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PEDIATRIC UROLOGY

Influence of diuretic (furosemide) on contrast medium distribution in computed tomography urography of high-grade hydronephrosis in children

Przemysław Bombiński[1], Michał Brzewski[1], Stanislaw Warchol[2], Agnieszka Biejat[1], Marcin Banasiuk[3], Marek Gołębiowski[4]

[1]*Department of Pediatric Radiology, Medical University of Warsaw, Warsaw, Poland*
[2]*Department of Pediatric Surgery and Urology, Medical University of Warsaw, Warsaw, Poland*
[3]*Department of Pediatric Gastroenterology and Nutrition, Medical University of Warsaw, Warsaw, Poland*
[4]*1st Department of Clinical Radiology, Medical University of Warsaw, Warsaw, Poland*

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Corresponding author
Przemysław Bombiński
Department of Pediatric Radiology
Medical University of Warsaw
63a Żwirki i Wigury Street
02-091 Warsaw, Poland
phone: +48 506 691 059
przebom@op.pl

Introduction Diuretics improve visualization of the urinary tract in computed tomography urography in adults, as well as in magnetic resonance urography in adults and children. Also, diuretics can help to diagnose upper urinary tract obstruction in intravenous urography, ultrasonography or dynamic scintigraphy. However, there are still missing data on evaluation of furosemide usefulness in computed tomography urography examinations in children with suspected congenital anomalies of the urinary tracts.
The aim of this study was to compare the homogeneity of contrast medium distribution in high-grade hydronephrosis in pediatric computed tomography urographies performed with and without use of diuretic (furosemide).

Materials and method We have restrospectively analyzed computed tomography urography image series performed in the Department of Pediatric Radiology, in children with suspected congenital anomalies of the kidney and the urinary tract. Kidney units with high-grade hydronephrosis were divided in two groups: non-furosemide (n = 25) and furosemide (n = 28) group, where diuretic in dose 1 mg/kg, with maximum 20 mg, was administered intravenously 3–5 min before contrast medium administration. Subjective image quality and diagnostic confidence were evaluated by two independent radiologists and compared between study groups.

Results There were no significant differences in subjective image quality and diagnostic confidence between furosemide and non-furosemide groups.

Conclusions Addition of furosemide to computed tomography urography does not improve homogeneity of contrast medium distribution in hydronephrotic kidneys in children.

Key Words: children ‹› computed tomography urography ‹› congenital anomalies of kidney and urinary tract ‹› diuretics

INTRODUCTION

Diuretics increase urine flow rate and allow better visualization of urinary tracts in conventional intravenous urography (IVU), as well as in nuclear medicine, Doppler ultrasonography, computed tomography (CT) and magnetic resonance (MR) urography (CTU, MRU). Furosemide improves distention and opacification of the collecting systems and ureters. In adults, use of furosemide in CTUs is widely discussed in diagnosis of urothelial cancers [1–10]. In present-day diagnosis of congenital anomalies of kidneys and urinary tract (CAKUT) in children, usefulness of furosemide is analyzed in particular in MRU [11, 12, 13] and dynamic scintigraphy [12, 14, 15] functional examinations – use of furosemide in pa-

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tients with high-grade hydronephrosis can differentiate a true obstruction (ureteropelvic junction obstruction – UPJO), requiring surgical intervention, from a dilated non-obstructed system. CTU can provide anatomic information about suspected CAKUT and can be performed in children in some specific indications or in case MRU is not available [16]. However, usefulness of furosemide has been assessed in a very limited manner. Also, it is highlighted that increased diuresis caused by furosemide may increase distention of the urinary tract and reduce contrast medium (CM) concentration, resulting in decreased opacification and poorer visualization of the collecting system [17].

The aim of this study was to analyze whether addition of furosemide improves homogeneity of CM distribution in high-grade hydronephrosis (HN) in pediatric CTUs.

MATERIAL AND METHODS

Study design

This was a retrospective study comparing the subjective image quality and diagnostic confidence between furosemide and non-furosemide CTU examinations performed in children with high-grade HN. CTUs were performed between 2011 and 2016 in selected patients before qualification to surgical treatment. There was no access to MRU.

Ultrasonography and dynamic renal scintigraphy were performed in all analyzed patients. All kidneys with impaired renal function (i.e., <40% of split renal function at DMSA scintigraphy) were excluded from this analysis. Grade of HN was assessed in ultrasonography according to the grading system described in the European Society of Pediatric Radiology (ESPR) guidelines [18]. Kidney units with high-grade HN (grade 3–5) were included into final analysis. Results of functional scintigraphy, graded as follow: normal, delayed or impaired excretion, were analyzed to compare the types of urinary tract abnormalities between the study groups (no obstruction, partial or total obstruction).

Our study was accepted by the institutional ethics review board.

Computed tomography urography protocol

Our standard CTU protocol included acquisition made from the diaphragm or the top of the kidney to the symphysis pubis. Excretory phases were performed 15–30 min after intravenous (iv) administration of contrast material (CM). Iomeron 300 (iomeprolum) in a standard dose of 1 ml/kg of body weight was used. Diuretic (furosemide) in dose 1 mg/kg, with maximum 20 mg, was administered intravenously 3–5 min before CM administration.

Our 64-MDCT scanner (Brilliance CT 64, Philips Healthcare, Best, The Netherlands) had iterative reconstruction algorithm (iDose4), and the 4th reconstruction level was implemented in all analysed examinations [19]. Scanning parameters (including tube voltage kV and tube current mAs) were different, depending on the standard department's CT protocols adequate to patients' weight. Image evaluation was performed on diagnostic workstation (IntelliSpace Portal, Philips, Netherlands).

Image quality analysis

The evaluation was performed independently by two radiologists (Observer A – A.B. and Observer B – P.B., with 17 years and 7 years of experience in pediatric CT, respectively), who were blinded to the group information.

Overall subjective image quality and diagnostic confidence were evaluated. Criteria were based on reported previously abdominal CT studies [20–30]. Overall subjective image quality was defined as the presence of motion artefacts, image noise and beam-hardening streak artefacts and was rated on

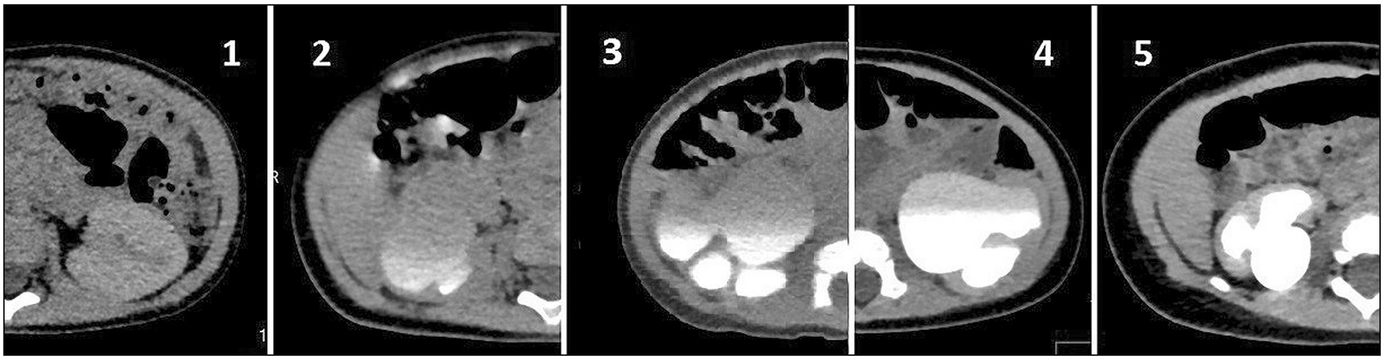

Figure 1. *Grades 1–5 in diagnostic confidence grading scale. Scores 1 and 2 were deemed as non-diagnostic in clinical practice.*

a 5-point scale (1 – unacceptable quality, non-diagnostic; 2 – poor quality, affecting the interpretation; 3 – moderate quality, not affecting the interpretation; 4 – good; 5 – excellent). Diagnostic confidence was defined as reader confidence in visualization of anatomical structures (calyces, pelvis, megaureters) and was associated with CM distribution within the collecting system (Figure 1). Grading scale was adapted from previous urinary tract studies and modified as presented in Table 1. For both scales, scores 1 and 2 were deemed as non-diagnostic in clinical practice.
Grading scores and interobserver agreement were evaluated between the study groups.

Statistical analysis

Continuous variables were tested by the Shapiro-Wilk test for normality. Data were then expressed as median and range. Comparisons between nominal variables were tested with χ^2 statistics. The weight Kappa was used to determine agreement between observers. Statistical analysis was performed using Statistica 12 (Tulsa, USA). Kappa coefficients were calculated by using PQStat 1.6 (Poznań, Poland). P-value of <0.05 was defined as statistically significant. Strength of interobserver agreement was indicated with kappa values as follows: <0 – poor; 0–0.2 – slight; 0.2–0.4 – fair; 0.41–0.6 – moderate; 0.61–0.8 – substantial; 0.81–1.0 – almost perfect.

RESULTS

A total of 101 CTU examinations in 93 patients were assessed for eligibility. A total of 51 image series in 51 patients with high-grade HN and preserved renal function were identified and included for the final analysis. There were 17 girls and 34 boys, median age 2.3 years, IQR 0.8–8.1, range 0.2–12.2 years (Table 2). There were 53 collecting systems with HN grade 3–5 (furosemide group n = 28, non-furosemide group n = 25). Two patients had bilateral high grade HN (one boy in furosemide group and one girl in non-furosemide group).
There was no significant difference in terms of age (p = 0.08) and gender (p = 0.2) between the study groups.
Also, there were no significant differences in results of functional scintigraphy (p = 0.8), making both study groups similar with regard to the types of urinary tract abnormalities.
None of the image series were rated as non-diagnostic in overall subjective image quality scale (all were rated as scores 3–5). One collecting system in the non-furosemide group was rated as poor (score 2) in diagnostic confidence scale, while all other kidney units were evaluated as diagnostic (scores 3–5).
Median (IQR) scores in subjective image quality scale were 4 (3–4) for both observers. Median (IQR) scores in diagnostic confidence scale were 5 (5–5) for Observer A and 5 (4–5) for Observer B.
General interobserver agreement between study groups was substantial for subjective image quality (kappa = 0.78) and almost perfect for diagnostic confidence (kappa = 0.91). Interobserver agreement within the study groups is presented in Table 3.
Subjective image quality and diagnostic confidence scores were not significantly different between the study groups (p = 0.96 and p = 0.1 for Observer A; p = 0.9 and p = 0.3 for Observer B, respectively).

Table 1. *Diagnostic confidence grading scale*

Grade		
1	No opacification	Non-diagnostic
2	Incomplete opacification – contrast medium present only in several calyces or part of the pelvis	Poor, affecting the interpretation
3	Complete, but inhomogeneous opacification, with contrast medium layering in calyces or pelvis – layering effect in 1–50% of collecting system volume	Acceptable, diagnostic
4	Complete, almost homogeneous opacification, with contrast medium layering in calyces or pelvis (layering effect in 51–99% of collecting system volume	Good
5	Complete and homogeneous opacification, no layering effect	Excellent

Table 2. *Characteristics of patients included in this study*

	Furosemide Group (n = 28)	Non-furosemide Group (n = 25)	p
Sex (M:F)	16 : 12	19 : 6	p = 0.2
Age (years)	3.0 (1.2–9.3)	1.5 (0.5–5.8)	p = 0.08
Age (range in years)	0.2–12.2	0.2–10.5	

Table 3. *Interobserver agreement within the study groups (kappa)*

	Furosemide Group	Non-furosemide Group
Subjective image quality	0.85 (almost perfect)	0.69 (substantial)
Diagnostic confidence	0.86 (almost perfect)	0.96 (almost perfect)

DISCUSSION

We have shown that there was no difference in homogeneity of CM distribution in hydronephrotic kidneys in pediatric CTUs performed with and without use of diuretic.

There are several techniques to improve opacification and distention of urinary tracts in CTU, including oral and intravenous hydration, use of compression belts and administration of diuretics [1, 2, 8, 20, 31, 32]. Also, reduction of contrast layering effect may result in improving diagnostic accuracy of CTU [17, 20, 33]. It is highlighted in evaluation of ureters in adults, where suboptimal distention and peristaltic waves may limit visualization of small urothelial tumors [32, 34]. The role of CTU in children with suspected CAKUT is different – it is performed to visualize the anatomy of the abnormality [35] and adequate and homogeneous opacification of the hydronephrotic collecting system is crucial. In MRU studies, furosemide causes uniform distribution of the gadolinium contrast within the urinary tract and it is recommended in adults and children, for non-dilated as well as obstructed urinary tract evaluation [7, 11, 13, 36]. However, our analysis showed that there can be no similar effect in CTUs performed in hydronephrotic kidneys in children, and use of furosemide does not change CM distribution in a dilated collecting system. To the best of our knowledge, there was only one publication describing usefulness of furosemide-enhanced multi-slice CTU in children. Kosucu et al. [37] described a series of 19 CTUs performed with furosemide in children with suspected urinary tract obstruction and dilatation, which clearly depicted urinary tract abnormalities. However, opacification and CM distribution in the renal collecting systems and ureters was evaluated in a limited manner and there are still missing data on comparison of furosemide and non-furosemide examinations.

There are different proposed doses of furosemide, varying between 5 mg and 40 mg [2, 12, 13, 32]. In children, it should be adapted to the patient's weight, and in our department a standard dose was 1 mg/kg, with maximum 20 mg.

There were limitations to our study. First, scanning parameters were different between patients and radiation exposure assessment was not a goal of this study. However, our recent research already confirmed that there are no significant differences in subjective image quality and diagnostic confidence between lower dose and higher dose examinations [38]. Second, we did not perform objective density measurements of the collecting systems, as there were different doses of furosemide, adapted to patients' weight. Third, we did not analyse the objective change in collecting system dimensions, in comparison to initial ultrasound evaluation, which potentially could have an impact on CM concentration due to increased diuresis in the furosemide study group. However, we have confirmed that both study groups were similar with regard to the types of urinary tract abnormalities (there were no significant differences in results of functional scintigraphy between the study groups). Fourth, only kidneys with preserved renal function (≥40% at DSMA) were evaluated in our study, which is a substantial limitation in comparison to MRU [13, 39].

CONCLUSIONS

We do not suggest the use of diuretics in CTUs of hydronephrotic kidneys in children, as this does not improve homogeneity of CM distribution in dilated collecting systems.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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