

Colour Doppler and Biomarkers Utility for Renal Damage due to Congenital Hydronephrosis

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ABSTRACT

Objective: To determine colour doppler and serum biomarkers spectrum in children with congenital hydronephrosis.

Study Design: An observational study.

Place and Duration of Study: Department of Pediatric Nephrology, West China 2nd University Hospital of Sichuan University and Key Laboratory of Birth Defects and Related Disease of Women and Children (Sichuan University), China, from January to December 2017.

Methodology: A total of 95 children with hydronephrosis were selected as case group. According to the degree of hydronephrosis, the patients were divided into mild hydronephrosis group, moderate hydronephrosis group, and severe hydronephrosis group. Forty children with normal renal function were selected as normal comparison group. Peak systolic velocity (V_{max}), end diastolic velocity (V_{min}), resistance index (RI), pulsatility index (PI), and serum cystatin C (CysC), β_2 -microglobulin (β_2 -MG), and α_1 -microglobulin (α_1 -MG) of all subjects in both groups were recorded and compared.

Results: The V_{max} , V_{min} of main renal artery (MRA) and interlobar renal artery (IRA) in case group were lower than those of normal group (all $p < 0.001$). RI of MRA and IRA in case group were higher than those of normal control group (both $p < 0.001$). There were no significant differences in the PI of MRA and IRA between the two groups ($p = 0.700$, and 0.250 respectively). The levels of serum CysC, β_2 -MG and α_1 -MG in normal control group, mild hydronephrosis group, moderate hydronephrosis group, and severe hydronephrosis group were significantly different (all $p < 0.001$), and the levels of serum CysC, β_2 -MG, α_1 -MG were also different in children with different degrees of hydronephrosis.

Conclusion: Combined detection of colour doppler and serum biomarkers CysC, β_2 -MG and α_1 -MG in the diagnosis of renal damage in congenital hydronephrosis is feasible and reliable.

Key Words: Congenital hydronephrosis, Colour doppler, CysC, β_2 -MG, α_1 -MG.

INTRODUCTION

Congenital hydronephrosis, as one of the most common urinary system abnormalities is often found in children with ureteropelvic junction obstruction.¹⁻³ Finding effective, safe and minimally invasive indicators for congenital hydronephrosis evaluation has become a hotspot in current clinical research. Ultrasonography is an easy-to-use, non-invasive and non-radioactive means of examination that can detect morphological damage of hydronephrosis. However, using grayscale ultra-sonography to distinguish cases of mild hydronephrosis from normal cases showing fullness only, is relatively difficult.⁴⁻⁶ Studies show that the levels of serum biomarkers, such as cystatin C (CysC), β_2 -micro-

globulin (β_2 -MG) and α_1 -microglobulin (α_1 -MG) could be used to effectively evaluate renal function.⁷⁻⁸ Previous studies find that serum CysC, β_2 -MG may be potential biomarkers of obstruction in hydronephrosis.⁹

The aim of this study was to evaluate the clinical value of colour doppler combined with serum CysC, β_2 -MG and α_1 -MG in the evaluation of congenital hydronephrosis, with a view to provide a reference for management of congenital hydronephrosis.

METHODOLOGY

This study was conducted at the Department of Pediatric Nephrology, West China Second University, Hospital of Sichuan University and Key Laboratory of Birth Defects and Related Disease of Women and Children (Sichuan University), Ministry of Education, Chengdu, China, from January to December 2017. A total of 95 children with hydronephrosis were selected as the case group. Inclusion criteria were patients with congenital hydronephrosis, no obvious abnormalities on grayscale ultrasound of the liver, gallbladder, pancreas, spleen, chest X-ray or heart and lung, who could tolerate the examination. Exclusion criteria were patients with immune dysfunction, severe liver and kidney damage, and urinary tract infections, recent history of trauma or surgery, or hydronephrosis caused by other causes such

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as urinary tract infections or tumors. Hydronephrosis was graded as mild on ultrasound when the renal collection system was 1.0-2.0 cm in dimension, and renal parenchyma and kidney shape was normal. Moderate hydronephrosis was ultrasound showing separation of the renal collection system by 2.1-3.5 cm, and the renal parenchyma thinner, and kidney enlarged. Severe hydronephrosis was labelled when ultrasound showed separation range of the renal collection system ≥ 3.6 cm, the kidney enlarged, and the renal parenchyma thinned by compression or completely shrunk. A total of 40 children with normal kidney function and having checkups in the hospital over the same period were selected as the normal control group. The study was approved by the Hospital Ethical and Research Committee, and family members of the subjects all signed the informed consents.

Colour doppler diagnostic system was used for examination. The abdominal convex array probe was used at a frequency of 3-5MHz, sampling volume 3mm, wall filter 100Hz, and the angle between blood flow and acoustic beam $\leq 30^\circ$. First, the shape and various diameters of the kidneys were observed by two-dimensional ultrasonography, and blood flow measurements were made after obtaining a standard coronal section. The sampling frame was placed at the main renal artery (MRA) of the renal hilum and the interlobar renal artery (IRA) of the renal parenchyma to obtain a

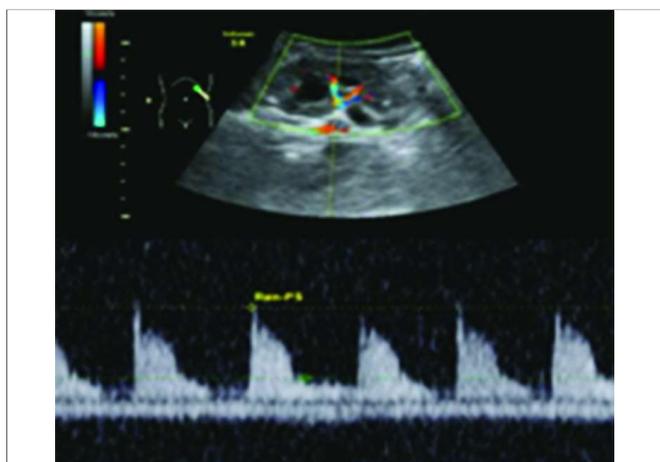


Figure 1: RI of intra renal arteries in children with hydronephrosis.

satisfactory blood flow spectrum (3 to 5 consecutive waveforms similar to each other). The peak systolic velocity (V_{max}), the end diastolic velocity (V_{min}), resistance index (RI), and pulsatility index (PI) were measured. The levels of CysC, β_2 -MG and α_1 -MG in the serum of the subjects were measured by the double-antibody sandwich enzyme-linked immunosorbent assay (ELISA).

SPSS 21.0 statistical software was used for data analysis. Measurement data were expressed as mean \pm standard deviation. The independent samples t-test was used for comparison between two groups and one-way ANOVA was used for comparison among multiple groups. A difference with a p-value less than 0.05 was considered statistically significant.

RESULTS

The 95 children in the case group were divided into the mild hydronephrosis group 30 cases (31.58%), the moderate hydronephrosis group 31 cases (32.63%), and the severe hydronephrosis group 34 cases (35.79%).

In case group, there were 60 males (63.16%) and 35 females (36.84%); aged from 4 months to 11 years, mean 5.26 ± 0.97 years; 46 cases (48.42%) of ureteropelvic junction obstruction (UPJO), 40 cases (42.11%) of UVJO (ureteropelvic junction obstruction) and 9 cases (9.47%) of ureteroceles; 50 cases (52.63%) of unilateral hydronephrosis, 45 cases (47.37%) of bilateral hydronephrosis; 58 cases (61.05%) of hydronephrosis in the left kidney and 37 cases (38.95%) of hydronephrosis in the right kidney. In normal control group, there were 25 males (62.50%) and 15 females (37.50%); aged 4 months to 10 years, mean 5.17 ± 0.62 years.

The V_{max} , V_{min} of main renal artery (MRA) and interlobar renal artery (IRA) in case group were lower than those of normal control group (all $p < 0.001$). The RI of MRA and IRA in case group were higher than those of normal control group (both $p < 0.001$). There were no significant difference in the PI of MRA and IRA between the two groups ($p = 0.700$ and 0.250 , respectively, Table I and Figure 1).

The levels of serum CysC, β_2 -MG and α_1 -MG in normal control group, mild hydronephrosis group, moderate hydronephrosis group, and severe hydronephrosis group were significantly different (all $P < 0.001$), and the

Table I: Comparison of kidney colour doppler parameters between case group and normal control group.

Parameter	Groups	MRA		IRA	
		Mean \pm SD	p-value	Mean \pm SD	p-value
Vmax	Normal control group (n=40)	53.76 \pm 6.08	<0.001	28.02 \pm 2.53	<0.001
	Case group (n=95)	40.12 \pm 3.26		14.08 \pm 1.30	
Vmin	Normal control group (n=40)	24.18 \pm 2.94	<0.001	13.92 \pm 1.47	<0.001
	Case group (n=95)	16.03 \pm 1.31		9.27 \pm 0.39	
RI	Normal control group (n=40)	0.63 \pm 0.05	<0.001	0.56 \pm 0.11	<0.001
	Case group (n=95)	0.74 \pm 0.06		0.71 \pm 0.05	
PI	Normal control group (n=40)	1.26 \pm 0.19	0.700	1.21 \pm 0.14	0.250
	Case group (n=95)	1.27 \pm 0.11		1.23 \pm 0.07	

Table II: Comparison of the levels of serum CysC, β_2 -MG and α_1 -MG in each group.

Groups	n	CysC (mg/L)		β_2 -MG (mg/L)		α_1 -MG (mg/L)	
		Mean \pm SD	p-value	Mean \pm SD	p-value	Mean \pm SD	p-value
Normal control group	40	0.79 \pm 0.05	<0.001	1.82 \pm 0.32	<0.001	19.93 \pm 2.04	<0.001
Mild hydronephrosis group	30	0.92 \pm 0.10		2.16 \pm 0.71		23.07 \pm 5.20	
Moderate hydronephrosis group	31	1.01 \pm 0.26		3.04 \pm 0.63		25.02 \pm 4.28	
Severe hydronephrosis group	34	1.09 \pm 0.41		5.54 \pm 0.96		26.73 \pm 5.22	

levels of serum CysC, β_2 -MG and α_1 -MG were also different in children with different degrees of hydronephrosis (Table II).

DISCUSSION

Congenital obstruction is the most common cause of congenital hydronephrosis. Congenital obstruction can lead to poor urine excretion, increase the expansion pressure in the pelvis, compress the renal parenchyma, and cause changes in multiple vascular factors such as angiotensin II in the kidney, then it will cause renal vasoconstriction, promote a further increase of renal vascular resistance and decrease renal function.^{10,11} Without timely treatment, congenital hydronephrosis may cause renal failure. So it is extremely important to determine the degree of obstruction and renal function in clinical practice.^{12,13} The conventional B-scan ultrasonography can easily detect the extent of water accumulation, but it cannot evaluate renal function; Intravenous pyelography (IVP) and radioisotope renography can be used to understand renal function; but in cases of severe hydronephrosis, IVP cannot visualise the calyceal system because of poor excretion of contrast.^{14,15} The results of this study showed that there were significant differences in the V_{max} , V_{min} and RI under colour doppler between normal control group and case group. The V_{max} and V_{min} in case group were both lower than those of normal control group, while there were no significant difference in the PI of MRA and IRA between the two groups. The RI of the MRI and IRA in case group were both higher than those of normal control group, suggesting that RI was of practical significance as an indicator of vascular resistance. This conclusion is in accordance with the view proposed by Kawai *et al.*¹⁶

According to the related research results, the expression of CysC was closely related to the glomerular filtration rate, and it could be used as an objective indicator to evaluate the glomerular filtration function.¹⁷ Parvex *et al.* concluded that CysC was a promising marker of renal function, at birth, in neonates prenatally diagnosed with congenital kidney anomalies.¹⁸ The results of this study were shown that the levels of serum CysC in normal control group, mild hydronephrosis group, moderate hydronephrosis group, and severe hydronephrosis group had statistically significant differences; and the levels of serum CysC in children with different degrees of hydronephrosis were higher than those in normal

control group. This illustrates that the CysC is an important biomarkers to assess congenital hydronephrosis.

Elevated serum β_2 -MG levels suggested a decrease in glomerular filtration rate, while elevated urinary β_2 -MG levels reflected damaged renal tubular reabsorption function.¹⁹ Bartoli *et al.* substantiated that the role of β_2 -MG as marker of tubulointerstitial damage in human obstructive nephropathy.²⁰ The results of this study suggested that children's damaged glomerular function was caused by the inability of normal glomeruli to compensate for β_2 -MG excretion; the results also indicated that the serum β_2 -MG levels were different in children with varying degrees of hydronephrosis and the degrees of glomerular function damage would also vary. This study found that β_2 -MG was a promising marker of congenital hydronephrosis.

The protein α_1 -MG is a glycoprotein with small molecular weight, it is mainly synthesised in liver and lymphoid tissues.²¹ It is widely present in various body fluids of the human body and can freely pass through the glomerular filtration membrane. However, most of such proteins are reabsorbed and decomposed by proximal convoluted tubules. Under normal circumstances, α_1 -MG is rarely seen in urine. Its content in urine can only increase when the renal tubular is injured. So, it is currently widely believed that α_1 -MG is an indicator to reflect glomerular and renal tubular functions. The results of this study demonstrated that the serum α_1 -MG levels could well indicate whether the renal tubule was damaged; and the severer the damage was, the higher the α_1 -MG level would be.

It can be seen that the detection on the levels of serum CysC, β_2 -MG and α_1 -MG can well distinguish cases of mild hydronephrosis from normal cases, and can make up for the deficiency of kidney ultrasonography in this aspect. Therefore, colour doppler combined with serum CysC, β_2 -MG and α_1 -MG has important clinical significance on the evaluation of congenital hydronephrosis. At the same time, this study also has many limitations and shortcomings; for instance, the number of the studies is less, and future still has many aspects to perfect.

CONCLUSION

Combined detection of colour doppler and serum biomarkers CysC, β_2 -MG and α_1 -MG in the diagnosis of

renal damage in congenital hydronephrosis is feasible and reliable.

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