Is a Reassuring MAG-3 Diuretic Renal Scan Really Reassuring?

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Key Words

MAG-3 diuretic nuclear scan • Hydronephrosis • Ureteropelvic junction obstruction

Abstract

Objective: The mercaptoacetyltriglycine-3 (MAG-3) diuretic renal scan is frequently used to diagnose obstruction in children with hydronephrosis. However, it remains unclear whether a reassuring MAG-3 diuretic scan in the presence of high-grade hydronephrosis accurately predicts the absence of obstruction. We sought to determine if a reassuring nuclear scan can accurately identify patients with high-grade hydronephrosis that can be safely observed. **Materials and Methods:** We retrospectively reviewed the course of 22 children (25 renal units) ages 0–3 months with significant hydronephrosis (Society of Fetal Urology grade 3–4) detected prenatally. All patients underwent a MAG-3 diuretic nuclear renal scan. **Results:** Twenty-two patients with 25 renal units were included, 19 with grade 3 and 6 with grade 4 hydronephrosis on ultrasound. Sixteen renal units had a reassuring nuclear scan ($T \frac{1}{2} < 10$ minutes, average 5.9, range 2–9). Nine renal units had indeterminate scans ($T \frac{1}{2}$ 10–20 minutes, average 12.8, range 10–17). Fifteen of 16 (94%) kidneys with a reassuring nuclear scan had complete resolution of their hydronephrosis. One patient with an initially reassuring nuclear scan underwent pyeloplasty after persistent grade 4 hydronephrosis one year later prompted a repeat MAG-3 indicating obstruction. Eight of 9 (89%) patients with an indeterminate $T \frac{1}{2}$ of 10–20 minutes had complete resolution of their hydronephrosis. One patient was lost to follow up. Average length of follow up and time to resolution was

23.6 months (range 4–61 months). **Conclusion:** In pediatric patients with persistent antenatally detected hydronephrosis, a reassuring MAG-3 can allow for safe observation in the vast majority. Only one of 24 renal units with follow-up progressed to obstruction. All patients treated without surgery had complete resolution of their hydronephrosis. Observation with serial ultrasounds may be an appropriate alternative to operative management, even in patients with moderate to severe hydronephrosis in the presence of a reassuring or indeterminate MAG-3 diuretic scan.

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Introduction

Hydronephrosis is the most common genitourinary abnormality found on prenatal ultrasound [1] with an incidence of 1/100 to 1/500 [2, 3]. Transient (48%) and physiologic (15%) hydronephrosis account for the vast majority of cases, followed by ureteropelvic junction obstruction (UPJO) in approximately 11% of cases [4]. Other causes of prenatal hydronephrosis include: vesicoureteral reflux, ectopic ureter, posterior urethral valves, ureterocele, mega-ureter, urethral atresia, retrocaval ureter, and prune belly syndrome [1].

UPJO occurs in approximately 1 in 750–2,000 children [4–6]. Blockage of the ureteropelvic junction causes dilation of the kidney from poor drainage of urine, which can potentially damage the affected kidney and lead to progressive loss of renal function. The cause of the ob-

struction may be intrinsic, such as an aperistaltic segment of abnormal ureter, or extrinsic from a crossing vessel, both of which impede forward flow of urine [2]. Less common causes of obstruction include ureteral valves or polyps [1]. UPJO is more common in boys, with a male to female ratio of 3:1, and more often affects the left kidney, though it can occur bilaterally in ten percent of cases [6].

Prior to the widespread use of ultrasound, UPJO typically presented with urinary tract infection or abdominal mass in children ages 12–24 months; however with the widespread use of prenatal ultrasound, a majority of UPJOs are identified prenatally [1]. Despite this early detection, difficulty remains in determining which cases of hydronephrosis are pathologic and require further intervention [7]. In patients with moderate to severe urinary tract dilatation (Society of Fetal Urology Grade 3 and 4), diuretic renography in the form of diethylenetriaminepentaacetic acid and ^{99m}Tc mercaptoacetyltriglycine-3 (MAG-3) diuretic scans are used to identify or confirm obstruction. Two metrics from these scans are evaluated to determine the presence of an obstructive process: half time of the radiotracer to washout and differential renal function. A time for half of the radiotracer to clear ($T_{1/2}$) of less than 10 minutes is considered non-obstructive while a $T_{1/2}$ greater than 20 minutes suggests the presence of obstruction [8–10]. A $T_{1/2}$ between 10 and 20 minutes is indeterminate and requires follow-up [8–10]. The second parameter for determining significant obstruction is differential renal function, which is felt to be significant if renal function is decreased to < 35–40% of the overall function [11, 12]. It is believed that conservative measures are safe when a differential function is greater than 40% and the anterior posterior diameter is less than 12 mm [13].

While there has been much attention to the accuracy of an abnormal nuclear scan in identifying obstruction, to our knowledge, it is unclear whether a reassuring or indeterminate MAG-3 diuretic scan in the presence of high-grade hydronephrosis accurately predicts the absence of obstruction. The purpose of this study is to determine if a reassuring or indeterminate nuclear scan can accurately identify patients with high-grade hydronephrosis that can be safely observed without surgical intervention.

Materials and Methods

After institutional review board approval, we retrospectively reviewed the charts of 160 patients with a history of prenatal hydronephrosis who had a MAG-3 diuretic renal scan treated be-

tween 2003 and 2010. Patients with concomitant urologic conditions such as vesicoureteral reflux, multicystic dysplastic kidney, posterior urethral valves, megaureter, and ureteral duplication were excluded. Hydronephrosis was assessed using the Society of Fetal Urology (SFU) grading system [14]. Ultrasounds were performed by a single pediatric urologist (A.F.) with the patient in the supine position using a 4–8 MHz Micro Convex ultrasound transducer probe. MAG-3 diuretic scans were performed within six weeks of diagnosis using a standard “well tempered” diuretic renogram protocol [15]. Specifically, according to the parameters of the “well tempered” diuretic renogram protocol, patients are allowed to orally hydrate ad lib prior to the study and during the study will have dilute normal saline instilled intravenously at a rate of 200 ml/kg/hour. A bladder catheter is placed for drainage and patients are placed in the supine position. The region of interest will include the entire kidney and the background subtraction will be 2 pixels wide around the entire perimeter of the region of interest of the kidney. The renogram activity curve and images will be acquired for 20–30 minutes at intervals determined by the practitioner, after which the diuretic furosemide will be administered at a dose of 1 mg/kg and the remainder of the images obtained at 5 minute intervals for 20 minutes. Differential function is calculated by subtracting background from the total counts of the renogram curve between one minute and the appearance for radioactivity in the calyces [15]. All patients were followed with serial ultrasounds at three-month intervals for the first year of life, then six-month intervals for the subsequent 2 years and yearly thereafter until resolution of their hydronephrosis. MAG-3 diuretic scans were repeated if hydronephrosis worsened or failed to improve. Indications for surgical intervention included a $T_{1/2}$ indicating obstruction, a differential renal function of 40% or worse, worsening of hydronephrosis or failure to improve on repeat ultrasound, and febrile urinary tract infection.

Results

Twenty-two children with 25 hydronephrotic renal units were included in the study. The male to female ratio was 10:1. Hydronephrosis was left sided in 13 patients (59%), right sided in 6 patients (27%), and bilateral in 3 patients (14%). Average patient age at initial presentation after neonatal detection of hydronephrosis was 4 ± 2 weeks (95% confidence interval) (range 0–3 months). All patients had initial detection of hydronephrosis on prenatal ultrasounds. All patients had severe hydronephrosis according to the SFU grading system (grade 3 and 4). Nineteen renal units (76%) had grade 3 hydronephrosis and 6 renal units (24%) had grade 4 hydronephrosis on ultrasound.

Sixteen renal units (64%) had a reassuring nuclear scan with a $T_{1/2}$ less than 10 minutes (average 5.9, range 2–9 minutes). Nine renal units (36%) had indeterminate scans with a $T_{1/2}$ of 10–20 minutes (average 12.8, range 10–17 minutes) (table 1). All patients had a differential renal function above 40% on the affected kidney, with the

Table 1. Breakdown of renal units by SFU grade hydronephrosis and MAG-3 diuretic scan results

Hydronephrosis on ultrasound	Normal (T ½ < 10 minutes)	Indeterminate (T ½ 10–20 minutes)
Grade 3	10 renal units	9 renal units
Grade 4	5 renal units	1 renal unit

Table 2. Demographic and follow-up datas

Total patients	Number	Percentage
Gender	22	
Males	20	91%
Females	2	9%
Position	22	
Bilateral	3	14%
Unilateral	19	86%
Total renal units	25	
SFU Grade 3	19	76%
SFU Grade 4	6	14%

SFU = Society of Fetal Urology; Mean age for postnatal follow-up is 4 weeks $\pm$ 2 weeks (95% CI); Mean follow-up is 24 months $\pm$ 7 weeks (95% CI).

exception of one patient whose differential renal function was 35%. Notably, this was in a horseshoe kidney. All scans were performed with background subtraction using a crescent shaped area adjacent to the kidney. Patients were followed for an average of 24 ± 7.1 months (95% confidence interval) (range 4–61 months). Follow up continued until the hydronephrosis resolved or progressed, in which case diuretic renography was repeated (table 2). Eighteen of 19 patients (95%) with grade 3 hydronephrosis had complete resolution of their hydronephrosis. The remaining patient was lost to follow up. In this patient, at 56 months of follow up, the hydronephrosis was stable and had decreased to grade 2. Five of 6 patients (83%) with grade 4 hydronephrosis had complete resolution of their hydronephrosis. One patient required surgery after an initial MAG-3 diuretic scan showed a T ½ of 7 minutes; however after persistent grade 4 hydronephrosis at 1 year, a repeat MAG-3 revealed a T ½ of 34 minutes despite a normal differential renal function and the patient underwent pyeloplasty (fig. 1). The patient has recovered well since surgery and has stable SFU grade 2 hydronephrosis and normal renal function.

Fig. 1. Outcome of conservatively managed high-grade hydronephrosis with reassuring or indeterminate MAG-3 diuretic scans.

Fig. 2. Patient with a grade 4 hydronephrotic right kidney and indeterminate MAG-3 diuretic scan (fig. 3). The hydronephrosis completely resolved after 38 months.

Discussion

SFU grade of hydronephrosis has been shown to correlate with the severity of renal cortical damage and decreased renal function on dimercaptosuccinic acid scans [16]. Furthermore, previous authors have found SFU grade 3–4 hydronephrosis to be independent risk factors

Fig. 3. Indeterminate renal scan with a $T_{1/2}$ of 12 minutes after lasix administration corresponding to a severe (SFU grade 4) hydronephrotic right kidney with complete resolution of hydronephrosis after a trial of observation.

for surgery [17]. Some authors believe that grade 3–4 hydronephrosis is an indication for surgery [5]. In fact, some have argued that early surgical intervention is actually a more conservative approach than non-operative, expectant management [18]. The debate of early surgical intervention versus observation is ongoing and two distinct camps have emerged [7].

Many believe that early surgical intervention is the preferred management of patients with high-grade hydronephrosis. In one study of 205 patients, 181 (88%) with SFU grade 3–4 hydronephrosis required pyeloplasty [17]. The majority of these patients were followed with ultrasound only, as progressive worsening on ultrasound was accompanied by deterioration in renal function [17]. The authors recommend initially performing diuretic renography and ultrasound every 3–6 months during the first 2 years of life [17, 19]. Furthermore, in a randomized trial of 32 infants with obstructive drainage patterns on renography randomized to surgery versus observation, there was a 25% crossover rate from the observation to surgery group and the authors concluded that unilateral obstructive hydronephrosis is better managed with pyeloplasty [20].

However, there are also those who believe observation is a more appropriate approach in these patients. Chertin et al. [17] have argued that in a patient with stable renal function and hydronephrosis, ultrasound examinations every 6 months are acceptable for 2 years [17, 19, 21]. A

prospective study of 26 children with unilateral hydronephrosis and a $T_{1/2}$ less than 10 minutes showed that only 6 (23%) ultimately needed a pyeloplasty at 6 year follow up, due to a decrease in renal function or an increase in hydronephrosis [22]. Patients with indeterminate scans ($T_{1/2}$ 10–20 minutes) were not included and the grade of hydronephrosis was not available. The authors concluded that children with unilateral hydronephrosis thought due to UPJO with a differential renal function of 40% or higher and with a $T_{1/2}$ less than 10 minutes can be safely followed up [22]. Another study of 19 children with bilateral grade 3–4 hydronephrosis showed that 65% of kidneys were able to be safely observed with close follow up in the first two years of life [23].

While surgery is indicated in unequivocally obstructed patients, we sought to further define the subpopulation of significantly hydronephrotic children that can be safely observed. We believe that those with high-grade hydronephrosis who have a reassuring or indeterminate Mag-3 scan can be safely observed without long-term renal damage (fig. 2, 3). Limitations to our study include the small number of patients and retrospective nature. Patients with SFU grade 4 have an overall 50–55% chance of needing pyeloplasty according to currently available data [24]. However, in our study, 83% of patients with reassuring scans despite grade 4 hydronephrosis were successfully managed conservatively.

Conclusion

In pediatric patients with prenatally diagnosed high-grade hydronephrosis (SFU grade 3–4), a reassuring or indeterminate MAG-3 diuretic scan can allow for safe observation in the vast majority of patients. The present study shows that only one of 24 renal units (4%) with follow-up progressed to obstruction. The remaining 96% of children treated without surgery had complete reso-

lution of their hydronephrosis. It is important to closely follow children with prenatally diagnosed hydronephrosis with serial ultrasonography. Repeat diuretic renography may be indicated if hydronephrosis does not resolve or progresses. The majority of children with high-grade hydronephrosis can be safely managed with observation in the presence of a reassuring or indeterminate MAG-3 diuretic scan.

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