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Radionuclide Assessment of Urethral Urinary Transit in Children Having Obstructive Uropathies

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Congenital abnormalities, including obstructive uropathies, play a leading role among the causes of chronic renal failure in childhood. This article describes the modern capabilities of diagnostics of obstructive uropathy associated with the pathology of vesicoureteral junction in children. The article provides data on the advantages and disadvantages of different diagnostics methods, and emphasizes the need to choose a particular method while following strict indications and preferring less invasive and more informative methods to others. Being based on the results of their own studies, the authors have proved the high efficiency of the dynamic nefroscintigraphy for the assessment of urodynamics with obstructive uropathies of vesicoureteral reflux.
***Key words**: obstructive uropathy, megaureter, vesicoureteral reflux, dynamic nefroscintigraphy.*

The group of congenital obstructive uropathies is widely represented among the congenital urological diseases in children. According to recent data, the frequency range of these diseases varies from 1 to 5.4% of all pediatric population [1].

Obstructive uropathies are described in modern literature as a set of structural and functional changes in renal tissue, which develop due to the disruption of normal urine passage. At the same time the barriers for normal urine flow may be functional or organic in nature; they concentrate at the level of pyelocaliceal, pelvic, urethral, and vesico-ureteral segments or may be a consequence of bladder outlet obstruction. Such definition originated due to the expansion of knowledge about the mechanisms of kidney damage in obstructive uropathies, where urodynamic disorders play the largest role in their formation [2].

Disorders of fetal organogenesis, or sclerotic processes in vesico-ureteral segment, that develop postnatally, form the basis of obstructive uropathy development [3]. This leads to the obstruction formation of a functional or organic type. Obstruction can be complete or partial, to be one-or two-sided.

Forecast on obstructive uropathies treatment and quality of life of patients with this pathology is largely determined by the nature and severity of renal parenchymal lesions. Urinary tract infection in the form of cystitis, urethritis, and pyelonephritis often serves as the first evidence of obstructive uropathy. Urodynamics disorders, along with ineffective antibiotic therapy, contribute to long-term persistence of pathogenic bacteria and to the development of

microbic and inflammatory process with formation of kidney tissue multiple sclerosis and pyelocaliceal system deformation. Urinary tract infection is the first symptom of obstruction for more than 25% of children [4].

Severe cases of obstructive uropathies lead to patients' disability, as clearly presented urodynamic disorders lead to a drastic reduction or even loss of renal function with the formation of end-stage chronic kidney disease (CKD). Thus, according to M.S. Ignatova, a group of children with III, IV and V CKD mostly suffered from congenital kidney disease [5].

It was indicated in the works of R. Chevalier and S. Klahr, that obstructive uropathies are the major cause of development of chronic kidney disease in children, especially in infants and at early childhood. All these factors prove the social significance of the problem [6-8].

Pathology of vesico-ureteral segment causes obstructive uropathies, among which there are vesicoureteral reflux (VUR) and various forms of primary megaureter.

Currently, ultrasonography (USG) is widely used for the examination of urological patients. The method is relatively simple and not invasive. Extension of lower parts of ureter, renal pelvis and also calyces expansion along with a full bladder, as well as the expansion or size increase of pyelocaliceal system after urination are the signs of VUR, that can be seen during ultrasound of the urinary tract. Renal parenchymal disorder may be identified during kidneys ultrasound. Many authors believe ultrasound should be considered as a screening test for early diagnosis of VUR. However, it is relatively low sensitivity of this method and similar echographic picture of the high VUR degrees and various megaureter forms, that cast doubt on its suitability concerning this disease [9, 10].

The X-ray methods, such as excretory urography and voiding cystourethrography, are considered to be a «Gold standard» method of obstructive uropathy diagnosis.

X-ray cystography is the main method of VUR diagnosis and the differential diagnosis of various megaureter forms (refluxive and obstructive). Its main advantage is obtaining data on the structure of bladder, urethra and ureter anatomy [9, 11-13].

However, interpretation of data obtained is based solely on visual assessment of X-ray by a specialist, which reduces the reproducibility of study results [13]. In addition, in some cases, reflux lasts for less than a minute, which does not allow to identify the pathology, or diagnosis is formed if Xray-contrasting substances are detected in ureter. It is important to note that when Xray-contrasting substances of a low temperature are injected into the bladder, there can be determined a transient vesicoureteral reflux, which the patient does not have under normal conditions, that is a false-positive test result. This is due to the negative influence of low temperature solutions on the bladder and vesico-ureteral segment (similar to anticholinergic drugs) [14]. One should also note a significant radiation dose to the patient (2-4 mSv), which puts a constraint on the repeat study for a certain time period. All of the above caters for further search for new methods in the diagnosis of retrograde urine flow in the ureter [6, 15-17].

Excretory urography is included into in the complex examination of patients with obstructive uropathy along with the X-ray cystography. Children urologists often use a jet research version for the preservation of renal function. At the same time it is possible to achieve tight filling of pyelocaliceal system on one of the urograms [18].

Using excretory urography a specialist makes it possible to evaluate the structure of anatomical pyelocaliceal system, ureters and bladder. In addition, basing on the rate of Xray-contrasting substance excretion, one can get understanding of renal excretory function. However, excretory urography provides only an indirect view of the upper urinary tract urodynamics ("gap" of nefrophase does not undermine a necessary disorder of urine outflow from the upper urinary tract), and provides no information about the presence of retrograde urine flow from the bladder into the ureter [9]. Other deficiencies of this method are the need of intravenous injection of Xray-contrasting substance (invasiveness), the risk of allergic reactions, as well as the inability of usage on children with azotemia. According to several authors, complications and side effects, when using Xray-contrasting substance, was observed in approximately 25% of all cases [12, 18]. In modern conditions excretory urography can be replaced by magnetic resonance urography (which is a highly informative non-invasive method that does not require injection of the contrast).

Static nefroscintigraphy with Tc-99m-DMSA (dimerkaptosuktsinatatsetate) is used to determine the severity of nephrosclerosis processes on the basis of the detection of sites with a reduced radiopharmaceuticals accumulation during a complex examination of patients with obstructive uropathies [19-21]. The method relies on the use of radiopharmaceuticals that can join 99mTc. Such radiopharmaceuticals are evenly distributed in the functioning renal parenchyma. Removing them takes a few hours, which allows a specialist to visualize the renal parenchyma without imposing image of a collecting system. [22].

According to several authors, static nefroscintigraphy is the best method for nephrosclerosis determination [23]. Investigation of renal scarring detection efficiency by ultrasound and static nefroscintigraphy with Tc-99m-DMSA showed that the radionuclide method revealed umbilicus kidney in 35% of cases, while the results of the ultrasound pointed to the lack of organ damage. Gomes et al. (1994) showed that the sensitivity of excretory urography for diagnosis of sclerotic changes of the renal tissue in children with VUR comprised 60.2%, and 96.9% for radioisotope studies with DMSA.

Dynamic nefroscintigraphy is widely used in pediatric urological practice in addition to static scyntigraphy of the kidneys. The method is based on registration of the dynamics of the radioactivity in the kidney and blood after intravenous injection of the radiopharmaceutical (hippuran), and on computer processing of the images [24].

Ability to visualize the kidneys and upper urinary tract is the main advantage of this technique, allowing them to evaluate the anatomic and topographic condition and level of ureter obstruction or stenosis. In addition, the dynamic nefroscintigraphy provides the evidence of organ blood flow disorders. This method allows to determine the functional difference between the kidneys in 5% of cases, that is it identifies disorders, which are likely for early-stage disease.

However, the technique has several disadvantages. In particular, the results of the study get influenced by the degree of hydration, diuresis, and emotional condition of the patient.

It should be noted that the use of dynamic nefroscintigraphy along with diuretic load, as well as functional tests along with other types of research, should be limited to cases requiring a differential diagnosis:for example in patients with severe organic obstruction, such samples may lead to a non-occupied attack of renal colic or pyelonephritis exacerbation [25].

Thus, despite the variety of proposed methods for visualizing obstructive uropathies, the problem of diagnosis of these diseases remains outstanding. Today, none of the proposed

methods allow to evaluate ureter transit function, basing on objective indicators of urodynamics. In modern literature there is indicated a possibility of an objective assessment of urine movement along the upper urinary tract. To do this, the authors evaluated the rate of transit of radiopharmaceutical through ureters, using the method developed by them. However, studies were conducted on adult patients, and there is no data on the use of this method for children [26].

The aim of this study was to explore the possibilities of radionuclide method for assessing the upper urinary tract urodynamics in children having obstructive uropathies. To solve the abovementioned problem there were examined 82 patients (47 boys and 35 girls). Age of the surveyed varied from 3 months to 17 years 11 months

All patients included in the research work, were hospitalized in Urinary&Andrological Department of FSBI Child Health Research Center of RAMS on various forms of obstructive uropathy, namely, vesicoureteral I-IV degree reflux (according to the classification by P.E. Heikkel and K.V. Parkkulainen, 1966), obstructive megaureter, refluxing megaureter form (classification by Smith, 1977). All patients were examined before and after surgery.

A complex survey of children included laboratory research methods (clinical blood and urine tests, blood chemistry, urine culture for sterility) and instrumental research methods (sonography, voiding urethrography, excretory urography, the static and dynamic renal scintigraphy with nefroscintigraphy with voiding cystography). Complex urodynamic study was applied to all patients, while neurogenic bladder disorders were criteria for exclusion of a child from the study.

There was added in the standard protocol of dynamic nefroscintigraphy a definition of ureteral transit parameter (PMT) - an indicator of ureteral urine transit. The study was conducted for a child sitting or lying on their back. Zones of interest were on the upper and lower thirds of both ureters, the size of the zone of interest corresponded to approximately a third of ureter (Fig. 1). We used a matrix of 64 × 64 pixels. The duration of the serial frame was 5 s.

Data analysis consisted of constructing curves of "activity-time" with the zones of interest. Next, subtract the curve was carried out with the upper third of the ureter from the curve of the lower third, followed by the construction of the resulting graph (see Fig. 1).

This parameter characterizes the average range of ureteral transit under the integral mean value obtained during subtraction of the resulting curve. If ureteral transit is normal, then the quantity of “activity”, passing through the interest zone, should be approximately the same, while integral value should differ little from "0" or to be in the range of positive values because of the uneven background on the different segments of the ureter and the background "flare" from the bladder.

Thus, the parameters of ureteral transit through the upper and lower third of the ureter should be equal to or greater than 0. Negative values indicate a delay in urine outflow through the ureter.

All children under this survey were divided into four groups. It should be noted that party of defeat was considered the unit of study, so the number of children examined and the number of observations do not match.

The first group (n = 30, number of observations is 54) included children having urinary tract infection, who have not shown any urodynamic disorders of the upper urinary tract during a comprehensive survey.

This group was prescribed as a comparison group, and rates of ITP in these children have been set as a standard (average rate 0.58).

The second group (n = 10, the number of observations of 12) included patients with obstructive megaureter form.

The third group (n = 14, the number of observations 23) consisted of children hospitalized with refluxing megaureter form.

The fourth group comprised of patients with the I-IV degree of vesicoureteral reflux. There were developed two subgroups: patients with VUR of I-III degree (n = 45, number of observations is 70) and children with VUR of IV degree (n = 13, the number of observations 19).

All children with obstructive uropathies were examined before surgery and 6 months after it.

Indexes of inflammatory activity and biochemical indexes of renal function were evaluated in groups throughout all scientific working process. According to the imaging techniques (ultrasound, X-ray and radionuclide techniques) there was assessed the state of renal tissue and renal blood flow states. Also there was analyzed the severity of urodynamic disorders of the upper urinary tract (the degree of collecting system and ureter expansion, reduction of radiolabel excretion, retrograde urine flow into the ureters, diffuse changes in renal tissue, impaired intra-and extrarenal outflow RFID). During dynamic nefroscintigraphy UTP (ureteral transit parameter) was determined for all children. Surgical correction of obstructive uropathy was carried out by endoluminal surgery methods (endoscopic correction of the TMR, and the balloonage and bougienage of vesicoureteral anastomosis with obstructive megaureter), and by means of the open surgery. Ureter neoimplantation into the bladder was carried out according to the method of Cohen and Politan-Leadbettera.

During obtained data analysis it was found that the most evident urodynamic disorders were determined in patients with obstructive megaureter form (Fig. 2). Children being up to surgery had the mean value of -14.8 UTP in this group. By the first follow-up examination (6 months after surgery) there has place a maximum recovery of ureters transit functions, which indicated by the mean value of UTP after surgery (-1.1).

In the group of children with a refluxing megaureter form, urodynamics disorders were less evident; however, they still indicate a significant ureter transit functions disorder. Hence, the average rate of ureteral transit before surgery was -12.45. After surgical correction, recovery of transit ureter is much slower than in patients having obstructive megaureter form. Children had the mean value of UTP equal to - 7.45 at the first follow-up examination.

Patients having I-III degree VUR had an average preoperative value of the parameter under study at the level of -4.74, which indicates the least urodynamics disorder. It should be noted that surgical treatment of VUR, samely as for refluxing megaureter, leads to the long-term restoration of ureter transit functions. After surgery, the average value of the ureteral transit parameter was equal to -3.5, which is the rate of urine passage to the ureter increased by less than 2 times.

In the subgroup of children having IV degree VUR, ureteral transit function severity was comparable to that of refluxing megaureter form. The average value of the ureteral transit index before surgery was -11.15 and after surgery it was - 7.25. Thus, the duration of urodynamics

recovery with VUR of the IV degree is similar to that of other reflux degrees (change by less than 2 times, see Fig. 2).

In addition, upon the data analysis there has been received no reliable statistical relationship ($p > 0.05$) between ureteral transit parameter and chronic obstructive pyelonephritis course (clinical and laboratory remission, recurrent or latent course).

According to the analysis performed, the following conclusions can be made:

1. Radionuclide techniques are highly informative for obstructive uropathies diagnosis.
2. Ureteral transit parameter (UTP) is a sensitive parameter, that does not depend on the clinical inflammation course type in the kidney parenchyma. UTP characterizes the rate of urine passage through the ureter, basing on objective urodynamics measures, and can be used in the diagnosis of obstructive uropathies, caused by vesicoureteral segment pathologies.
3. The most evident disorders of the upper urinary tract urodynamics were observed in patients with obstructive megaureter form, while patients with VUR of the I-III degrees have the smallest decrease of ureteral transit function.
4. The most evident effect of the effected surgical treatment can be seen in patients with obstructive megaureter form.
5. UTP indicates the longest recovery of urodynamics after surgical treatment in children with refluxing megaureter form.

Finally, it is important to note that use of UTP allows to perform an objective assessment of upper urinary tract urodynamics for patients having a pathology of vesicoureteral junction, and that UTP plays an important role in assessing and optimizing the results of surgical correction of obstructive uropathy.

Fig. A. The scheme of resulting curve formation in the assessment of ureteral transit indicators

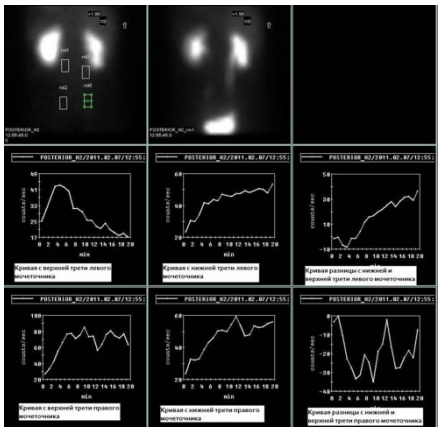
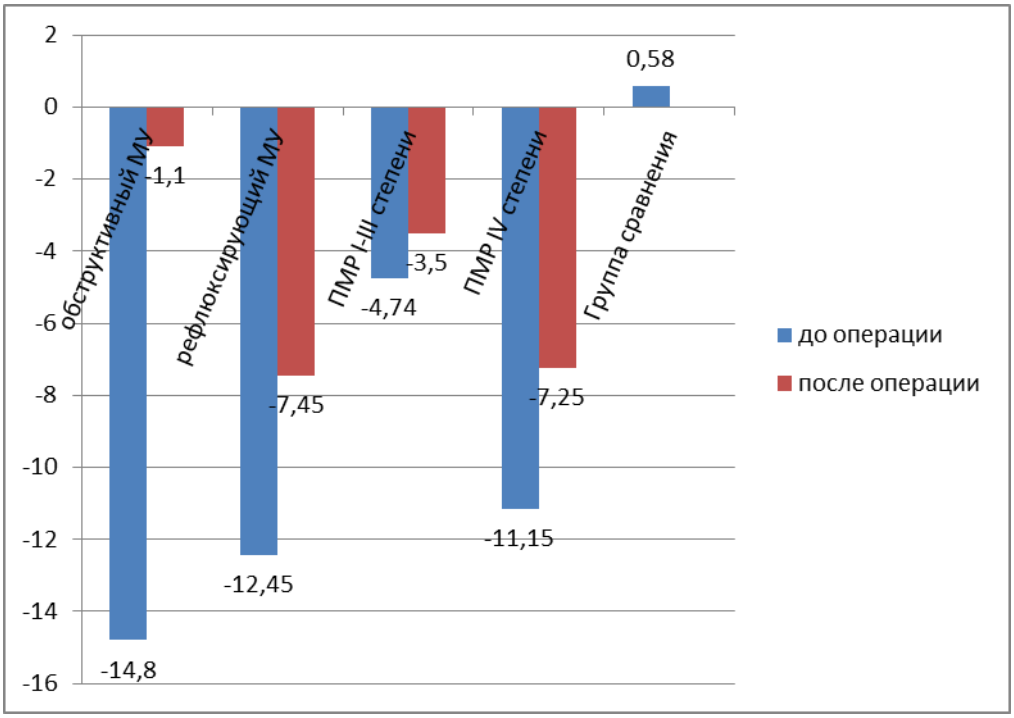


Fig. Two. The dynamics parameters of ureteral transit before and after surgical treatment in children with megaureter and vesicoureteral reflux (VUR), p <0,05 in the Figure



Note: **обструктивный МУ –** obstructive MU**; рефликсирующий МУ –** reflux MU
ПМР I-III степени – I-III degree VUR**; ПМР IV степени –** IV degree VUR
Группа сравнения– comparison group; **до операции** – before surgery**;** после операции – after surgery

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