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Original Article

Role of renal dynamic imaging in evaluation of impairment of renal function in pediatric congenital hydronephrosis

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Abstract: Objective: Congenital hydronephrosis is a common prenatally diagnosed anomaly associated with an incidence of approximately 0.5-1% in newborns. The purpose of this study was to clarify the value of 99 m diethylenetriamine pentaacetic acid (^{99m}Tc-DTPA) in the assessment of renal function impairment of pediatric hydronephrosis. Methods: A total of 48 children with unilateral ureteropelvic junction obstruction were enrolled and subjected to ^{99m}Tc-DTPA diuretic renography examination. The glomerular filtration rate (GFR), renal blood perfusion rate (BPR) and peak uptake rate (PUR) were quantitatively analyzed with the aid of renal dynamic imaging system. The blood urea nitrogen (BUN), serum creatinine (Scr) and hemoglobin (Hb) in each patient were also measured. Correlation analysis was used to evaluate the relationship of GFR, BPR, PUR with BUN, Scr and Hb. Results: Diuretic renography results showed that GFR, BPR and PUR in children with hydronephrosis were gradually reduced with the aggravation of the hydronephrosis. The BUN and Scr were negatively, but the Hb was positively relevant with the GFR, BPR and PUR in children with severe hydronephrosis. The GFR, BPR and PUR in children with mild or moderate hydronephrosis were negatively related with Scr. Conclusion: Diuretic renography with ^{99m}Tc-DTPA may effectively reflect the degree of hydronephrosis and impairment of renal function, and may be employed as an ancillary diagnostic tool for pediatric congenital hydronephrosis. It is also used for evaluation of improvement in renal function after operation.

Keywords: Hydronephrosis, renal function, diuretic renography, ^{99m}Tc-DTPA renal dynamic imaging

Introduction

The obstruction of the urinary tract can lead to kidney failure and infant death in the newborns, as well as chronic kidney disease and early heart disease in adolescence and adulthood [1]. The obstructive diseases of the urinary tract contribute to end-stage kidney disease in most cases and exert a big burden on public health all world round [2]. The obstructive urinary tract lesions lead to varying degrees of hydronephrosis, renal atrophy and renal functional impairment [3]. The congenital hydronephrosis is one of the most identified anomalies detected on antenatal ultrasound scan. The underlying etiology of congenital hydronephrosis remains elusive [4]. The unilateral ureteropelvic junction obstruction is considered as one of the most common prenatally detected diseases associated with hydronephrosis [5]. It is accepted that early detection of unilateral ureteropelvic junction obstruction are critical and feasible strategies with long-term benefits to the patients and society. The prenatal ultrasound became widely available in the 1980s and was recognized as a necessary tool for evaluation of the urinary tract obstruction in recent years [6].

The renal ultrasound is intensively used for detection antenatal hydronephrosis in infants due to its low risk, availability and the absence of radiation exposure [7]. However, the ultrasound quality hinges on the status of patient hydration or operator experience, which substantially limited the separate application of ultrasound [8]. The ^{99m}Tc-DTPA renal dynamic imaging system is increasing popular in the evaluation of congenital hydronephrosis and treated as the gold standard for renal function

Table 1. Clinicopathologic characteristics of the patients

Characteristic	Healthy controls (n=13)	Hydronephrosis (n=48)	χ^2, t/*P*
Gender			
Male (%)	9 (69.2%)	28 (58.3%)	0.059/0.476
Female (%)	4 (30.8%)	20 (41.7%)	
Age (months)	27±12	27±9	0.942/0.127
Ethnicity			
Han (%)	8 (88.9%)	45 (93.8%)	0.274/0.600
Minorities (%)	1 (11.1%)	3 (6.2%)	
Family religious			
Yes (%)	6 (66.7%)	33 (68.8%)	0.015/0.902
No (%)	3 (33.3)	15 (31.2)	
Family economic status			
Poor (%)	2 (22.2%)	9 (18.8%)	0.070/0.966
Fair (%)	6 (66.7%)	34 (70.8%)	
Good (%)	1 (11.1%)	5 (10.4%)	

Note: All values are expressed as mean ± SD or percentage. The data in baseline patient characteristics between groups were compared with χ^2 test or paired-T test.

assessment in clinical practice [9, 10]. However, the relationship between clinical biochemical indexes and renal function parameters evaluated by ^{99m}Tc-DTPA renal dynamic imaging inpatients with congenital hydronephrosis are largely unknown.

The present study was designed to explore the relationship between the haematological indexes in congenital hydronephrosis caused by ureteropelvic junction obstruction and different parameters of renal function impairment measured by ^{99m}Tc-DTPA.

Patients and methods

Ethics statement

The approval of this study protocol was received from the Ethics Committee of the affiliated hospital of Nantong University and the institutional review board. The written informed consent was provided from parents of the children. The study procedures complied with the guidelines and regulations provided by the affiliated hospital of Nantong University.

Participants

We retrospectively collected the medical records of 48 pediatric patients with unilateral ureteropelvic junction obstruction between November 2006 and December 2012. Inclusion criteria was shown as follows: (1) all children had a prenatal diagnosis of unilateral hydronephrosis during routine fetal ultrasound and the unilateral hydronephrosis was reconfirmed with a postnatal examination including ultrasound or intravenous renal pelvis radiography; (2) there was no abnormal morphology and function of the contralateral kidney. The patients with ureterovesical junction obstruction, posterior urethral valves obstruction, vesicoureteral reflux, bilateral hydronephrosis and previous operation on the urinary system were excluded from this study. Renal dynamic imaging of ^{99m}Tc-DTPA was performed on all children initially before pyeloplasty. Of the patients, 28 were boys (28±12 months old) and 20 girls (27±11 months old). The children's average age at the time of surgery was 27 months. The left kidney was affected in 22 patients and the right kidney in 26. Renal controls images with ^{99m}Tc-DTPA were obtained from 13 children (9 boys and 4 girls, average age: 27±9 months), who underwent nephrectomy for nephroblastoma and the histological results were normal. The clinicopathologic characteristics of the patients were shown in **Table 1**.

^{99m}Tc-DTPA renal dynamic imaging

The unilateral ureteropelvic junction obstruction was confirmed by ^{99m}Tc-DTPA as previously described [11]. All children were given a single bolus injection of ^{99m}Tc-DTPA (Technescan DTPA; Mallinckrodt Medical, Hazelwood, MO, USA) intravenously at a dose of 5 MBq/kg for body weight lower than 20 kg and 4 MBq/kg for body weight excess of 20 kg. The syringe was then flushed and the subsequent 20-minute images were collected using a gamma camera equipped with high-resolution collimators (HawKeye VG5 SPECT/CT, GE, USA). The digital data were obtained with each second for the first minute and then at a 15-second frame rate. The digital images were stored in a 64×64

Table 2. Laboratory renal function parameters in pediatric hydronephrosis

	n	BUN (mmol/L)	Scr (μmol/L)	Hb (g/L)
Healthy controls	16	3.84±1.21	53.81±6.78	130.24±24.52
Mild hydronephrosis	25	3.98±1.16	59.26±6.17	117.84±18.58
Moderate hydronephrosis	14	4.29±1.87*	73.54±7.93*	102.55±13.16*
Severe hydronephrosis	9	9.15±2.31*,†	117.8±13.45*,†	88.95±10.43*,†
F		5.584	9.138	4.174
P		0.008	0.000	0.013

Note: All values are expressed as mean ± SD. Blood urea nitrogen, BUN; serum creatinine, Scr; hemoglobin, Hb. One-way ANOVA was used to compare the differences in Healthy controls, Mild hydronephrosis, Moderate hydronephrosis and Severe hydronephrosis groups, and the comparisons between two groups were analyzed by One-way ANOVA post hoc Bonferroni test. *P < 0.05 compared to Healthy controls, †P < 0.05 compared to Mild hydronephrosis.

Table 3. Diuretic renography parameters in pediatric hydronephrosis

	n	GFR (ml/min)	BPR (%)	PUR (%)
Healthy controls	16	50.59±8.75	49.62±11.23	52.7±13.17
Mild hydronephrosis	25	48.33±7.92	43.67±12.19	47.82±11.52
Moderate hydronephrosis	14	34.56±7.18*	34.61±10.47*	40.17±9.44*
Severe hydronephrosis	9	28.74±6.25*,†	20.92±7.18*,†	23.58±6.84*,†
F		11.242	3.115	4.195
P		0.000	0.021	0.012

Note: All values are expressed as mean ± SD. Glomerular filtration rate, GFR; renal blood perfusion rate, BPR; peak uptake rate, PUR. One-way ANOVA was used to compare the differences in Healthy controls, Mild hydronephrosis, Moderate hydronephrosis and Severe hydronephrosis groups, and the comparisons between two groups were analyzed by One-way ANOVA post hoc Bonferroni test. *P < 0.05 compared to Healthy controls, †P < 0.05 compared to Mild hydronephrosis.

pixel matrix. The original data, the dynamic image of the kidney, renal artery perfusion curve, glomerular filtration rate (GFR), renal blood perfusion rate (BPR) and peak uptake rate (PUR) were measured with the Gates method and corrected for surface area. In addition, the assessment for renal function impairment (RFI) was determined with shape of the time activity curve (TAC) and time of peak (TOP) in ^{99m}Tc-DTPA renal dynamic imaging. The patients were divided into the mild hydronephrosis; moderate hydronephrosis or severe hydronephrosis based on the RFI value according to the previous report [12].

Laboratory measurements

Laboratory parameters including serum BUN, Scr and Hb were determined in each patient within 2 days on admission for evaluating renal disease. The venous blood samples were centrifuged at 4,000 rpm for 10 min and stored at -80°C until analysis. Both blood Scr and BUN were analyzed using an enzymatic method [13, 14].

Statistical analyses

Data were expressed as mean ± SD or percentage. Statistical analysis was conducted by using SPSS 17.0 (SPSS Inc., Chicago, IL, USA). The Kolmogorov-Smirnov test was used to check the data distribution normality. Comparisons between two groups were made by Student's t test. The test for categorical variables was made by chi-square test, and the small cell variables were compared by Fisher's exact test. One-way ANOVA followed by post hoc Bonferroni test was used when multiple comparisons were made. The correlation of GFR, BPR and PUR with the clinicopathological variables of the patients was assessed using Spearman's rank correlation test. A value of $P < 0.05$ was considered as statistically significant.

Results

Laboratory renal function parameters in pediatric hydronephrosis

Compared with the healthy controls, the levels of serum BUN and Scr were significantly

Table 4. Correlations between GFR and laboratory parameters (r/*P*)

	n	Years	Hb	BUN	Scr
Healthy controls	16	(0.949/0.001)	(0.260/0.573)	(-0.248/0.591)	(-0.963/0.002)
Mild hydronephrosis	25	(-0.256/0.579)	(0.308/0.502)	(0.208/0.655)	(-0.892/0.017)
Moderate hydronephrosis	14	(0.231/0.617)	(0.337/0.482)	(0.411/0.360)	(-0.840/0.018)
Severe hydronephrosis	9	(0.212/0.622)	(0.992/0.000)	(-0.898/0.006)	(-0.968/0.000)

Note: Glomerular filtration rate, GFR; blood urea nitrogen, BUN; serum creatinine, Scr; hemoglobin, Hb. The correlation between GFR and the clinicopathological variables of the patients was assessed using Spearman's rank correlation test.

Table 5. Correlations between BPR and laboratory parameters (r/*P*)

	n	Years	Hb	BUN	Scr
Healthy controls	16	(0.892/0.007)	(0.542/0.209)	(-0.198/0.632)	(-0.695/0.019)
Mild hydronephrosis	25	(-0.127/0.683)	(0.314/0.499)	(0.324/0.575)	(-0.745/0.018)
Moderate hydronephrosis	14	(0.245/0.595)	(0.392/0.451)	(-0.216/0.618)	(-0.624/0.024)
Severe hydronephrosis	9	(0.108/0.732)	(0.872/0.019)	(-0.723/0.016)	(-0.668/0.021)

Note: Renal blood perfusion rate, BPR; blood urea nitrogen, BUN; serum creatinine, Scr; hemoglobin, Hb. The correlation between BPR and the clinicopathological variables of the patients was assessed using Spearman's rank correlation test.

Table 6. Correlations between PUR and laboratory parameters (r/*P*)

	n	Years	Hb	BUN	Scr
Healthy controls	16	(0.841/0.018)	(0.174/0.687)	(0.118/0.743)	(-0.694/0.018)
Mild hydronephrosis	25	(0.173/0.687)	(0.331/0.559)	(-0.223/0.602)	(-9.679/0.000)
Moderate hydronephrosis	14	(0.125/0.726)	(0.318/0.494)	(0.154/0.697)	(-0.815/0.014)
Severe hydronephrosis	9	(0.069/0.894)	(0.913/0.000)	(-0.845/0.011)	(-0.743/0.018)

Note: Peak uptake rate, PUR; blood urea nitrogen, BUN; serum creatinine, Scr; hemoglobin, Hb. The correlation between PUR and the clinicopathological variables of the patients was assessed using Spearman's rank correlation test.

increased in children with moderate or severe hydronephrosis, the severe hydronephrosis children had higher levels in both BUN and Scr. However, the moderate or severe hydronephrosis group exhibited a lower Hb level and the Hb in children with severe hydronephrosis decreased to an even lower level. It is interesting that no significant differences in BUN, Scrand Hb between the control group children with mild hydronephrosis (**Table 2**).

Diuretic renography parameters in pediatric hydronephrosis

Diuretic renography results showed that GFR, BPR and PUR in children with hydronephrosis were gradually reduced with the aggravation of the hydronephrosis. The GFR, BPR and PUR in children with mild hydronephrosis were only slightly declined (**Table 3**).

Correlation of GFR, BPR, and PUR with laboratory parameters

Correlation analysis indicated that the GFR (**Table 4**), BPR (**Table 5**) and PUR (**Table 6**) were positively correlated with the ages, but negatively associated with Scr in normal children. The GFR (**Table 4**), BPR (**Table 5**) and PUR (**Table 6**) in children with mild or moderate hydronephrosis were negatively related with Scr. The BUN and Scr were negatively, but the Hb was positively relevant with the GFR (**Table 4**), BPR (**Table 5**) and PUR (**Table 6**) in children with severe hydronephrosis.

Diagnostic efficacy of GFR in pediatric congenital hydronephrosis

The ROC curve analysis revealed that area was 0.612 (95% CI=0.512-0.836, P=0.000). When the cutoff value =1.12, the diagnostic sensitivity (68.2%) and specificity (82.3%) reached their peak values (**Figure 1**).

Discussion

The advanced imaging and prenatal maternal sonography are clinically used to evaluate the renal function in pediatric congenital hydronephrosis [15]. The diuretic renography of ^{99m}Tc-

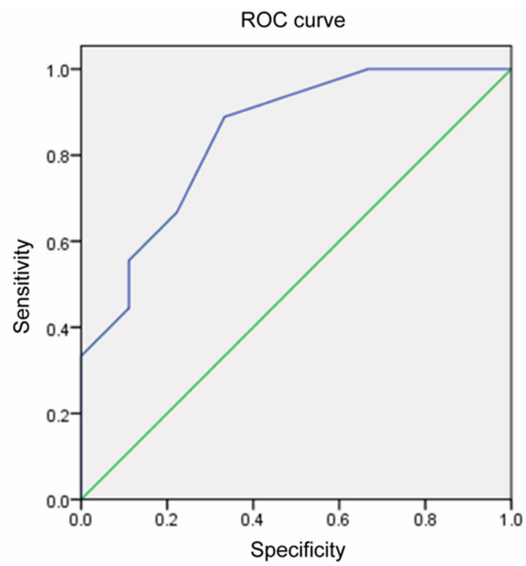

Figure 1. Assessment of the diagnostic efficacy of GFR in pediatric congenital hydronephrosis by calculating the area under the receiver operating characteristic curve. (AUC=0.612, P=0.000, Sensitivity =0.682; Specificity =0.823).

DTPA is currently recognized as the most reliable method for determination of GFR [16]. However, it is still unknown that the relation between the renographic and clinicopathologic laboratory findings in children with congenital hydronephrosis. The present study demonstrated that the GFR, BPR and PUR measured by diuretic ^{99m}Tc-DTPA renography and Scr are ideal indexes assessing the renal function in pediatric congenital hydronephrosis. The BUN and Hb are not suitable for detection of early hydronephrosis in children.

Renography has been identified as a noninvasive approach to observe subjects with renal abnormalities, including pediatric congenital hydronephrosis [17]. The ^{99m}Tc-DTPA renography has been intensively advocated as a simple and noninvasive technique for the detection of hydronephrosis [18]. Diuretic renography with ^{99m}Tc-DTPA provides not only renal perfusion function and morphological data, but also serves as an effective mean for differentiating obstructive from nonobstructive hydronephrosis by calculating differential renal function parameters including GFR, BPR and PUR [9]. It is also proposed that diuretic renography of ^{99m}Tc-DTPA is an independent factor associated with relative renal function improvement in patients with unilateral ureteropelvic junction obstruction (UPJO) who underwent surgery [19, 20]. Our results showed that GFR, BPR and PUR in children with hydronephrosis were significantly decreased in moderate or severe hydronephrosis and the severe hydronephrosis children had a worse renal function. The GFR, BPR and PUR in children with mild hydronephrosis were only slightly declined. These results suggested that the confirmed mild hydronephrosis should be operated as early as possible to prevent continuous renal function damage. In addition, despite no statistically significant difference were found between mild renal hydronephrosis and normal controls. Future large scale studies should be collaborative in order to set a boundary point as a critical point for decompensated renal function.

The measurement of BUN, Scr and Hb are often used as a supplementary means for detection of hydronephrosis [21]. The unilateral ureteropelvic junction obstruction is closely related with renal dysfunction reflected by significant increases in BUN and Scr [22]. Our data presented that the levels of serum BUN and Scr were significantly increased in children with moderate or severe hydronephrosis and the moderate or severe hydronephrosis group exhibited a lower Hb level. Correlation analysis suggested that GFR, BPR and PUR were negatively correlated with Scr in all children, but negatively associated with BUN only in severe hydronephrosis. Furthermore, the Hb was positively relevant with the GFR, BPR and PUR only in severe hydronephrosis. These results hinted that the BUN and Hb were not suitable for detection of early hydronephrosis in children. BUN and Hb may be dramatically changed only when severe impairment of renal function occurred. The GFR, BPR and PUR measured by diuretic ^{99m}Tc-DTPA renography and Scr are ideal indexes assessing the renal function in pediatric congenital hydronephrosis. It is noted that the GFR, BPR and PUR were positively associated with the ages in healthy controls. The results suggested that the renal function is gradually increasing with the growth and development of children. It is interesting that GFR, BPR and PUR had no relationship with years in children with congenital hydronephrosis. It may be attributed to the different physiological and pathological characteristics of the children. But to be sure, early diagnosis and early treatment should be done in children with congenital hydronephrosis. The correlation analysis between the diuretic renography and laboratory measurement may provide a new approach for the guidance and management of congenital hydronephrosis patients. In addition, ROC curve analysis showed that GFR measured by ^{99m}Tc-DTPA renography exhibited high sensitivity and specificityin the diagnosis of congenital hydronephrosis patients. The comparisons of ^{99m}Tc-DTPA diuretic renography examination and other method in predicting renal injury of hydronephrosis will be explored in our further research.

In conclusion, the GFR, BPR and PUR measured by diuretic ^{99m}Tc-DTPA renography were credible for renal function assessment, and GFR, BPR and PUR were negatively associated with the Scr in normal, mild, moderate and severe hydronephrosis children. Surgical treatment should be accepted as soon as possible in case that the children with congenital hydronephrosis are confirmed, in order to prevent local and systemic damage caused by the decline of renal function to the loss of compensation. Diuretic renography of ^{99m}Tc-DTPA may be a promising tool in postnatal follow up in antenatally detected hydronephrosis.

Disclosure of conflict of interest

None.

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References

[1] Cachat F, Ramseyer P, Meyrat BJ, Frey P, Boubaker A, Lepori D, Parvex P, Bugmann P and Girardin E. [Antenatally detected hydronephrosis: practical approach for the pediatrician]. Rev Med Suisse 2005; 1: 505-506, 509-512.

[2] Mesrobian HG and Mirza SP. Hydronephrosis: a view from the inside. Pediatr Clin North Am 2012; 59: 839-851.

[3] Asl AS and Maleknejad S. Clinical outcome and follow-up of prenatal hydronephrosis. Saudi J Kidney Dis Transpl 2012; 23: 526-531.

[4] Wen JG, Li ZZ, Zhang H, Wang Y, Wang G, Wang Q, Nielsen S, Djurhuus JC and Frokiaer J. Expression of renal aquaporins is down-regulated in children with congenital hydronephrosis. Scand J Urol Nephrol 2009; 43: 486-493.

[5] Assmus MA, Kiddoo DA, Hung RW and Metcalfe PD. Initially Asymmetrical Function on MAG3 Renography Increases Incidence of Adverse Outcomes. J Urol 2016; 195: 1196-1202.

[6] Pohl HG and Belman AB. Congenital anomalies of the urinary tract. Curr Pediatr Rev 2014; 10: 123-132.

[7] St Aubin M, Willihnganz-Lawson K, Varda BK, Fine M, Adejoro O, Prosen T, Lewis JM and Shukla AR. Society for fetal urology recommendations for postnatal evaluation of prenatal hydronephrosis--will fewer voiding cystourethrograms lead to more urinary tract infections? J Urol 2013; 190: 1456-1461.

[8] Hiraoka M. Medical management of congenital anomalies of the kidney and urinary tract. Pediatr Int 2003; 45: 624-633.

[9] Al-Mashhadi A, Neveus T, Stenberg A, Karanikas B, Persson AE, Carlstrom M and Wahlin N. Surgical treatment reduces blood pressure in children with unilateral congenital hydronephrosis. J Pediatr Urol 2015; 11: 91.e91-96.

[10] Piepsz A. Antenatal detection of pelviureteric junction stenosis: main controversies. Semin Nucl Med 2011; 41: 11-19.

[11] Gheissari A, Nematbakhsh M, Amir-Shahkarami SM, Alizadeh F and Merrikhi A. Glomerular filtration rate and urine osmolality in unilateral ureteropelvic junction obstruction. Adv Biomed Res 2013; 2: 78.

[12] Li ZZ, Xing L, Zhao ZZ, Li JS, Xue R, Chandra A, Norregaard R and Wen JG. Decrease of renal aquaporins 1-4 is associated with renal function impairment in pediatric congenital hydronephrosis. World J Pediatr 2012; 8: 335-341.

[13] Tezuka M, Murata Y, Ishida R, Sawada Y and Shibuya H. Tc-99m DTPA renography in patients with collagen disease. Clin Nucl Med 2001; 26: 187-192.

[14] Inal S, Altuntas A, Kidir V, Ozorak A, Ilgin Y and Sezer MT. Utility of serum creatinine/cystatin C ratio in diagnosis of postrenal acute kidney injury. J Res Med Sci 2014; 19: 1086-1089.

[15] Nguyen HT, Benson CB, Bromley B, Campbell JB, Chow J, Coleman B, Cooper C, Crino J, Darge K, Herndon CD, Odibo AO, Somers MJ and Stein DR. Multidisciplinary consensus on the classification of prenatal and postnatal urinary tract dilation (UTD classification system). J Pediatr Urol 2014; 10: 982-998.

[16] Radulovic M, Pucar D, Jaukovic L, Sisic M, Krstic Z and Ajdinovic B. Diuretic 99mTc DTPA renography in assessment of renal function and drainage in infants with antenatally detected hydronephrosis. Vojnosanit Pregl 2015; 72: 1080-1084.

[17] Chandrasekharam VV. Laparoscopic repair of congenital midureteric strictures in infants and children. J Pediatr Surg 2015; 50: 1909-1913.
[18] Yazici B, Oral A, Gokalp C, Akgun A, Toz H and Hoscoskun C. A New Quantitative Index for Baseline Renal Transplant Scintigraphy With 99mTc-DTPA in Evaluation of Delayed Graft Function and Prediction of 1-Year Graft Function. Clin Nucl Med 2016; 41: 182-188.
[19] Liu M, Fu ZL, Di LJ, Zhang JH, Fan Y, Zhang XC and Wang RF. [Efficiency evaluation of diuretic renography in the operative or conservative treatments of unilateral ureteropelvic junction obstruction patients]. Beijing Da Xue Xue Bao 2015; 47: 638-642.
[20] Liu M, Fu Z, Li Q, Di L, Zhang J, Fan Y, Zhang X and Wang R. Delayed renal tissue tracer transit in Tc-99m-DTPA renography correlates with postoperative renal function improvement in UPJO patients. Nucl Med Commun 2015; 36: 833-838.
[21] Kochakarn W, Ratana-Olarn K, Lertsithichai P and Roongreungsilp U. Follow-up of long-term treatment with clean intermittent catheterization for neurogenic bladder in children. Asian J Surg 2004; 27: 134-136.
[22] Wongmekiat O, Leelarungrayub D and Thamprasert K. Alpha-lipoic acid attenuates renal injury in rats with obstructive nephropathy. Biomed Res Int 2013; 2013: 138719.