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Original scientific paper

The Evolvement of the Renographic Curve Pattern in Early Childhood

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A B S T R A C T

The purpose of this study was to evaluate renographic parameters obtained from healthy renal units (RUs) in newborns and infants with unilateral kidney condition. Thirty three children including twenty newborns, referred to Technetium-99m mercaptoacetyltriglycine (Tc-99m MAG3) diuretic scintigraphy due to unilateral kidney condition entered the study. Only contralateral, healthy RUs were analyzed. Since many children returned for follow up, there were altogether 78 dynamic studies included. Kidney length was compared to ultrasound measurements. Renographic curve parameters (time to maximum counts, T max and time to half maximum counts, T½ max) were evaluated. The results showed that the kidney length measured on Tc-99m MAG3 scintigraphy correlated well with ultrasound measurements. Regarding the renographic curve parameters, in the newborn period a significantly shorter T max (mean T max 3.65±1.2 min, p=0.026) was found compared to the group of two months old infants (5.12±2.2 min). In older age groups mean T max gradually shortened again. On the contrary, T½ max was significantly longer in newborn and early infant period than in older age groups (16.7±8.2 min, p=0.018), but generally showed variable values until the age of three years. It can be concluded that it is important to be aware of possible diversities of renographic curve pattern of healthy kidneys in early childhood, especially in the elimination part. Therefore, when interpreting a dynamic renal study, one should also consider other parameters like kidney growth, morphology and differential function, which can be reliably monitored with repeated Tc-99m MAG3 scintigraphy, to discern between normal and pathologic finding.

***Key words**: kidney, radionuclides, Tc-99m MAG3, diuretic scintigraphy, newborns*

Introduction

Tc-99m MAG3 diuretic scintigraphy is a well established diagnostic tool in pediatric nephrourology, predominantly used in the evaluation of prenatally diagnosed hydronephroses. It has considerable advantages over other diagnostic methods since it is not invasive and gives the possibility to assess a number of parameters with one study[1]. Among them, differential kidney function and drainage pattern are considered most important[2,3]. When decisions in clinical setting have to be taken, especially when operative treatment is planned, the information obtained from the renogram, particularly after diuretic challenge is frequently considered crucial. Therefore, different parameters are introduced in order to make interpretation of the renogram more reliable[4]. Also, efforts have been made to improve inter-observer reproducibility in interpreting renal drainage[5,6]. However, the concept of obstruction appears progressively to be difficult to define, except when dealing with total obstruction[7].

Moreover, changes can be also noted in healthy kidneys, or at least clinically assumed normal, especially in the early age. Although without real drainage impairment, in such kidneys considerable variations of renographic curve pattern can be observed, particularly in the newborn period. These can sometimes be difficult to differentiate from real pathological finding, especially because data on how renographic curves should look like and what are the normal parameters for this age group are lacking. To our knowledge, only one study addressing

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this problem can be found[8]. Therefore, the aim of our study was to evaluate renographic parameters obtained from contralateral, normal renal units in newborns and their evolvement until the age of 3 years and beyond.

Patients and Methods

Patients

Thirty three children (9 girls, 24 boys), including twenty newborns (mean age 28 days; range 7–62 days), referred to dynamic scintigraphy due to mild unilateral kidney condition (pyelon fissus, double or slightly dilated collecting system), entered the study. In this prospective study, only contralateral, healthy renal units (RUs) were included. The inclusion criteria were: no clinical and laboratory signs of urinary tract infection at the time of scintigraphy (normal parameters from blood and urine samples), all examined RUs without signs of dilatation or other pathology – hence sonographically normal, without parenchymal lesions in parenchymal phase image of Tc-99m MAG3 study[9]. Serum urea and creatinine levels as a global kidney function indicators were normal in all participants. Differential kidney function values in all examined RUs have not superated 55%, which implied well preserved function of the diseased kidney.

Twenty four children returned for follow up, 13 of them up to five times. Altogether, there were 78 dynamic studies, or a total of 78 healthy RUs included, grouped according to age at the time of scintigraphy in 6 groups: newborns, 7–28 days (N= 20); 29–60 days (N=13); 2–12 months (N=17); 13–24 months (N=11); 25–36 months (N=11) and 4–6 years (N=6). Each child has had kidney ultrasound examination performed 1–3 days prior to scintigraphy.

Methods

Tc-99m MAG3 diuretic scintigraphy was performed according to the standard European Association of Nuclear Medicine (EANM) protocol[10] modified only for the time of diuretic application. There were no intravenous fluids for prehydration used, but oral fluid intake was encouraged on the day of study. Newborns and infants were offered additional bottle or breastfeed, while older children were ecouraged to drink liberally water or fruit juice. There were neither salt nor water depleted at the time of the renogram.

Newborns and children, whose body weight did not exceed 6 kg, were positioned directly on the detector surface (Siemens Orbiter and Diacam single head cameras). Zoom 1.5 or 2 was applied according to the size of the child laying supine with the kidneys and bladder in the field of view. Dynamic acquisition was acquired in a 128x128 and byte mode matrix for 90 frames, 30 seconds per frame, with total study duration of 45 min. The application of diuretic, when necessary, was postponed to the 30th minute (F+30), which is the standard procedure in the authors' department.

After motion correction, kidney regions of interest were drawn and split function with and without background subtraction calculated using uptake ratio method with one large region between kidneys. Kidney length was measured in the »line profile« application from ICON renal package program, as number of pixels from upper to the lower pole contours, multiplying with the camera calibration factor.

Renographic curves were constructed and time from zero to maximum counts (Tmax) and time from Tmax to half of the maximum counts (T½ max; reflecting the elimination rate) were determined. These parameters, including kidney length, were analyzed for different age groups and statistically evaluated. In all healthy observed units, sum of Tmax and T½ max was shorter than 30 minutes; therefore any possible influence of the furosemide application on the drainage could be neglected.

Kidney length data obtained from ultrasound were available for only 54 RUs, therefore only these were included in comparisons with scintigraphy and statistically analyzed.

This study was approved by the ethical committee of the School of Medicine, Rijeka, and University Hospital Centre Rijeka. All parents have signed consent for the tests undertaken during the child's stay in the hospital.

Statistical analysis

Statistical analysis was performed using Statistica for windows, release 8.1 (Stasoft, Inc., Tulsa, OK, USA). The normal distributions of Time to maximum, Time to half-maximum and kidney length were checked by Kolmogorov Smirnov test with Lillieforse correction. Data are presented as a mean and standard deviation (SD). To test the differences of the time to maximum counts, time to half-maximum and of the kidney length between the age groups, one way analysis of variance (one-way ANOVA) was used. For post hoc analyses Tukeys' test was used. The regression analysis was done using linear reggresion equation and Pearsons' coefficient of correlation.

All statistical values were considered significant at the p level of <0.05.

Results

Time to maximum counts (Tmax) and age

For the group of newborns Tmax was 3.65±1.2 min and was significantly shorter (P=0.026) than in the second month of life (5.12±2.2 min). In the older age groups (by the end of the first, second year and after) mean Tmax was significantly shorter compared to the second month of life (all $p<0.05$).

The calculated means for Tmax were significantly different between all groups (p=0.040) (Figure 1).

The correlation coefficient between Tmax and age was negative, meaning that Tmax shortens with age (r=–0.254; p=0.015.; Figure 2).

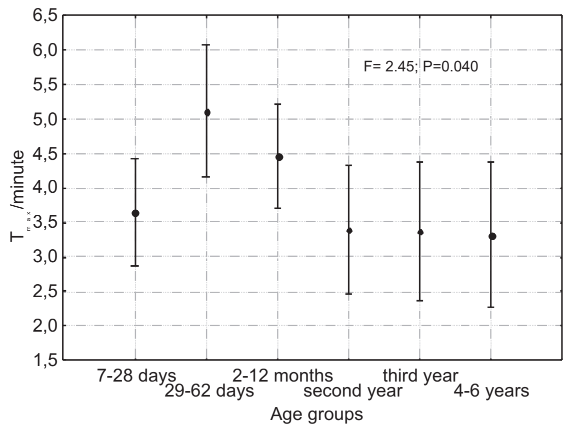

Fig. 1. Values of Tmax (min) in different age groups ($\overline{X}$±SD).

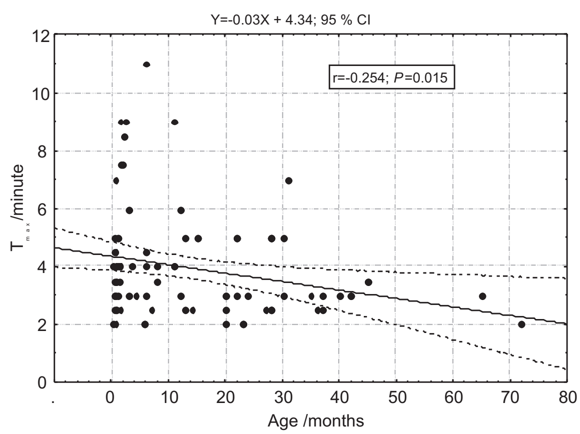

Fig. 2. Correlation between Tmax and age.

Time to half-maximum counts (T½ max) and age

The mean T½ max was calculated for each age group, showing great variability of results. In the group of newborns mean T½ max was 16.7±8.2 min, which is longer than in the following three age groups (15.2±6.7, 9.9±5.5, 9.2±4.8 min, respectively) (Figure 3).

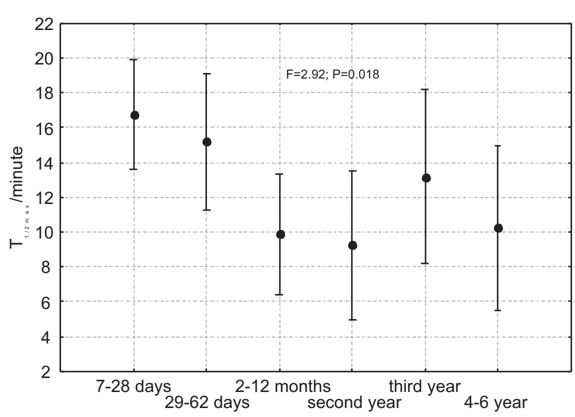

Fig. 3. Values of T½ max (min) in different age groups ($\overline{X}$±SD).

In the Figure 4 the correlation between time to half maximum counts (T½ max) and age is showed: T½ max shortens with age (r=–0.286; p=0.011).

Kidney length and age

The mean kidney length was measured for each age group. The mean kidney length does not change significantly between the first and the second month of age (p=0.971). The change is also not significant after the third year (p=0.996). In the age groups between second month and third year, kidney length significantly increases (p<0.001) (Figure 5).

In the Figure 6 the positive correlation (r=0.892) between kidney length and age is showed.

The expected kidney length for the child of the particular age can be calculated from the graph using the above linear regression equation (Figure 6). For example, for two months old infant, the expected kidney length on scintigraphy would be 0.78x2+4.88=6.4 cm.

Comparison of kidney length measured on scintigraphy and ultrasound

Kidney length measured on scintigraphy and ultrasound correlates with high significance. There were no

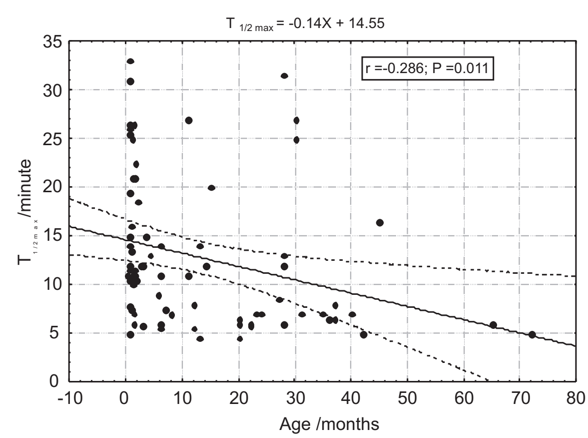

Fig. 4. Correlation between mean T½ max and age.

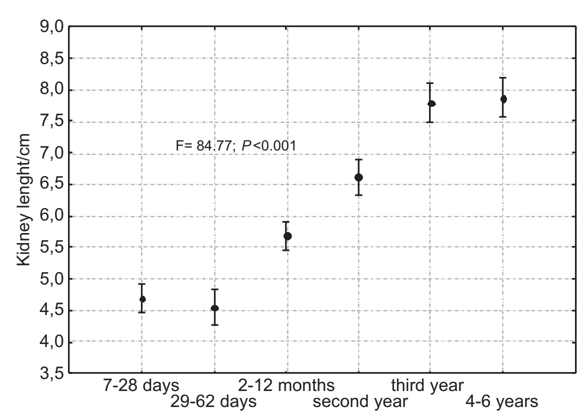

Fig. 5. Kidney length measured on MAG3 scintigraphy and age ($\overline{X}$±SD).

TABLE 1
KIDNEY LENGTH DETERMINED ON PARENCHYMAL PHASE OF MAG3 SCINTIGRAPHY AND ULTRASOUND

Age	Scintigraphy (cm) N=78		Ultrasound (cm) N=54		Statistics
	N	$\overline{X}$±SD	N	$\overline{X}$±SD	p
7–28 days	20	4.7±0.5	12	4.6±0.7	0.999
29–62 days	13	4.6±0.5	9	5.1±0.5	0.734
2–12 months	17	5.7±0.5	12	5.9±0.4	0.932
Second year	11	6.5±0.6	9	6.3±0.5	0.969
Third year	8	7.8±0.6	6	7.4±0.6	0.851
4–6 years	9	7.9±0.5	6	7.4±0.5	0.726

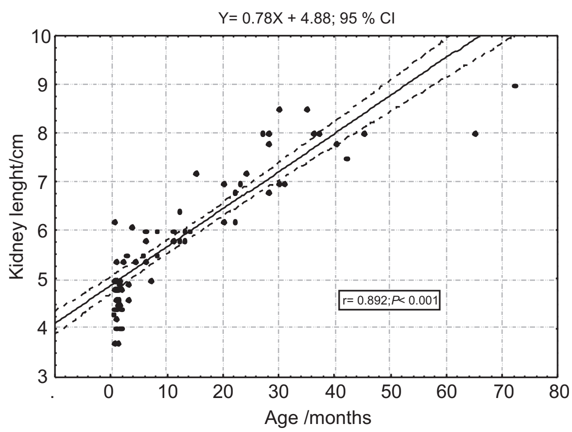

Fig. 6. Correlation between kidney length (cm) measured on scintigraphy and age (months).

statistically significant differences found between kidney length measured on scintigraphy and ultrasound in all age groups (all p>0.05) (Table 1).

Discussion

In this study, characteristics of the renographic curve parameters (T max, T½ max), observed in healthy kidneys, were analyzed. In newborns a significantly shorter mean T max and significantly longer T½ max were found than in the subsequent period. During second month of life, a transitory prolongation of T max was found, but after that it is gradually reaching adult values by the age of three years. T½ max in the early childhood is also variable but with a steady shortening trend by the age of three years.

We have also showed that kidney length can be reliably determined on the parenchymal phase image of Tc-99m MAG3 scintigraphy and it correlates with ultrasound measurements with high significance. Therefore, kidney growth can be monitored with repeated scintigraphy.

Our study was limited with relatively small number of patients in particular age groups. Although a satisfying number of MAG3 renograms was included, the result of transitory prolongation of Tmax for the second age group, which could not be explained with physiological factors, can be due to the above reason. Therefore, a larger patient group to confirm this finding should be included.

Although diuretic renography plays a mayor role in a workup of children with hydronephrosis, different opinions still exist on how to perform the exam, when to apply furosemide ((F–15, F+0, or F+20) and how to interpret the renographic curve, especially after the diuretic application[7]. Basically, one can rely on the diuretic response to discern between normal and obstructed finding. However, the interpretation of diuretic renogram is not always straightforward; it demands considerable experience and knowledge on the child's history and control over some external factors, like fluid intake. Some physiologic characteristics of newborn period also have to be taken into account. It has been demonstrated that even in the absence of hydronephrosis, physiologic dimensions of fetal renal collecting system are variable[11], even dependent on maternal hydration state[12]. Also, it is only at the very end of embryonal development period when a full canalisation of urether takes place, while maturation of it's walls continues well after the birth[13,14]. The embrional development disorders such as postponed maturation and canalisation of urether can cause transient drainage disturbances. Therefore, all these factors, together with a poor hydration of the child, could have impact on the renographic curve pattern of the healthy kidney.

Contralateral hydronephrosis is also frequently alluded to have impact on the drainage of the healthy kidney, but this thesis has not been proved so far. Therefore, many reasons for uncommon appearance of the newborn and infant renographic curve can be present and should not be interpreted as pathological. Indeed, successive dynamic scintigraphies show evolvement towards normalization, mostly by the age of three years (Figure 7).

Therefore, we recommend interpretation of renographic curve parameters only in conjunction with other data including the status of the parenchyma[9], kidney dimensions (growth) and differential function rather than to conclude on the kidney status solely from the curve appearance and diuretic response.

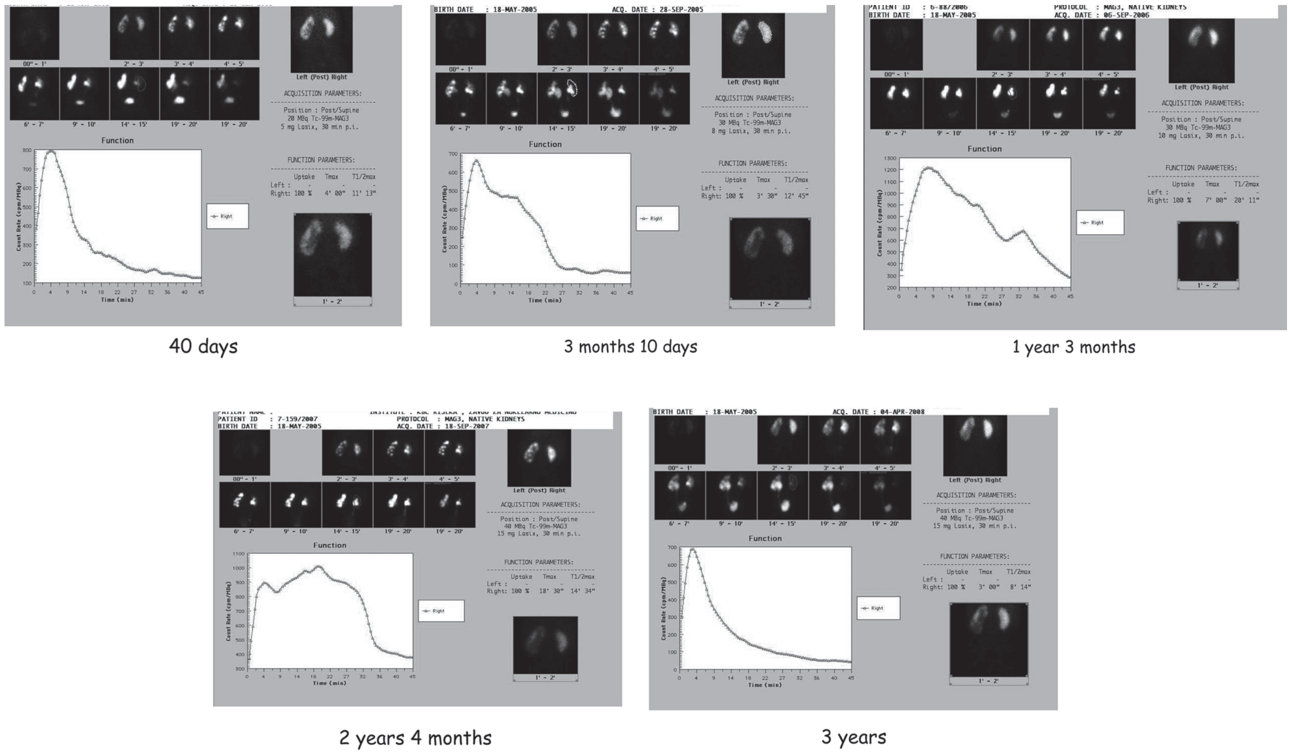

Fig. 7. Example of the evolvement of the renographic curve pattern of the healthy kidney on follow up in the same child from 40th day after birth until the third year of age.

Conclusions

Renographic curve parameters (T max, T½ max) obtained from healthy kidneys in newborn and early infant period are longer and more variable than in older age groups.

Generally, a »shrinking« trend for the whole renographic curve with age is present, but typical appearance in the majority of cases is not achieved earlier than three years of age.

Kidney length can be measured on the parenchymal phase of scintigraphy with Tc-99m MAG3; given the significant correlation with sonographic values, we can conclude that kidney growth can be reliably monitored with successive dynamic scintigraphies.

Therefore, when interpreting a renogram in the early age, one should also consider other parameters such as kidney growth, appearance of the parenchyma and split function in order to discern between normal and real pathological finding.

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RAZVOJ OBRASCA RENOGRAFSKE KRIVULJE U RANOM DJETINJSTVU

S A Ž E T A K

Cilj rada je bio procijeniti parametre renografske krivulje zdravi bubrežnih jedinica kod novorođenčadi i male djece s unilateralnom bubrežnom bolesti. U studiju je bilo uključeno trideset troje djece, uključujući dvadesetero novorođenčadi, upućenih na diuretsku scintigrafiju bubrega s Tc-99m metkaptoacetiltriglicinom (Tc-99m MAG3) zbog bolesti jednog bubrega. Ispitivane su samo zdrave bubrežne jedinice. Obzirom da je većina ispitanika dolazila na kontrolne scintigrafije, ukupno je analizirano 78 dinamičkih studija. Duljina bubrega dobivena scintigrafskom metodom uspoređena je s ultrazvučnim mjerenjem. Evaluirani su i parametri renografske krivulje, vrijeme do maksimalnog broja impulsa, Tmax i vrijeme potrebno da od časa Tmax broj impulsa padne na polovicu, T½ max. Rezultati su pokazali da je duljina bubrega mjerena scintigrafijom s Tc-99m MAG3 u visokoj korelaciji s ultrazvučnim mjerenjima. U novorođenačkoj dobi je Tmax značajno kraći (3,65±1,2 min, p=0,026) no u slijedećoj dobnoj skupini dojenčadi dva mjeseca starosti (5,12±2,2 min). U starijim dobnim skupinama Tmax se postupno skraćuje. Nasuprot tome, T½ max je u novorođenačkoj i dojenačkoj dobi znatno dulji no u ostalim dobnim skupinama (16,7±8,2 min, p=0,018), ali su vrijednosti varijabilne do treće godine života. Važno je poznavati varijabilnost obrasca renografske krivulje zdravih bubrega u ranom djetinjstvu, a posebno eliminacijskog segmenta. Stoga, da bi se lakše diferencirao uredan od patološkog nalaza, osim renografske krivulje, uvijek treba uzeti u obzir i druge parametre kao što su rast bubrega, izgled parenhima i vrijednost diferencijalne funkcije, koji se mogu pouzdano pratiti kontrolnim Tc-99m MAG3 scintigrafijama.