Original Article

Glomerular filtration rate and urine osmolality in unilateral ureteropelvic junction obstruction

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Abstract

Background: Renal maldevelopment, interstitial fibrosis, ischemic atrophy, decreased glomerular filtration rate (GFR), and renal blood flow (RBF) are inevitable consequences of chronic kidney obstruction that only partially improve after early intervention. There are only few studies that evaluated urine osmolality in affected kidney and its correlation with short-term outcome.

Materials and Methods: Thirty patients (age<1 year) with unilateral ureteropelvic junction obstruction (UUPJO) were enrolled in this study. UUPJO was confirmed using Technetium 99 isotope scans and the patients were indicated to be operated afterward. Urine and blood samples were obtained before, 24, 48, and 72 h after the surgery. The serum level of blood urea nitrogen, creatinine, and glucose were measured. GFR, urine osmolality (measured and calculated), and urine specific gravity were determined too.

Results: Cortical thickness of hydronephrotic kidney was significantly increased 6 months after the surgery. GFR was significantly increased 72-h postsurgery compared to before operation.

Neither means of calculated nor of measured urine osmolalities were significantly different in various stages. The last calculated urine osmolality (72 h) had significant correlation with the last measured osmolality (72 h); r=0.962, P=0.0001. The last GFR (72 h) had positive significant correlation with GFR before the surgery and GFRs at 24 and 48 h postsurgery.

Using regression tests, only the before surgery GFR was the predictor of the last GFR(72 h).

Conclusion: In UUPJO the measured and calculated urine osmolality of the affected kidney did not differ. In addition, GFR before surgery should be considered as the predictor of the GFR shortly after repair.

Key Words: Children, glomerular filtration rate, unilateral ureteropelvic obstruction, urine osmolality

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INTRODUCTION

Hydronephrosis is the most common abnormality in the urinary tract on prenatal screening by ultrasound. The differences in incidence rise from diversity in timing of ultrasonography and criteria for dilatation.[1] Nonetheless, the incidence of a considerable uropathy in association with hydronephrosis varies from

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0.2% to 0.92%.[1,2] Renal maldevelopment that is caused by chronic unilateral partial obstruction may recover after releasing the obstruction and saving the hemodynamics.[3,4] However, interstitial fibrosis, ischemic atrophy, decreased glomerular filtration rate (GFR), and renal blood flow are inevitable consequences of obstruction that only partially improve after early intervention.[5] Although the mortality of unilateral partial obstruction is not reported to be high, the morbidity is still significant.[6] Different clinical findings and urinary proteomics have been proposed to determine the outcome of obstruction, such as severity of oligohydramnios, urine transforming growth factor-β, and matrix protein.[7-10] Nevertheless, there are few studies evaluating the predicting factor of GFR and urine osmolality of the affected kidney in unilateral obstruction. Herein, we evaluated urine osmolality of the obstructed kidney before and after correcting the obstruction and its correlation with short-term GFR.

MATERIALS AND METHODS

Patients

In a longitudinally designed analytical study, 30 confirmed unilateral uretropelvic junction obstruction (UUPJO) patients younger than 1 year with no sex discrimination were enrolled in a 20-month study period (December 2009 to August 2011). They were selected from pediatric nephrology, pediatric surgery and neonatology wards, and clinics affiliated to the main medical university of Isfahan, Iran.

UUPJO was confirmed by Technetium 99 m-diethylene triamine pentaacetic acid dynamic renal scintigraphy (99 mTc-DTPA) with diuretic. The indication of surgery was proposed by pediatric nephrologist and fix pediatric urologist. The second confirmatory ultrasound study was performed by a fix radiologist just before performing surgery to determine the kidney size, cortical thickness, anteroposterior diameter of pelvic and grade of hydronephrosis.

Patients with single kidney, bilateral hydronephrosis, and cystic disease were not included. The standard surgical procedure was open dismembered pyeloplasty by a fix pediatric urologist.

The survey was performed in accordance with the ethical standards of the Helsinki Declaration (Seoul, 2008). The study approved by the institutional review boards and the Ethics Committee of the Research Department of Isfahan University of Medical Sciences. After complete explanation of the study objectives and protocols for parents, written informed consent was obtained.

Design

Urine and blood samples were obtained in 4 distinct phases; before, 24, 48, and 72 h after surgery. The first urine sample was drawn by the surgeon from the obstructed pelvic directly just before starting surgery and the 3 remaining samples were obtained from the urine collected by the nephrostomy tube placed in operated pelvic.

Blood samples were all taken from peripheral veins, which were not used to infuse medications. All samples were immediately centrifuged and extracted plasma was kept frozen in −20°C. Blood urea nitrogen (BUN) and creatinine were measured in the serum samples. Urine specific gravity was assessed by refractometer. In addition, urine osmolality were measured directly by Vapor Pressure Osmometer. Vapor pressure osmometer determines the concentration of osmotically active particles that reduce the vapor pressure of a solution. Wescore 5200 vapor osmometer (USA) was used and measurement procedure was done according to its instruction.

Urine osmolality was also calculated and compared with measured amounts. This formula could be used in case of urine osmolality measurement.[11]

$$\text{Osmolality} = [\text{SG } 1.000] \times 40$$

The final ultrasonoghraphic evaluation was performed 6 months after surgical repair to determine kidney size, cortex thickness, pelvic diameter, and grade of hydronephrosis.

Besides, the GFR was also calculated according to the Schwartz formula.[12]

GFR: K L/Cr

In which K is a constant changing with age (according to below 1 year it is 0.35 for female or 0.45 for male in this study) and L is length in centimeter and Cr is plasma creatinin level (mg/dL).

Statistical analysis

Quantitative data were compared using paired Student's *t* test and in case of qualitative, Chi-square test was administered. Also regression test was used to find independent variables.

All tests were performed using SPSS software (SPSS, Chicago, IL, USA), Version 18.

RESULTS

The mean ± SD of the age for 30 assessed cases was 4.3 ± 1.69 months with minimum and maximum of 2 and 8 months, respectively. Thirty kidney units were evaluated. Hydronephrosis was observed in 9 left kidneys (30%) and 21 right kidneys (70%).

The mean of hydronephrotic left kidney cortical thickness was significantly increased 6 months after surgery in comparison with thickness before surgery; 9.8 ± 0.8 mm versus 9.5 ± 0.58 mm, respectively, $P = 0.029$. Similar results were achieved between hydronephrotic right kidney cortical thicknesses before and 6 months after surgery; 8.69 ± 0.78 mm versus 8.34 ± 0.92 mm, respectively, $P = 0.024$. Anteroposterior diameter (APD) of right kidney was decreased significantly 6 months after surgery in comparison with AP diameter before surgery, 5.86 ± 1.84 mm versus 7.98 ± 3.03 mm, respectively; $P = 0.0001$. The same result was not observed in left kidney, $P > 0.05$.

The mean of GFR before performing surgery was significantly lower than the GFR at 72 h after surgery; 53.64 ± 5.04 mL/min/1.73 m^2 versus 56.84 5.14 mL/min/1.73 m^2, $P = 0.027$. The mean of GFRs in different stages of the study is shown in Table 1. Nonetheless, the means of urine specific gravity were not significantly different among different stages, $P > 0.05$; Table 2. Neither means of calculated nor of measured urine osmolalities were significantly different in various stages; $P > 0.05$, Tables 3 and 4.

The mean of urinary sodium excretion at the last phase (72 h) was not significantly different from the first stage (before performing surgery); 150.84 ± 6.9 meq/dL versus 153.40 ± 7.13 meq/dL, respectively, $P > 0.05$. The same results were achieved in other stages (after 24 and 48 h).

Table 1: Means of GFRs in different stages of the study

Pairs of GFRs	Mean±SD		95% confidence interval		Significance
			Lower	Upper	
GFR before and GFR 24 h	54.22±5.01	54.55±5.07	-0.74	0.07	0.107
GFR before and GFR 48 h	54.22±5.01	55.08±5.29	-0.88	-0.15	0.007
GFR before and GFR 72 h	54.22±5.01	56.53±5.52	-4.34	-0.28	0.27
GFR 24h and GFR 48 h	54.55±5.07	55.08±5.29	-0.54	-0.06	0.016
GFR 24h and GFR 72 h	54.55±5.07	56.53±5.52	-2.24	-0.08	0.036
GFR 48h and GFR 72 h	55.08±5.29	56.53±5.52	-1.54	0.21	0.126

The urine measured and calculated osmolalities were also had been compared with each other. Before surgery there was significant difference between measured and calculated amounts, $P = 0.013$. However, 24, 48, and 72 h after surgery no significant difference was seen between calculated and measured osmolalities, $P > 0.05$.

Neither calculated nor measured urine osmolality in different stages had significant correlation with GFRs, $P > 0.05$.

The last calculated urine osmolality (72 h) had significant correlation with the last measured osmolality (72 h); $r = 0.962$, $P = 0.0001$. No significant correlation was achieved between calculated and/or measured urine osmolality with parenchymal thickness, $P > 0.05$.

The last GFR (72 h) had positive significant correlation with the GFR before surgery and GFRs 24 and 48 h: $r = 0.707$, $P = 0.001$; $r = 0.923$, $P = 0.0001$; $r = 0.964$, $P = 0.0001$, respectively. However, the last GFR (72 h) had no correlation with parenchymal thickness before or after surgery; $P > 0.05$. Regression analysis showed that only GFR before surgery was the predictor of GFR 72 h, $P = 0.001$.

DISCUSSION

In this study, we assessed measured urine osmolality in UUPJO and its association with GFR. To the best of our knowledge, it is the first study that evaluates changes in urine osmolality obtained directly from renal pelvis, and the association between its concentration with GFR and AP diameter of pelvis after 6 months.

Dilatation of the renal pelvis is the most frequent finding of renal anomalies particularly obstruction of the urinary tract. Among causes of the obstructive uropathy, UUPJO is common in all races.[1,2] The importance of UUPJO is not only for the reason of its high prevalence

Table 2: Means of urine specific gravity through different stages of the study

Pairs of urine specific gravity (USG)	Mean±SD		95 % confidence interval		Significance
			Lower	Upper	
USG before and USG 24 h	1005.96±4.43	1006.68±5.06	-3.26	1.81	0.54
USG before and USG 48 h	1005.96±4.43	1007.79±5.73	-3.74	0.09	0.06
USG before and USG 72 h	1005.96±4.43	1007.45±5.86	-4.83	1.83	0.35

Table 3: Means of calculated urine osmolality in different stages of the study

Pairs of measured urine osmolality (C-UOSM)	Mean±SD		95% confidence interval		Significance
			Lower	Upper	
C-UOSM before and C-UOSM 24 h	238.62±177.43	248.88±181.39	-130.69	72.76	0.56
C-UOSM before and C-UOSM 48 h	238.62±177.43	303.70±232.77	-149.94	3.73	0.06
C-UOSM before and C-UOSM 72 h	238.62±177.43	298.94± 240.87	-193.27	73.27	0.35
C-UOSM 24 h and C-UOSM 48 h	248.88±181.39	303.70±232.77	-151.47	41.84	0.25
C-UOSM 24 h and C-UOSM 72 h	248.88±181.39	298.94±240.87	-161.79	98.63	0.61
C-UOSM 48 h and C-UOSM 72 h	303.70±232.77	298.94±240.87	-61.49	207.49	0.25

Table 4: Means of measured urine osmolality in different stages of the study

(M-UOSM)	Mean±SD		95% confidence interval		Significance
			Lower	Upper	
M-UOSM before and M-UOSM 24 h	186.58±106.76	269.29±184.80	-183.55	18.13	0.10
M-UOSM before and M-UOSM 48 h	186.58±106.76	259.26±162.22	-150.13	33.33	0.19
M-UOSM before and M-UOSM 72 h	186.58±106.76	286.25±170.87	-235.91	12.24	0.07
M-UOSM 24 h and M-UOSM 48 h	269.29±184.80	259.26±162.22	-162.53	65.58	0.38
M-UOSM 24 h and M-UOSM 72 h	269.29±184.80	286.25±170.87	-86.72	90.19	0.96
M-UOSM 48 h and M-UOSM 72 h	259.26±162.22	286.25±170.87	-61.49	207.49	0.25

but also for irreversible complications of the obstruction on renal blood flow, GFR, and urinary concentration and renal function.[5,13-15] In UUPJO different stages of increased intrarenal pressure, activation of renin–angiotensin system, and decreased renal blood flow have been observed.[16-19] Topcu *et al.* reported that GFR, urine osmolality, and urinary sodium excretion were reduced in solitary kidney with UUPJO.[20] In rodent models, both partial and complete obstruction resulted in alteration in urinary osmolytes.[21] While acute short-term unilateral obstruction in rats has not changed the permeability to water and reabsorptive capacity of terminal collecting duct, prolonged unilateral obstruction has resulted in increased cyclooxygenase and decreased permeability to water and urinary sodium excretion in obstructed kidney.[22,23] Since we calculated GFR based on Schwarz formula and selected unilateral obstruction, comparing GFRs in 2 kidneys (obstructed and nonobstructed) was unfeasible. However, we demonstrated that GFR after 72 h of releasing the obstruction increased significantly comparing with the previous stages. Perhaps, changes in vasoconstrictors and renin–angiotensin system after removing the obstruction resulted in increased GFR.[3-5] Nonetheless, we did not observe changes in the urinary excretion of sodium shortly after obstruction release.

We did not demonstrate changes in measured and/or calculated urine osmolality in different stages. Most studies that evaluated urine osmolality had been conducted on animal models. We evaluated the changes of urine osmolality in hospitalized patients that have been receiving intravenous water and electrolytes based on hydration status, urinary output, and serum sodium. Therefore, stable urine osmolality and sodium excretion in different stages are true scenarios that are observed in clinical setting after eliminating the obstruction. Furthermore, we observed that measured and calculated urine osmolality obtained from obstructed renal units was significantly different only before intervention. This difference was not seen after surgical repair.

Chevalier *et al.* reported that initial urinary tract lesion remained 1 month after surgical repair.[24] Chertin *et al.* demonstrated that improving renal function after surgical correction has been occurred just after turning to pubertal age.[25] Trusting on imaging findings after surgical repair is not sufficient to predict the results of reconstruction.[26] Indeed, most available data supported by both experimental and human studies suggested that UUPJO provokes permanent changes of the renal parenchyma.[27] We showed that parenchymal thickness was dramatically increased 6 months after surgery. Furthermore, APD of right kidney was lower 6 months after surgery compared with APD before surgery. The same result was not shown in the left kidney. The smaller sample size in left kidney unit (9 left units comparing with 21 right units) may describe the insignificant statistical result.

The volume of amniotic fluid has been introduced as the main predictive factor of fetus outcome in bilateral UUPJO.[28] However, in UUPJO methods of surgical repair have been proposed to affect the outcome.[29-31] We selected a fix surgical method. Consequently, the type of reconstruction method had no effect on renal function outcome. Evaluating final GFR (72 h) revealed that only GFR before surgery was the predictor of renal outcome.

CONCLUSION

We concluded that in UUPJO, the measured and calculated urine osmolality of the obstructed kidney did not differ during first 3 days postoperation. Therefore, calculated urine osmolality should be used unalterably for measured urine osmolality in UUPJO. Furthermore, GFR before surgery is the only predictor of short-term GFR after surgery. Nonetheless, parenchymal thickness, urine osmolality, and urine specific gravity were the predictors of GFR after surgery.

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