ACTUAL PROBLEMS OF THE PEDIATRIC NEPHROLOGYAND UROLOGY

30th Jubilee Meeting of the Czech Working Group for Pediatric Nephrology and 20th Meeting of the Czech Section of the Pediatric Urology, Třeboň, 22.-23.5. 2009

Editors: Jan Janda, Radim Kočvara, Zdeněk Doležel

Organizers:
Prof. Zdeněk Doležel, MD PhD
Prof. Jan Janda, MD PhD
Assoc. Prof. Radim Kočvara
Prof. Miloš Velemínský, MD PhD
Reviewer: Prof. Miloš Velemínský, MD PhD

1st Edition, May, 2009, **ISBN 978-80-7394-166-6**

Dear collegues!

It is our pleasure you have accepted our invitation to take part at the international joint meeting of pediatric nephrologists and urologists in Třeboň! The first meeting of Czech pediatric nephrology was organized in 1980 in Třeboň and the 30th jubilee anniversary 2009 was the reason to come to Třeboň again! So, this year it is a joint conference – the 30th Meeting of the Czech Working Group for Pediatric Nephrology and the 20th Meeting of the Czech Section for Pediatric Urology. Our meeting will host several renowned invited speakers from Austria, Canada, Germany, Italy, Poland, and Slovakia. The presentations are aimed at several main topics emphasizing practical approach to diagnostics and treatment. This year we have decided to let the aktive participants to create a short communication instead the traditional abstracts. The text is printed only in English and the Czech modified version will be later displayed on the official website of the Czech Pediatric Society. Some colourful social activities will be provided by the organizing committee during the meeting. A Get-together party with a dinner and music is planned on Friday evening. Being in Třeboň, you will have an opportunity to enjoy the historical town and enchanting countryside full of ponds (tied to the name of Jakub Krčín, famous pond builder in 16th century).

Prof. Zdeněk Doležel, MD PhD
Head of the WGPN

Prof. Jan Janda, MD PhD
President of the Czech Pediatric Society

Assoc. Prof. Radim Kočvara
Head of the Section Pediatric Urology at Czech Urological Society

Prof. Miloš Velemínský, MD PhD
Dean of the Faculty of Health and Social Studies

20. Annual Meeting of the Czech Working Group for Pediatric Urology with international participation. Třeboň 2009

PROGRAM

FRIDAY, MAY 22

8.25–10.00

Pediatric nephrology – section I (oral presentations)

chairmen: Janda J, Feber J

Janda J, Špatenka J: **History of the Czech Pediatric Nephrology** *(p. 11)*

Litwin M: **Cardiovascular complications of chronic kidney disease in children** *(p. 14)*

Šuláková T, Janda J, Feber J: **Recommendations on implementation of ABPM in practice and interpretation of results in children** *(p. 16)*

Feber J, Šuláková T, Litwin M: **Ambulatory blood pressure monitoring (ABPM) in children – easy for the computer, not so easy for the physician** *(p. 17)*

Šuláková T, Janda J, Černá J, Janštová V, Šuláková A, Slaný J, Feber J: **Arterial hypertension in children with diabetes mellitus type 1 – frequent and not easy to diagnose** *(p. 22)*

Storm J, Grepl J, Rejtar P, Doležal J: **Radiation safety in medical irradiation** *(p. 24)*

Coffee break 30 min

10.30–12.30

Pediatric nephrology – section II (oral presentations)

chairmen: Šuláková T, Kovács L

Kovács L: **Drinking regime in children (review)** *(p. 26)*

Feber J, Geier P: **Glucocorticoids in children with idiopathic nephrotic syndrome – dosing and adverse effects in the first 3 months of therapy** *(p. 27)*

Dušek J, Vondrák K, Seeman T, Zieg J, Janda J: **A hockey player with painful chest** *(p. 30)*

Malina M, Janda J, Seeman T: **Monogenous diseases of kidney in children** *(p. 33)*

Flögelová H, Hálek J, Šmakal O, Michálková K, Dubrava L, Janout V: **Effectiveness of postnatal renal ultrasound screening and criteria for diagnosing pathological renal pelvic dilatation – final report** *(p. 36)*

Kolský A, Najmanová S, Netvalová S, Rada T, Šilhánková I, Jiroušová K, Kučerová J, Heinige P,

Dejlová Kolská M, Skibová J, Lyer P, Houšťková H: **Acute pyelonephritis – analysis of patients admitted in the years 1997 and 2007** *(p. 38)*

Nebesář J: **Children's spa cure for kidney and urinary tract disorders** *(p. 40)*

Lunch 12.30–13.30

13.30–15.10

Pediatric urology – bladder pathology (oral presentations)
chairmen: Kočvara R, Morávek J

Rösch WH, Ebert AK: **Andrological, gynecological, psychosocial and psychosexual aspects in the long-term follow-up of patients with bladder-exstrophy and their impact on current approach** *(p. 41)*

Morávek J, Kříž J, Trachta J: **Urinary bladder defects in children** *(p. 44)*

Riccabona M*:* **Modern management of children with MMC** *(p. 46)*

Zerhau P, Husár M: **Contemporary possibilities of children's detrusor hyperactivity treatment by mini-invasive methods** *(p. 49)*

Dítě Z, Molčan J, Janů M, Kočvara R, Sedláček J, Dvořáček J: **The intravesical instillation of propiverin and oxybutinin in the treatment of neurogenic bladder dysfunction in children**
(p. 51)

Coffee break 20 min

15.30–16.45

Pediatric urology – kidney and upper urinary tract (oral presentations)
chairmen: Šmakal O, Zerhau P

J. Kříž, J. Morávek: **Use of renal scan to evaluate renal function in congenital hydronephrosis in children** *(p. 53)*

Šmakal O, Vrána J, Hartmann I, Tichý T, Flögelová H, Michálková K: **The importance of DMSA scans and ultrasound findings in the treatment of congenital anomalies of duplicated kidney associated with obstruction or reflux** *(p. 55)*

Svitač J, Javorka K jr., Kliment J: **Associated urological anomalies in children with unilateral renal agenesis** *(p. 58)*

Husár M, Zerhau P: **Multi cystic dysplasia – will histology aid in treatment indication?** *(p. 59)*

Sedláček J, Langer J, Kočvara R, Dítě Z, Molčan J, Jiskrová H, Doležal J: **Is the konservative approach to a high-grade neonatal hydronephrosis really safe? A prospective study** *(p. 61)*

Novák I, Skálová S, Šenkeřík M: **The treatment of total duplex kidney by the anastomosis of upper urinary tract** *(p. 64)*

Novák I, Janoušková L, Kuliaček P: **Endoscopic submucosal injection of dextranomer/hyaluronic acid copolymer (deflux): a long time follow up** *(p. 66)*

Coffee break 20 min

17.05–17.45

Pediatric urology – genital pathology (oral presentations)
chairmen: Kříž J, Novák I

Drlík M, Tichý S: **Are we able to performe orchidopexis at the optimal age?** *(p. 68)*

20.00 Get together party, dinner in the form of raut, dancing

---

SATURDAY, MAY 23
8.00–9.00 Ferring workshop (Enuresis) with breakfast

9.00–10.00 Poster session
Individual discussion by poster with authors

SHORT COMMUNICATIONS

HISTORY OF THE CZECH PEDIATRIC NEPHROLOGY

Jan Janda, Jaroslav Špatenka
Dpt. of Pediatrics and Transplant Center, University Hospital Motol and Charles University in Prague

As in other countries, the Czech pediatric nephrology arose from studies on elektrolyte and water balance, its regulation and clinical descriptive studies of children kidney diseases.
A leading role in the new pediatric subspeciality played the 1st Department of Pediatrics in the framework of Prague Children Hospital. In the early fifthies, e.g. Prof. Emil Poláček was one of pioneers of parenteral rehydration in infants and later he introduced the treatment of acute renal failure using successfully peritoneal dialysis in such cases (in 1962 Poláček and Milotová – the first peritoneal dialysis in a child with hemolytic uremic syndrome). The first section of pediatric nephrology in the former Czechoslovakia has been established in early sixthies and the communistic system some has allowed some pediatricians to get a stipendium abroad, even in USA (M. Ort, MD at Prof. Jack Mettcof, Chicago). Of course, the first time of development of the pediatric nephrology as a subspeciality was closely connected with nephrologists who were active at departments of internal medicine. The first renal biopsy in a child performed the renowned Professor Jan Brood in Prague in 1961. There was an intensive collaboration in the field of renal functions which was realized together with nephrologists and urologists for adults (L. Hradcová and O. Schück, E. Hradec). After the movement of the children hospital from Karlov to Motol, J. Švorc and J. Dušek were commissioned to develop pediatric nephrology in the framework of the 2nd Dptm. of Pediatrics. Other active pediatric nephrology facilities started their activities in Slovakia (Košice – F. Démant, E. Mathéová), Bratislava (M. Šašinka). Martin (J. Buchanec). Prof. Démant was the main local organizer of one of first meetings of the European Society for Paediatric Nephrology in the High Tetras in 1973. In early seventhies J. Janda came to Motol and continued with his coworkers further activities aiming to start renal replacement therapy in children with chronic renal failure as integrated chronic dialysis- transplantation network together with J. Kreisinger and J. Špatenka. A friendly help and support was provided by collegues from Charité- Hospital in Berlin (the former GDR) who organized later the 1st Pediatric Nephrology Symposium of the Socialist Countries in Eisenach (1977, P. Grossmann, S. Devaux), when it was not possible to visit western countries. This event was the first opportunity after the meeting in High Tatras, people from Eastern Europe could encounter renowned pediatric nephrologists from the West. In the same year the first child in the former Czechoslovakia was transplanated in Prague at Institute of Clinical and Experimental Medicine (IKEM) on 22nd of June 1977 after 4 months of manual chronic peritoneal dialysis (dialysis solution in bottles). The patient was a preschool child with chronic renal failure due to hemolytic uremic syndrome. Some renal transplantation were realized in IKEM before the transfer of program to a pediatric hospital in Motol. Since the eighties, an important role played contacts with Western Germany pediatric nephrologists

in Heidelberg (K. Schärer, O. Mehls), Hannover (J. Brodehl, J. Ehrich, P. Hoyer), Essen (H. Olbing, E. Bonzel). Introducing the regular chronic hemodialysis was an important help brought H. J. Stolpe (Rostock). Being supported by DAAD network, several Czech pediatricians spent a longer time at the Section for Pediatric Nephrology in Heidelberg. Later, contacts with USA (R. Fine) and France (P. Cochat) has been established and enabled longer stays for our young collegues. Close collaboration of pediatricians with surgeons J. Špatenka and M. Krolupper resulted in a regular chronic hemodialysis program in children in 1980, the first patient was succesfully transplanted in Motol 24th of Novemeber 1981 under assistance of V. Kočandrle and J. Špatenka.

Later, J. Feber took over the responsibility for pediatric renal transplantation program. Today, the pediatric nephrology as subspeciality is practised particularly at departments of pediatrics of major pediatric facilities (Prague, Plzeň, Brno, Olomouc and regional hospitals as well).

There are three specialized pediatric units providing elimination methods in acute and chronic renal failure (Prague-Motol, headed by K. Vondrák), Brno (headed by Z. Doležel) and Ostrava (headed by M. Hladík). These units in Brno and Ostrava have been attached to Faculty Departments of Pediatrics with special sections for kidney diseases in children and adolescents. Over the past decade, these sections for pediatric nephrology have become important centers for clinical pediatric nephrology practice and research as well.

Pediatric renal transplantations for all Czech Republic are concentrated at University Hospital Prague- Motol. Up to the end of 2008 altogether more than 210 successful renal transplantations in children and adolescents have been performed (T. Seeman is responsible for these activities in Motol). The technical background and modern equipment of our units matches similar facilities in western countries. Results of our patient survival and grafts reach the international standards. Since more than 20 years the Czech pediatric nephrologists are included in international cooperative research studies. Also publication activities in recognized international journals improved significantly. It is a good message, that the main topics of our publications activities during the last time are not only clinical studies, but also laboratory research, including molecular genetics of kidney diseases. Very vivid is the contact with the Slovak pediatric nephrologists, who are regularly guests of our annual meetings (L. Kovács, L. Podracká, O. Červeňová etc.).

The first meetings of a working group on pediatric nephrology was held in Třeboň 1980 and became a tradition, this year we do remember 30 years of our Working Days of Pediatric Nephrology. Since some years the abstracts of our conferences were printed paralelly in Czech and English as well. Recently, a new monograph on pediatric nephrology was published and Czech pediatric nephrologists contribute to monographs on nephrology edited by nephrologists for adult patients. The Czech pediatric nephrologists repeatedly applicate successfully for granted research projects. The postgraduate education of Czech

pediatricians in hospitals follows the standards of European Union (at least 6 years to be educated as pediatric nephrologists). Our pediatric nephrologists are members of international societies and associations (e.g. European Society of Paediatric Nephrology, International Pediatric Association, International Pediatric Transplantation Association, Deutsche Gesellschaft für Pädiatrische Nephrologie).

Increasingly, the future of the Czech pediatric nephrology will depend on the activities of our young collegues who will keep close contacts with the international clinical and research community. We would like to wish them to have more people who are committed to the right things and are ready to improve the level of pediatric nephrology in the Czech Republic.

_Notes

CARDIOVASCULAR COMPLICATIONS OF CHRONIC KIDNEY DISEASE IN CHILDREN

Mieczyslaw Litwin

Children's Memorial Health Institute, Warsaw, Poland

Cardiovascular disease is the main complication of chronic renal disease (CKD) and renal replacement therapy (RRT). From historical perspective the causes of morbidity and mortality in children with CKD and on RRT evolved from infections, through stroke, uremic cardiomyopathy to complications of widespread uremic arteriopathy. Uremic cardiomyopathy is characterized by left ventricular eccentric hypertrophy with systolic and diastolic failure with accompanying rhythm disturbances and valves calcifications. First, functional changes may be detected as early as CKD stage 3 but overt clinical symptoms may be undetected until CKD stage 5. The left ventricular biopsy shows widespread intermiocardiocyte fibrosis with increased collagen content up to 4–5%.The parallel process is development of uremic arteriopathy involving arterial tree from aorta to arterioles. The pathological basis of uremic arteriopathy is Moenckebergs sclerosis with calcifications in media and increased intima-media thickness (IMT). The functional consequences are increased stiffness of arterial tree, increased pulse wave velocity, increased systolic load to the ventricle and decreased coronary flow in diastole. Although children with CKD are exposed to many classical risk factors of cardiovascular disease including dyslipidemia, insulin resistance and hyperhomocystinemia, excluding arterial hypertension they play only minor role in pathogenesis of uremic cardio- and arteriopathy. The main risk factors are common both for cardio- and arteriopathy and include low GFR, calcium and phosphate metabolism abnormalities, hyperparathyroidism, vitamin D over- and underdosing and arterial hypertension. In case of cardiomyopathy important role is played by chronic volume overload, especially in dialyzed children. It is important to bear in mind that good ultrafiltration achieved by peritoneal dialysis at start of therapy steadily declines and after two years most of patients

are chronically overhydrated. The character of uremic cardiovascular disease changes after renal
transplantation. Although good graft function enables at least partial improvement with decrease of arterial IMT, increased elasticity and decrease of left ventricular mass, transplanted children are now exposed to risk factors related with immunosuppressive and corticosteroid treatment. Consequences of obesity, hypertension and metabolic complications caused by corticosteroids may be exaggerated by insulin resistance or new onset diabetes caused by cyclosporine or more often, by tacrolimus. This leads to development of metabolic syndrome. Cardiovascular uremic disease is closely related with CKD and its treatment. The early and strictly controlled antihypertensive treatment and therapy of mineral metabolism abnormalities is the mainstay of therapy. However, because the main and fundamental cause of disease is loss of kidney function the best treatment of uremic cardio-arteriopathy is early, even preemptive transplantation of well matched kidney enabling use of relatively safe steroid free or low dose steroid immunsuppressive regimen. In dialyzed children the mainstay of treatment is as good dialysis as possible together with pharmacological therapy of calcium-phosphate disturbances and antihypertensive treatment.

_Notes

RECOMMENDATIONS ON IMPLEMENTATION OF ABPM IN PRACTICE AND INTERPRETATION OF RESULTS IN CHILDREN

Tereza Šuláková1**, Jan Janda**2**, Janusz Feber**3
Departments of Pediatrics in Ostrava1, Prague2, Czech Republic and Ottawa3, Canada

Ambulatory blood pressure monitoring (ABPM) has been increasingly used for the diagnosis of hypertension (HTN) in children in both research and clinical settings. However, the use and particularly the interpretation of ABPM in clinical practice are not easy. ABPM may be useful in differentiating primary from secondary HTN (1, 2) and help to detect white coat HTN and masked HTN. In children with prehypertension (office blood pressure (BP) ranging between 90–95th percentile), the ABPM may also be valuable in stratifying the risk for target organ damage. Even with normal average ABPM values, an increased BP variability is associated with target organ damage in adults (4). This fact may be especially relevant if there is a strong family history of HTN. Careful selection of equipment for ABPM measurement is essential for accurate results in children. There are two different BP detection techniques in use: oscillometric (5) and auscultatory (6). Oscillometric devices usually have a lower percentage of erroneous readings than auscultatory devices and are easier to use than auscultatory devices. Moreover, the normative data for ABPM interpretation are based on oscillometric method (5). There are no normative

data for auscultatory devices in children. For these reasons, most centers performing ABPM in children and adolescents use oscillometric monitors (7). Whilst there are many different monitors on the market, only few have been validated in children (see www.dableducational.org). Similarly to the measurement of office BP measurement, the cuff size influences the accuracy of BP data. The width of the cuff should be at least 40% of the mid-arm circumference. The devices should be equipped with cuffs of various sizes designated for pediatric use. The ABPM software should enable to enter the 95th percentile (5, 8) and to record the measurement at variable time intervals. Most experts in pediatric ABPM consider the ABPM as valid if at least one BP reading per hour is obtained, including the sleep period (7). The routine use of ABPM is limited in children younger than 5–6 years due to technical problems and lack of normative data. The interpretation of ABPM recordings could be influenced by methods of dividing the recording into awake and sleep periods (fixed or according to patient's diary). It is necessary to underline, that the most recent normative data are based on a fixed nighttime period ranging from midnight to 6.00 AM and the daytime period from 8.00 AM to 8.00 PM. Consequently, several BP recordings measured in the transient periods (from 8.00 PM to 12PM and from 6.00 AM to 8.00 AM) are discarded from final analysis of the 24h BP (5, 8). Extreme deviations of BP readings during the ABPM are unlikely to be valid and are most likely artifacts. For these reasons a visual inspection is required before interpretation of the average BP. To avoid the need for manual editing of recorded BP values, the software of most ABPM devices accepts only BP measurements with systolic BP <240 and >70 mm Hg, diastolic BP <140 and >40 mm Hg, heart rate <125/min, and pulse pressure >40 but <100 mm Hg with a diastolic BP< systolic BP. However, these settings may not be appropriate for younger children whose normal resting values for heart rate and BP may differ significantly from adults. Interpretation of ABPM studies is usually based on a combination of criteria, including mean BP and BP loads. Average MAP, SBP and DBP are calculated by the ABPM software, but these values should be compared with ABPM normative data to determine whether a subject's BP is normal or elevated. The use of regular auscultatory resting (office) BP values from Fourth Report on BP in Children (9) may result in overdiagnosis of hypertension in children (10). ABPM values should be compared with gender- and height-specific data obtained in large pediatric populations using ABPM (5). BP loads for any given period are also calculated by the analysis software. Loads between 25% to 30% are considered elevated (11). Loads ≥50% were demonstrated to be predictive of left ventricular hypertrophy in one pediatric study (12). Most experts in pediatric ABPM use the combination of mean BP and BP load to categorize patients into normal or hypertensive. However, some patients with normal mean BP levels may have elevated BP loads. These patients may be truly hypertensive and at risk for target organ damage even if they do not fit into the proposed criteria for

analyzing ABPM studies (10). Normal dipping is generally defined as a decline of the mean systolic and diastolic ambulatory BP levels from day to night ([mean daytime ABPM mean nighttime ABPM]/mean day ABPM×100) by more than or equal to 10%. However, the classification of a pediatric patient as a dipper or nondipper may vary based on the definition of the daytime and nighttime periods.

Conclusion: The use and interpretation of ABPM in children is not easy in clinical practice and requires proper education of the personnel. It is absolutely essential that the ABPM technology is used by educated and experienced personnel in order to maintain the functionality of the equipment, to minimize measurement errors, and to obtain valid, reliable and reproducible BP data. A proper interpretation of the ABPM results by an experienced physician is crucial in order to make a correct diagnosis of hypertension/normotension in children.

References

1. Flynn JT: Differentiation between primary and secondary hypertension in children usány ambulatory blood pressure monitoring. Pediatrics. 2002; 110:89 – 93.

2. Seeman T, Palyzová D, Dusek J, Janda J: Reduced nocturnal blood pressure dip and sustained nighttime hypertension are specific markers of secondary hypertension. J Pediatr. 2005; 147:366–371.

3. Graves JW, Althaf MM: Utility of ambulatory blood pressure monitoring in children and adolescents. Pediatr Nephrol. 2006; 21:1640–1652.

4. Parati G, Faini A, Valentini M: Blood pressure variability: its measurement and significance in hypertension. Curr Hypertens Rep. 2006; 8:199–204.

5. Soergel M, Kirschstein M, Busch C, Danne T, Gellermann J, Holl R, Krull F, Reichert H, Reusz GS, Rascher W: Oscillometric twenty-four- hour ambulatory blood pressure values in healthy children and adolescents: a multicenter trial including 1141 subjects. J Pediatr. 1997; 130:178–184.

6. O'Sullivan JJ, Derrick G, Griggs P, Foxall R, Aitkin M, Wren C: Ambulatory blood pressure in school children. Arch Dis Child. 1999; 80:529–532.

7. Urbina E, Alpert B, Flynn J, Hayman L, Harshfield GA, Jacobson M, Mahoney L,McCrindle B, Mietus-Snyder M, Steinberger J, and Daniels S: Ambulatory Blood Pressure Monitoring in Children and Adolescents: Recommendations for Standard Assessment. A Scientific Statement From the American Heart Association Atherosclerosis, Hypertension, and Obesity in Youth Committee of the Council on Cardiovas. Hypertension. 2008, 52(3):433–451.

8. Wühl E, Witte K, Soergel M, Mehls O, Schaefer F: German Working Group on Pediatric Hypertension. Distribution of 24-h ambulatory blood pressure in children: normalized reference values and role of body dimensions. J Hypertens. 2002; 20:1995–2007.

9. National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The fourth report on the diagnosis,

evaluation, and treatmentof high blood pressure in children and adolescents. Pediatrics. 2004; 114 (suppl 4th Report):555–576.
10. Lurbe E, Sorof JM, Daniels SR: Clinical and research aspects of ambulatory blood pressure monitoring in children. J Pediatr. 2004; 144:7–16.
11. White WB, Dey HM, Schulman P: Assessment of the daily blood pressure load as a determinant of cardiac function in patients with mild-to-moderate hypertension. Am Heart J. 1989; 118:782–795.
12. Sorof JM, Cardwell G, Franco K, Portman RJ: Ambulatory blood pressure and left ventricular mass index in hypertensive children. Hypertension. 2002; 39:903–908 _____
_Notes

AMBULATORY BLOOD PRESSURE MONITORING (ABPM) IN CHILDREN – EASY FOR THE COMPUTER, NOT SO EASY FOR THE PHYSICIAN

Janusz Feber1**, Tereza Šuláková**2**, Mieczyslaw Litwin**3
1Children's Hospital of Eastern Ontario, Ottawa, Canada; 2Teaching Hospital Ostrava, Czech Republic; 3Children's Memorial Health Institute, Warsaw, Poland

Ambulatory blood pressure monitoring (ABPM) is relatively easy to perform in children above 5 years of age, who usually tolerate the cuff on the arm over the whole 24 hours period. ABPM results are then analyzed by the computer software, which produces reports of systolic, diastolic blood pressure (BP) and mean arterial pressure over 24h, daytime and nighttime periods with calculation of the BP load. The amount of data generated by the computer may be overwhelming for a busy clinician with limited experience with the ABPM interpretation. The aim of the presentation is to demonstrate the pitfalls of the conventional ABPM analysis in children and to outline the use of ABPM for a more sophisticated (advanced) analysis of the BP.

Conventional (linear) analysis Obtained ABPM results (average blood pressure for 24h, daytime and nighttime periods) should be compared with the normative values for ABPM (1). These new reference data were generated from the initial normative data (2) using the LMS method. The LMS transformation normalizes the distribution of data and therefore allows the reporting of BP in standardized deviation scores (SDS). Normal BP (50th percentile) equals zero SDS, whereas the upper limit of normal (95th percentile) corresponds to 1.65 SDS. The use of SDS enables a more accurate assessment of hypertension into true normotension (values around 0 SDS), pre-hypertension (values closer to the 95th percentile) and true hypertension (values above the 95th percentile), as the BP can be expressed as a continuous variable rather than abnormal or normal BP based on the 95th percentile from the older reference data (2).

Unfortunately, the use of these new reference SDS values is more complicated and requires the calculation of SDS values based on the Publisher equation (1). This

rather sophisticated calculation is prohibitive for physicians less experienced in computer technology. Consequently, most physician still use the old reference values in percentiles, which seem to be much easier to use in clinical practice, but may not provide as much information as the new, LMS transformed, reference values.

In addition to the average BP, the ABPM provides useful information on the BP load i.e. the number of BP readings exceeding the 95th percentile. Most experts agree that the normal BP load should be <25%, BP load >50% is clearly abnormal and associated with a higher risk for target organ damage (3). However, the use of BP load in the definition of hypertension in children has been a matter of debate and the consensus was not yet reached despite the most recent pediatric ABPM guidelines published in 2008 (3). In addition, some children cannot be properly classified as proposed by the guidelines such as children with normal average BP but abnormal BP load – they simply do not fit any definition as proposed by the guidelines. The calculation of the correct BP load is also dependent on the definition of daytime and nighttime periods, which is another topic of hot discussion among experts in ABPM. Whilst it seems appropriate clinically to use individualized time periods (every child has different daytime/nighttime habits), the normative values are based on fixed definition of the daytime and nighttime periods (1). Therefore, for a correct interpretation of the ABPM, the operator of the ABPM device should insert the individual 95th percentile for each child and adjust the daytime/nighttime periods in the computer software. Without these adjustments, the calculated BP load and daytime/nighttime BP difference (dipping) may not be correct and may lead to false conclusions.

Advanced ABPM analysis, Ambulatory stiffness index (AASI) In addition to the linear analysis described above, the ABPM can be used for assessment of arterial stiffness, which is recognized as a major determinant of cardiovascular risk (4). Arterial stiffness can be assessed with the AASI calculated from the ABPM data. Using the individual 24-h |BP readings, the diastolic BP is plotted against the systolic BP and the linear regression slope is calculated. The AASI is then defined as one minus the regression slope (5). The AASI has been found to be elevated in hypertensive children and correlates with the duration and the origin of hypertension in childhood (5).

BP variability BP variability has been shown to correlate with end-organ damage, cardiovascular morbidity and mortality. The BP variability can be assessed by ABPM using the standard deviation (SD) of the average ambulatory BP. Recently, correction of SD by the number of BP readings during daytime and nighttime periods (weighted SD) has been proposed (6). This index correlated better with end-organ damage and can be considered as a simple index of the 24-h BP variability (6). **BP rhythmicity** BP normally exhibits circadian rhythmicity (higher BP during the day, lower BP at night) which can be assessed with the conventional (linear) ABPM analysis (BP dipping). Assessment of

ultradian i.e. shorter than circadian, cardiovascular rhythmicity requires specialized software (Chronos-Fit) implementing Fourier analysis. This analysis enables to identify the presence of ultradian rhythms and measure their amplitudes and acrophases. First pediatric reports show that children with chronic kidney disease display disturbed circadian and ultradian rhythms (7). Studies of BP rhythmicity in other pediatric populations at risk for hypertension are in progress.
Conclusion: ABPM provides an excellent tool for assessment of the BP level, load, variability and rhythmicity. It can also be used for assessment of arterial stiffness (AASI). However, the analysis of ABPM requires computer skills and a proper use of normative data. The ABPM findings should be interpreted with caution by a physician who is aware of potential pitfalls of ABPM in children.

References

1. Wühl E et al.: Distribution of 24-h ambulatory blood pressure in children: normalized reference values and role of body dimensions. J Hypertens. 2002; 20:1995–2007.
2. Soergel M et al.: Oscillometric twenty-four hour ambulatory blood pressure values in healthy children and adolescents: A multicenter trial including 1141 subjects. J Pediatr 1997; 130:178.
3. Urbina et al.: Hypertension 2008; 52:433–451.
4. Boutouyrie P et al.: Aortic stiffness is an independent predictor of primary coronary event in hypertensive patients: a longitudinal study. Hypertension 2002; 39:10–15.
5. Simonetti et al.: Ambulatory arterial stiffness index is increased in hypertensive childhood disease. Pediatr Res 2008; 64:303.
6. Bilo G et al.: A new method for assessing 24-h blood pressure variability after excluding the contribution of nocturnal blood pressure fall. J Hypert 2007; 25:2058–2066.
7. Wühl E et al.: Ultradian but not Circadian Blood Pressure Rhythms Correlate with Renal Dysfunction in Children with Chronic Renal Failure. J Am Soc Nephrol 2005; 16:746–754.

_____

_Notes

22

ARTERIAL HYPERTENSION IN CHILDREN WITH DIABETES MELLITUS TYPE 1 – FREQUENT AND NOT EASY TO DIAGNOSE

Terezie Šuláková1**, Jan Janda**2**, Jana** Černá1**, Vlasta Janštová**1**, Astrid Šuláková**1**, Jaroslav Slaný**1**, Janusz Feber**3
Departments of Pediatrics in Ostrava1, Prague2, Czech Republic and Ottawa3, Canada

Background: There has been a worldwide increase in the incidence of type 1 diabetes, particularly among children younger than 5 years old (1, 2). Given

that duration of diabetes, rather than age of onset, is the more predominant risk factor for DKD (diabetic kidney disease), increasing rates of diabetes in children undoubtedly will lead to an increase in DKD in these age groups, a finding that is already being reported in some populations. Children with diabetes mellitus type 1 (DM1) are at risk for hypertension (HTN), because HTN is one of the most common comorbidities in DKD. Unlike adult population (3), there is a lack of data from children diabetic population related to hypertension prevalence (4–7). The main reasons for it are the complicated definition and interpretation of HTN on ABPM in children (8, 9).

Aim: to assess the prevalence, type and severity of hypertension and to evaluate the diagnostic efficacy of the office blood pressure (BP) measurement and ABPM in the assessment of HTN in a group of diabetic children referred to the nephrology clinic.

Methods: We analyzed office BP and ABPM measurements in 84 children (43 boys) obtained at a median age of 14.9 years and 6.3±3.5 years after diagnosis of DM1. office BP and ABPM results were converted into standard deviation scores (SDS). In addition, we analyzed blood pressure loads and nighttime dipping. The comparison between office BP and ABPM was performed using kappa coefficient and receiver operator curve (ROC) (10).

Results: HTN / prehypertension was diagnosed in 20/84 (24%) and 23/84 (27%) patients using office BP (>95th percentile and 90–95th percentile, respectively) and in 24/84 (29%) patients using ABPM (≥95th percentile during 24h, day or night). Both methods were in agreement in 33 ABPM normotensive and 16 ABPM hypertensive patients (most had nighttime HTN); 32% patients had white coat HTN and 9.5% patients had masked HTN. The kappa coefficient was 0.175 (95% CI -0.034 to 0.384) suggesting poor agreement between office BP and ABPM. Diastolic office BP was a better predictor of ABPM HTN (ROC AUC=0.71±0.06) than systolic office BP (AUC=0.58± 0.07). The percentage of non-dippers ranged from 7 to 23% in ABPM normotensive patients and 21–42% in ABPM hypertensive patients who also had significantly higher BP loads ($p<0.0001$).

Conclusion: The significant proportion of diabetic children suffer from hypertension, which can only be diagnosed with ABPM due to a high percentage of nighttime, white coat and masked hypertension. The office blood pressure can be used as a screening method for hypertension, but has a poor predictive value for either normotension or hypertension on the ABPM. Despite the fact that the availability of pediatric normative values and the use of SDS BP values significantly improved the diagnostic accuracy, the interpretation of ABPM in diabetic children is not easy in clinical practice due to increased complexity of the ABPM interpretation in children.

References

1. NEU A: Rising Incidence of DM1 in Germany. Diabetes Care, 24, 4, 2001.

2. Gale EA: The rise of childhood type 1 diabetes in the 20th century. Diabetes 51:3353–3361,2002.
3. KDOQI Clinical Practice Guidelines and Clinical Practice Recommendations for Diabetes and Chronic Kidney Disease. AJKD 2007.
4. 17. Knerr I, Dost A, Lepler R, Raile K, Schober E, Rascher W, Holl RW: Tracking and Prediction of Arterial Blood Pressure From Childhood to Young Adulthood in 868 Patients With Type 1 Diabetes. A multicenter longitudinal survey in Germany and Austria. Diabetes Care 2008, 31, 726–727.
5. Dost A, Klinkert Ch, Kapellen T, Lemmer A, Naeke A, Grabert M, Kreuder J, Holl RW: Arterial Hypertension determined by Ambulatory Blood Pressure profiles.Contribution to microalbuminuria risk in a multicenter investigation in 2,105 children and adolescents with type 1 diabetes. Diabetes Care 2008, 31:720–725.
6. Darcan S, Goksen D, Mir S, Serdaroglu E et al.: Alterations of blood pressure in type 1 diabetic children and adolescents. Pediatr Nephrol 2006, 21:672–676.
7. Šuláková T, Janda J: Ambulatory blood pressure in children with diabetes 1. Pediatr Nephrol 2008, 23, 12:2285–2286.
8. Urbina E, Albert B, Flyn J, Hayman L, Harshfield GA, Jackson M et al.: Ambulatory Blood Pressure Monitoring in Children and Adolescents: Recommendations for Standard Assessment. A Scientific Statement from the American Heart Association Atherosclerosis, Hypertension, and Obesity in Youth Committee of the Council on Cardiovascular Disease in the Young and the Council for High Blood Pressure Research. Hypertension published online Aug 4, 2008; DOI: 10.1161/HYPERTENSIONAHA.108.190329.
9. Acosta AA, McNiece KL: Ambulatory blood pressure monitoring: a versatile tool for evaluatin and managing hypertension in children. Pediatr Nephrol 2008, 23:1399–1408.
10. Landis JR, Koch GG: The measurement of observer agreement for categorical data. Biometrics 1977, 33:159–174.

_Notes

24

RADIATION SAFETY IN MEDICAL IRRADIATION

J. Storm, J. Grepl, P. Rejtar – Clinic of radiology, J. Doležal
Department of nuclear medicine, UH Hradec Králové

Present radiology and nuclear medicine are inseparable parts of modern medicine. Using the properties of ionizing radiation is their elemental and essential component. Increase of the risk appears with utilization of ionizing radiation on human body because medicine irradiation represents the majority (more than 90 percents) of irradiation from man-made sources and is approximately 11 percent of whole irradiation from all sources. Optimalization of the radiation safety of persons, which are indicated to the medical irradiation, is one of the most important tasks, which are in relation to

application of ionizing radiation. Indication to investigation is the first way to reduce radiation load of persons.
Level of the risk of each investigation is too different and its knowledge and ability to inform about radiation load should belong to skills of physicians, radiological assistants and others. Elemental information about radiation load and applicability of investigative methods are content of bulletin of Ministry of Health, issue 11 from November 2003.
Efficient dose in major part of examinations (cystourethrography, intravenous pyelography, scintigraphy of kidneys) in pediatric nephrology is approximately 1–2mSv (includes radiology and nuclear medicine). Patients are much lower irradiated at direct radionuclide cystography. Average efficient dose at intravenous excretory urography, computed tomography and angiography is approximately 10mSv. Risk of fatal tumor is about 5,5 percent/1Sv. Children's risk of fatal tumor is greater (2–3 times) because of higher radiosensitivity.
Evaluation and optimalization of the risks related with medical irradiation belong to basic rules of the modern medicine. Choice and conditions of technical equipment are always as important to minimize radiation load as choice of investigation method. Enhanced attention should be pay to the medical irradiation of children, searching investigation with using high patient doses and computed tomography. Good chaise of exposure parameters, minimize of irradiated volume and correctly using of skiascopy is the right way to optimize radiation load in radiology.
Application of the right amount a radionuclide, which warrants good diagnostic information and low radiation load, is a basic parameter in nuclear medicine. Erudition of medical team and preparation of patient are also very important.
Tabulation of radiation load, which is in relation to investigation method, is complicated question. All notes about medical irradiation must by archive. Notes about height and weight are very important too. Another factors which have effect on radiation load, are health state, preparation of patient, patient's cooperation etc. Medical team cannot influence these and more other factor. For this reason it is not possible to determinate limits of radiation load. Referential levels were made in place of limits. Frequently overflowing of these levels gets impulse to optimalization of radiation safety.

_Notes

DRINKING REGIME IN CHILDREN (REVIEW)

L. Kovács
2nd Department of Pediatrics, Comenius University Medical School, Bratislava, Slovakia

Probably everybody is familiar with the concept of „drinking regime", even

though not everybody respects its principles. It appears that our contemporary, civilized society does not assigns appropriate importance to such basic, natural physiological needs, as ingestion and excretion of water and food are. Ingestion of water in proper quality and amounts is an important prerequisite for maintaining somatic health, mental wellbeing and physical performance.
The aim of this contribution is to support the appropriate drinking regime and use common physiological sense in the world of pervasive advertisements on the so-called „best“ and „most healthy“ drinks (at least by means of the advertisers). Consumption of sugar-sweetened beverages, particularly carbonated soft drinks, may be a key contributor to the epidemic of overweight and obesity, by virtue of these beverages' high added sugar content, low satiety, and incomplete compensation for total energy. Moreover, their "taste-induced drinking" may overwhelm normal thirst sensation and lead to excessive fluid intake, not infrequently associated with development of symptomatic hyponatremia due to water intoxication.

_Notes

GLUCOCORTICOIDS IN CHILDREN WITH IDIOPATHIC NEPHROTIC SYNDROME – DOSING AND ADVERSE EFFECTS IN THE FIRST 3 MONTHS OF THERAPY

Janusz Feber, Pavel Geier
Departments of Pediatrics, Children's Hospital of Eastern Ontario, Ottawa, Canada

Background: Adverse effects of glucocorticoids (GC) are mostly studied in children with long-term or recurrent use of GC, in whom problems with statural growth and bone disease are observed. However, little is known about early/short-term effects (within the first 3 months of GC therapy). We aimed to review various dosing regimens of prednisone (PRED) and to evaluate the effects of GC on bone health, body mass index (BMI) and blood pressure (BP) in children with the first episode of idiopathic nephrotic syndrome (INS).
Prednisone dosing: Prednisone (PRED) represents the mainstay of standardized GC therapy for the 1st episode of INS in children. The usual PRED dose is 60 mg/m2/day given for 4 weeks (ISKDC protocol) or 6 weeks (APN protocol) followed by 40 mg/m2/every 2nd day for 4 (ISKDC) or 6 weeks (APN) (1, 2). However, many physicians/centers use alternative PRED dosing based on weight (2 mg/kg/day) (3, 4), mainly at the initiation of the PRED therapy, when the statural height is not readily available. This dosing of PRED in mg/kg/day is probably easier to use in daily clinical practice, but the calculated total daily PRED dose is significantly lower (approximately 80%) compared to the total daily PRED calculated per m2, mainly in children below 30 kg of weight (5). This may result in PRED underdosing of children with an initial episode of INS, which in turn may affect the long-term prognosis, mainly the relapse rate.

Bone health: Bone disease/fractures are known adverse effects of long-term GC therapy. The short-term GC administration is usually well tolerated and consequently less studied. A multicenter, prospective observational study (Steroid induced Osteoporosis in Paediatric Population – STOPP) is currently in progress in Canada (6). There are 3 arms in the study: patients with leukemia, rheumatic conditions and nephrotic syndrome. Patients with the 1st onset of INS have been prospectively followed for 4 years since the initiation of the GC therapy. The first preliminary results in 63 children already show a significantly decreased lumbar spine bone mineral density (BMD) during the first 30 days of GC therapy. The decreased BMD persists during the first 3 months of the standard PRED therapy and correlates with the cumulative PRED dose: an increase of the GC dose by 1g/m2 is associated with a decrease of BMD by 0.14 SDS (multivariate analysis, p=0.023). Moreover, 3 out of 63 patients had asymptomatic fractures during the first 3 months of GC therapy. These results suggest that even short-term GC therapy may have significant adverse effects on the bone metabolism in children with INS (6).

Arterial hypertension and body mass index: Hypertension and weight gain are the two other common adverse effects of long term GC treatment. However, there is limited information on blood pressure (BP) and body mass index (BMI) during the short-term high-dose GC treatment of the first episode of INS. In our study, the casual BP, height and weight were measured in all children presented with new onset INS treated with PRED 60 mg/m2/day for 6 weeks daily + PRED 40 mg/m2/every 2nd day for another 6 weeks. BP, weight and height were taken at presentation (T0), at the time of remission (T1), on the 42nd day (T2) and on the 84th day (T3) of GC therapy. Each recorded BP and BMI value were converted into Z-scores (SDS) based on age and height related reference values (7, 8). Mean systolic BP was 1.54±1.45 SDS at T0, 0.65±1.60 SDS at T1, 1.52±1.25 SDS at T2 and 1.48±0.90 SDS at T3. Hypertension (BP>1.65 SDS) was diagnosed in 38% at T0, 28% at T1, 52% at T2 and 36% of patients at T3 (9). The median BMI was 1.19 SDS at T0, 0.44 SDS at T1, 1.70 SDS at T2 and 1.32 SDS at T3 (values at all time intervals are higher than the population mean except for T1, Anova for repeated measures = 0.0008). The percentage of obese children (BMI>1.65 SDS) was 29% at T0, 23% at T1, 50% at T2 and 28% at T3.

In summary, hypertension and weight gain is frequently observed in children with an initial episode of INS. The increased BMI and hypertension is likely secondary to fluid overload at presentation of INS. However, significant changes in BMI and BP are observed during the initial GC treatment and approximately 1/3 of children with INS are obese and hypertensive at the end of 3-month long GC treatment.

Conclusion: Children with a new onset of idiopathic nephrotic syndrome receive standardized prednisone treatment over 2 to 3 months depending on the protocol. The dosing of prednisone in mg/m2/day is recommended, as the

dosing in mg/kg/day may result in prednisone underdosing and potentially higher rate of relapses compared to the dosing in mg/m2/day. Even a relatively short treatment with prednisone can cause significant abnormalities of bone metabolism, body composition and blood pressure early in the course of the disease/treatment.

References

1. Report of the International Study of Kidney Disease in Children (ISKDC). J Pediatr 1979;
95:239.
2. Arbeitsgemeinschaft für Pädiatrische Nephrologie (APN). Lancet 1988; 1:8582:380.
3. Bagga A et al.: Pediatr Nephrol 1999; 13:824.
4. Matsukura H et al.: Am J Nephrol 2001; 21:362.
29
5. Feber J et al.: Pediatr Nephrol 2009; 24:1027.
6. Feber J et al.: Abstract submitted to the 5th International Conference on Children's Bone
Health, June 23–26, 2009, Cambridge, UK.
7. http://www.cdc.gov/GrowthCharts
8. National High Blood Pressure Education Program Working Group in High Blood Pressure
in Children and Adolescents. Pediatrics 2004; 114(Suppl 2):555.
9. Geier P et al.: Pediatr Nephrol 2007; 22:1493.

_Notes

A HOCKEY PLAYER WITH PAINFUL CHEST

J. Dušek, K Vondrák, T. Seeman, J. Zieg, J. Janda
Pediatric Department, Medical School Charles Univ. Prague and Univ. Hosp. Motol

Our patient played ice hockey from his age 6 years and his family supported him a lot. He trained ice hockey for 6 days a week. He had to travel for his training in other city 80 kilometers far. His secondary school was submitted to his ice hockey as well. Presently he was attended to "Vladimir Ruzicka´s hockey school" in Prague. He started to complain for pain on the right side of lower part of his chest. Due to his hobby (hockey) he was examined on surgery as a first step. A chest X- ray was done and because he was crushed into boards during his last hockey match the examination was concluded as a rip injury maybe fracture. For persisted the pain he was admitted on pediatric department of district hospital. The second chest X- ray revealed a rather big infiltration in the area of his pain, in the right lung base. Moreover bilateral effusions with the right effusion lager than the left one were confirmed. An edematous and painful ankle without any injury was found during the history examination. The examination continued and due to positive of antinuclear antibodies (ANA) and

anti-dsDNA antibody, the diagnosis of systemic lupus erythematosus (SLE) became suspicious. He was transferred to our ward and the diagnosis of SLE has been confirmed. A percutaneous biopsy of his right kidney was performed uneventfully. The biopsy showed focal segmental necrotizing SLE glomerulonephritis with active extracapillary proliferation (WHO IIIB). He was immediately treated by Solu-Medrol pulses followed by Prednisone and he got one i.v. Cyclophosphamide pulse (CF). The pulmonary infiltration disappeared, a chest X ray was clear, contrary to our expectation, the pulmonary function test showed severe restrictive lung disease, in spite of that he got well and his family was happy for a few days. Candida albicans has been proved in his throat already in the district hospital. About ten days after a beginning of his immunosuppressive treatment he had a sore throat and got a caught. He was treated by antimycotics locally because Candida albicans became suspicious from this infection. Another complication was deep vein thrombosis on his right leg. Two days later he became suddenly dyspnoic, his chest had absent breath sounds on the right side and was tympanic to percussion on the side. The pneumothorax (PNO) was diagnosed by a chest X- ray, right lung was completely collapsed, without mediastinal shift. He was transferred to surgical department for chest tube placement. A continuous suction was started immediately. The right lung unfolded only partially and air in the pleural cavity persisted. Therefore prolonged chest tube drainage was necessary. Quite a big amount of the air was still escaping from lung, for more than a week. When drainage was stopped the PNO reappeared again. In the same place of previous lung infiltration the CT scan discovered a disintegrated cavity. Finally open thoracotomy under general anesthesia was only a solution of this problem and a resection of destroyed lung was performed. Meantime he was treated successfully by i.v. ketoconasol for Candida esophagi is. We felt an anxiety about possible serious adverse event of the second pulse of CF. Therefore CF was replaced by mycophenolat mofetil, steroids continued for all the time but the total dose was slowly tapered down. Presently this boy has no problem, the urine analysis is normal (urine is protein free), all clinical signs of SLE disappeared. Only slightly increased serum creatinine and border value of ANA still persisted. Our boy fulfilled following classification criteria of the American College of Rheumatology: arthritis, pleuritis, proteinuria (above 0.5 g/24 h), hemolytic anemia with reticulocytosis, lymfopenia, ds- DNA and antinuclear antibodies and lupus anticoagulans was presented.

SLE is chronic systemic disease which can involve multiple organs. The kidneys, liver, skin, brain, joints, bone marrow and polyserositis are well known affected organs by SLE. Pulmonary involvement is relatively frequent in adult patients (50–70%) but in children is scarce. A number of the pulmonary complications have been reported, although it usually runs a benign course, pulmonary lupus sometimes caries a serious prognosis. Lupus pulmonary involvements include pleuritis, pneumonitis, infectious pneumonia,

pulmonary hemorrhage, pulmonary hypertension and PNO. Even dysfunction of the neuromuscular control of respiration has been published. The PNO is however, is one of the less frequently reported complications in adult and rare in children. Until now only a few anecdotic cases of PNO have been published in children The PNO may occur only in children with high disease activity. The reported outcome of patients with SLE who developed PNO is dismal. The complication of PNO in patients with SLE is infrequent but, from limited number of patients reported in the literature, appears to carry a grave prognosis. Only two reports of survivors exist in English literature. A number of putative mechanisms have been presented previously. Patients who have had pulmonary function test prior to the pneumothorax have had distinct evidence of restrictive lung disease. Our case confirmed this observation. Almost all previous reports describe a typically fatal course in this setting; our case illustrates the fourth successful management of PNO in a child with SLE.
Conclusions: We would like to draw attention to PNO as one of life threatening complication of SLE even in children. Our boy is the **fourth survival child** with this complication in the literature. Our observation fully confirmed fact that serious restrictive lung disease precedes a development of PNO.

References

1. Sawkar LA, Eason HF: Recurrent spontaneous pneumothoraces in systemic lupus erythematosus. Chest, 1971 60:604–605.
2. Wilhelm M, Scott K, Why V: Pneumothoraces complicating systemic lupus erythematosus with nephritis. Padiatr Nephrol 2002, 17:261–263.
3. Ciftci E et al.: Pulmonary involvement in childhood-onset systemic lupus erythematosus: a report of five cases. Rhevmatology 2004, 43:587–591.
4. Paira S, Roverano S: Bilateral pneumothorax and mediastinal emphysema in systemic lupus erythematosus. Clinical Rheumatology 1992, 11:571–573.
5. Yen JH, Tsai WC, Ou TT, Lin SC, Chen JC, Liu HW: Systemic lupus erythematosus complicated by recurrent spontaneous pneumothorax – a case report. Kaohsiung J Med Sci 2001, 17:540–544.
6. Passero FC, Myers AR: Hemopneumothorax in systemic lupus erythematosus. J Reumatol 1980, 7:183–186.

_Notes

33

MONOGENOUS DISEASES OF KIDNEY IN CHILDREN

M. Malina, J. Janda, T. Seeman
Dpt. of pediatrics, University Hospital Motol and Charles University in Prague

Introduction: Role of genetics in kidney pathology is known for a long time. Many severe kidney diseases show some form of inheritance and many different syndromes have been described. Presently, molecular genetics is an

important part of standard diagnostic procedures in framework of kidney diseases in children.

Monogenous kidney diseases: About 40 monogenous kidney disorders are known presently and new findings are added to this broad spectrum every year. This review summarizes genetic chronic kidney diseases with most relevant clinical impact.

Nephrotic syndrome (NS) is a common glomerulopathy in childhood. Beside idiopathic forms with unclear etiology, genetically determined forms occur. These monogenic forms essentially differ in treatment and patient's prognosis from the idiopathic ones. They are clinically and histologically indistinguishable. The only option of differential diagnosis is molecular genetic testing. The most prominent genes causing genetically determined nephrotic syndrome are ***NPHS1, NPHS2, WT1*** **and** ***LAMB2***. All but one of genetic caused NS are resistant to initial steroid therapy. In all patients with steroidresistant nephrotic syndrome (SRNS) genetic background should be examined and genetically caused NS should be taken to differential diagnosis. Patients with SRNS should be tested using molecular genetics, at best at the time of renal biopsy.

Mutations in the ***NPHS2*** gene (called also podocine gene) are known to cause about 20% of the SRNS. NS mostly occur in infant and preschools age. The second most common gene causing SRNS is ***WT1***. Mutations in exon eight and nine of this well-known oncogene can cause sporadic SRNS and are also present in syndromes Denys-Drash and Frasier. Patients with this mutation must be observed very carefully for occurrence of Wilms tumor. The most severe nephrotic syndrome with earliest manifestation is congenital nephrotic syndrome of Finnish type due to mutations in the ***NPHS1*** gene. These patients are lacking protein of the slit diaphragm called nephrin resulting in a very poor prognosis. Some presentations of SRNS are also connected with syndromic diseases. For example mutations in ***LAMB2*** gene are causing Pierson syndrome (SRNS+microcoria). In adolescence, SRNS with FSGS could be caused by mutations in genes for α-actinin (***ACTN4***) and TRPC6 calcium channel (***TRPC6***).

Molecular genetic testing in Czech Republic is available for ***NPHS2, WT1*** **and** ***ACTN4*** **genes**.

Atypical hemolytic uremic syndrome (aHUS, D-HUS) is a complement dysregulation disorder with a major impact of genetic background. In contrast to typical forms (D+HUS), where the major pathogenic factor is microbial infection, about 50% of the aHUS are caused by mutations in currently known five genes (***CFH, CFI, MCP and CFB*** and ***C3***).

Differential diagnosis of D+ and D- HUS is of great clinical importance as the children with D- HUS have very poor prognosis (without specific treatment mortality up to 90%) and need aggressive therapy including plasmapheresis. All the patients with D- HUS must be investigated for the underlining cause.

Hereditary tubulopathies are a very broad group of disease comprising of pathologies involving renal tubules. Most of these diseases are connected with disorders in sodium, potassium and calcium handling. Most of them also show syndromic pattern with involvement of many organ systems.
In Czech Republic molecular genetic testing is available for **Lowe syndrome** and **Dents disease**. These diseases are closely related and both present with symptoms of hypercalciuria and nephrocalcinosis. While the Dents disease shows only renal involvement, Lowe syndrome comprises of triad of nephrocalcinosis, congenital cataract and central nervous system pathology resulting in heavy mental retardation.
Alport syndrome is a syndromic monogenous disease manifesting as hematuria, sensorineural deafness and ocular abnormalities. This disease is caused by mutations in genes for collagen IV chains. It shows all forms of inheritance (X-linked (85%), autosomal dominant (14%) and autosomal recessive (1%).
Polycystic kidney disorders are a heterogeneous group of single gene diseases characterized by development of multiple renal cysts. **Autosomal recessive polycystic kidney disease** (ARPKD) is early onset form with involvement of kidney and biliary tract. Majority of patients does reach end stage renal disease at early age. **Autosomal dominant polycystic kidney disease** (ADPKD) is caused by mutations in two genes (*PKD1, PKD2*). It is a live shortening disease with much milder phenotype than the ARPKD. DNA analysis in the Czech Republic is available only for ADPKD. Molecular genetic testing of ARPKD is available abroad.
Nephronophtisis is the most frequent monogenic cause of end stage renal disease in children (ca 10%). It shows an autosomal recessive inheritance. At least five genes (*NPHP1–NPHP5*) are known presently with different age of onset of the symptoms. The most common form is the juvenile form (mean age of onset of ESRD is 13 years).
Pediatricians should be aware of the facts given above and contact pediatric nephrology centers asking for the possibility to perform molecular genetic testing in suspected cases, either in this country or to establish contact to a center abroad. One of the most important tools of molecular genetic testing is the possibility to offer prenatal diagnostics to families, where already one handicapped child has been born.

References

Literature review

Genetic Diseases of the Kidney Edited by: Richard P. Lifton, Stefan Somlo, Gerhard H. Giebisch and Donald W. Seldin, 2009.

Original articles

1. Ruf RG et al.: Patients with mutations in NPHS2 (podocin) do not respond to standard steroid treatment of nephrotic syndrome. J Am Soc Nephrol, 2004. 15(3): p. 722–732.

2. Mucha B et al.: Mutations in the Wilms' tumor 1 gene cause isolated steroid resistant nephrotic syndrome and occur in exons 8 and 9. Pediatr Res, 2006. 59(2): p. 325–331.
3. Hinkes BG et al.: Nephrotic syndrome in the first year of life: two thirds of cases are caused by mutations in 4 genes (NPHS1, NPHS2, WT1, and LAMB2). Pediatrics, 2007. 119(4): p. e907–919.
4. Kaplan JM et al.: Mutations in ACTN4, encoding alpha-actinin-4, cause familial focal segmental glomerulosclerosis. Nat Genet, 2000. 24(3): p. 251–256.
5. Mukerji N, TV: Damodaran, and M. P. Winn, TRPC6 and FSGS: the latest TRP channelopathy. Biochim Biophys Acta, 2007. 1772(8): p. 859–868.
6. Philippe A et al.: Nephrin mutations can cause childhood-onset steroid-resistant nephrotic syndrome. J Am Soc Nephrol, 2008. 19(10): p. 1871–1878.
7. Zenker M et al.: Human laminin beta2 deficiency causes congenital nephrosis with mesangial sclerosis and distinct eye abnormalities. Hum Mol Genet, 2004. 13(21): p. 2625–2632.
8. Loirat C, Noris M, and Fremeaux-Bacchi V: Complement and the atypical hemolytic uremic syndrome in children. Pediatr Nephrol, 2008. 23(11): p. 1957–1972.
9. Cho HY et al.: Renal manifestations of Dent disease and Lowe syndrome. Pediatr Nephrol, 2008. 23(2): p. 243–249.

Notes

36

EFFECTIVENESS OF POSTNATAL RENAL ULTRASOUND SCREENING AND CRITERIA FOR DIAGNOSING PATHOLOGICAL RENAL PELVIC DILATATION – FINAL REPORT

H. Flögelová1**, J. Hálek**2, 3**, O. Šmakal**4**, K. Michálková**5**, L. Dubrava**2**, V. Janout**

1Dept. of Pediatrics, 2Neonatal Dept., 3Dept. of Medical Biophysics, 4Dept. of Urology, 5Dept. of Radiology, 6Dept. of Preventive Medicine, Faculty of Medicine and Dentistry, Palacký University in Olomouc and University Hospital Olomouc

The aim of the study: To assess whether ultrasound (US) examination of the kidneys in newborns is effective as a screening test for detecting kidney disorders related to renal pelvic dilatation (RPD) and to establish criteria for pathological magnitude of dilatation.

Methods: A prospective study of 6,088 newborns examined in the University Hospital Olomouc in 2005–2008. In all newborns, renal US was performed 72 hours after birth. Included were children with RPD of 5 mm and more on a transverse scan, the so-called anteroposterior intrarenal diameter (APIRD). Records of all the infants were checked for RPD detected by prenatal US examination. And all of them (regardless of the results of US screening) were checked for surgeries to treat kidney disorders. The number of cases of RPD

revealed by postnatal US screening was recorded and the proportion of newborns with prenatally detected RPD was calculated. The number of infants with surgically treated kidney disorders was determined. The receiver operating characteristic (ROC) curve was plotted and the discriminating ability of the screening to detect infants in need of surgery was assessed. The ROC was used to define the APIRD cut-off point to select children requiring further follow-up. Statistical analysis was performed using the XLstat2006 software.
Results: The absolute and relative RPD incidence rates were as follows: less than 5mm 5,854 (96.2%), 5–7mm 146 (2.4%), 7–10mm 70 (1.15%), 10–15mm 13 (0.21%), 15mm and more 5 (0.08%).
Of the screened infants, 16 (0.26%) were surgically treated for kidney disorders, of whom 9 (56%) were detected prenatally and 16 (100%) postnatally.
The numbers of surgically treated infants were as follows: 1 (0.68%) in the 5–7mm RPD group, 6 (8.6%) in the 7–10mm group, 4 (30.8%) in the 10–15mm, and 5 (100%) in the 15mm and more group.
The basic statistical parameters (sensitivity, specificity, positive and negative predictive values) were calculated for the individual RPD values. The ROC curve for postnatal US screening was plotted and the area under the curve (AUS = 0.995) was calculated (excellent discriminating ability of the test to detect severe abnormalities of the kidneys requiring surgery).
Based on the analysis of statistical data and the ROC, the ideal APIRD cutoff point for detecting severe abnormalities appears to be 7mm and more.
Conclusion: The ability of prenatal US examination to detect significant urinary tract abnormalities has been confirmed by numerous studies. Postnatal screening is only carried out in certain regions and countries (1, 2). In the Czech Republic, standard care in pregnancy comprises 2–3 US examinations of the fetus, with at least one being performed in the third trimester. However, it is often carried out by inadequately trained professionals using equipment of varied quality. Many congenital developmental abnormalities, often severe ones, remain undetected (3). This may be one of the reasons why early postnatal renal screening is performed in as many as half of all neonatal departments. Our findings concerning the relatively low number of abnormalities detected by prenatal US examination are not unusual (4).
Based on our findings postnatal renal US is an adequate screening test to detect severe abnormalities of the urinary tract requiring surgery (excellent sensitivity, good discriminating ability). The recommended cut-off point for RPD suitable for further surveillance is 7mm (transverse scan, APIRD).
Prenatal detection of severe abnormalities is extremely low in our study. The results of postnatal renal US screening represent a challenge to improve prenatal US screening in our region.
** Supported by the IGA grant No. NR 9512-3.).*
References

1. Riccipetitoni G, Chierici R, Tamisari L, De Castro R, Manfredi S, Veroni G, Susini P, Georgacopulo P, Vigi V: (1992) Postnatal ultrasound screening of urinary malformations. J Urol 148:604–605.
2. Tsuchiya M, Hayashida M, Yanagihara T, Yoshida J, Takeda S, Tatsuma N, Tsugu H, Yoshiaki H, Munakata E, Murakami M: (2003) Ultrasound screening for renal and Urinary tract anomalies in healthy infants. Pediatrics International 45:617–623.
3. Flögelová H, Smakal O, Halek J, Michalkova K, Geier P, Koranda P, Dubrava L, Janout V: (2008) Pitfalls of Prenatal Ultrasound Screening in Diagnostics of Serious Inborn Developmental Defects of the Kidney and Urinary Pathways – Prospective Study and Preliminary Results. Ces-slov Pediat 11:606–613.
4. Bhide A, Sairam S, Farrugia MK, Boddy SA, Thilaganathan B: (2005) The sensitivity of antenatal ultrasound for predicting renal tract surgery in early childhood. Ultrasound Obstet Gynecol 25:489–92.

ACUTE PYELONEPHRITIS – ANALYSIS OF PATIENTS ADMITTED IN THE YEARS 1997 AND 2007

A. Kolský1**, S. Najmanová**2**, S. Netvalová**1**, T. Rada**2**, I. Šilhánková**1**, K. Jiroušová**1**, J. Kučerová**1**, P. Heinige**1**, M. Dejlová Kolská**2**, J. Skibová**3**, P. Lyer**2**, H. Houšťková**1

1Dept. of Pediatrics Thomayer Teaching Hospital, Prague 4; 2Dept. of Pediatrics, District Hospital, Kladno; 3Institute for Clinical and Experimental Medicine, Prague 4

The Aim of the study: A retrospective analysis of group of children admitted in 1997 and 2007 for acute pyelonephritis (APN) to two pediatric departments (a teaching hospital and a district hospital).

Methods: We reviewed data of children with the first attack of APN. All children met the clinical and laboratory criteria of APN (significant bacteriuria, CRP, FW, fever). In 1997, there were 9 children from Prague 4, aged 2.94±4.03 yrs (median 0.92), 55.6% of boys, and 16 children from Kladno, aged 4.39±4.53 yrs (median 3.44), 50% of boys (n.s.). In 2007, there were 72 children from Prague 4, aged 5.86±7.38 yrs (median 1.35; range 0.09–18.9 yrs) and 34 children from Kladno, aged 7.24±7.38 yrs (median 3.36; range 0.08–18.7 yrs). Younger than 3 months were 20% of patients (1997) and 5.7% (2007). There were 76% of patients younger than 6 years (52% of boys) (1997) and 52% (40% of boys) (2007). All boys were uncircumcised.

Results: A comparison of the two departments revealed no statistical difference in the age of children in 1997 and 2007. In 1997, the number of patients with APN admitted to hospital in both districts was very low, only 9 children in Prague 4 (65,249 children in the district, 2,379 were hospitalized) and 16 in Kladno (26,197 children in the area, 2,674 were hospitalized), $p<0.001$. In 2007, 72 children were admitted to hospital in Prague 4 (the district of Prague 4 had 38,269 children, a decrease by 41.3%) and, in Kladno, there were 34 children admitted to hospital (the district had 30,220 children, an

increase by 13.3%), $p<0.05$. When comparing 1997 and 2007, we can see a higher incidence of APN in Prague 4 (0.14 vs. 1.9 children/1,000/year; $p < 0.001$) and a lower incidence in Kladno (0.6 vs. 1.1; $p=0.057$). *E. coli* was identified in 60% and 68.9% of cultures in 1997 and 2007, respectively. Initial antibiotic therapy was started as i.v. in 48% of patients in 1997, and in 27% of patients in 2007. Sixty-eight percent of children (1997) and 61% (2007) were treated with aminopenicillins plus beta- lactamase inhibitors, and 28% (1997) and 17% (2007) (second- or third-generation) with cephalosporins, combined with an aminoglycoside in 8% (1997) and 2.8% (2007) of children. Using a standard algorithm of examination, we found vesicoureteral reflux (VUR) in 5 children (20%) in 1997, and in 6 children in 2007 (5.7%); 4 (16%) children had bilateral VUR in 1997 and 2 children (1.9%) in 2007. Two children were indicated for surgery in 1997 (one grade V bilateral VUR and hydronephrosis with megaureter each). One girl was indicated for surgery in 2007 (nephrolithiasis) and 3 children are being followed for hydronephrosis and megaureters. DMSA was performed in 76% of patients, with pathological findings demonstrating kidney injury in 37% (1997) and, in 38% of patients, with pathological results in 4.7% of children (2007). In children with VUR, pathological DMSA findings were made in only 43% (1997) and 17% of patients (2007). APN recurrence was observed in only 1 patient (4%) in the year 1997. Eight percent (1997) and 4.7% (2007) of children were patients with a low birth weight and at risk due to their perinatal history. Among boys, the incidence of APN was highest within the first year of life and declined thereafter. Comparing our data with the literature, we think that the number of children with APN should have been higher.

Conclusion: Comparing two pediatric departments, no statistical difference concerning the age of patients, ultrasound, DMSA, and voiding cystourethrography was found. This may mean that children with APN are not diagnosed or are being treated in outpatient departments. Consequently, our data may implicate that children with APN are not appropriately assessed by primary care pediatricians so the diagnosis can be missed. The situation with APN is perhaps already improving thanks to better information of primary care pediatricians.

References

1. Hoberman A, Chao HP. Keller D et al.: Prevalence of urinary tract infection in febrile infants. J. Pediatr. 123, 1993, 17–23.

2. Janda J: Infekce močových cest u dětí. In: Infekce ledvin a močových cest v dospělém a dětském věku. Ed: V. Teplan, M. Horáčková, E. Bébrová, J. Janda a kol. Praha, Grada, 2004.

3. Nuutinen M, Uhari M, Murphy MF, Hey K: Clinical guidelines and hospital discharges of children with acute urinary tract infections. Pediatr. Nephrol., 13, 1999, 45–49.

4. Rushton HG: Urinary Tract Infections in Children (Epidemiology, Evaluation and Management). Pediatr Clin. North Am. 44, 1997, 1133–1169.
5. Uhari M, Nuutinen M: Epidemiology of symptomatic infections of the urinary tract in children. BMJ, 297, 1988, 450–452.
6. Velemínský M, Janda J: Infekce močových cest u dětí. Praha, Avicenum, 1978.

_Notes

40

CHILDREN'S SPA CURE FOR KIDNEY AND URINARY TRACT DISORDERS

Josef Nebeská
Pediatric Spa Lázně Kynžvart, Lázeňská 295, 354 91 Lázně Kynžvart

We use the positive effects of natural medicinal sources (mineral water, peloids) for the complex spa cure of children and adolescents, which are combined with other methods of medical rehabilitation and physical medicine. The aim is after-treatment or decreasing activity, stopping or at least slowing down the progress of kidney and urinary tract diseases in children.
Training of voiding is performed using method of myo-feedback, its process is uroflowmetrically evaluated and postvoiding residuum is measured by ultrasound.
An integral part of the spa cure in the children's health resort is pedagogical, psychological and educational care with recommendation for accompanying persons how to arrange free time, children's education, with regard to nursing techniques and daily regimes.

_Notes

ANDROLOGICAL, GYNECOLOGICAL, PSYCHOSOCIAL AND PSYCHOSEXUAL ASPECTS IN THE LONG-TERM FOLLOW-UP OF PATIENTS WITH BLADDEREXSTROPHY AND THEIR IMPACT ON CURRENT APPROACH

Wolfgang H. Rösch, Anne-K. Ebert
Department of Paediatric Urology, Klinik St. Hedwig, University of Regensburg, Germany

The Exstrophy-Epispadias Complex (BEEC) is comprised of a spectrum of anomalies involving the abdominal wall, pelvis, urinary tract, genitalia and occasionally the spine and anus. Major surgical issues are secure abdominal wall closure, achievement of urinary continence with preservation of renal function, and finally adequate cosmetic and functional genital reconstruction. The following approaches are currently used for the management of the BEEC: variations of a staged approach, primary one-stage reconstruction during newborn period and removal of the bladder template with complete urinary diversion in a rectal reservoir. Further understanding of the complex anatomy

and analysis of initial follow-up results helped to improve operative techniques, so that nowadays continence rates of 70 to 80% during childhood can be expected. Though spontaneously voiding is the main issue, additional surgery might be needed to gain continence like catheterisable channels, bladder augmentation or bladder neck closure. In cases of definite failed reconstruction however, urinary diversion provides finally continence and secure upper urinary tract protection. In addition to continence, during puberty genital and reproductive function gain naturally in importance for both sexes. However, there is still an ongoing debate, whether a specific surgical approach has a more favourable outcome and less long-term complications compared to others in this respect. However, despite intense clinical and basic research many clinical problems remain unsolved.

Andrological aspects: We evaluated 21 adult male BEEC patients. 17 patients had a single stage reconstruction, 1 had a staged approach, 2 got primarily a urinary diversion and 1 had only an external genital reconstruction in epispadias. All were evaluated with a semi-structured questionnaire, a clinical examination, ultrasound, hormone and semen analysis (1).

Results: All patients reported erections, 19 were sure about ejaculation (90.5%). 18 patients proved antegrade and 1 patient retrograde ejaculations; 2 patients were not able to retrieve their specimen. 15 patients had regular

testicular size, 4 had unilateral and 2 bilateral small testicles. 4 had irregular intratesticular sonographic findings, one of these had a testicular intraepithelial neoplasia which was treated with radiation. 17 patients had normal hormone analysis, whereas 4 showed elevated follicle-stimulating hormone. Semen analysis showed normozoospermia in 3, asthenozoospermia in 5, oligoasthenozoospermia in 6 and azoospermia in 5. Seminal parameters included fructose on average 1441.8 μg/ml (normal 1200–4500), zinc 43.3 μg/ml (normal 70–250) and α-glucosidase 19.13 mU/ml (>20).

Conclusions: Our long-term data suggest that functional bladder neck reconstruction with a consequent anatomical placement of the colliculus seminalis in the posterior urethra allows antegrade ejaculations in 94.1% of the patients. So not only for continence, but also for ejaculation and fertility the primary successful and anatomical correct approach to the bladder neck seems to be the key point.

Due to the severely impaired sperm quality and hormonal findings we should offer the BEEC patients adequate diagnostics and treatment options.

Gynecological aspects: The congenital bony pelvis and pelvic floor defect highly predisposes females in the BEEC to uterine prolapse. There is a paucity of knowledge about pelvic floor anatomy after reconstruction of the BEEC. Therefore we conducted a cross-sectional study using 3D sonography and MRI to describe pelvic floor anatomy. The aim was to determine whether perineal 3D sonography is a reliable diagnostic tool compared to MRI and to proof

whether previously defined pelvic floor parameter can predict the postoperative risk for uterine prolapse (2).
Conclusion: This is the first study showing that perineal 3D- sonography is useful for pelvic floor imaging in BEEC. Established pelvic floor parameter may predict the risk for pelvic organ prolapse in BEEC. Again pelvic ring closure seems to play an important role in prevention of uterine prolapse and the overall functional outcome results.
Psychosocial and psychosexual aspects: In a long-term retrospective follow-up of an average of 11.1yrs. 100 patients with BEEC (mean age 14.5) were evaluated with respect to medical history, and received a general questionnaire concerning their social and psychosocial situation. A total of 54 pts. who were 15yrs. Or older received an additional questionnaire to assess detailed sexual history (3).
Conclusion: Despite a high degree of social integration and adult adaptation, children and adolescents with BEEC suffer from psychosocial and psychosexual dysfunction. Anxiety about genital appearance and sexual activity is a common phenomenon among adolescents with BEEC. Due to their specific developmental implication genitourinary malformations may create vulnerabilities to psychosexual dysfunction due to prolonged incontinence, residual genital defects and postsurgical genital appearance. As a consequence 4support from a multidisciplinary team, helping these affected individuals and parents through the whole childhood and adolescence, is mandatory. Therefore a prospective analysis of clinical predictive factors in gender-related long-term outcome is needed to provide an individualised flexible treatment strategy with predictable success and quality of life. Besides the paediatric urologist, this must also comprise the paediatric orthopedic surgeon, the paediatrician, the urologically experienced paediatric psychologist, experienced paediatric nurses and urotherapists.

References

1. Ebert AK, Bals-Pratsch M, Seifert B, Reutter H, Rösch WH: Genital and reproductive function in males after functional reconstruction of the Exstrophy-Epispadias-Complex –long-term results. Urology 2008, 72(3):56–69.
2. Ebert A, Falkert A, Brandl R, Hirschfelder H, Koller M, Rösch WH: Pelvic floor imaging using 3D sonography and MRT in long-term follow-up of the Bladder-Exstrophy- Epispadias-Complex (BEEC), BJU 2009, in press.
3. Ebert A, Scheuering S, Schott G, Rösch WH: Psychosocial and psychosexual Development in childhood and adolescence within the exstrophy-epispadias complex. J Urol 2005, 174(3):1094–1098.

_Notes

URINARY BLADDER DEFECTS IN CHILDREN

J. Morávek, J. Kříž, J. Trachta
Department of Paediatric Surgery, 2nod Medical Faculty, Charles University,

Prague, University Hospital Motol

Introduction, aim of the study: Urinary bladder defects represent exstrophy of the bladder and cloacal exstrophy. They occur due to impaired ingrowth of the mesenchyme between ectodermal and entodermal layers of the cloacal membrane in 6th–7th. week of embryonic development. If this impairment takes place sooner, the urorectal septum is involved and cloacal exstrophy is the result. Both malformations represent major involvement of the urogenital or gastrointestinal systems leading to different degree of impaired quality of life. In our cohort of patients we would like to demonstrate the surgical correction of the defects as well as its complications and the results of the treatment.

Methods: Between march 1994 and march 2009 we have performed 53 surgical procedures in 25 children with inborn defects of the urinary bladder. 17 children were newborns with these defects 13 of them had bladder exstrophy (9 boys, 4 girls) 4 children had cloacal exstrophy (2 boys, 2 girls) 1 female patient had combination of bladder exstrophy and anorectal atresia.

The primary reconstruction of the bladder was performed within 24–48 hour limits in all children. Once the paraexstrophy flaps were used, twice an iliac osteotomy was necessary to reconstruct the bladder. The reconstruction of the epispadiac urethra is done 2–3 years later in our institution (Cantwell.-Ransley procedure, twice after Mitchell). Then we try to increase the outflow resistance by bladder neck plasty (Young-Dees- Leadbetter procedure) together with bladder neck suspension (Marshall- Marchetti- Krentz procedure). If the continence remains unsatisfactory a continent vesicostomy with bladder neck occlusion is the option. Cloacal exstrophy is treated by an excision of the omphalocele, reduction of the ileocaecal intususception and terminal colostomy and reconstruction of the bladder from two hemibladders and plasty of the urethra.

Results: One female patient had recurrent dehiscence of the reconstructed bladder (4 times), bilateral pyohydronephrosis with septic shock was solved in her by bilateral ureterostomy. All children are incontinent at first. Vesicoureteral reflux occurs in almost 100% of patients (in one patient we have not confirmed it). Correction of the reflux by reimplantation of the ureters together with bladder neck plasty is effective in more than 90% of patients as well as in case of primary reflux.One patient has unilateral lowered renal function on MAG3 renal scan (33%) despite of successful antireflux plasty. One female patient with cloacal exstrophy had duplex uterus with ectopy of the right ureter in one uterus. In her the reimplantation of the ureter was performed during primary reconstruction of the bladder. An intestinal obstruction due to adhesions followed, it was solved by excision of the adhesions and placement of the gut in non-rotation position. One girl underwent a continent vesicostomy by excluded ileum loop with occlusion of the bladder neck. One boy with cloacal exstrophy died of intractable septic shock. Socially acceptable continence (patients remains dry more than 1 hour) is to be achieved in most

patients with bladder exstrophy. In cloacal exstrophy patients the solution is usually permanent colostomy and continent vesicostomy.
Discussion: Reconstruction of the bladder is possible even in very small exstrophy targets in almost all cases. Pelvic osteotomy is usually necessary for reconstruction after 24–48 hours after birth. The reconstructed bladders have tendency to expand even if the remain empty due to incontinence, which is the rule. Vesicoureteral reflux is also the rule as there is the malformation of the ureterovesical junction. After reconstruction of the bladder its dysfunction may contribute also to aetiology of the VUR. The urinary incontinence paradoxically protects the kidneys that are usually intact in patients with bladder defects at birth. Socially acceptable continence (i.e. dry interval more than 1 hour) is usually possible to be achieved by increased outflow resistance by bladder neck plasty and suspension. The tubularisation of the intersymphyseal bands seems to contribute to continence mechanism, nevertheless this seems to be more a controlled stricture than true continence.
Conclusion: Urinary bladder defects represent a permanent problem for the involved individuum. Its corrections must be performed step by step or single staged procedure (1, 2). Usually it results in preserved renal functions as well as socially acceptable continence. A permanent follow up of these patients is necessary.

References

1. Gearhart JP: Complete repair of bladder exstrophy in the newborn: complications andmanagement. J Urol. 2001 Jun; 165(6 Pt 2):2431–2433.
2. Husmann DA: Surgery Insight: advantages and pitfalls of surgical techniques for thecorrection of bladder exstrophy. Nat Clin Pract Urol. 2006 Feb; 3(2):95–100. Research No.:00064203/6310.

Contact: jiri.moravek@lfmotol.cuni.cz

_Notes

MODERN MANAGEMENT OF CHILDREN WITH MMC

Prof. Dr. Marcus Riccabona
St. Vinzenz Hospital Linz/Austria, Department of Peadiatric Urology

Introduction: The incidence of spina bifida ranges between 1 and 4 out of 1000 live born children.
The spinal cord lesion is localized at variable levels. Depending on the level of the lesion the detrusor, the bladder neck and pelvic floor can be overactive or inactive. Overactivity of the bladder can result in damage of the kidneys, especially in combination with overactivity of the sphincter complex. Recurrent urinary tract infection and reflux form a continuous threat to the kidneys.
An active treatment of detrusor and sphincter overactivity from birth on is mandatory. This implies that every neonate with MMC is treated by clean intermittent catheterisation (CIC) and pharmacological suppression of detrusor overactivity from birth on.

The main objectives in the urological management of children with MMC are preservation of renal function, quality of life, preferably with urinary continence at school age and independence at older age in respect to bladder and bowel management.

Work-up and start of therapy: The first assessment should take place 6 weeks after closure of the lesion and includes urinalysis, 4 – hour voiding observation, ultrasound of the kidney and the bladder, kidney function and basic videourodynamics with a VCUG. CIC and Oxybutynin 0,3mg/kg 2× daily or Tolterodine 0,1mg/kg 2× daily is started, no antibiotic prophylaxis. After 3 months a reevaluation is performed with an additional DMSA Scan, optional MR-urography and recommendation of circumcision in boys.

Botulinum-A Toxin: Botulinum-A Toxin blocks presynaptic parasympathetic release of acethylcholine and may affect sensory nerve fibers. It is indicated in nonresponder to orally or intravesically administered anticholinergic medication. We injected 10U/kg of Botulinum-A Toxin diluted in 1ml saline into the detrusor at 25–40 sites, sparing the trigone via a 3.7, 25cm needle (Cook®). Several studies confirmed the safety of the therapeutic and minimally invasive BTX-A treatment of detrusor hyperreflexia in children affected by spina bifida, and showed astonishing improvement in urodynamic parameters like reflexvolume, maximum detrusor pressure, detrusor compliance, bladder capacity and incontinence score. The efficacy remains constant for a mean of 9 months but results return to baseline levels after 11 months.

Incontinence Surgery: Different surgical options exist.

Sling Suspension: Patients with a paralytic pelvic floor need bladder neck surgery to reach continence. In male patients an abdominoperineal puboprostatic and in female patients a transvaginal sling procedure is recommended. A 10–15 cm long and 2 cm wide paramedian strip of the rectus abdominis fascia is used leaving the caudal end fixed to the pubic bone.

Bulking agents: When, after a sling procedure, some leakage persists this is cured by injection of a bulking agent in the bladder neck. This can be obtained by either the transurethral or suprapubic route or both. As bulking agent Macroplastique® or Deflux® are used.

Catheterisable Stoma: The need for transfers from a wheel chair to do CIC is the most important indication to make a catheterisable stoma. In patients with a large bladder capacity for age a continent stoma can be constructed from a bladder tube (continent vesicostomy). Patients with a normal or reduced bladder capacity (augmentation) can be treated by cutaneous appendicovesicostomy (Mitrofanoff) or by an ileal tube (Monti). The stoma is either placed in the midline (umbilicus) or on the right side of the lower abdominal wall using the VQZ-technique. In selected cases a ureter can be used as a catheterisable stoma.

Autoaugmentation of the bladder: This procedure is indicated in selected

cases to lower intravesical pressure in low compliance bladder and secondly to get patients off antimuscarinic therapy. Not much extracapacity can be achieved.

Ileocystoplasty (Clam cystoplasty): This is indicated when bladder capacity is too small to reach acceptable numbers of catheterisation/day and the leak point pressure is < 25cm H2O. It is performed with ileum or colon. In general, 25cm of ileum is used, opened antimesenterically, and constructed in a ushaped cup. In case of a short ileal mesentery, sigmoid colon can be used easily. The bladder has to be opened and transsected until to the bladder neck to avoid an hourglass-shaped bladder.

Bowel management: The first 2 years of life a wait and see policy is done, often supported by chronic use of laxatives. At age 3, bowel management can be done with retrograde colonic enemas with success in the vast majority of cases. As an alternative and in the older children an antegrade colonic stoma (ACE) is offered. The simplest way to create an ACE is to bring the tip of the appendix to the abdominal skin by laparoscopy. Alternatives are an open procedure and in the absence of the appendix the creation of a transverse tube from the colon (Monti). Some authors have good experience with several types of buttons that are put into the colon.

A modern protocol for the management of children with MMC is mandatory. Urinary and faecal dryness and finally independence are important factors for optimal quality of life in spina bifida patients.

References

1. Kaplan GW: A pragmatic approach to myelomeningocele. Dialogues in Pediatric Urology
23, number 11, 2000. 2. Kurzrock EA: Clean Intermittent Catheterization of Infants with Myelodysplasia. Dialogues in Pediatric Urology, Vol 23, Number 11, November 2000.
3. Lapides J et al.: Clean intermittent self-catheterization in the treatment of urinary tract disease. J Urol 107:458, 1972.
4. Hopps C, Kropp K: Preservation of renal function in children with myelomeningocele managed with basic newborn evaluation and close follow-up. J. Urol. 2003: 169, 305–308.
5. Riccabona M, Koen M, Schindler M, Goedele B, Pycha A, Lusuardi L, Bauer SB: Botulinum-A toxin injection into the detrusor: a safe alternative in the treatment of children with myelomeningocele with detrusor hyperreflexia. J Urol. 2004 Feb; 171 (2 Pt1): 845– 848; discussion 848.
6. Dik P, Klijn AJ, van Gool JD, de Jong-de vos van Steenwijk, De Jong IP: Early Start to Therapy Preserves Kidney Function in Spina Bifida Patients. Eur Urol. 2006, Jan 19.
7. Muller T, Arbeiter K, Aufricht C: Renal function in myelomeningocele: risk factors,

chronic renal failure, renal replacement therapy and transplantation, Curr. Opin.Urol, 2002
Nov; 12 (6): 479–484.

_Notes

CONTEMPORARY POSSIBILITIES OF CHILDREN'S DETRUSOR HYPERACTIVITY TREATMENT BY MINI-INVASIVE METHODS

Pavel Zerhau, Matej Husár
Department of Paediatric Urology, University Children's Hospital Brno

Introduction: Until recently, a highly invasive surgical procedure was considered as the only possibility of severe detrusor hyperactivity therapy upon the failure of pharmacologic treatment. Of recent years, however, neuromodulatory and neurostimulative methods as well as a direct detrusor influence by botulinum-toxin A application have been preferred. The most efficacious biologic toxin inhibits acetylcholine liberation on presynaptic cholinergic endings, which results in reduced muscle contractility in the place of application. Especially, it reduces excessive abnormal musculature contractions. The arisen chemical denervation is a reversible process with axonal regeneration, enduring in laboratory conditions for 3 to 6 months. Such features have been utilized in urology since the 1980s, when the BTA application into the musculature of sphincter ani externus muscle was described for the first time. The intradetrusor application results in a considerable reduction of non-inhibited contractions, intravesical pressure, extension of bladder capacity and improvement of urinary continence.

Objective: A survey of contemporary possibilities in view of mini-invasive method influence on detrusor hyperactivity and description of the own experience related to botulinum-toxin A intra-detrusor application in children.

Material and methods: During 2008/2009, botulinum-toxin A was applied to 7 children (5 boys, 2 girls) at the age between 5 and 12 years. The used method was an endoscopic botulinum toxin A application into the children's detrusor. In three cases, the bladder hyperactivity was neurogenic, the other four patients have shown no signs of any neurogenic origin. All the children patients underwent an unsuccessful long-lasting conservative treatment (Propiverin, Oxybutinin, Tolterodin). Botulotoxin was applied in a dose of 10 IU (Botox)–30 IU (Dysport)/kg, as per the actual children body weight into 25–30 detrusor points. In case of two patients, the application followed repeatedly. The subsequent evaluation considered the continence effect, urodynamic parameters and duration effect.

Results: 6 patients have shown an improvement of continence problem, 1 patient was continent before. An enlargement of cystometric capacity by 73% on the average was reached with all patients. 6 children have shown reducing of intravesical pressure by 54% on the average. In two cases, a considerable

dwindle of bladder wall appeared; in other cases this problem was detectable. The above mentioned improvement was detected by testing done within 3 months after the botulotoxin application. The test results gained 6 months after the botulotoxin application showed much lower values and after 9 months, an improvement due to the application of Botox vaccine was detectable with 3 patients only. The repeated applications resulted in an effect, comparable with that of the first given injection.

Conclusion: Botulinum toxin A may be considered as a safe and effective substance to be alternatively applied in connection with detrusor hyperactivity treatment with children, resistant to a drug therapy. It is usable for both, the neurogenic and non-neurogenic pathologies. Applications done in cases of low bladder compliance or already made remodeling of fibrous wall are less effective. Detrusor hyperactivity with absence of frequent non-inhibited contractions is an ideal indication. Treatment standardization, especially in the field of dosage, re-application and combining with drug therapy is a great challenge for the contemporary pediatric mini-invasive urology.

The work is supported by the Grant No. NS 9845-3

References

1. Schulte-Baukloh H, Michael T, Schubert J, Stolze T, Knispel HH: Efficacy of botulinum-a toxin in children with detrusor hyperreflexia due to myelomeningocele: preliminary results.Urology 2002, 59:325–327.
2. Krhut J: Hyperaktivní močový měchýř. Jessenius Maxdorf, Praha 2007, 148 s.
3. Riccabona M, Koen M, Schindler M, Goedele B et al.: Botulinum-A toxin injection into the detrusor: a safe alternative in the treatment of children with myelomeningocele with detrusor hyperreflexia. J Urol 2004, 171:845–848.
4. Altaweel W, Jednack R, Bilodeau C, Corcos J: Repeated intradetrusor botulinum toxin type A in children with neurogenic bladder due to myelomeningocele. J Urol 2006, 175:1102–1105.
5. Hoebeke P, De Caestecker K, Vande Walle J, Dehoorne J, Raes A, Verleyen P, Van Laecke E: The effect of botulinum-A toxin in incontinent children with therapy resistant overactive detrusor. J Urol. 2006, 176(1):328–330.

_Notes

THE INTRAVESICAL INSTILLATION OF PROPIVERIN AND OXYBUTININ IN THE TREATMENT OF NEUROGENIC BLADDER DYSFUNCTION IN CHILDREN

Z. Dítě
1**, J. Molčan**1**, M. Janů** 2**, R. Kočvara**1**, J. Sedláček**1**,J. Dvořáček**1
1Department of Urology, General Teaching Hospital and 1st Medical, School of Charles University, Prague 2, Czech Republic; 2Department of Preparing Sterile Drugs, Hospital Pharmacy, General, Teaching Hospital, Prague 2, Czech Republic

The aim of the study: Propiverin hydrochloride and oxybutinin hydrochloride are frequently used perorally, reducing effectively symptoms of bladder overactivity. Parenteral administration has potential to decrease anticholinergic side effects.
We report and compare short time results of intravesical instillation of propiverin hydrochloride or oxybutinin hydrochloride in neurogenic bladder dysfunction.
Methods: Eighteen patients with neurogenic bladder were enrolled into the study between 2004 and 2008. Twelve children suffered from myelodysplasia, two from myelodysplasia together with tethered cord syndrome, two patients from sacral agenesis and two from neuroinfection. Seven children were previously unsuccessfully treated with oral oxybutinin and five with oral propiverin. All children absolved clinical investigation, urinalysis, ultrasound and videourodynamic investigation before and three months after treatment.
Group 1: 13 patients, aged 4–18 (Ř11.3) years, were treated using intravesical instillation of propiverin hydrochloride during 11 months in average; Group 2: five patients, aged 2–12 (Ř6.6) years, received oxybutinin hydrochloride intravesically during 14 months in average. Children in Group 1 were treated with intravesical sterile solution of propiverin hydrochloride instilled (0.03g diluted into 50 ml of saline solution), prepared by Hospital Pharmacy. Average dose administered was 13 mg (4–15 mg) twice a day. Children treated in Group 2 instilled oxybutinin hydrochloride by intermittent catheterisation three-times daily in average 4.5 mg (2.5–5 mg, the pill crushed and dissolved in saline solution). The children with urinary tract infection were on antibacterial chemoprophylaxis.
In Group 1, 12 (92.3%) children suffered from intractable urge incontinence and 13 (100%) from hyperactivity or bladder small capacity. Seven (53.8%) patients presented with faecal incontinence and 7 (53.8%) with chronic constipation.
In Group 2, there were 5 (100%) children with intractable urge incontinence, hyperactivity or bladder of small capacity. Three (60%) patients suffered from faecal incontinence and four (80%) from chronic constipation.
Results: In Group 1 (propiverine), daytime incontinence improved in 9 out of 12 (75.0%). Night-time leaks diminished in 5 (50.0%) children. Urodynamic parameters improved in 8 patients (61.5%). Maximal cystometric volume on filling cystometry increased from 265.4 ml to 304.2 ml (by 14.9 %, p=0.124) in average. Maximal detrusor pressure decreased from 36.5cm H2O in average to 26.3cm H2O (by 28.3%, p=0.079). Faecal incontinence was diminished in two (28.6%) and constipation in five (71.4%) patients out of seven.

In Group 2 (oxybutinin), daytime incontinence improved in four out of five patients (80.0%). Night-time leaks diminished in two (40.0%). Urodynamic parameters improved in one patient (20.0%). Maximal cystometric volume increased in average from 269.4 ml to 317.6 ml (by 17.8%, p=0.097). Maximal detrusor pressure decreased from 61.2cm H2O in average to 54.0cm H2O (11.8%, p=0.226). Faecal incontinence was diminished in two (40.0%) and constipation in one (20.0%) patient.
No adverse effects were recorded (headache, impaired salivation, blurred vision) in both propiverin and oxybutinin groups.
Statistic method used: T-test.
Conclusions: Similar positive effect on urinary incontinence has been registered in both propiverin and oxybutinin groups with prevailing effect on day-time incontinence without any adverse events regarding side-effects or infection. In the Group 1, good therapeutical impact was observed in reducing detrusor pressures comparing with Group 2 (p=0,002) and, moreover, positive effect of propiverin instillation on constipation was registered.

References

1. Amarenco G, Adba MA, Kerdraon J: Value of intravesically instilled oxybutynin in refractory
bladder hyperactivity. Study of 15 cases. Prog Urol. 1992, 2, p. 660–663.
2. Guerra LA, Moher D, Sampson M, Barrowman N et al.: Intravesical oxybutinin for children with poorly compliant neurogenic bladder: a systematic review. J. Urol. 2008, 180, p. 1091–1097.
3. Haferkamp A, Hohenfellner M: Intravesical treatment of overactive bladder syndrome. Urologe A. 2006, 45, p. 1283–1288.

USE OF RENAL SCAN TO EVALUATE RENAL FUNCTION IN CONGENITAL HYDRONEPHROSIS IN CHILDREN

J. Kříž, J. Morávek
Department of Paediatric Surgery, 2nd Medical Faculty, Charles University, Prague, University Hospital Motol

Introduction, aim of the study: Renal functions represent the main criteria to evaluate the possible benefit from surgery for congenital hydronephrosis in children. For investigation of separate renal function a dynamic renal scan is routinely in use. The aim of our study is to evaluate the results of MAG3 renal scan in unilateral congenital hydronephrosis in children so as to exclude the possible functional overvalue of the affected kidney.
Methods: We compare the function of the obstructed kidney before surgery and 6 months after dismembering pyeloplasty. A successful pyeloplasty is followed by improved wash-out curve, provided that separate renal function remains the same or was also improved, especially in small children. The investigation with 99m Tc MAG3 was performed in supine position of the

patient, a diuretic was applied in selected cases. A relative renal function was calculated either from surface area under the curve between 1st and 3rd minute after intravenous administration of the radio-pharmaceutical. A subtraction of the activity of the background in the secretory phase has been performed (area method) or we have calculated the steep gradient of the curve in the same intervals (slope method). The normal values are 50% to 50% with fluctuations within 5%.

Results: We have investigated 47 children (31 boys, 16 girls) between 1 month and 18 years of age (average 5,5 yrs). The unilateral hydronephrosis was 22 × right sided, 25 × on the left, the function of the contralateral kidney was normal. The function of the affected kidney preoperatively was 7× supranormal (i.e. over 53% separate renal function). In 5 of these children it has dropped by more than 5% postoperatively. The postoperative result was also worse in 5 children with preoperative lowered or normal separate renal function. In 35 children with worsened or normal renal function preoperatively the postoperative scan revealed improvement or stable functions. In children with preoperative supranormal function of the affected kidney an additional investigation with DMSA renal scan may be considered (2).

Discussion: We have confirmed the supranormal function of the obstructed kidney to be usually false. In five children from seven (70%) it has dropped sharply by more than 5% postoperatively. In 5 children from 40 with normal or lowered function preoperatively (12,5%) it was also falsely overvalued. So the obstruction with urine retention devalues functional investigation. The false overvalue of the renal function of the obstructed kidney is in connection with enlargement of this organ. The US investigation of this kidney reveals its enlargement but dilatation of the pelvicalyceal system and thinning of the parenchyma. According to accepted classification it is consistent with hydronephrosis of the 4th degree. The explanation of this phenomenon is unclear (1). The static renal scan using DMSA is more exact investigation for the renal function but a greater radiation exposure especially in small children is the main drawback of it.

Conclusion: The preoperative separate renal function on MAG3 renal scan is overvalued in 20% of children with congenital obstructive hydronephrosis. So the false overvalue of the enlarged hydronephrotic kidney is frequent. In our experience the decision to correct surgically the hydronephrotic kidney is made in children with increasing dilatation of the hollow system and thinning of the renal parenchyma despite normal or even supranormal function on MAG3 renal scan.

References

1. Seung-Juna Oh, Dae Hynk Moon, Weechang Kang, Young Seo Park at al.: Supranormal differential renal funtion is real but may be pathological: Assesment by 99m Technecium nMercaptoacetyl triglycine renal scan of congenital unilateral

hydronephrosis. Journal of Urology, Vol 165, issue 6, supp1, June 2001, p. 2300–2304.
2. Bouisson F, Julian A, Ouhayoun E: Supranormal renal function in unilateral hydronephrosis in children. Study with MAG3 and DMSA. Alasbium Journal, year 6, No 25, July 2004. ISSN: 0717-4055.
**Support by VZ MZO 00064203/6310*
Contact: kriz.uro@seznam.cz

_Notes

THE IMPORTANCE OF DMSA SCANS AND ULTRASOUND FINDINGS IN THE TREATMENT OF CONGENITAL ANOMALIES OF DUPLICATED KIDNEY ASSOCIATED WITH OBSTRUCTION OR REFLUX

O. Šmakal1**, J. Vrána**1**, I. Hartmann**1**, T. Tichý**2**, H. Flögelová**3**, K. Michálková**4
1Dpt. of Urology, 2Dpt. of Pathology, 3Dpt. of Paediatrics 4Dpt. of Radiology, Teaching Hospital Olomouc

The aim of the study:
1) Evaluate ultrasound (US) findings, DMSA scans and renal histology findings in kidneys after heminephrectomy for obstructive or reflux uropathy.
2) Establish criteria for ablative procedure.

Methods: We prospectively evaluated 28 children (aged 3 month-14 years) with duplicated kidneys associated with obstructive or reflux uropathy. They underwent surgery between 2002 and 2008. The procedures performed were resections of the lower pole of the kidney in 6 cases, resections of the upper pole of the kidney (22). To diagnose the cause of obstructive or reflux uropathy all children were examined with the US, DMSA scan and voiding cystography. Cystoscopy was performed in 27, MAG3 diuretic scintigraphy in 6, magnetic resonance urography in 6.
The grade of interstitial fibrosis in renal histology was assessed according to Zhang. Endoscopic incisions of ureteroceles were performed up to 6 weeks of age in all cases.

Results: US findings: the thickness of renal parenchyma varied from 1 to 6 mm, the pelvic dilatation was of grade 4 according to Society for Fetal Urology in all observed renal segments.
Based on DMSA scan, the functions of these renal segments were 0–28% of relative function of the duplicated kidney (0–13% of total renal function).
The following uropathies were found:
vesicoureteral reflux (VUR) grade IV–V in the lower pole of the kidney in 5 patients, obstruction in pelvi-ureteric junction in the lower pole of a duplicated collecting systeme in 1 patient and ectopic ureterocele in 6, ectopic megaureter with ureterovesical obstruction in 13, ectopic megaureter with VUR

in 3 patients in the upper pole of the kidney.
Renal histology findings showed dysplasia with fibrosis (6), interstitial fibrosis grade G4 and G3 ≥ 90% (9), interstitial fibrosis grade G4 and G3 ≥ 70% (13).
The correlations between US parenchymal thickness and histological findings (Table l) and between DMSA scans and histological findings (Table 2) are documented.
Table 1
Correlation of ultrasound and histological findings
parenchymal thickness no. patients histological findings (Zhang)
1 mm 2
G4 + dysplasia (1),
G4 and G3 ≥ 90% (1)
2–3 mm 15
G4 + dysplasia (2),
G4 and G3 ≥ 90% (5),
G4 and G3 ≥70% (8)
4–5 mm 10
G4 + dysplasia (3),
G4 and G3 ≥ 90% (3),
G4 and G3 ≥70% (4)
6 mm 1 G4 and G3 ≥70% (1)
Table 2
Correlation of DMSA scans and histological findings
affected segment –
share in relative
function of kidney no. patients histological findings (Zhang)
0–10% 20
G4 + dysplasia (5),
G4 and G3 ≥90% (8),
G4 and G3 ≥70% (7)
10–20% 5
G4 and G3 ≥90% (1),
G4 and G3 ≥70% (4)
20–28% 3
G4 and G3 ≥70%+dysplasia (1),
G4 and G3 ≥70% (2)
57
Conclusion: Thank to the standardized renal US a DMSA scintigraphy we should be able to asses serious and irreversible impairment of the relevant renal segment prior to surgery and to determine whether to use reconstructive or ablative procedure.
Renal ultrasound documenting severe parenchymal thinning, and DMSA

scans confirming a poorly or nonfunctioning upper or lower pole of kidney, are reliable tests for predicting severe histological lesions.
Based on our findings, US parenchymal reduction is consistent with the changes in renal histology. The DMSA findings reflect renal histology. Renal segment hypofunction up to 10% of the total renal function (the only exception was 1 child 13%) indicate a serious diffuse impairment of the parenchyma, mostly justifying the ablative procedure. The most serious histological changes are detected in the ectopic ureterocele. The development of renal parenchyma is not improved even by early endoscopic incision in these cases.

References

1. Bolduc S, Upadhyay J, Restrepo R, Sherman C, Farhart W, Khoury AE, Ghoneimi AE: The predictive value of diagnostic imaging for histological lesions of the upper poles in duplex systems with ureteroceles. BJU International 2003; 91:678–682.
2. Bolduc S, Upadhyay J, Restrepo R, Sherman C, Farhart W, Khoury AE, Ghoneimi AE:
Histology of upper pole is unaffected by prenatal diagnosis in duplex system ureteroceles.
J.Urol 2002; 168:1123–1126.
3. Abel C, Lendon M, Gough D: Histology of the upper pole in complete urinary duplicationdoes
it affect surgical management? Br J Urol 1997; 80:663–665.
4. Fernbach SK, Zawin JK, Lebowitz RL: Complete duplication of the ureter with ureteropelvic junction obstruction of the lower pole of the kidney: imaging findings. AJR
1995; 164:701–704.
5. Zhang PL, Peters CA, Rosen S: Ureteropelvic junction obstruction: morphological and
clinical studies. Pediatr. Nephrol. 2000; 14:820–836.

_Notes

58

ASSOCIATED UROLOGICAL ANOMALIES IN CHILDREN WITH UNILATERAL RENAL AGENESIS

Juraj Svitač, Kamil Javorka jr., Ján Kliment
Department of Urology, Faculty Hospital and Jessenius School of Medicine, Martin, Slovakia

The aim of the study: Unilateral renal agenesis (URA) is a relatively frequent anomaly of urogenital tract. In some studies an increased incidence of associated urological abnormalities (AUA) were reported in these patients. We evaluated the incidence of AUA in children with URA in our hospital.
Methods: We retrospectively analysed cases of URA diagnosed and treated in our department between January 1995 and December 2008. Age of patients

at the time of diagnosis varied from newborn to 12 years (mean 6,2 years). There were 13 boys and 7 girls. The left kidney was absent in 8 patients and the right one in 12. The diagnosis was made in all children by abdominal ultrasound and renal scintigraphy using MAG3 as radionuclide. In patients with the history of urinary tract infections we performed also voiding cystography and excretory pyelography.
Results: AUA were present in 10 out of 20 patients with URA (50%). Hydronephrosis was detected in 6 cases, vesicoureteral reflux in four, and megaureter in three children. Surgical treatment was indicated in five patients.
Conclusion: In agreement with the data found in literature, we diagnosed a large number of AUA in children with URA (50%). Because of these results, complete urological examination with the consequent therapy is recommended in all children suffering of URA.

References

1. Atiyeth B, Husmann D, Baum M: Contralateral renal abnormalities in patients with renal agenesis and non cystic renal dysplasia. Pediatrics, 91, 1993, 1, 4–8.
2. Cascio S, Paran S, Puri P: Urological anomalies in children with unilateral renal agenesis. J. Urol., 162, 1999, 3, 1081–1083.
3. Del Rossi C, Attanasio A, Domenichelli V, De Castro R: Treatment of the Mayer-Rokitansky-Kuster-Hauser syndrom in Bangladesh: results of 10 total vaginal replacement with sigmoid colon at a missionary hospital. J Urol., 162, 1999, 3, 1138–1140.
4. Oshima K, Miyazaki Y, Brock JW, Adams MC, Ichikawa. I, Pope JC.: Angiotensin type II receptor expression and ureteral bulding. J. Urol., J. Urol., 166, 2001, 5, 1848–1852.
5. Robson WL, Leung AK, Rogers RC: Unilateral renal agenesis. Adv. Ped., 42, 1995, 3, 575–579.
6. Song JT, Ritchey MI, Zerin M, Bloom D: Incidence of vesicoureteral reflux in children with unilateral renal agenesis. J Urol., 153, 1995, 4, 1249–1251.

MULTI CYSTIC DYSPLASIA – WILL HISTOLOGY AID IN TREATMENT INDICATION?

M. Husár, P. Zerhau
The Clinic of Children Surgery, Orthopaedics and Traumatology, UH Brno/Department of paediatric urology

Introduction: There is no unified approach of surgical therapy of patients suffering from multi cystic dysplasia. Permanent discussions on grounds for and against nephrectomy have been hold. Multi cystic dysplasia may be diagnosed as early as in the prenatal period – ultrasound detection is possible from 20 weeks gestation (1). It may be associated with other urinary tract abnormalities (obstructive uropathy, vesicoureteral reflux, megaureter) (2) or as a part of syndromes (Meckel-Gruber sy., Potter sy.) (3, 4). References to incidence of tumorous changes in relation to a multi cystic kidney are hardly to

trace in the literature. This paper refers to incidence of embryonic tissue, pyelonephric process in kidneys afflicted by multicystic dysplasia and to cases of kidney removal for other reasons.

Material and methods: A retrospective study evaluates histological findings with patients after (hemi) nephrectomy. The heminephrectomy resp. nephrectomy was done in case of patients having suffered from multi cystic dysplasia, reflux nephropathy or kidney afunction due to other causes. From 2000 to 2007, 50 patients underwent a (hemi) nephrectomy. The sample of patients was divided into 2 groups. Group A contained patients with diagnosis of multi cystic dysplasia (n = 19), group B included patients who underwent nephrectomy for other reasons (n = 31). The taken up tissue was histologically tested by dyeing it with haematoxylin-eosin and then assessed. In group A, nephrectomy was done in the way of laparoscopy; the patients of group B underwent surgical intervention mostly. The average age of patients in group A was 3.46 years (modus 1.5 y, median 2 y); the average age of patients in group B was 5.04 years (modus 1y, median 2 y).

Results: In group A (n = 19, multi cystic dysplasia), embryonic tissue was proved in case of 15 patients (79%), histological finding of chronic pyelonephritis occurred in 3 patients (20%). In group B (n = 31), embryonic tissue was indicated with 6 patients (19%), histological picture of chronic pyelonephritis occurred in case of 19 patients (61%). Additionally, patients with indicated heminephrectomy for partial afunction of kidney with dual hollow system (15 patients, group B, reflux nephropathy, non-reflux megaureters) have been followed-up extra. 4 patients with indicated embryonic tissue underwent upper polar heminephrectomy. No embryonic tissue was traced in patients having undergone lower polar heminephrectomy. No patient of the sample (n = 50) has shown any histological finding of malignancy.

Conclusion: No correlation between tumorous disease and diagnosis of multi cystic dysplasia was proved till now. However, should we consider the embryonic tissue as a precancerosis, then we should speak about a risk of 79%. On the other hand, it also should be pointed out that embryonic tissue incidence in kidneys of patients who underwent nephrectomy for any other reason is 20%. Perez et al. mention similar incidence of Wilms tumour in patients with or without multi cystic dysplasia. They recommend ultrasound control every 3 months till 8 years of age (5). Homsy et al. say that decision on nephrectomy depends on various factors – infection, hypertension, abdominal pain and hematuria (6). Cambio in his publication points out that the incidence of infection is correlated with vesicoureteral reflux, not with the presence of multi cystic dysplasia (7). Finally we can say that there is no consensus in management of patients with multi cystic dysplasia, but more authors incline towards conservative strategy.

References

1. Hajek Z, Kulovany E, Macek M: Textbook-Basics of prenatal diagnosis, Grada Publishing, 2000, p. 116.
2. Calisti A, Perrotta ML, Oriolo L, Inqianna D, Miele V: The risk of associated urologicalabnormalities in children with pre and postnatal occasional diganosis of solitary, small or ectopic kidney: is a complete urological screening always necessary?, World J Urol., 2008 Jun, 26(3):281–284.
3. Kumari N, Pradhan M, Shankar VH, Krishnani N, Phadke SR: Post-mortem examination of prenatally diagnosed fatal renal malformation, J Perinatol, 2008 Nov, 28(11), 736–742.
4. Kuwertz-Broeking E, Brinkmann OA, Von Lengergke HJ, Sciuk J, Fruend S, Bulla M, Harms E, Hertle L: Unilateral multicystic dysplastic kidney: experience in children, BJU Int, 2004 Feb, 93(3), 388–392.
5. Pérez LM, Naidu SI, Joseph DB: Outcome and cost analysis of operative versus nonoperative management of neonatal multicystic dysplastic kidneys, J Urol, 1998 Sep,
160(3 Pt 2):1207–1211, discusion 1216.
6. Homsy YL, Anderson JH, Oudjhane K, Russo P: Wilms tumor and multicystic dysplastic
kidney disease, J Urol, 1997 Dec, 158(6):2256–2259, discusion 2259–2260.
7. Cambio AJ, Evans CP, Kurzrock EA: Non-surgical management of multicystic dysplasia
kidney, BJU Int, 2008 Apr, 101(7):804–808. Epub 2008Jan8.

_Notes

61

IS THE CONSERVATIVE APPROACH TO A HIGHGRADE NEONATAL HYDRONEPHROSIS REALLY SAFE? A PROSPECTIVE STUDY

J. Sedláček2**, J. Langer**2**, R. Kočvara**1**, Z. Dítě**1**, J. Molčan**1**, H. Jiskrová**3**,**
J. Doležal4
1Dpt. of Urology, General Teaching Hospital and 1st School of Medicine, Prague; 2Dpt. of Pediatrics, General Teaching Hospital and 1st School of Medicine, Prague; 3Dpt. of Nuclear Med., General Teaching Hospital and 1st Faculty of Medicine, Prague; 4Dpt. of Urology, Hospital České Budějovice

The aim of the study: To compare development of hydronephrosis, differential renal function, grow up of affected and contralateral not-affected kidney and changes of TGF beta 1 in serum and urine in a group of conservatively and surgically treated children with unilateral high-grade neonatal hydronephrosis.
Methods: Between years 2005–2008, 52 newborns with unilateral hydronephrosis grade III–IV (S.F.U. classification) with good differential renal function (> 40%) were followed up prospectively. Children were randomized into two groups.

Group I of 25 newborns who underwent an early surgical treatment – dismembered pyeloplasty at an average age of 4.6 months (range 1.5–8.2). Group II of 27 patients, who were treated conservatively. Children, in whom increasing dilatation or decreasing function was encountered during follow up, were indicated for subsequent surgery. Children in both groups were followed by series of clinical, ultrasonografic and radionuclid studies using MAG-3. Blood and urine samples were collected from children in both groups repeatedly for TGF beta 1 measurements. Urine samples were obtainted from dilated renal pelvis during surgical procedures as well.
An overall follow up was 18 months (4–44 months).
Results: In group I, we did not record any complications during or after surgery. After 18 months (range 4–44) of follow up, we confirmed decrease in dilatation in all patients and a stable differential renal function before (Ř 49%, range 41–55%) and after the procedure (Ř 51%, range 46–58%) (1, 2).
A total number of 7 (25%) children in conservative group required surgical intervention during follow up. Three for decreasing differential renal function and four for increasing dilatation. In all three cases of decreased function we recorded its complete restoration to initial level, but not before 19, 19 and 12 months, respectively. A significant decrease in hydronephrosis to grade I or II was found in five (18.5%) children only; remaining 15 (56.5%) children in conservative group demonstrated a stable high-grade hydronephrosis (3, 4).
62
Comparison of group I and II:
We found significant difference in initial levels of serum TGF beta-1 between surgical and conservative group of children – Ř 33,1 ng/ml vs Ř 20,7 ng/ml (p= 0,0002); it can be associated with parent preference for surgical approach in case of higher grade of dilatation. Surgical resolution of the obstruction was associated with a significant decrease of serum TGF beta-1 in group I (Ř 33,1 ng/ml vs Ř 20,5 ng/ml, p = 0,0005) (5, 6).
During follow up, there was an non- signficant increase of serum TGF beta-1 levels in conservative group (20.7 ng/ml vs. 25.9 ng/ml, p = 0.16). Similarly in group of 7 children converted to surgical treatment for increasing obstruction, a further increase of serum TGF beta 1 occurred even after the procedure. (Ř 16,8 ng/ml and Ř 21,4 ng/ml praeoperatively versus Ř 23,9 ng/ml postoperatively).
We compared development of contralateral non-affected kidneys and find-out a faster grow-up of the kidneys in conservatively followed children (Ř 49.5 mm vs Ř 62.6mm in group I and Ř 52.7 mm vs Ř 65.8 mm in group II), but the difference was not statistically significant (p = 0,293).
From total number of 42 samples in group I and 52 samples in group II, only 17 (40%) and 10 (19%), respectively, contained detectable levels of this marker. Urine levels of TGF beta 1 were nearly 1000 times lower than serum levels.

Conclusions: Surgery is a safe and effective alternative for children with high-grade hydronephrosis, which may prevent any deterioration of the kidney and increase of obstruction.
During conservative follow up, up to 25% of children have to be converted to surgical treatment for signs of increasing obstruction. Decrease of differential renal function is completely reversible after a postponed repair if a close follow up is adhered to. A conservative approach brought significant decrease of hydronephrosis in only 18.5% of cases and further close follow-up is required in these children.
Surgical resolution of the obstruction caused significant decrease of serum TGF beta-1. Monitoring of urine TGF beta-1 seems to be not reliable because of very low detectable levels.
Supported by grant IGA MZ No NR 8320-4.

References

1. Hanna MK: Antenatal hydronephrosis and ureteropelvic junction obstruction: the case
for early intervention. Urology. 2000; 55:612–615.
2. Castagnetti M, Novara G, Beniamin F, Vezzú B, Rigamonti W, Artibani W: Scintigraphic renal function after unilateral pyeloplasty in children: a systematic review. BJU Int. 2008 Sep; 102(7):862–868.
3. Ulman I, Jayanthi VR, Koff SA: The long-term followup of newborns with sewere unilateral hydronephrosis initially treated nonoperativelly. J Urol. 2000; 164:1101–1105.
4. Sedláček J, Kočvara R, Langer J, Dítě Z, Dvořáček J: Výsledky léčby neonatální hydronefrózy. Čes.-slov. Pediat. 2008; 63(12):653–659.
5. Taha MA, Shokier AA, Osman HG et al.: Pelvi-ureteric junction obstruction in children: the role of urinary transforming growth factor-beta and epidermal growth factor. BJU Int. 2007; 99(4):899–903.
6. Murer L, Benetti E et al.: Clinical and molecular markers of chronic interstitial nephropathy in congenital unilateral ureteropelvic junction obstruction. J Urol. 2006; 176:2668–2673.

Contact: josef.sedlacek@vfn.cz

_Notes

THE TREATMENT OF TOTAL DUPLEX KIDNEY BY THE ANASTOMOSIS OF UPPER URINARY TRACT

I. Novák, S. Skálová1**, M. Šenkeřík**1
Children´s Department of Urology, 1Department of Paediatrics, Teaching Hospital, Hradec Králové, Czech Republic

The aim of the study: Congenital urinary tract anomalies and congenital heart diseases are the most common defects in childhood. Duplications in some parts of urinary tract are the most frequent.
A complete duplication of an upper urinary tract is one of the frequent

congenital anomaly. There is coincidence of structural abnormalities and functional abnormalities – obstruction in the upper segment of ureter and vesicoureteral reflux of different grade in the lower segment of ureter. Ureterocele is the most frequent cause of obstruction of upper part and is accompanied with the development of megaureter (dilatation of ureter more than 10mm). Heminephroureterectomy (an ablation of an dilated part of kidney and ureter) is the treatment choice in the case of afunctional segment of ureter. Anastomotic operations (connection of both ureters) are one of the treatment options in a case of functional dilated upper ureteral segment and in the absence of vesicoureteral reflux in the lower ureteral segment. Uretherocystoneostomy is another surgical technique in treatment of duplication anomalies. Laparoscopic surgery can be used in all these surgical techniques. Our experiences with salvage anastomotic operations of an upper urinary tract are shown below.

Methods: We have evaluated four patients after the anastomotic surgery at the Children's Department of Urology in Hradec Kralove retrospectively from May 2000 to February 2009. All of them were girls of age from 10 months to 11 years (average age 42,5 months).

Causes of the upper ureteral segment obstruction were: ureterocele in two cases and ureteral ectopia in another two cases. Recurrent urinary tract infections were the main symptoms, in one case (in 11 years old girls) we found ureteral incontinence too.

We used this diagnostic method in all patients: ultrasonography, voiding cystography and kidney scintigraphy. In two patients we used intravenous urography for the diagnosis of duplication in urinary tract, in remaining two patients we used magnetic resonance imaging (MRI) which was more sensitive for evaluation of the kidney anatomy and function. All patients were treated surgically – classic open surgery.

The anastomosis end to side and one pyelo-ureteroanastomosis were performed with standard postsurgical care.

All patients had a retroperitoneal drain for 3–5 days, a permanent bladder catheter for 10 days and an ureteral splint for month after surgery. Antibiotics were used before and one month after surgery.

The average hospitalization duration was 10 days.

Results: All operations were without substantial intraoperative problems, postoperative healing was without complication too. Only one complication was observed – a dislocated stent.

The significant decrease of dilatation was found in all our patients. Control static scintigraphy showed good function of upper kidney segment in all patients. Ureteral incontinence and urinary tract infections disappeared. All patients had negative results of screening examinations (ultrasound, urinary biochemistry, microbiology) after surgery. Nobody in our study population require reoperation for new reflux or stricture.

Conclusion: The anastomotic surgery should be recommended as the primary choice in surgical treatment of a functional dilated upper ureteral segment and the lower ureteral segment without reflux. The described ureteroureteroanastomosis
or uretero-pyeloanastomosis seems to be the most effective surgical method with good results in function after surgery a no troubles of operated patients.
Uretero-cystoneostomy of both ureters is an alternative surgical treatment method. In all operations is necessary to calculate with possible complications. New stricture or reflux are the most common postoperative complications which need reoperation and in these cases laparoscopy should not be used.

References

1. Braga LH, Moriya K, El-Hout Y, Farhat WA: Ureteral duplication with lower pole ureteropelvic junction obstruction: laparoscopic pyeloureterostomy as alternative to open approach in children. Urology. 2009 Feb; 73(2):374–376.
2. Escala JM, Cadena González Y, López PJ, Retamal G, Letelier N, Zubieta R: Ectopic ureter in pediatrics. A change in the way of presentation Arch Esp Urol. 2008 May; 61(4):507–510.
3. Komiakov BK, Novikov AI, Guliev BG, Popov SV: Upper ureteropyeloureteroanastomosis in obstruction of the ureter of the lower half of the double kidney. Urologiia. 2008 Jan–Feb; (1):20–23.
4. Merrot T, Diakité M, Chaumoître K, Panuel M, Alessandrini P: Value of low ureteroureterostomy in 5 cases of functional ectopic ureter on duplicated collecting system in children. Conservative management of ectopic ureter]Prog. Urol. 2007 Sep; 17(5):987–991.
5. Prieto J, Ziada A, Baker L, Snodgrass W: Ureteroureterostomy via inguinal incision for ectopic ureters and ureteroceles without ipsilateral lower pole reflux. J Urol. 2009 Apr; 181(4):1844–1848.

ENDOSCOPIC SUBMUCOSAL INJECTION OF DEXTRANOMER/ HYALURONIC ACID COPOLYMER (DEFLUX): A LONG TIME FOLLOW UP

I. Novák, L. Janoušková, P. Kuliaček
Children´s Department of Urology, Teaching Hospital, Hradec Králové, Czech Republic

The aim of the study: The dextranomer/hyaluronic acid (Dx/HA) copolymer was used for endoscopic treatment of vesicoureteral reflux (VUR) by Stenberg in 1995. Many different chemical substancies can be used for treatment of VUR. This substancies can be divided in two main groups: resorbable and nonresorbable. More efficient are the nonresorbable substances for example Teflon, silicone particles etc. Small nonresobable balls were constructed for implantation too. The main advantage of this group is the stable mechanical effect after implantation. Migration of particles seems to be the substantial

disadvantage of this group and it can be the cause of embolisation of material deposits to the lung or brain. Dextranomer/hyaluronic acid copolymer, cartillage, bovine collagen, blood, fat etc. are in the second (resorbable) group. Dextranomer/hyaluronic acid copolymer is the most common used substance in clinicians from this group. Diasadvantages of these substances were allergic reactions. Only autologous blood and Dextranomer/hyaluronic acid copolymer have no allergic complications. The main limitation of this treatment is time dependent effect (in time the effect is lower due to the reassertion). Today Dextranomer/hyaluronic acid copolymer is most commonly used for treatment in urology.

Recently in selected patients the endoscopic submucosal injection of Dextranomer/hyaluronic acid copolymer seems to be primary therapy of VUR after failure of pharmacologic treatment. The aim of our study was to evaluate the efficacy of above mentioned method in children. The results were compared with an effect of use of the autologous blood injection in our previous studies.

Methods: In a group of 66 patients 101 refluxes were treated by submucosal injections of 0,3–1,5ml Dextranomer/hyaluronic acid copolymer from June 2002 to December 2005 in the Children´s Department of Urology, Teaching Hospital, Hradec Kralove. Only 61 patients with 96 refluxes (grade of I–V) were evaluated, all included children were examined by voiding cystography (VCG).

The indications for endoscopic application of Dextranomer/hyaluronic acid copolymer were: VUR grade I (in 2 refluxes), grade II (in 10 refluxes), grade III (in 53 refluxes), grade IV (in 28 refluxes) and grade V (in 3 refluxes).

67

Refluxes of I and II grade were treated only in coincidence of high reflux on the opposite side.

After the injection we evaluated: grade of reflux, number of completely cured patients without reflux, cases of endoscopic or classical surgery and necessity of following pharmacologic treatment.

Results: After the first injection: in 19 (31%) patients (with 25 refluxes) we found no reflux (they were so called completely cured). In other patients the grade of reflux changed: grade I (in 20 refluxes.), grade II (in 21 refluxes), grade III (in 11 refluxes) and grade IV (in 10 refluxes).

In cases of persisting reflux (10/16%) endoscopic injection was repeated. Uretherocystoneostomy was indicated in 4 (6%) patients with persisting high symptomatic reflux (of grade IV).

Conservative (pharmacologic) treatment need to continue in the other 29 (47%) patients. Grade of refluxes decreased in 18 cases (in approximately about 1–2 grade), unchanged refluxes persisted in 11 cases. Morbidity or complications were not found in all 29 patients on a conservative treatment.

Conclusions: Although only small number of completely cured patients were found, there is trend to decrease in reflux grade in study population. The results

of Dextranomer/hyaluronic acid copolymer treatment seem to be same as results of blood injection treatment of VUR. The main advantage is the low incidence of complications and decrease in antiobiotic treatment.
Today there is trend to reduction in antibiotics treatment strategy according to the new guidelines.
The main advantage of the endoscopic submucosal injection is short learning curve for the surgeon, the main disadvantage of Dextranomer/hyaluronic acid copolymer is the cost of the method compared with the blood.
Of course persistence of the high grade reflux is an indication in both groups for the classical surgery (uretherocystoneostomy).

References

1. Benoit RM, Peele PB, Docimo SG: The cost-effectiveness of dextranomer/hyaluronic acid copolymer for the management of vesicoureteral reflux. 1:substitution for surgical management. J. Urol. 2006; 176:1588–1592.
2. Capozza N, Lais A, Matarazzo E, Nappo S, Patricolo M, Caione P: Treatment of vezicoureteric reflux: a new algorithm based on parenteral preference. BJU Int. 2003; 92:285–288.
3. Perez-Brayfield M, Kirsch AJ, Hensle TW, Koyle MA, Furness P, Scherz HC: Endoscopic treatment with dextranomer/hyaluronic acid for complex cases of vesicoureteral reflux. J. Urol. 2004; 172:1614–1616.
4. Stenberg A, Hensle TW, Lackgen G: Vesicoureteral reflux: a new treatment algorithm. Curr. Urol. Rep. 2002; 3:107–114.

ARE WE ABLE TO PERFORME ORCHIDOPEXIS AT THE OPTIMAL AGE?

M. Drlík, S. Tichý
Department of Pediatric and Trauma Surgery, Thomayer Teaching Hospital, 3rd Faculty of Medicine, Charles University, Prague, Czech Republic

Background: Cryptorchidism is the most common congenital anomaly associated with the genitalia of newborn males. At the age of 1 year almost 1% of all full-term male infants are affected (1). At the age of 1 year there is no significant difference in the number of spermatogonia in undescended and normally descended testis. After this age reduced numbers of Leydig cells, delayed disappearance of gonocytes, failure of primary spermatocytes to appear, and reduced total germ cell counts in the undescended testis were described (2). In past years there is a net trend to reduce the recommended age for orchidopexy. The treatment can be started at the age of six months as spontaneous testicular descent after this age is rare (3). Recent EAU guidelines recommend that treatment of every child with undescended testis should be finished at the age between of 12 to 18 months to prevent histological deterioration of testicular tissue. However in practice we observe many patients coming to orchidopexy at a later age (4).
Aim of the study is to investigate how many children we operate on in the

recomended age, whether a trend exists toward reduction in the age at which orchidopexies are carried out and why some children were operated on beyond the recomended age range.

Methods: All boys who underwent an orchidopexy for an undescendend testis at Department of Pediatric and Trauma Surgery of Thomayer Teaching Hospital at Prague between January 2004 and December 2008 were identified through a retrospectively collected database. They were analysed according to the age at the time of operation and year of surgery. The proportions of children younger than 18 months and older than 18 months were calculated for each year. The apparent reason for the delay of orchidopexis was checked in the office medical records.

Results: In total 233 boys underwent orchidopexis for undescendend testes with 176 (75%) of the boys having sugery after the recomended age of 18 months. During a period of 5 years we observed a significant increse in the proportion of boys having surgery before the age of 18 months. As former guideliness allowed the orchidopexy till the age of 2 years, we calculated two separate categories of children having delay in orchidopexy. The first group of children that were operated between the ages of 19 and 24 months consisted of 69

44 patients, the second group of children that were operated on between the ages of 25 months and 18 years consisted of 132 patients. The principal reasons for the late orchidopexy in the first category were late decision of our department in 28 (68%), late refferal in 4 (10%), preceding ineffective hormonal treatement in 3 (7%) and other complicating illness in 3 (7 %) cases. The principal reasons in the second category were late refferal in 51 (38%), confirmed ascending testis in 30 (22%), probable ascending tesis in 24 (18%), preceding ineffective hormonal treatment in 17 (12,5%), and other complicating illness in 7 (5%)cases.

Conclusion: The number of children operated on after the recomended age remains markedly high, although we observe significant increase of patients operated on before the age of 18 months. The high incidence of late refferals points to the importance of the education of primary care providers on the benefit of early orchidopexy. The high incidence of ascending testes proves the importance of the examination of testicular position during regulary follow ups by primary care providers.

References

1. Berkowitz GS, Lapinski RH, Dolgin SE, Gazella JG, Bodian CA, Holzman IR: Prevalence and natural history of cryptorchidism. Pediatrics 1993; 92:44–49.
2. Huff DS, Hadziselimovic F, Snyder HM 3rd, Blythe B, Ducket JW: Histologic maldevelopment of unilaterally cryptorchid testes and their descended partners. Eur J Pediatr 1993; 152 (Suppl): S11–S14.
3. Kočvara R: Kryptorchizmus: kdy načasovat a jakou léčbu provést? Urol List 2007; 5 (1):30–33.

4. Bruijnen CJ, Vogels HD, Beasley SW: Review of the extent to which orchidopexy is performed at the optiml age: implications for health services. ANZ J Surg. 2008 Nov; 78(11):1006–1009.

_Notes

TESTICULAR SIZE AND CATCH-UP GROWTH AFTER LYMPHATIC-SPARING AND LYMPHATIC NONSPARING VARICOCELE REPAIR IN CHILDREN AND ADOLESCENTS

R. Kočvara1, 2**, J. Sedláček**1**, Z. Dítě** 1**, J. Molčan**1**, J. Dvořáček**1, 2
1Department of Urology, General Teaching Hospital and 1st Medical School of Charles University, Prague 2; 2Department of Urology, Institute for Postgraduate Medical Education, Prague

Aims: Division of lymphatic vessels during varicocelectomy may lead to hydrocele formation and development of testicular hypertrophy associated with intratesticular oedema. We studied the testicular growth through the adolescence in relation to the pubertal stage and to the type of the repair (lymphatic sparing and lymphatic non-sparing).

Patients and methods: 174 children and adolescents with primary unilateral grade II-III varicocele were prospectively studied between 1997 and 2007 with a minimal follow-up 1 year after varicocele repair. Laparoscopic high ligation was used in 37 patients (at mean age 13.6, pubertal stage-PS 2.6) during 1997 to 3/1999 (LNS group). Microsurgical repair (both laparoscopic and microscopic subinguinal) was used in 137 patients (mean age 14.1, mean pubertal stage 3.3) between 4/1999 and 2007 (LS group). Patients with another testicular pathology were excluded. Testicular size was assessed by ultrasound. A testicle with an atrophy index greater than 25% or with a difference in testicular size greater than 2 cc was considered hypoplastic. Hypertrophy of the left testicle after varicocelectomy was defined as at least a 10% increase in size over the right testicle.

Results: Before repair, the mean left testicular size (LTS) was 7.2 cc; the atrophy index (AI) 19.7% and difference in testicular size (DTS) 1,7 cc in the LS group, and 5.4 cc, 21.1% and 1,4 cc in the LNS group, resp. After the mean follow-up of 2.1 y in LS and 3.7 y in the LNS group, the LTS reached 12.2 cc; AI 11.2% and DTS 1.3 cc in the LS group (mean age 16.8 y, PS 4.7) and 16.3 cc; -6.8% and -0.9 cc in the LNS group (mean age 17.5 y, PS 4.7), resp. Differences in all parameters were highly significant. Similar significant differences were found in each pubertal stage, as well as in 104 patients (78 from the LS and 27 from the LNS group) older than 17 years (range17 to 21). In these patients, testicular hypoplasia was detected in 41 (51.2%) before and in 26 (33.3%) at follow-up in the LS group, in 14 (51.9%) and 4 (14.8%) in 71
the LNS group; testicular hypertrophy in 2 (2.6%) and 7 (25.9%) in the LS and LNS group, resp.

Conclusions: After lymphatic non-sparing repair, higher increase in testicular size has been found in all pubertal stages, exceeding mostly the size of the right testis. The real catch-up growth can be assessed in microsurgical lymphatic-sparing repairs only, though the absolute difference between the both testes remains in most patients.

** Supported by grant IGA MZ No: NR 8817-4.*

References

1. Cayan S, Akbay E, Bozlu M, Doruk M, Erdem E, Acar D, Ulusoy E: The effect of varicocele repair on testicular volume in children and adolescents with varicocele. J. Urol., 168, 2002, 731–734.
2. Gershbein AB, Horowitz M, Glassberg KI: The adolescent varicocele I: Left testicular hypertrophy following varicocelectomy. J. Urol., 162:1447–1449, 1999.
3. Glassberg KI, Poon SA, Gjertson CK, Decastro GJ, Misseri R: Laparoscopic Lymphatic Sparing Varicocelectomy in Adolescents. J Urol. 2008; 180:326–330.
4. Kass EJ, Belman AB: Reversal of testicular growth failure by varicocele ligation. J. Urol., 137: 475–476, 1987.
5. Kočvara R, Doležal J, Hampl R, Povýšil C, Dvořáček J, Hill M, Dítě Z, Staněk Z, Novák K: Division of lymphatic vessels at varicocelectomy leads to testicular oedema and decline in testicular function according to the LH-RH analogue stimulation test. Eur. Urol., 43, 2003, 430–435.
6. Kočvara R, Dvořáček J, Sedláček J, Dítě Z, Novák K: Lymphatic sparing laparoscopic varicocelectomy: a microsurgical repair. J. Urol., 2005, 173, 1751–1754.
7. Kočvara R, Sedláček J, Doležal J, Staněk Z, Dítě Z, Dvořáček J: Mikrochirurgická subingvinální varikokélektomie u dětí a dospívajících Čas. Lék. Čes., 146, 2007, č. 10, s. 763–766.
8. Riccabona M, Oswald J, Koen M, Lusuardi L, Radmayr Ch, Bartsch G: Optimizing the operative treatment of boy with varicocele: sequential comparison of 4 techniques. J. Urol., 169, 2003, 666–668.
9. Schwentner C, Oswald J, Lunacek A, Deibl M, Bartsch G, Radmayr C: Optimizing the outcome of microsurgical subinguinal varicocelectomy using Isosulfan Blue: a prospective randomized trial. J. Urol., 2006, 175:1049–1052.
10. Zampieri N, Mantovani A, Ottolenghi A, Camoglio FS: Testicular Catch-up Growth After Varicocelectomy: Does Surgical Technique Make a Difference? Urology. 2009; 73:289–292.

Contact: radim.kocvara@lf1.cuni.cz

_Notes

TUBULARIZED INCISED PLATE URETHROPLASTY (SNODGRASS) IN PRIMARY HYPOSPADIAS REPAIR

P. Kuliaček1, 2**, I. Novák**1**, M. Králová**2**, L. Janoušková**1**, M. Toušek**2**, K. Baker**1
1Department od Paediatric Urology, University Hospital, Hradec Králové;

2Department od Paediatric Surgery, University Hospital, Hradec Králové
The Aim of the Study: To report the outcomes in a large series using a modified tubularized incised plate (TIP) urethroplasty (Snodgrass) technique mostly without a dartos flap or local de-epithelialized skin flap to cover the urethroplasty. In the past 10 years TIP urethroplasty became a preferred technique for distal hypospadias repair and subsequently gained worldwide popularity and acceptance. The procedure gives good functional results and a cosmetic appearance that is superior to that obtained by MAGPI, Mathieu or onlay preputial flap repairs. In addition, this procedure is associated with a fairly low rate of complications. The reported experience with this surgical modification has been primarily in cases of distal hypospadias.
Material and method: We retrospectively reviewed consecutive patients with hypospadias presenting between 2000 and 2008. 160 hypospadias boys were treated with tubularized incised plate urethroplasty for primary repair of hypospadias over a 9 years period.
The surgical technique was similar to that described previously by Snodgrass. A bloodless field was maintained during surgery with a penile tourniquet. An artificial erection was induced to confirm a straight penis as necessary. Urethral plate preservation is the principle concept of this technique and the entire length of the urethral plate was incised along the midline and the neourethra was tubularized over an 8 or primarily a 10 Fr. short silicone stent. Soft stent was inserted in 148 boys.
The curvature (chordee) usually disappeared after the penis was degloved. Fibrous chordee was excised in 6 cases. Dorsal plication wasn´t performed. Urethroplasty was performed using double-layered subcuticular 7/0 polyglactin running sutures. To cover the neourethra, a dartos flap was used in 10 and spongioplasty in 57 patients. A dartos flap was mobilized from the dorsal prepuce to cover the neourethra.
The surgical technique for spongioplasty was similar to that described previously by Yerkes and colleagues. The spongiosa were then rotated toward the midline to wrap the neourethra as well as the hypoplastic portion of the native urethra.
The thin distal urethra was preserved and incorporated as part of urethroplasty. The glans is then closed in two layers. For diversion a percutaneos suprapubic catheter was placed in 148, a dipping stent in 3 and urethral catheter in 9 cases. Stent through the uretroplasty was removed on the 10–14th post-operative day. Suprapubic catheter was taken off the same or next day after stent removal.
Results: TIP urethroplasty was performed in 160 boys. There were 151 distal penile, 5 midshaft and 4 penoscrotal types. The operative time was 70 to 180 minutes. Mean patient age at surgery was 35 months (range 7 months to 17 years). 14 patients had complications.
The fistulas were noticed in 9 patients (5,6%). All but one fistulas were repaired successfully at a later date. Two cases had meatal stenosis (1,25%) and

underwent meatotomy procedure.
Two children (1,25%) had dehiscence of the glanular portion of the repair and 1 child (0,62%) had a bleeding from urinary bladder which was repaired. No urethral diverticulum was noticed during follow-up. A higher complication rate wasn‘t found after TIP urethroplasty procedures with foreskin preservation (150 boys).
All penises had excellent cosmetic appearance, even in complicated cases. Follow-up ranges from 5 months to 8 years. The overall complication rates were 8,75%.
Conclusion: Tubularized incised plate urethroplasty is currently one of the most popular techniques for hypospadias repair. The advantages of this technique include its simplicity, low complication rate, very good appearance of the glans penis and normal meatus in most boys.
Key steps include preservation of the urethral plate, midline incision of the plate for urethroplasty, and subsequent glansplasty. Attention to important surgical details is needed to obtain optimal functional and cosmetic results. Complications of the primary repair developed in only 14 of 160 patients (8,75%).
Tubularized incised plate urethroplasty is now the procedure of choice for distal and some proximal hypospadias repair at our institution.

References

1. Snodgrass W: Tubularized, incised plate urethroplasty for distal hypospadias, J Urol 151, (1994), pp. 464–465.
2. Snodgrass W, Koyle M and Manzoni G et al.: Tubularized incised plate repair: results of a multicenter experience, J Urol 156 (1996), pp. 839–841.
3. Yerkes EB, Adams MC and Miller DA et al.: Y to I wrap: use of distal spongiosum for hypospadias repair, J Urol 163 (2000), pp. 1536–1539.
4. Yang SS, Chen YT, Hsieh CH et al.: Preservation of the thin distal urethra in hypospadias repair. J Urol 2000; 164:15–13.
5. Kocvara R, Dvoracek J, Dite Z et al.: Comprehensive long-term analysis of hypospadias repair using vascularized flaps and tubularized incized plates – report on 588 cases. Cas Lek Cesk 2005; 144(Suppl 2):7–11.
6. Snodgrass WT: Tubularized incised plate (TIP) hypospadias repair. Urol Clin North Am 2002; 29:285–290.
7. Baskin LS, Ebbers MB: Hypospadias: anatomy, etiology, and technique. Journal of Pediatric Surgery. 2006; 41(3):463–472.
8. Hadidi AT, Azmy AF, editors: Hypospadias Surgery: An Illustraded Guide. Berlin, Germany: Springer; 2004.
9. Snodgrass W, Koyle M and Manzoni G et al.: Tubularized incised plate hypospadias repair for proximal hypospadias, J Urol 159 (1998) (6), pp. 2129–2131.

_Notes

75

THE TESTICLE SPARING OPERATION IN A CASE OF ISOLATED TESTICULAR LYMPHOMA

I. Novák, J. Hak1**, E. Šimáková**2**, P. Rejtar**3**, J. Krejsek**4

Children´s Department of Urology, 1Department of Paediatrics; 2Fingerland´s Department of Pathology; 3Department of Radiology; 4Department of Clinic Immunology, Teaching Hospital Hradec Králové, Czech Republic

The aim of the study: Testicular tumors are not common in childhood. Prepubertal testicular tumors are frequently benign. Yolk sac tumors, which are always malignant, are the most common germ cell testicular tumors in prepubertal males. Teratomas are benign in pediatric patients and are the second-most commonly reported testicular tumors. The remaining tumor types are rare. Leukemia and lymphoma are the most common malignancies which affect the testis secondarily. Because the blood-testis barrier may protect the intratesticular cells, the testis may be the site of residual tumor in children after therapy. The radical inquinal orchiectomy is the standard first part of treatment of testicular tumors.

An isolated testicular lymphoma is a very rare disease. There are only few cases described in the urological literature.

In this case report we are presenting nonstandard surgical treatment (testicle sparing operation) of the isolated testicular lymphoma at the Children´s Department of Urology of Teaching Hospital in Hradec Kralove.

Case report: 2 years old boy was admitted to our department due to left testicular scirrhus expansion. He had no history of pain, fever or trauma. All biochemical parameters were normal.

Left testicle was exactly enlarged and of hard consistency. We used ultrasound in testicular examination. In the left testicle a tumor formation of 10mm in diameter was described. Blood tumor markers (AFP, β-HCG) were negative, no metastatic changes were found on X-ray examination. Surgical treatment (from inguinal access) was indicated.

The affected testicle was enlarged by a tumour. The tumour was of hard consistency, was encapsulated inside the testicle. Perioperative biopsy was done (the diagnosis of malignat lymphoma was done). Testicle sparing operation was indicated (in agreement with the recommendation of hematologist) - the whole tumor was excised and the rest of the testicle was resutured and was kept in the scrotum. There were no complications after operation and the set of subsequent examinations was done. We found no other focus of lymphoma. CT scan was negative (without lymphomatic expansion), bone marrow examination was negative. Definitive biopsy results and flowcytometry examination results confirmed the diagnosis of non-Hodgkin lymphoma of early B-cellular line.

We started with two-year chemotherapy according to the protocol NHL-NBBFM-95. The cytostatic therapy is dividend in 4 phases: induction phase with

combination of 5–8 cytostatics, followed by consolidation phase, reinduction phase and maintenance phase. This hematooncologic treatment was without any complication. This patients is under the control of urologist and hematologist.

Result: We reached so called complete remission in this patient. After 8 years (now the boy is of 10 years old). The left (prior affected testicle) has a normal ultrasound structure and is of normal size compared with the contralateral site. The palpation findings and ultrasound scans show only moderately smaller testicular proportions. Spermiogram examination is being planned after the age of 17 years.

Conclusion: We reported a very rare cause of the isolated testicle enlargement - malignant lymphoma in a case of two years old boy. In this case no radical surgical treatment (orchiectomy) was chosen. The affected testicle was spared instead. Now the boy is in a complete remission (8 years after the oncologic treatment).

Although the orchiectomy is usually indicated as a standard surgical treatment of testicular tumors, in our case we shown the potential same effect of testicular sparing operation.

References

1. Hasselblom S, Ridell B, Wedel H, Norrby K, Sender Baum M, Ekman T: Testicular lymphoma a retrospective, population-based, clinical and immunohistochemical study. Acta Oncol. 2004; 43(8):758–765.

2. Lu D, Medeiros LJ, Eskenazi AE, Abruzzo LV: Primary follicular large cell lymphoma of the testis in a child., Arch Pathol Lab Med., 2001, 125(4), 551–554.

3. Vitolo U, Ferreri AJ, Zucca E. Primary testicular lymphoma. Crit Rev Oncol Hematol. 2008 Feb; 65(2):183–189.

4. Zucca E, Conconi A, Mughal TI, Sarris AH, Seymour JF, Vitolo U, Klasa R, Ozsahin M, Mead GM, Gianni MA, Cortelazzo S, Ferreri AJ, Ambrosetti A, Martelli M, Thiéblemont C, Moreno HG, Pinotti G, Martinelli G, Mozzana R, Grisanti S, Provencio M, Balzarotti M,Laveder F, Oltean G, Callea V, Roy P, Cavalli F, Gospodarowicz MK: International Extranodal Lymphoma Study Group. Patterns of outcome and prognostic factors in primary large-cell lymphoma of the testis in a survey by the International Extranodal Lymphoma Study Group. J. Clin. Oncol. 2003 Jan 1; 21(1):20–27.

_Notes

77

ENURESIS THROUGH THE AGES

J. Dušek

Pediatric Dept 2nd Medical School Charles University and Univ Hospital Motol, Prague, Czech Republic

Enuresis is a really old and stressful problem as old as mankind itself. It is not known when enuresis became a medical problem, but it has been recognized as

a disturbance of childhood necessitating medical treatment since the time of the Papyrus Eber's, which is dated 1550 B.C. Although the pediatric section of this ancient volume is, at best, tiny, yet it contains therein a remedy for treatment of enuresis. For treatment enuresis in ancient Egypt was used the mixture of Juniper berries, Cyprus and Beer in ratio 1:1:1. From contemporary point of view this therapeutic approach to enuresis seems to be a little funny. We will see in the following, how have been changed attitudes and therapeutic modalities in the evolution of medicine. Even in ancient Egypt enuresis was considered of great enough importance to gain mentioned in one of few medical texts of the day. The Eber's Medical Papyrus is named after the German Egyptologist Georg Moritz Ebers who acquired the Papyrus in 1872. The oldest known scientific treatise containing case studies on anatomy and the appropriate remedies, together with formulas for making medicines are contained within the 110 page. Thought to have been copied some parts from a much earlier document as it has a reference to the pharaoh Den, who reigned during the 1st dynasty c. 3000 BC. The document is written in hieratic script measures some 20.23 m in length and 30 cm in height. It contains a remarkably accurate description of the circulatory system, noting that the heart is the centre of the blood supply. Surprisingly, it also has a small section on psychiatry and other fields such as obstetrics, contraception, dentistry, and the digestive system.

In the West African Kingdom a child with enuresis aged more than 4–5 years, was first at beaten, if no response, ashes were put on water and the mixture was poured over head of the offending child and this child was driven in the street, where all the children clapped their hands and run after the child and singing a mocking song.

In Whydah the child is taken to the lagoon and washed repeatedly if necessary. If the bad habit continues a large frog was attached to the child's waist to frighten offender. Navaho Indian's enuretic child had to stay naked with his spread legs over a burning nest of the phoebe. The nests of the swallows or of the nighthawks were also used. It was believed to be helpful because these birds do not wet their nests.

78

The therapeutic approach to bedwetting children has been changed through the ages. For example medieval treatments seem to be looked for some a medicinal remedy to strength the urinary blader of enuretic child. Phaer (1954) recommended a drahm of powered goat claw and cock trachea. Fontanus (1642) suggested sprinkling roasted pig bladder. Primerose (1659) prescribed hare's testicle with brain and wine, taken by mouth. The treatment of enuresis in the nineteenth century seems to have been in the main mechanical and medically unhelpful. Distinctly punitive treatments advocated the Victorian era included a steel spike in the bed (to prevent masturbation) a steel yoke over the penis, silver nitrate and painful cautery of the anaterior meatus.

Next possibilities for enuresis treatment were nerve tonics (strychnine) or sheep fat suppository. Trousseau (1870) said "enuresis I consider a nervose, the first precaution is to break the bad habit of the organs. That time was belladonna honored and pharmacologically acceptable remedy. Numerous reliable drugs were used for enuresis treatment for example urotropin, santonin, nux vomica, potassium bromide, salix nigra and more others. Guillameau advised walking children during the night, as well as threatening and shaming them, but he warned against harsh treatment. Louis XIV suffered from enuresis as well. In that time was advised to boys with enuresis tie a cord around his penis to prevent accidents. Adams (1844) accepted that children never willingly wet their beds, were not lazy.

The middle part of the last century represented the urological era in nocturnal enuresis. Cystoskopies, cystometrograms, bladder stretching and dilatation, bladder neck stimulation and diathermy and number of other urological intervention have been therefore advocated. This rather strange idea persists in some doctor's mind up to now and their patients with enuresis are still underwent useless and invasive urologic examination.

The history of the treatment enuresis has demonstrated many therapeutic approaches; even rituals and many "drugs" were used. We can snicker or laugh at these practices, which were used, in the past centuries but they less or more worked. Therefore it is no wonder that so many peculiar treatments have been tried, and so many odd practices have persisted especially in some countries or cultures.

Unfortunately the medical literature related to a history and treatment of enuresis is scarce. Consequently of this fact some practices and remedies, successfully used in the past, can remain unknown.

References

1. Glicklich LB: An historical account of enuresis. Pediatrics (1951), 8:859–876.
2. Gill D: Enuresis through the ages. Pediatr Nephrol (1995), 9:120–122.
3. Graaf MJM de: 40 years of being treated for nocturnal enuresis. Lancet 340:957–958.
4. Gut J: Pomočování u dětí.
5. Treatment for enuresis: Criteria, Maechanism and Health Care: http://jpepsy.oxfordjournals.org/cgi/content/full/25/4/219
79

NOCTURNAL ENURESIS – SELECTED CASES I

Ilona Novotná
M.D. / Středomoravská nemocniční a. s., odštěpný závod Nemocnice Přerov / Department of Paediatrics

Nocturnal enuresis in the pediatric consultation room and its case report

Children with primary nocturnal enuresis - basic inspection and therapy.

The inspection of a child with nocturnal enuresis includes a profound

anamnesis, a physical inspection, the chemical examination of urine, sediment, bacteriology and osmolality, the ultrasound examination of kidneys and bladder with post micturition residual and the correct filling of the drinking and micturition card.
The therapy begins with an adjustment of drinking and micturitionhabits, it continues with the removal of diapers and the positive motivation of the child and its family.
In pharmacotherapy nocturnal enuresis is treated with desmopressine – Minirin MELT, prob. anticholinergics.

_Notes

80

NOCTURNAL ENURESIS – SELECTED CASES II

Marie Kmoníčková
M.D. / Pardubická krajská nemocnice a. s. / Department of Paediatrics and Nephrology

Initially, we mention general data focused on the preparation MINIRIN (desmopressine) in a form of "MELT".
After that we are going to demonstrate short/condensed statements taken out of our practice concerning to the preparation use.
The first case refers to the treatment of the boy´s NOCTURNAL ENURESIS, who has been examined for the first time at the age of 14, but whose parents did not agree with following medicament treatment.
At the same time we present possibility of the preparation use with lower quantity of the effective drug owing to the successive medication termination.
The second case refers to so called RESISTANT NOCTURNAL ENURESIS, that is very difficult to be influenced. Eventually, this case has been successfully treated by means of combination Minirin MELT + oxybutinin.
The last case demonstrates possibilities of Mirinin medication in the case of the nocturnal enuresis influence occurred in children´s psychomotoric retardation.

_Notes

81

HYPERCALCIURIA – A CLUE TO DIAGNOSIS

Sylva Skálová1**, Lenka Minxová**1**, Štěpán Kutílek**2
Department of Paediatrics Charles University in Prague, Faculty of Medicine and University Hospital in Hradec Králové1, Center for Clinical and Basic Research, Pardubice2, Czech Republic

Introduction: Hypercalciuria is defined as urinary calcium excretion ≥ 0.1 mmol/kg/24hours. Hypercalciuria can be a result of various disease states. The most frequent clinical manifestations of hypercalciuria include hematuria,

abdominal pain, urolithiasis, nephrocalcinosis, dysuria, enuresis, urinary tract infection. Three case reports of hypercalciuria of different origin are presented.
Case reports: Patient No.1 had a history of urinary tract infection at the age of four years, persistent microscopic hematuria with recurrent episodes of macroscopic hematuria, and nephrolithiasis of the right kidney. The results of basic biochemical indices of renal functions and imaging methods were normal, same as S-Ca, ALP, PTH, however calciuria was in the range of 0.18–0.23 mmol/L. Therefore a diagnosis of **idiopathic hypercalciuria** was established. Nephrolithiasis was treated by shock wave lithotripsy. Hematuria and hypercalciuria resolved after initiation of hydrochlorothiazide treatment.
Patient No. 2 suffered from recurrent abdominal pain, at the age of 5 years ultrasonography revealed nephrocalcinosis, further assessment revealed normocalcemic hypercalciuria (0.23 mmol/kg/24h), hypermagnesiuria, secondary hyperparathyroidism and chronic renal insufficiency. This combination pointed to the very rare diagnosis of **familial hypercalciuria with hypermagnesiuria and nephrocalcinosis (FHHNC),** which was later confirmed by finding of claudin 16 (CLDN16) gene mutation.
Patient No. 3 was a boy with a history of prematurity (35th gestational week, 1860 g birthweight). He had persistently high U-Ca/U-cr ratio (6.96), hypophosphataemia, low S-PTH and X-ray revealed forearm fracture. The above findings were suggestive of **metabolic bone disease of prematurity.** Phosphate supplementation rapidly improved biochemical abnormalities and clinical state. Currently the child is thriving and has no alterations of Ca/P metabolism.
Conclusion: Assessment of hypercalciuria is essential in all children with urolithiasis and nephrocalcinosis. It should be also a part of differential diagnostic procedure in hematuria, recurrent abdominal pain, urinary tract infection and enuresis in childhood.

WHAT IS THE BETTER METHOD FOR ESTIMATION SERUM CREATININE FOR CLINICIANS: ENZYMATIC OR JAFFE ONE?

J. Dušek1**, K. Vondrák**1**, T. Seeman**1**, J. Zieg**1**, R. Průša**2**, B. Jedličková**2**, J. Janda**1
1Pediatric Dept. and 2Dept. of clinical Biochemistry and Pathobiochemistry; IInd Medical School Charles Univ Prague and Univ Hosp Motol
Modified Jaffe method is commonly used for a long time for serum creatinine estimation. It is well known that Jaffe method is not exact, its reproducibility is lower and real level of serum creatinine is overestimated by 20–30%.Worldwide used Schwartz formula for calculation of glomerular filtration rate in children was created on the base of the Jaffe serum creatinine estimation. Enzymatic method is modern, exact and more reliable, however 10× more expansive. In clinical praxis this new methods slowly replace the old one.

Enzymatic method has been introduced by our dept. of biochemistry in University hospital Motol. Because normal values of serum creatinine given by enzymatic methods are lower, we wanted to know what the exact difference is. In the same blood sample was serum creatinine level examined by the both methods (enzymatic and Jaffe). All blood samples were taken in children with kidney diseases followed in our out patients department or in children admitted in the nephrology ward. The children were aged 0.5–21 years (median 12.5 y.). Altogether 169 blood samples have been examined. An automatic analyzer ADVIA 1650 (Siemens Medical Solutions Systems) was used for creatinine analysis. The kit CREA_2 nr. 03039070 were used for Jaffe kinetic method and ECRE_2 nr. 04992596 for colorimetric enzymatic method.

As we expected serum creatinine values estimated by enzymatic method were mostly lower than values estimated by Jaffe method. Obviously the difference was lower with increasing serum creatinine levels (with higher serum creatinine the difference was smaller). From practical reasons all serum creatinine results were divided into the three groups dependently on the serum creatinine level. We studied these differences in each group separately. Serum creatinine levels in our groups were 0–100, 101–200 and 201–800 μmol/l. The results are shown on figures 1, 2 and 3.

Serum creatinine 0 - 100 umol/l- Average difference + 19 umol/l (min. + 0,5- max. + 31,6)

Serum creatinine 101 - 200 umol/l- Average difference + 10 umol/l (min. + 0,1 - max.+ 19,9)

Serum creatinine 201 - 900 umol/l, Average difference - 23 umol/l (min. + 10,2 max. - 158)

The mean differences were 19 μmol/l (0.5–31.6 μmol/l), 10 μmol/l (0.1–19.9 μmol/l) and – 23 μmol/l (10.2 till–158 μmol/l) respectively in our three groups. In the range of normal or slightly higher serum creatinine levels the enzymatic method gives results about 20 μmol/l lower, than Jaffe method and on the contrary in children with the high creatinine levels (above 200 μmol/l) are results provided by enzymatic method about 23 μmol/l higher than estimated by Jaffe method.

Conclusions:

1) The difference between enzymatic method and Jaffe method strongly depends on serum creatinine level.

2) It is difficult to use old Schwartz formula for calculation of GFR in children if enzymatic method for serum creatinine estimation is used.

3) It is necessary to revised Schwartz formula for calculation for GFR in children with serum creatinine values obtained by enzymatic method.

References

1. Cobbaert CM, Baadenhuijsen H, Weykamp CW: Prime time for enzymatic creatinine methods in pediatrics. Clin Chem. 2009 Mar; 55 (3):549–58.

2. Srivastava T, Alon US, Althahabi R, Garg U: Impact of standardization of creatinine methodology on the assessment of glomerular filtration rate in children. Pediatr Res. 2009 Jan; 65 (1):113–116.
3. Myers GL, Miller WG, Coresh J et al.: Recommendations for improving serum creatinine measurement: a report from the Laboratory Working Group of the National Kidney Disease Education Program. Clin Chem. 2006 Feb; 52 (2):169–170.
4. Panteghini M: Enzymatic assays for creatinine: time for action. Clin Chem Lab Med. 2008; 46 (4):567–572.

_____

_Notes

RENAL VEIN THROMBOSIS WITH PULMONARY EMBOLISM – FIRST MANIFESTATION OF LUPUS NEPHRITIS

Sylva Skálová1**, Lenka Minxová**1**, Antonín Lukeš**1**, Petr Dědek**1**, Miroslav Podhola**2
Department of Paediatrics, Fingerland´s Department of Patology, Charles University in Prague, Faculty of Medicine and University Hospital in Hradec Králové, Czech Republic

Introduction: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that can affect almost any organ system with renal involvement occuring in up to 70% of patients. Membranous lupus nephropathy (MLN) represents 10–20% cases of lupus nephritis. Renal vein thrombosis and severe hypoalbuminaemia at presentation are considered to be markers of poor prognosis in membranous MLN.

Case report: 11-year old girl was admitted for shortness of breath, posttraining dyspnea and nonspecific symptoms including fatigue, headache, myalgia and oedema. On admission, she was pale with oedema of eyelids and lower extremities, Palpation of the left part of abdomen was painful and there was positive tapottement on the left lumbar side.
Left renal vein thrombosis was diagnosed by ultrasonography. Laboratory investigation revealed nephrotic syndrome with proteinuria 16g/24h and hypoalbuminaemia 11.8g/l. She fullfilled 6 of 11 criteria for SLE. Bilateral pulmonary embolism was diagnosed subsequently by lung perfusion scan. Renal biopsy revealed pure membranous nephropathy (WHO type Va). Treatment with low-molecular weight heparin was initiated together with immunosupressive therapy consisting of methylprednisolone pulses followed by intravenous cyclophosphamide pulses. Antithrombotic therapy resulted in complete recanalisation of left renal vein. Complete remission of lupus nephritis was achieved after five months from starting immunosupressive therapy.

Conclusion: Thromboembolism can be one of the first manifestations of SLE. Paediatricians, rheumatologists and nephrologists should be aware of this

fact.

RELATION BETWEEN DONOR/RECIPIENT BODY MASS AND KIDNEY GRAFT FUNCTION IN PEDIATRIC RENAL TRANSPLANTS

J. Špatenka, E. Foltýnová, T. Seeman, J. Janda, K. Matoušovic
Transplant Center and Department of Pediatrics, University Hospital Motol, Prague

Background*:* An average kidney weight in newborns is 26.6 g and increases with age, reaching 269 g at the age of 20 y. The kidney weight rise is caused by a growth of all kidney tissue components, e.g. glomerular basement membrane width increases from 150 nm after the birth, to 300 nm at the age of 5 years, up to 400 nm in adults. Glomerular filtration rate also increases with growth of a subject. In 1994, H. S. Mackensie et al. showed that function and morphology of the rat kidney graft are significantly influenced by a transplanted kidney mass. Also in men, many findings indicate a positive influence of the transplanted kidney mass on the kidney graft function and survival (Chertow GM et al. 1996, Taal MW et al. 1998). This knowledge may be important especially in pediatric kidney transplantation, as renal transplant centers prefer adult grafts even for small pediatric recipients. We hypothesized that transplanted kidney parenchyma mass may influence GFR in a post transplant period in children, and therefore, we tested this hypothesis.

Cohort of patients and methods*:* In 1997–2007, kidney transplantation was performed in 66 children aged 8–19 y (average 18.3±4.47, median 19.43.), of them 36 were male and 30 female. At transplantation, the body weight of recipients ranged from 13 to 112 kg (39.37±17.90, median 40.0)). Four transplantations were from a living and 62 from a cadaveric donor. The age of living donors varied from 37 to 41 y (median 40), their body weight was from 51 to 87 kg (70.5±17.7, median 72). Age of cadaveric donors was 11 to 52 y (30.85±12.06, median 29.05).

We retrospectively evaluated serum creatinine levels (S-cr, measured at Dept. Biochemistry and Pathobiochemistry of the University Hospital Motol) and creatinine clearance calculated according to Schwartz formula at the end of hospitalization, 12 months after transplantation, and at the end of follow-up. All findings were evaluated with regard to a donor/recipient body masses ratio (D/R BMR).

Results: Ccr directly correlated with a D/R BMR at the end of hospitalization ($r = 0.6125$, $P = 0.0071$) and 1 y after transplantation ($r = 0.5938$, $P = 0.0059$), but not at the end of follow up.

88

Summary: We found a very significant direct correlation between the D/R BMR at transplantation and Ccr early and 1 y after transplantation, but this functional dependence disappeared in the late post transplant period.

References

1. Chertow GM, Milford EL, Mackenzie HS, Brenner BM: Antigen-independent determinants of cadaveric kidney transplant failure JAMA. 1996, 4:1732–1736.
2. Taal MW, Tilney NL, Brenner BM, Mackenzie HS: Renal mass: an important determinant of late allograft outcome. Transplant Rev 1998; 12:74–84.

Graph 1 **GFR vs. D/R BMR (end of hospitalisation)**
y = 15,238x + 52,094
GFR (ml/min/1.73 m2 89
Graph 2
GFR vs. D/R BMR
(end of follow-up) y = 8,196x + 92,422, r = 0.2362 N.S.
D/R BMR
GFR m l/m in /1.73 m 2

_Notes

HEREDITARY VITAMIN D-RESISTANT RICKETS WITH ALOPECIA – AN INTERESTING DISEASE FOR PEDIATRIC NEPHROLOGISTS

Z. Doležel, D. Feldman1, D. Dostálková, J. Štarha
Dept. of Pediatrics, Medical School Masaryk's Univ. and Univ. Hosp. Brno, Dept. of Medicine, Stanford Univ. Sch. Med., USA1; zdoleze@fnbrno.cz

Hereditary vitamin D – resistant rickets (HVDRR) is a rare recessive genetic disorder caused by mutations in the vitamin D receptor (VDR). In this case study, we examined the VDR in a young girl with clinical features of HVDRR including rickets, hypophosphatemia, and elevated serum 1,25(OH)2D. The girl also had total alopecia. Two mutations were found in the *VDR* gene: a nonsense mutation (R30X) in the DNA-binding domain and a unique 3-bp in-frame deletion in exon 6 that deleted the codon for lysine at amino acid 246 (ΔK246). The child and her mother (origin from Indonesia) were both heterozygous for the 3-bp deletion, whereas the child and her fater (origin from Czech Republic) were both heterozygous for the R30X mutation. Fibroblasts from the patient were unresponsive to 1,25(OH)2D3 as shown by their failure to induce *CYP24A1* gene expression, a marker of 1,25(OH)2D3 responsiveness. [3H]1,25(OH)2D3 binding and immunoblot analysis showed that the patient's cells expressed the VDRΔK246 mutant protein; however, the amount of VDRΔK246 mutant protein was significantly reduced compared with wildtype controls. In transactivation assays, the recreated VDRΔK246 mutant was unresponsive to 1,25(OH)2D3. The ΔK246 mutation abolished heterodimerization of the mutant VDR with RXRα and binding to the coactivators DRIP205 and SRC-1. However, the ΔK246 mutation did not affect the interaction of the mutant VDR with the corepressor Hairless (HR). In summary, we describe a patient with compound heterozygous mutations in the VDR that results in HVDRR with alopecia. The R30X mutation truncates the

VDR, whereas the ΔK246 mutation prevents heterodimerization with RXR and disrupts coactivator interactions.
A part of this case was published in J Bone Miner Res 2009; 24:643–651.

References

1. Holick MF: Resurrection of the vitamin D deficienty and rickets. J Clin Incest 2006; 116:2062–2071.
2. Valdivielso MJ, Fernandez E: Vitamin D receptor polymorphisms and disease. Clin Chim Acta 2006; 371:1–12.
3. Bora G et al.: Vitamin D receptor gene polymorphisms in Türkish children with vitamin D deficient rickets. The Türkish Journal of Pediatrics 2008; 50:30–33.

MONOGENIC HYPERTENSION

Z. Doležel, J. Štarha, D. Dostálková
Dept. of Pediatrics, Medical School Masaryk's Univ. and Univ. Hosp. Brno; zdoleze@fnbrno.cz

Hypertension (H) has become an epidemic affecting nearly 1 milliard individuals worldwide. Uncontrolled H increases the risk of cardiovascular and chronic kidney disease, and there is a direct relationship between the risks of stroke, heart attack, heart failure, kidney disease and the severity of H. Recent studies have shown that end organ damage such as atherosclerosis and left ventricular hypertrophy are common in the setting of mild H in children and adolestents, increasing their risk of cardiovascular disease as adults. H is usually an asymptomatic disease but children with severe uncontrolled H may present with seizures, stroke, encephalopathy and heart failure. Moreover, recent studies have shown that appropriate treatment of H results in significant reductions in the risks of stroke, heart failure, myocardial infarction and endstage kidney disease.
Primary H is currently the most common cause of H in children. Usually is mild and associated with overweight or obesity. Children with severe H, unlike adults, usually have secondary causes of H. Of the secondary causes of H in pediatrics, the majority include diseases that affect glomerular filtration, ion transport or hormonal messages to the kidney.
Based on plasma renin level measured as plasma renin activity (PRA), hypertensive individuals can be classified as low, normal or high-renin hypertensives. This classification system is relevant and widespread, as PRA status is related to distinct pathophysiological mechanisms that sustain high blood pressure and may even predict responsiveness to different antihypertensive treatments.
Some children develop H because of a defect in a single gene, so called monogenic H. The genes responsible for these disorders have all been cloned and all participate in pathways involved in heightened renal sodium reabsorption. The increased sodium reabsorption arises in the distal nephron and leads to volume expansion and H. This review will briefly explore the

recently indentified molecular mechanisms and pathogenesis of genetic disorders that cause H in children. Monogenic forms of H are: Familial hyperaldosteronism type I, II, and III, Liddle's syndrome, Gordon's syndrome, Apparent mineralocorticoid excess, Congenital adrenal hyperplasia type IV and V, and Mineralocorticoid receptor-activating mutation.
92

References

1. Williams SS: Advances in genetic hypertension. Curr Opin Pediatr 2007; 19:192–198.
2. Garovic VD, Hiliard AA, Turner S: Monogenic forms of low-renin hypertension. Nature Clinical Practice Nephrology 2006; 2:624–630.
3. Mulatero P, Verhovez A, Morello F et al.: Diagnosis and treatment of low-renin hypertension. Clinical Endocrinology 2007; 67:324–334.

_Notes

93

PROMETHEUS – NOT JUST A MYTH

M. Hladík, T. Zaoral, M. Nowaková
Dept. of Pediatric Intensive Care, Faculty Hospital, Ostrava

For centuries, people would read stories about the Titan Prometheus who was commanded to be chained in the Caucasus for having given the gift of fire to mankind. There, each day, an eagle would fly and feast on Prometheus´ liver; yet each day, this organ would renew itself. This story raises a question: did old Greeks know about the outstanding regeneration capacity of this vital organ? Subsequently in modern times Prometheus stands for a device which substitutes renal as well as liver functions. through the combination of two elimination methods: albuminopheresis (with the consecutive treatment of albumin by adsorption) and hemodyalysis. The fundamental principle of the whole issue is the evidence that the majority of toxic substances are transported albumin- bound within the blood stream. The idea first sprung into life through Falkenhagen in 1999 and it has been known as FPSA (Fractionated Plasma Separation and Adsorption [1, 2]). An indication for this elimination device is primarily hepatic failure; in case of accompanying renal failure (3).

Table 1: Etiology of hepatic failure (4)

Etiology	**Possible disease**
Infection	Hepatitis, sepsis,varicella, morbilli, ebola
Toxic	Amanita phalloides, paracetamol, valproate
Metabolic	Galaktosaemia, fruktosaemie, Wilson´s disease
Tissue infiltration	Leukemia, hemangioendotelioma, hepatoma, metastasis
Autoimmune	Antihepatic and antorenal antibodies in autoimmune disease
Ischemia	Budd-Chiari syndrome, shock

Nowadays, there are no explicit criteria for the commence of the elimination

in hepatic failure. The decision is based on clinical signs and symptoms of encephalopathy and laboratory markers. The King´s College Criteria is the auxiliary method to allow for a prognosis estimation in acute liver failure; this scoring system has been also used as a criterion for urgent liver transplantation. The Prometheus device consists of 2 filters and 2 adsorption capsules. The whole circuit is shown in figure 1.

The "artificial liver" treatment falls into the group of so called „bridging therapy" which enables either liver regeneration or liver transplantation in favourable conditions of stable metabolic homeostasis. It is not any reparative 9treatment for a severely damaged liver, the cornerstone of which still largely remains within the limits of supportive conservative approach, but with the unexceptionable participation of the liver – self autoreparative ability.

Figure 1: Prometheus circuit. Blood flows through extracorporal circuit into AlbuFlow filter whichenables albumin with bound toxins to enter a close-loop circuit with 2 adsorption capsules wherethe removal of these toxins takes place. Once cleansed, albumin returnes into blood. Then follows the removal of water-soluble toxins, urea and creatinin through the process of hemodialysis.

Prometheus device is accesible in 6 towns in the Czech Republic: Pilsen, Prague (2), Hradec Králové, Brno and Ostrava; here the device itself is located at the pediatric department. This distribution is fully sufficient from the perspective of both the accesability and the frequency of its usage. The total number of children treated with Prometheus so far in CR does not extend beyond 5 patients.

We report a case study of a seven-year-old girl with a severe diphasic alimentary intoxication with Amanita Phalloides. With this patient, Prometheus was used for the first time at our department. Unfortunately the course of the intoxication was fatal due to extensive latency between intoxication itself and the hospital admission. We verified the elimination efficiency of this method.

The Prometheus treatment should be restricted to a few centers around the country, also for the fact that the one-day expenses for this method is approximately 80 000 CZK (2860 Euros).

References

1. Falkenhagen D et al.: Fractionated plasma separation and adsorption system: a novel systém of blood purification to remove albumin bound substances. Artif Organs 23, 1999, s. 81-86

2. Kinan R et al.: Prometheus – a new extracorporeal system for the treatment of liver failure. Journal of Hepatology, 39, 2003, s. 984–990

3. Stadlbauer V et al.: Effect of Extracorporeal Liver Support by MARS and Prometheus on Serum Cytokines in Acute-on-Chronic Liver Failure. Crit Care, 2007, 6, 10.

4. Fedor M et al.: Intenzivní péče v pediatrii. Osveta Martin, 2006, 461.

_Notes

MEDULLARY CYSTIC KIDNEY DISEASE WITH SIGNIFICANT PROTEINURIA: CASE REPORT

H. Flögelová1**, T. Tichý**2**, K. Michálková**3
1Dept. of Paediatrics, 2Dept. of Pathology, 3Dept. of Radiology, University Hospital in Olomouc

Objectives and study: Medullary cystic kidney disease (MCKD) is hereditary chronic tubulointerstitial nephritis with slow progression to renal failure. The disease has characteristic renal histology and an autosomal dominant or sporadic pattern of inheritance (gene loci MCKD1, MCKD2). The clinical features are polyuria and nocturia. Normal or mild proteinuria is typical for the disease. We report a case of MCKD which presented atypically as significant proteinuria.

Methods: A 15-year-old boy presented to our hospital with significant proteinuria (1.5g/day). He had not suffered from polyuria or nocturia. The 24-h urine volume was 1400mL and the blood pressure was normal. The laboratory analysis showed a serum creatinine of 58μmol/L and urea of 5.1mmol/L. Serum sodium, potassium, calcium, phosphorus, uric acid as well as blood count was normal. Haematuria and leukocyturia were absent. Ultrasound examination of the kidneys revealed bilateral increased parenchymal echogenicity. The first renal biopsy (at 16 years of age) was consistent with hereditary nephropathy and suggestive of Alport syndrome. However, the diagnosis was not supported by the boy's family history and audiometry results. Proteinuria increased to 3g/day despite the medication (ACE-inhibitor, AT1 receptor antagonist). Polyuria of 3800mL/day and hyperazotaemia (serum creatinine of 146μmol/L, cystatin C relative glomerular filtration rate of 48mL/min/1.73m2) were documented. The ultrasound finding developed into hyperechoic renal medullary pyramids (serum and urine calcium concentrations were normal).

Results: The second renal biopsy revealed changes typical for MCKD (tubular basement membrane disintegration, tubular atrophy with cyst development, interstitial lymphocyte infiltration). Significant proteinuria (mixed, glomerulotubular) was partly explained by secondary diffuse glomerulosclerosis. Changes in the tubular basement membrane in MCKD are analogous to those in the glomerular basement membrane in Alport syndrome (explaining the wrong first diagnosis).

Conclusion: Based on the literature review, this is the first case of significant proteinuria in a child with MCKD.

A NEW MUTATION OF THE *COL4A5* GENE IN A FAMILY WITH ALPORT SYNDROME (CASE REPORT)

A. Bosáková, T. Šuláková, P. Plevová1**, J. Dvořáčková**2
Dpt. of Pediatrics, 1Dpt. of Medical Genetics and 2Dpt. of Patology, Teaching Hospital Ostrava, Czech Republic

Introduction: Alport syndrome is a clinically and genetically heterogeneous

nephropathy. The majority of cases are transmitted as an X-linked condition due to *COL4A5* mutations.
Case report: We report on an 11-year-old girl who has been followed since the age of 4-years for repeated urinary tract infections (cystitis), microscopic hematuria and later also proteinuria (< 0.5g/day) and hypertension. The ultrasound examination and the audiogram have been normal. She was treated with ramipril with a good effect on hypertension (ABPM). Renal biopsy revealed changes typical for Alport syndrome.
Father of the girl has been suffering from perceptive hearing loss and glomerulonephritis since childhood. He underwent two renal transplantations. There are also 3 relatives with a similar symptomatology in the family. Molecular genetic analysis of the *COL4A5* gene was performed and revealed a germline nonsense mutation c.372–373del.CA(p.C124X) in exon 6 of the gene. This mutation results in the synthesis of a shortened protein (123 amino-acid versus normal 1691 amino-acid chain). Based on the biopsy findings and molecular genetic analysis the diagnosis of X-linked Alport syndrome has been proved.
Conclusion: The mutation found in the observed family is a new one and has not been previously described. The mutation has deleterious effect on the protein level. It may be considered to be the cause of Alport syndrome due to the segregation of the mutation with the disease in the presented family.

_*Notes*

SURPRISING POSITIVE EFFECT OF NOOTROPICS IN CHILDREN WITH RESISTANT ENURESIS
J. Liška, V. Holeček, Š. Sobotová
*Mulač Hospital, Plze*ň
Sixty two patients aged from 8 to 17 years, being 42 boys and 20 girls with resistent enuresis (EN) were studied. After two years of experience with Minirin spray to resistant enuresis we were successful in 65%. The original treatment included desmopressin combined with oxybutinin. In spite this combination the positive effect did reach only 77%. We have observed following sleeping disorders: according to the work of Watanabe different types of arousal reactions especially EEG changes were observed. Having had only moderate effect using the above mentioned combination we decided to add piracetam. 20 μg/daily of desmopressin, 0,2 mg/kg of oxybutinin and 30–40 μg of piracetam were administrated at bedtime. The application of this combination continued for one and a half year. Standard proceedings as awards, approbations, calendar evidence, awaking from parents at 23 o´clock were used. Side effects (sleeping disturbances) were observed only in two children. Due to this effect we eliminated after 6 months from this combination oxybutinin, after 9 months of therapy we reduced desmopressin to the half.

After one year we eliminated desmopressin at all and after 15 to 18 months we stopped the application of piracetam. No relaps of EN occurred.
Conclusion: Our limited experience showed surprising good effect of combination desmopressin, oxybutinin and piracetam in resistant enuresis resulting in positive effect in 96%.

APPARENTLY LIFE THREATENING EVENT OF THREE WEEKS OLD BOY

Luděk Ryba
Dptm. of Pediatrics, District Hospital Ústí nad Orlicí, Eastern Bohemia
A fullborn breastfed healthy boy fell ill on the 18th day of his life. The pediatrician thought the temperature 38,9 °C was due to catarrhal otitis media. Without accomplishing any tests she advised the parents to give him antipyretics and ear drops. She didn´t suggest a date of clinical control. Three days later the parents called the emergency. After two days of moderate restlessness the boy ceased to breathe and turned blue. The emergency physician found him comatose, atonic and hypoxemic (saturation of oxygen was 70%), fortunately before the arrival of the ambulance he spontaneously regained respiratory movements. He was put on oxygen and transported to ICU at children´s hospital. At reception his circulation was failing, he was anuric, tachycardic with hearth rate 190/min., blood pressure was immeasurable. Laboratory tests revealed high inflammatory markers – CRP 286 mg/l, ESR 130/136 – and breakdown of the ECF compartment – sodium 118 mmol/l, potassium 7,9 mmol/l, blood urea 21 mmol/l and serum osmolarity 240 mOsm/l.
Fluid and antibiotic therapy was started "blind". After completion of further tests the therapy proved itself as causal and efficient.
The boy is now one year old, completely healthy, showing no consequences of this apparently life threatening event (ALTE) of undue origin.

_Notes

FIBRILLARY GLOMERULONEPHRITIS IN AN 18 YEARS OLD BOY WITH CORTICOID RESISTANT NEPHROTIC SYNDROME

V. Jankó1**, D. Daniš**2**, L. Kovács**1
2nd Department of Pediatrics1, University Hospita and Institute of Pathology2, Bratislava, Slovakia
Introduction: Organized fibrillar or microtubular glomerular deposits may be encountered in a variety of renal disorders, including amyloidosis, cryoglobulinemic glomerulonephritis, lupus nephritis, collagen glomerulopathies, and the entities of fibrillary and immunotactoid glomerulonephritis. Fibrillary glomerulonephritis (FGN) is a distinctive but controversial glomerulopathy first reported by Rosenmann and Eliakim in 1977. This rare disorder comprises less than 1% in renal biopsy series and

usually presents with renal insufficiency, nephrotic range proteinuria, and microhematuria. It is characterized pathologically by the deposition in glomeruli of fibrillar deposits that generally range from 10 to 24 nm in diameter. These fibrils usually stain for immunoglobulin G (IgG) and C3, with more variable and weaker positivity for other immunoglobulins. By definition, the glomerular deposits are Congo red–negative, allowing their differentiation from amyloid. Hence, synonyms for FGN include "nonamyloidotic fibrillary glomerulonephritis" and "Congo red–negative amyloidosis-like glomerulopathy".

Case: 18 years old male patient with the spastic form of infantile cerebral palsy was admitted admitted to our department for a mild face swelling. Laboratory studies revealed hypoalbuminemia (21.1 g/l), hypercholesterolemia (8.95 mmol/l) and nephrotic range proteinuria (6.4 g/day). Neither there were clinical nor laboratory clues for secondary nephrotic syndrome. Because of the corticoresistant nature of the disease, kidney biopsy was performed. The histological evaluation was consistent with either amyloidosis or fibrillary glomerulonephritis. Electron microscopy revealed presence of fibrillar deposits in glomeruli in the range of 10 to 16 nm, on average of 12 nm in diameter. On account of rapidly worsening renal failure he was started on cyclophosphamide along with ACE inhibitors and angiotensin II receptor blockers, which led to the partial recovery and stabilization of his renal function and reduction of proteinuria to 0.7 g/day.

Conclusion: This case highlights the need for routine electron microscopy in native renal biopsies, where the differential diagnosis is wide and varied and the light and immunofluorescence microscopic findings may be non specific.

PSEUDO-BARTTER SYNDROME AS A PRESENTATION OF CYSTIC FIBROSIS

Z. Doležel, J. Štarha, D. Dostálková

Dept. of Pediatrics, Medical School Masaryk's Univ. and Univ. Hosp. Brno; zdoleze@fnbrno.cz

Introduction: The term Bartter syndrome (BS) denotes a group of renal diseases which share a common denominator of hypokalemia and metabolic alkalosis. Terms such as Bartter-like syndrome do little to help the clinician identify the specific metabolic defect and treat the patient's illness correctly. Biochemical abnormalities similar to those found in BS, i.e. hypokalemic metabolic alkalosis, are also encountered in another group of patients so-called pseudo-Bartter syndrome with no pathology in the renal tubules. It is therefore very important to identify any other cause that may produce such a metabolic derangement. We present two children with pseudo-Bartter syndrome.

Case 1: a 5-month-old boy presented with anorexia, irritability and 4 episodes of dyselektrolytemia (hyponatremia, hypokalemia, metabolic alkalosis). No correct diagnose was established. On physical examination by

5th-episode, the infant was well hydrated with body weight and body height at 10th percentile.

Case 2: a 4-month-old girl was admitted for vomiting, poor feeding and failure to thrive. At admission she was apathic, hypotonic and with signs of 5% dehydration. Her body weight and body height were at 25th percentile.

Laboratory data of our two patients were:

Case Blood (mmol/l) Urine (mmol/24hrs)

Na+ K+ Cl- HCO3- Na+ K+ Cl-

1. 117 2.6 79.8 36.2 2.19 2.04 0.47

2. 118 2.5 77.0 34.5 3.14 2.25 0.68

With parenteral application of fluids and salt supplementation, dyselektrolytemia was achieved in our patients and they have no other similar episodes. After DNA analysis cystic fibrosis (CF; delta F508 in both infants) was confirmed.

Conclusion: In CF, electrolyte abnormalities and acid-base disturbances may be due to:

1. increase losses through excessive sweating;
2. acute intercurrent gastrointestinal processes accompanied by a low dietary intake and insufficient salt supply;
3. secondary hyperaldosteronism resulting from chronic sodium and acute water and salt depletion which increases the renal potassium and hydrogen losses for the exchange with sodium in the distal tubule.

Besides CF is pseudo-Bartter syndrome possible by surreptitious diuretic use, chronic administration of a chloride-deficient diet, bulimia, cyclic vomiting, congenital chloridorrhea, and abuse of laxatives. In all of these conditions, except diuretic use, the chloride content of urine will be low, and this is contrary to all forms of BS.

References

1. Amirlak I, Dawson KP: Bartter syndrome. Q J Med 2000; 93:207–215.
2. Haycock GB: Hyponatraemia: diagnosis and management. Arch Dis Child Educ Pract Ed 2006; 91:37–41.
3. Kovács L, Robertson GL: Disorders of water balance- hyponatremia and hypernatremia. In: Burger AG a Phillipe J (edit): Endocrine Emergencies, Bailliere‘s Clinical Endocrinology and Metabolism, Saunders, Philadelphia 1992:107–127.
4. Seyberth HW: An improved terminology and classificatoion of Bartter-like syndromes. Nature Clinical Practice Nephrology 2008; 4:560–567.

_Notes

IMAGING METHODS IN PEDIATRIC RENAL DISEASES

A. Bosáková1, **T. Šuláková**1, **V. Dedek**2, **P. Širůček**2, **J. Havelka**3, **J. Krhut**4, **M. Pětroš**5

1Dpt. of Pediatrics, 2Dpt. of Nuclear Medicine, 3Dpt. of Radiography, 4Dpt. of Urology, 5Dpt. of Gynecology University Hospital Ostrava

Imaging methods form part of the fundamental examinations in children with kidney diseases on the basis of high incidence of congenital defects. The most frequently used tests are:

Ultrasonic Detection – fundamental method used in patient examination in a pediatric nephrology clinic which detects some pathological defects already during the first examination. The kidney size is determined by the Dinkel's graph.

X-ray of the abdomen – the native image of the abdomen is of lesser importance these days, we use it when there is a suspicion of renal stones; renal stones can be detected by the ultrasound as well.

MCUG – is an invasive method where a catheter is inserted into the bladder and physiological solution with contrast is infused. We can show passive or active vesicoureteral reflux. At our clinic we perform this examination on a skiascopy where a transient VUR can be captured.

Isotopic Cystourethrography is a very appropriate method for VUR (vesicoureteral reflux) control examination. It is not suitable as a first examination because it does not provide the degree of reflux.

Intravenous Urography – we see the shape of the cup kidney and the possible obstruction of the urine outflow by the stone in blockade of the ureter. The size of kidneys is determined by the Clare graph.

Uroflowmetry – where a pathological curve shows the need for further examination of the lower urinary tract.

MAG 3 – (mercaptoacetyltriglycine) – is a dynamic scintigraphy of kidneys – kidney plasma flow – resulting in nephrographic curves.
The examination can show possible obstruction in the ureter (we can see the dilatation of the pelvis on the USG) and the kidney hypofunction or afunction can be depicted by an atypical curve shape. Each kidney can be examined separately.

DMSA – static scintigraphy (dimercaptosuccinic acid) – depicts the shape, location, size and intensity of the indicator uptake. It shows scars in kidney parenchyma (filling defect) post kidney inflammation, dystopia and kidney shape deviation. It evaluates the difference in the function of each kidney – we regard as a significant difference when the function of a diseased kidney is lowered under 45%.

CT – computer tomography – demonstrates tumors, and complicated anomalies of the urinary tract.

Angio- CT – demonstrates anomalies of renal vessels with a possibility of a follow up correction (percutaneous transluminal angioplasty)

NMR – nuclear magnetic resonance – and magnetic resonant angiography (**MRA**) non-invasive demonstration of vessel bed pathology. The contrast material is given intravenous into the periphery.

_Notes

RENOVASCULAR HYPERTENSION AND MID-AORTIC SYNDROME IN A 12-YEAR-OLD GIRL: A CASE REPORT

A. Kolský1**, J. H. Peregrin**2**, V. Smrčka**3**, J. Korda**3**, K. Jiroušová**1**, J. Kováč** 2**, H. Houšťková**1**, M. Kolská**4

1Dept. of Paediatrics, Thomayer Teaching Hospital, Praha 4; 2Institute for Clinical and Experimental Medicine, Praha 4; 3Regional Hospital České Budějovice; 43rd Medical Faculty Charles Univ Praha 10

The aim of the study: We report the case of a 12-year-old girl (171 cm, 46.5 kg, BMI 15,1), who presented with seizures due to a hypertensive crisis (blood pressure /BP/ reached 190/110 mmHg). The girl had experienced frequent headaches for 6 months. She was treated this time for headache, but BP was not measured. Physical examination demonstrated abdominal bruit, normal femoral pulses and no significant pressure gradient between the upper and lower extremities. Serum creatinine was 107 μmol/l, GFR 1.0 ml/s/1.73 m2, elevated plasma renin activity and hypokalemia were observed.

Methods: Two weeks later, selective renal arteriography (RA) showed a 99% renal artery stenosis (RAS) causing fibromuscular dysplasia of the upper hand from two right renal arteries as a part of mid-aortic syndrome (without aortic pressure gradient) was diagnosed. At the same time, occlusion of the superior mesenteric artery was found and Riolani anastomosis was detected as well.

Results: Percutaneous transluminal angioplasty of the renal artery (PTRA) was performed by balloon dilatation (balloon Savvy and Opera, pressure 13 atm.) via the right femoral access immediately without complication. Successful dilatation of the RAS was seen after the procedure. Clinical condition and laboratory results were favourable (serum creatinine 76 μmol/l, GFR 1.8 ml/s/1.73 m2, no signs of inflammation). Echocardiogram: mild left ventricular wall hypertrophy with a lowering of ejection fraction (EF) (40%). BP was controlled by 5mg of amlodipine. Follow-up computer tomography (CT) RA 3 months later showed proximal restenosis of renal artery. BP was also increased. Another PTRA was performed 4 months after the first one with stent implantation (BLUE 18 × 5 mm). CT RA 2 months later showed a new RAS proximal to the stent and another stent placement (ostially) is planned.

Conclusion: The girl´s condition 10 months after the 1st PTRA was good (no headache, normal echocardiogram, EF 61%), but BP based on 24h-ABPM all her values were above the 95th percentile. She is now being treated with amlodipine of 7.5 mg daily. Nevertheless, her long prognosis is dubious.

107

URINARY TRACT INFECTION IN THE NEWBORN INFANT AND IN CHILDREN L. Cataldi, M. Zaffanello, V. Fanos

Study Group for Neonatal Nephrology of the Italian Society of Neonatology,

*Dept. of Pediatric Sciences, Division of Neonatology, Catholic University of Sacred Heart, Rome, and **Laboratory Medicine, University-Hospital San Martino, Genova*

The authors present some data concerning urinary tract infections (UTIs) in the newborn infants and children. Diagnosis is frequently difficult to be obtained on the basis of the clinical findings. Being the paediatrician's goal to reduce the risk of renal scarring, prompt diagnosis and treatment is important. data about recent Italian trials on early Treatment of Acute Pyelonephritis, Prophylaxis After First Febrile Urinary Tract Infection in Children, and Value of Imaging Studies After a First Febrile Urinary Tract Infection, are shown.

The UTIs' incidence in infants ranges approximately from 0.1 to 2.0 percent in all newborn infants to as high as 20 percent in preterm newly born infants and neonatal at risk population (i.e. low-birth-weight infants) as experienced by Cataldi et Al. (1–2). UTIs occurs more frequently in boys than in girls before age one. After this age, both bacteriuria and UTI are more common in girls. Usually, infections that involve the kidney (pyelonephritis) may cause both acute morbidity and lead to scarring with the consequences of hypertension, preeclampsia, and chronic renal disease (4).

Ultrasonography, voiding cystography, and DMSA scintigraphy have been recommended after febrile UTIs, although evidence of their value is limited. Furthermore, recent trials suggest that antibiotic prophylaxis does not reduce the incidence of UTIs in children with low-grade vesicoureteral reflux. Renal scarring is a frequent outcome of acute pyelonephritis in children. The American Academy of Pediatrics expressed concern regarding any delay in the treatment of febrile UTIs, supporting the concept that such delay increases the subsequent risk of kidney damage. Antibiotic prophylaxis has been widely used after a febrile urinary tract infection, despite the evidence supporting that its efficacy is weak.

Based on recent studies and trials here are some of the Italian Study Group's suggestions

1) About the benefit of performing ultrasonography and scintigraphy in the acute phase or cystourethrography is minimal.

Italian study's findings support (a) technetium-99mdimercaptosuccinic acid scintigraphy 6 months after infection to detect scarring that may be related to long-term hypertension, proteinuria, and renal function impairment (although the degree of scarring was generally minor and did not impair renal function) and (b) continued surveillance to identify recurrent urinary tract infections that may warrant further investigation.

2) About early treatment of acute pyelonephritis in infants and young children had no significant effect on the incidence of subsequent renal scarring. Furthermore, no difference in scarring rates was observed when infants and young children were compared with older children.

3) Antibiotic prophylaxis, commonly used to reduce the risk for repeat febrile

urinary tract infections, does not reduce the rate of recurrence during 12 months after the first episode in children with or without the presence of primary non severe reflux.

References

1. Cataldi L, Salvaggio E, Prota M: L'infection urinaire du prematuré: existe-t-elle? Progres en Néonatologie 10:271, 1990.
2. Cataldi L, Salvaggio E, Prota M: Il neonato con infezione delle vie urinarie. Riv. Ital. Ped. (I.J.P.) 16:354, 1990.
3. Fanos V, Cataldi L: Antibiotics or surgery for vesicoureteric reflux in children. Lancet. 2004 Nov 6-12; 364(9446):1720–1722. Review.
4. Agostiniani R, Fanos V, Cataldi L: Imaging strategies in urinary tract malformations. Pediatr Med Chir. 2005 Sep-Oct; 27(5):72–74. Review.
5. Cataldi L, Agostiniani R, Fanos V: Urinary tract malformation and infection.Pediatr Med Chir. 2005 Sep-Oct; 27(5):67–70. No abstract available.
6. Fanos V, Atzei A, Zaffanello M, Piras A, Cataldi L: Cranberry and prevention of urinary tract infections in children. J Chemother. 2006 May; 18 Spec no 3:21–24. Review.
7. Aranda JV, Cataldi L, Fanos V: Clinical pharmacology of antimicrobials for urinary tract infections in newborns and young infants. J Chemother. 2006 May; 18 Spec no 3:14–15. Review.
8. Mussap M, Cataldi L, Plebani M, Fanos V: Laboratory investigation for the early diagnosis and monitoring of neonatal urinary tract infections: the present situation and future perspectives.J Chemother. 2006 May; 18 Spec no 3:9–13. Review.
9. Cataldi L, Mussap M, Fanos V: Urinary tract infections in infants and children. J Chemother. 2006 May; 18 Spec no 3:5–8.
10. Montini G, Toffolo A, Zucchetta P et al.: Antibiotic treatment for pyelonephritis in children: multicentre randomized controlled non-inferiority trial. BMJ 2007 August 25; 335:386.
11. Hewitt IK., Zucchetta P, Rigon L: Early Treatment of Acute Pyelonephritis in Children Fails to Reduce Renal: Scarring: Data From the Italian Renal Infection Study Trials Pediatrics 2008; 122; 486–490.
12. Montini G, Rigon L, Zucchetta P et al.: Prophylaxis After First Febrile Urinary Tract Infection in Children? A Multicenter, Randomized, Controlled, Noninferiority Trial. Pediatrics 2008 122:1064–1071.
13. Montini G, Zucchetta P, Tomasi L et al.: Value of Imaging Studies After a First Fibrile Urinary Tract Infection in Young Children: Data From Italian Renal Infection Study 1 Pediatrics 2009; 123; e239-e246.
14. Montini G, Cataldi L, Pennesi M et al.: "Raccomandazioni per la diagnosi, il trattamento e il follow-up delle IVU febbrili in bambini di eta compresa fra i 2 mesi e i 3 anni" Medico e Bambino 2009 (in press).

HIDDEN HIGH-GRADE VESICOURETERAL REFLUX IS

THE MAIN RISK FACTOR OF CHRONIC RENAL DAMAGE IN INFANTS WITH FIRST URINARY TRACT INFECTION

Marco Zaffanello, MD

Department of Mother-Child and Biology-Genetics, University of Verona, Verona, Italy. E-mail: marco.zaffanello@univr.it

The aim of the study: The aim of the present trial was to investigate, in a cohort of infants with first UTI and negative prenatal history, the role of US, VCUG and renal scintigraphy in screening babies at risk of hypertension and renal deterioration in the long term.

Methods: The prospective clinical trial took place between 2001 and 2008 at the Department of Mother-Child and Biology-Genetics at the Verona University medical clinic. We enrolled infants who had experienced the first febrile UTI at less than 3 years of age. All infants underwent urinalysis and microbiological analyses. Other inclusion criteria were negative history for adverse events during pregnancy and delivery, and normal foetal routine US. All infants with febrile UTI, after becoming part of the cohort, underwent renal ultrasound. Exclusion criterion was sonographic signs of obstruction. The VCUG was performed approximately one month after the urinary infection. Furthermore, to screen for parenchyma loss or renal scarring, a renal DMSA scintigraphy was performed in all children approximately six months after the UTI episode.

Sixty-nine infants (49.3% males) were prospectively followed-up. They were born at 38.7±1.3 (range 35-41) weeks of gestational age. The age of the first febrile UTI was 0.77±0.75 years (range 1 month–3 years).

Statistical analysis was performed using SPSS v. 17.0 software for Windows.

Results: The renal pelvis was unremarkable in 55.1% of cases. In 14.5% and 30.4% of cases it was ≤7 and >7 mm in diameter, respectively. The ureter was dilated in 11.6% of infants. Furthermore, in 5.8% of cases bladder examination disclosed abnormalities.

VUR was detected in 56.5% of the infants. In 40.6% of babies, the VUR was ≥ 3 degrees.

Renal scarring was observed in 21.7% of infants. Infants with renal scarring showed unilateral renal function significantly lower than those with non scarred kidneys (45.5±6.3 vs 42.3±5.6, $P<0.05$).

110

Stepwise binary logistic regression analysis showed that the severity of VUR correlated significantly with renal scarring. Sex, gestational age and age at first UTI, US kidney ratio, US pelvis dilation, US ureter dilation and bladder anomaly categories, reflux grading and position, and scintigraphy confirmed function were excluded from the model. In our cohort of infants with first UTI, the severity of VUR could double the risk of renal damage (OR=1.998, 95% CI= 1.286-3.103, P=0.002).

Conclusion: Scintigraphy can predict severe VUR in infants showing renal

scarring. Follow-up renal scintigraphy 6 months after a UTI is able to screen infants with permanent renal damage due to a febrile UTI to detect those who are at risk of loss of kidney function and who would require long-term assessment. VCUG may be performed as second line investigation to detect infants with hidden high-grade VUR and worse prognoses. After the first episode of UTI, the practice of performing VCUG in infants with normal US and late DMSA scintigraphy is of doubtful value.

_____

_Notes

TRANSIENT HYPERPHOSPHATASEMIA IN PEDIATRIC RENAL TRANSPLANT PATIENTS – IS THERE A NEED FOR CONCERN?

Sylva Skálová1, 2**, Štěpán Kutílek**3, 4**, Jennifer Vethamuthu**2**, Janusz Feber**2**, Abdelbaset Aborawi**2**, Pavel Geier**2

1Department of Paediatrics, Charles University in Prague, Faculty of Medicine in Hradec Králové, Czech Republic; 2Division of Nephrology, Children´s Hospital of East Ontario (CHEO), Ottawa, Canada; 3Department of Paediatrics, Pardubice Hospital, Czech Republic; 4 Center for Clinical and Basic Research (CCBR), Pardubice, Czech Republic

Introduction: Transient hyperphosphatasemia (TH) of infancy and early childhood is characterized by transiently increased serum activity of alkaline phosphatase (S-ALP) in children mostly under 5 years of age. There are no signs of metabolic bone disease or hepatopathy corresponding with the increased S-ALP, nor there is a disease common to all children with TH. Similarly to TH, the transiently increased S-ALP can be observed in patients post kidney transplantation (Tx). The elevation of S-ALP is quite dramatic which raises significant caregiver‘s anxiety and dictates the need for an extensive work-up. The goal of the study was to analyze the prevalence, severity and natural course of TH post Tx.

Patients, methods: We performed a retrospective chart review of all Tx children currently followed in CHEO. TH was diagnosed in 4/28 children post Tx at the age of 2.7, 4.0, 7.0 and 3.4 years, respectively. TH occurred at 10, 26, 34 and 21 months (median = 24) after Tx. The S-ALP peaked to 6628, 6200, 2900 and 4378 IU/L (normal values 129–291 IU/L), and returned to normal levels after 150, 90, 60 and 60 days (median = 75), respectively. Further analysis of the S-ALP isoenzymes confirmed the elevation of the bone-specific S-ALP. In all cases, the elevation of S-ALP was not associated with any changes in serum parathyroid hormone, calcium and phosphate levels, liver and kidney function, and all patients remained asymptomatic and had normal wrist X-rays.

Conclusion: TH post Tx is a benign condition with spontaneous recovery within 3–4 months. Initial work-up (bloodwork and wrist X-ray) is recommended to rule out other conditions, but a more extensive work-up

(including bone biopsy) should be postponed and considered only if there is no spontaneous recovery.

ANNUAL 2008 REPORT ON RENAL REPLACEMENT THERAPY IN CHILDREN IN THE CZECH REPUBLIC

K. Vondrák1**, Z. Doležel**2**, J. Dušek**1**, P. Dvořák**1**, M. Hladík**3**, T. Seeman**1**, E. Šimková**1**, J. Štarha**2**, T. Zaoral**3**, J. Zieg**1**, J. Janda**1
1Dpt. of Pediatrics Univ. Hospital Prague-Motol; 22nd Dpt. of Pediatrics, Univ. Hospital Brno; 3Dpt. of Pediatric ICU, Univ. Hospital Ostrava, Czech Republic

2008 annual report on renal replacement therapy in children under19 years of age in the Czech Republic.

The aim of the annual report is to give medical (particularly pediatric) community data regarding the renal replacement therapy and to analyze them. On the annual report data collection participated all (3) Czech pediatric dialysis centers – Prague (Dpt. of Pediatrics, University Hospital Motol), Brno (2nd Dpt. of Pediatrics, University Hospital Brno) and Ostrava (Dpt. of Pediatric ICU, University Hospital Ostrava).

Results: 2008 incidence of chronic renal failure (CRF) in children in the Czech Republic (CZ): renal replacement therapy has been commenced in 18 children (0–19 years), similar number compared to 2007 year (19 children). PD as a first choice in 14, HD in 4 children. 3 neonates died due to renal failure based on congenital kidney anomaly. No pre-emptive transplantation has been introduced.

The prevalence (number of children surviving on any of RRT modality – dialysis or transplantation with functional graft) referred to the 31. 12. 2008: altogether 62 children under 19 years were identified as having CRF. Of these 14 were on peritoneal dialysis (PD), 4 children on hemodialysis (compared to 2007 data with 11 children on HD), 3 neonates died and 41 children after successful kidney transplantation (50 children in 2007).

Kidney transplantation in 2008 underwent 6 children. In all 6 children from cadaver donor, no one from living related donor.

The 2008 incidence of „new" pediatric patients under 19 years (population of 1,99 million) suffering from ESRD either requiring RRT or died was 10,5 pmarp (per million age related population) in the Czech Republic (CZ). The incidence of ESRD in the CZ reached for the second time an equal rate comparing to the ERA-EDTA data. The ERA-EDTA incidence of CRF has remained stabile (9,4–9,8 pmarp) for 10 years.

By the end of 2008 the prevalence of CRF in children under 19 years in the CZ was 31,2 pmarp with continuously increasing tendency. In 1999 the

113

prevalence of ESRD was "only" 19,5 pmarp, in 2004 26,5 pmarp, in 2007 exceptional 37,2, and recently 31,2 pmarp (tab. No.1).

The ERA-EDTA 2006 Annual Report reports the ESRD prevalence in children under 19 years 55,4 pmarp, in 1997 it was 59,3 pmarp and the

prevalence remains stabile as well as the ERA-EDTA incidence of ESRD as mentioned above.
One can speculate about the difference of the prevalence of ESRD in children in the CZ and ERA-EDTA Report. One of the possibilities could be a different attitude to the RRT initiation with respect to the ethically questionable patients. Current CZ ESRD incidence 10,5 pmarp gives the chance to equilibrate Czech and ERA-EDTA data on the prevalence of ESRD.
Conclusion: the 2008 incidence of ESRD in children in the CZ (10,5 pmarp) is equal to the incidence reported in ERA-EDTA Report. The prevalence of ESRD in the Czech pediatric population (31,2 pmarp) has a constantly increasing tendency. PD is the most common first choice modality of RRT in children with ESRD in the CZ. RRT is a generally reasonable method for the children with ESRD in the CZ. Dialysis is the modality to ensure successful kidney transplantation
** Supported by the Grant FNM 64203/6906*

Notes

NEPHROLOGICAL AND UROLOGICAL COMPLICATIONS IN KAWASAKI DISEASE

Josef Gut, Lenka Kocinová, Šárka Kučerová, Jaroslav Popelka
Department of Pediatrics, District Hospital Česká Lípa

Kawasaki disease (KD), first described in 1967, is one of the most common acute systemic vasculitis of unknown etiology in childhood. The diagnosis is purely clinical, based on six diagnostic criteria, predominantly fever, rash, swollen hands and feet, conjuctivitis, cervical lymphadenopathy, inflammation of the mouth and lips. The most serious and life- threatening pathology is the development of arteritis and aneurysmal dilatation of the coronary vessels. Inflammatory lesion can affect various organs including genitourinary tract in large spectrum of forms.
From point of nephrological view: Histological findings included significant renal vascular involvement (panarteritis of the interlobar and smaller arteries, arteriolitis, thrombarteritis), intersticial infiltration, mild mesangial expansion, various grade of tubular necrosis in some patients. Rare cases KD complicated HUS, acute renal failure, renovascular hypertension, nephrotic syndrome and interstitial nephritis were published. It is well known that sterile leucocyturia is very common findings during acute febrile period (30–80% of cases), hematuria and proteinuria are lesser frequent manifestations. Sterile leucocyturia is seldom the sole laboratory presentation of KD. On the other hand, when the patients present with fever and leucocyturia, the diagnosis of urinary tract infection (UTI) is usually in suspicion. Formerly sterile leucocyturia in KD considered to be due to uretritis, because spontaneously voided urine samples contain leucocytes whilst catheterised ones from the bladder does not. Study of Watanabe et al (2007) suggested that some

patients develop sterile leucocyturia that originates from urethra and/or from the kidney as a result of mild and subclinical renal pathology. Overall, the presence of leucocyturia was neither specific nor sensitive as a marker for KD. Recently Wang et al (2007) brought a quite new idea in the view on renal complication in KD. They examined DMSA scan in consecutive patients with KD in acute febrile phase and revealed that 52% of them had renal inflammatory foci. Although all patients were free of clinical symptoms, follow-up DMSA scan after 6 months suprisingly showed renal scarring in 46% of them with acute changes. There was no significant predictive value of clinical or laboratory parameters for renal involvement, except the presence of coronary lesions. Renal inflammation was not also significantly correlated with leucocyturia and erythrocyturia. Although hyponatremia frequently occurs in KD, the clinical characteristics of these patients remains undescribed. The etiology of hyponatremia has probably complex cause, but renal parenchymal involvement is also suggested.

From urological point of view: The first case of hydrocele during the course of KD was that described in 1990. Bilateral hydrocele can be proven by ultrasonography examination in children with scrotal edema. Hydrocele had to be added in the list of possible (but rare) signs associated with KD. Its etiology is unknown but it is usually present in context of large peripheral edema of hands and feet.

Above mentioned changes we demonstrate in the case 24 months old boy with fully blown clinical picture of KD. Isolated sterile leucocyturia in initial investigation suggested suspicion to UTI. Prominent peripheral edema occurred at 7th day of fever stadium concurrently with large scrotal and facial edema without signs of renal functional deterioration or nephrotic syndrome. Boy´s weight increased by 1 Kg. At this time an ectasia of left-side coronal artery was revealed and prompt intravenous application of gammaglobulins started. Fever and irritability diminished in 24 hours and then gradually edema disappeared. Coronal artery lumen normalised in the next 7 days period with concurrent peripheral hand skin desquamation. In the laboratory thrombocytosis (to 1 000 000/mm3) occurred and inflammatory markers diminished to normal level. Leucocyturia also disappeared.

We observed 10 patients with Kawasaki disease (5 girls and 5 boys) during period 2001–2009. We found in six of them sterile leucocyturia and in 2 children transient erythrocyturia and proteinuria without deterioration of renal function and elevation of blood pressure. Two children had transient coronary arterial dilatation and one boy had prominent edema and bilateral hydrocele.

References

1. Wang JN, Chiou YY et al: Renal scarring in childhood Kawasaki disease. Ped Nephrol. 22, 5,2007, 684–689.

2. Watanabe T et al: Sterile pyuria in patiens with Kawasaki disease originates from both the urethra and the kidney. Ped Nephrol. 22, 7, 2007, 987–991.

_Notes

CLINICAL QUIZ: ACUTE RENAL FAILURE AND HEPATOPATHY

T. Šuláková, D. Barnetová, P. Širůček1, A. Bosáková, J. Slaný, J. Tylečková *Department of Paediatrics, 1Department of Infectious Diseases, FN Ostrava*

15 yrs old boy, previously fit and well, no significant family and past medical history, was admitted to Infectious Diseases Unit with suspected neuroinfection. He presented with pyrexia (39 °C) and fatigue since 7th August. Was seen by his GP on 12th August and he was prescribed antipyretics since his CRP was low (8mg/l). He suffered from nausea and vomiting on the following day, had facial paraestesias and was unable to walk. He was referred and admitted to hospital with very likely neuroinfection. He was still pyrexial, had positive meningism signs and nasopharyngitis symptoms on admission. His lab results showed leucopenia (WBC 2,8 × 10 9/l), thrombocytopenia (Plts 45 × 10 6/l), mild coagulopathy, normal urea (6,5 umol/l), raised creatinine (123 umol/l), elevated ALT (10,7 ukat/l) and AST (12,28 ukat/l); proteinuria (3+), haematuria (1+), negative inflammatory markers (CRP-3,8 mg/l) and LP. Full septic screen was sent (including bacteriology, virology and hepatitis screen).

Based on the facts stated above a diagnosis to consider could be:

1. Acute viral hepatitis.
2. Acute tubulointerstitial nephritis.
3. Ehrlichiosis?

Considering the clinical status and laboratory results (negative hepatitis tests), our diagnosis was Ehrlichiosis, the patient was started on doxycycline. Despite antibiotics patient remained pyrexial (39 °C), fatigued, nauseous and vomited. On 17th August he was oliguric, his renal function tests elevated significantly (creatinin 388 umol/l, urea 22.8 umol/l), however improved LFTs and FBC (WCC 4,8 × 10 9/l Plts 90 × 10 6/l). In the view of decreased renal function, patient was consulted with renal unit and transferred there to prepare haemodialysis treatment. Consultant Microbiologist recommended to continue with doxycycline and send a sample for Leptospirosis.

Your next diagnostic steps would be:

1. Immunological tests and renal biopsy (renal failure of unknown origin and systemic symptoms).
2. Systematic detailed review of patient's history and complex microbiological test (to exclude zoonoses)?

The admission diagnosis to Paediatric renal unit was acute tubulointerstitial nephritis. Toxic etiology (drugs, fungi) was excluded. Detailed review of last days history revealed history of old shed demolition 2 weeks before first symptoms occurred. Sample to check for Letospirosis, Hantavirosis and others

zoonoses was sent. Renal biopsy was indicated as the cause of renal impairment was still unclear (histology showed acute tubular damage, significant interstitial oedema and diffuse medullary haemorrhage).

What diagnosis would you consider following the histology result?

1. Autoimmune disease.

2. Zoonosis.

Your final diagnosis would be:

1. Autoimmune tubulointerstitial nephritis and hepatitis.

2. Ehrlichiosis.

3. Haemorrhagic fever complicated with acute renal failure?

_Notes

ACTUAL PROBLEMS OF THE PEDIATRIC NEPHROLOGY AND UROLOGY

30th Jubilee Meeting of the Czech Working Group for Pediatric Nephrology and 20th Meeting of the Czech Section of the Pediatric Urology

Reviewer: Miloš Velemínský

Editors: Jan Janda, Radim Kočvara, Zdeněk Doležel

Published by: University of South Bohemia České Budějovice

Faculty of Health and Social Studies

1st Edition, May, 2009

Print Retisk, Prague

ISBN 978-80-7394-166-6