DUAL-TIME ^{99M}TC-MAG3 DIURETIC RENOGRAPHY AND NEW CRITERIA IN THE ASSESSMENT OF OBSTRUCTIVE UROPATHY

Khaled Alkhawaldeh MD, Samir Khraisat MD*, Issa Hazza MD***

ABSTRACT

Objective: Obstructive pattern within hydronephrotic non-obstructed kidney is frequently encountered during ^{99m}Tc-MAG3 diuretic renography. The aim of this study was to assess the value of applying new protocol and criteria on dual-time imaging in ruling out obstruction.

Methods: We included 53 children (56 kidneys) in this study (28 boys and 25 girls with age range three weeks to 12 years). All had hydronephrosis, which was bilateral in three children. Eighteen children had pyeloplasty, while 35 children had no previous surgical interventions. All children were referred for assessment of renal outflow obstruction and kidney function. All children underwent routine diuretic ^{99m}Tc-MAG3 renal renography. All had obstructive patterns during diuretic ^{99m}Tc-MAG3 renography and underwent a second dynamic study 30 minutes later for 10 minutes. Non obstructive criteria were set as down sloping second time renogram with drop of kidney counts by ≥ 30% during the 10 minute second time renogram, or flat renogram but with drop of kidney counts by > 50% of peaked activity in first time renogram. Obstructive criteria on dual-time imaging were set as progressive rising second time renogram or flat second time renogram with drop of kidney counts by less than 30% compared to first time study. Equivocal criteria were set as flat renograms with drop of kidney activity by 30-50% or down sloping renogram with drop of kidney counts by < 30% over 10 minutes.

Results: Non obstructive patterns were noticed in 16 kidneys 15 (patients), with down sloping curves during second time renograms in seven kidneys and flat second time renogram with drop of activity by > 50% in 9 kidneys. Obstructive patterns on dual time point ^{99m}Tc-MAG3 renography were noticed in 31 kidneys (29 patients). Eleven kidneys (six patients) were false positive, since three patients had neurogenic bladder with no obstruction, two patients had long standing severe hydronehrosis with no obstruction and one patient had glomerulonephritis. Equivocal patterns were noticed in nine patients, four of them were turned to have significant obstruction, while five had no obstruction.

Conclusion: Dual-time ^{99m}Tc-MAG3 diuretic renography can increase the efficiency in differentiating between obstructed and non-obstructed hydronephrosis compared to routine single time study.

Key words: ^{99m}Tc-MAG3, Diuretic renograph, Hydronephrosis, Obstructive uropathy

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Introduction

The distinction between renal outflow mechanical obstruction and dilation not associated with obstruction is critical to patient management.(1) ^{99m}Tc-MAG3 diuretic renography is an established method for investigation of hydronephrosis. The

From the Departments of:
*Radiology, Nuclear Medicine division, King Hussein Medical Center, (KHMC), Amman-Jordan
**Pediatrics, King Hussein Medical Center, Amman, Jordan
Correspondence should be addressed to Dr. K. Alkhawaldeh, (KHMC), E-mail: khaledk73@gmail.com.
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renogram pattern during ^{99m}Tc-MAG3 diuretic renography is usually related to the degree of obstruction; an non-obstructed system is easily assessed by prompt tracer washout, whereas in cases of obstruction, washout after diuretic remains slow and there will be prolonged retention of the radiopharmaceutical resulting in raising curve.[1-3] However, obstructive pattern in non-obstructed hydronephrotic kidney is frequently encountered during diuretic renography,[1,4-8] and early differentiation between non-obstructed and obstructed kidney without follow up scanning can be considered a diagnostic challenge in a lot of cases.

We conducted this study to assess the added information achieved by performing delayed (second time) renography. Our aim was to try to differentiate between obstructed and non-obstructed hydronephrotic kidneys, by setting new criteria depending on second time renography findings.

Methods

This study was conducted in the nuclear medicine division at King Hussein hospital, in the period between August 2006 and October 2007. Fifty three children with 56 hydronephrotic kidneys were included in this study (28 boys and 25 girls with age range three weeks to 12 years). All children had hydronephrosis and three had bilateral hydronephrosis. Eighteen children had pyeloplasty, while 35 had no previous surgical interventions. All patients were referred for assessment of renal outflow obstruction and function. All patients underwent routine ^{99m}Tc-MAG3 diuretic renography. All patients had obstructive patterns (upsloping renogram) during routine diuretic ^{99m}Tc-MAG3 renography.

Routine ^{99m}Tc-MAG3 diuretic renography was performed following the standardized protocol, and bladder catheterization was not performed. All patients were hydrated by oral fluids before the injection of ^{99m}Tc-MAG3. Furosemide (1mg/kg) was intravenously administered 15 min before the injection of ^{99m}Tc-MAG3 radiopharmaceutical (F-15 protocol). We administered about 1.85 MBq/kg (50 µCi/kg) ^{99m}Tc-MAG3 and a minimum dosage of 37 MBq (1mCi) intravenously. All patients tolerated the procedure well and all acquisitions were conducted without the use of sedation. Movement was minimized by using ribbons in addition to the assurance effect of parents near the child. Dynamic study was set as two second/frames for the first minute followed by one min/frame for 20 minutes. For measurement of differential renal function and renogram generation, regions of interest were drawn over the entire kidney and background on each side. The kidney background was manually drawn on 1-2 minute images in a crescent shape over the outer aspect of the kidney. All patients underwent second time dynamic study, conducted 30 minutes later (50 minutes after radiotracer injection). This time was set to allow performing the new study for new patients, and improve patients' throughput in a busy departments like ours. Second time study acquisition was conducted by the same standard protocol except for the duration (without administration of new dose of radiotracer or Furosemide). During the time interval between the two studies, children were allowed to move, stand and walk according to the child's age.

For the purpose of this study, we set six criteria for the diagnosis of significant renal outflow obstruction during dual-time ^{99m}Tc-MAG3 diuretic renography. Non obstructive kidney criteria were set as: (a) any down-sloping second time renogram with rate of drop in counts by $\geq$ 30% /10 min (regardless of starting counts), or (b) flat second time renogram but with drop of counts by more than 50% of peaked counts on first time renogram.

Obstructive criteria were set as: (a) progressively raising second time renogram with no drop of kidney counts, or (b) flat second time renogram with drop of kidney counts by less than 30% of peaked first time renogram counts. Equivocal criteria were set as: (a) flat second time renogram with drop of counts by 30-50%, or (b) down sloping second time renogram with drop of counts by < 30%/10 min.

All patients were followed-up for 6-12 months, and the results of the dual-time ^{99m}Tc-MAG3 renography were compared with the final diagnoses. All patients had clinical follow-up and sonographic examinations performed at intervals of 3-6 months. Repeated diuresis renography was performed if there was increasing dilatation on the sonographic study.

The final diagnoses were based on either surgical findings or conservative management with repeated sonography and ^{99m}Tc-MAG3 examinations. Diagnosis of obstruction was made if: (a) further impairment of renal function (>10%) or hydronephrosis on follow up ^{99m}Tc-MAG3 scanning, or ultrasonography, or (b) improved postoperative drainage and hydronephrosis were found.

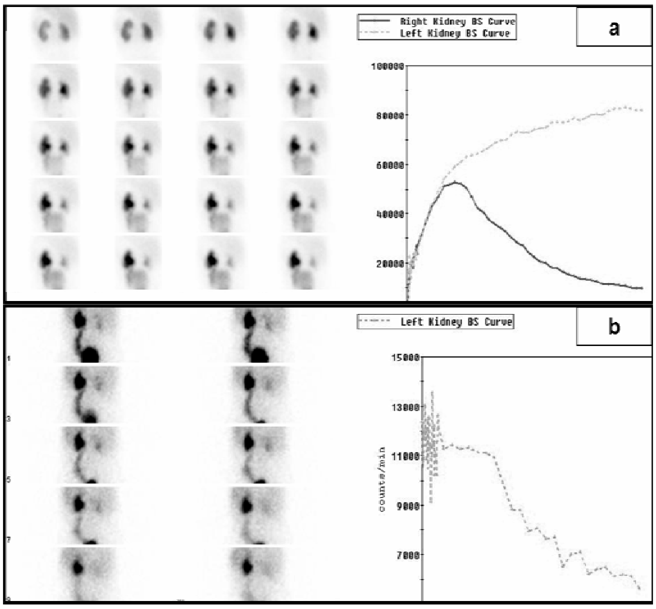

Fig. 1: Six years old boy with left kidney hydronephrosis and hydroureter. First time renogram (a) shows obstructive renogram pattern, while second time renogram (b) shows down sloping renogram (non obstructive criterion).

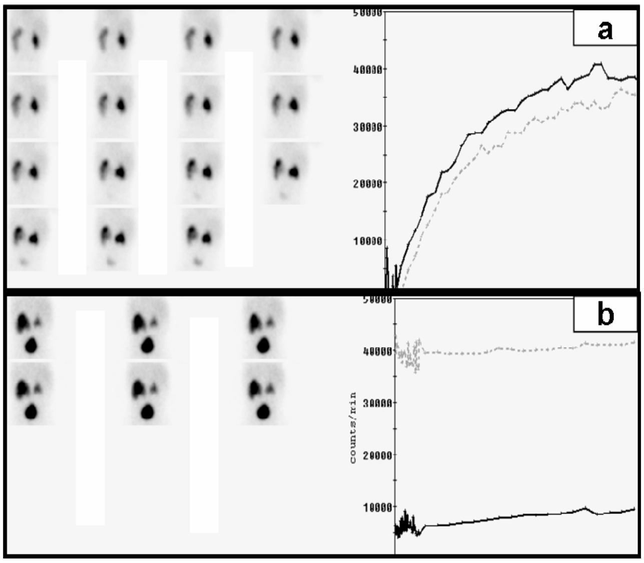

Fig. 2: Three weeks old newborn with bilateral hydronephrosis. First time renogram (a) shows bilateral obstructive renograms pattern, while second time study (b) shows flat renograms for both kidneys, with no drop of activity compared to first time renogram in the left (obstructive criterion), and drop of activity by about 75% in the right kidney (nonobstructive criterion)

Final diagnosis of non-obstructive hydronephrosis was made when there was no change in differential renal function on follow-up ^{99m}Tc-MAG3 diuretic renography and stationary or improved hydronephrosis on ultrasonography at 6-12 months in patients with presumed non obstructive hydronephrosis.

The decision for surgical intervention or conservative management was determined by the pediatric urologist, who considered the results of the diuresis renography, including the relative function of the kidney, the child's clinical findings and serial sonographic examination appearances before making the management decision.

Results

Dual-time ^{9m}Tc-MAG3 diuretic renography revealed non obstructive patterns in 16 kidneys (15 patients); with down sloping curves during second time renograms and drop by ≥ 30%/10 min in seven

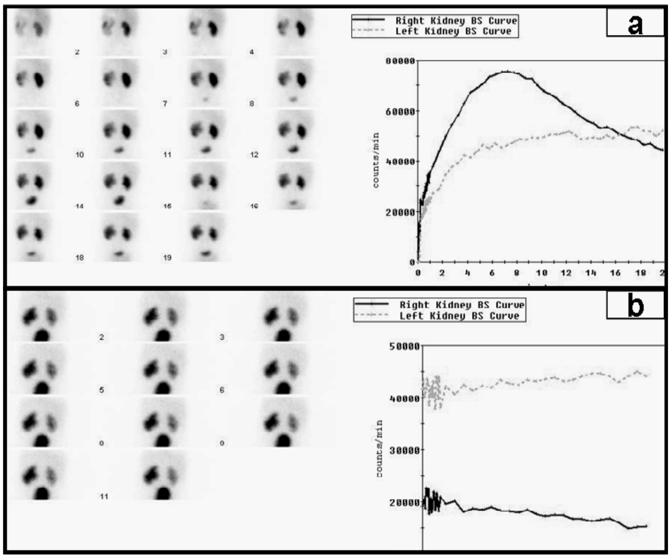

Fig. 3: Three month neonate with left hydronephrosis. First time renogram (a) shows obstructive renogram pattern. Second time renogram (b) shows progressively raised left renogram (obstructive criterion)

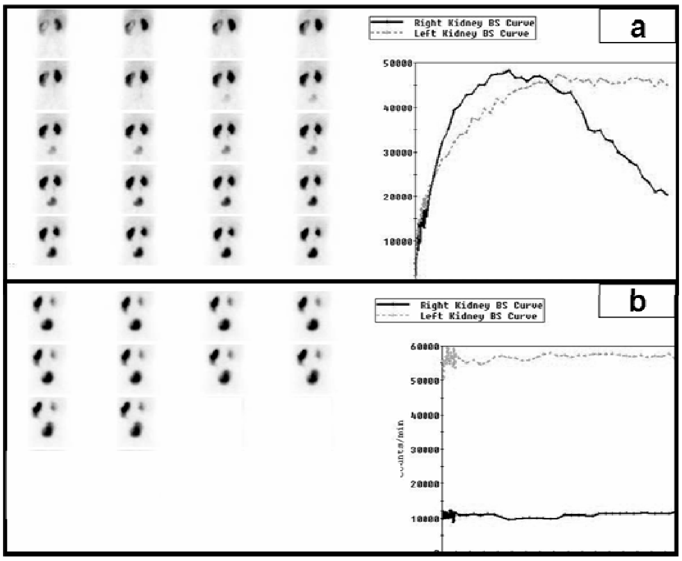

Fig. 4: Eight years old boy with left hydronephrosis. First time renogram (a) shows obstructive renogram pattern in the left kidney, while second time renogram (b) shows flat renogram with no drop in renal counts (obstructive pattern)

kidneys (seven patients) (Fig.1). The second non obstructive criteria with flat second time renogram but with drop of activity by ≥ 50% of peaked counts on first time renogram, was noticed within nine kidneys in eight patients (Fig. 2).

Obstructive patterns were noticed in 31 kidneys (29 patients); progressive raising renogram was noticed in 17 kidneys (Fig. 3), 12 of them where obstructed while five where not. Second obstructive criterion with flat renogram with drop by < 30% (Fig. 4) was noticed in 14 kidneys (12 patients), eight of them were obstructed and six were not. The six kidneys (in four patients) were considered as false positive, since two patients had long standing severe hydronephrosis with no obstruction (on follow up), while two patients (four kidneys) had neurogenic bladder with no obstruction (Fig. 5).

Equivocal patterns were noticed in nine patients, four of them turned out to have significant obstruction, while five had no obstruction. Table I and II show the distribution of patients and kidneys according to dual-time ^{99m}Tc-MAG3 diuretic renography results and final diagnosis.

Discussion

The management of ureteropelvic junction obstruction is difficult because the diagnosis of a significant obstruction cannot always be established

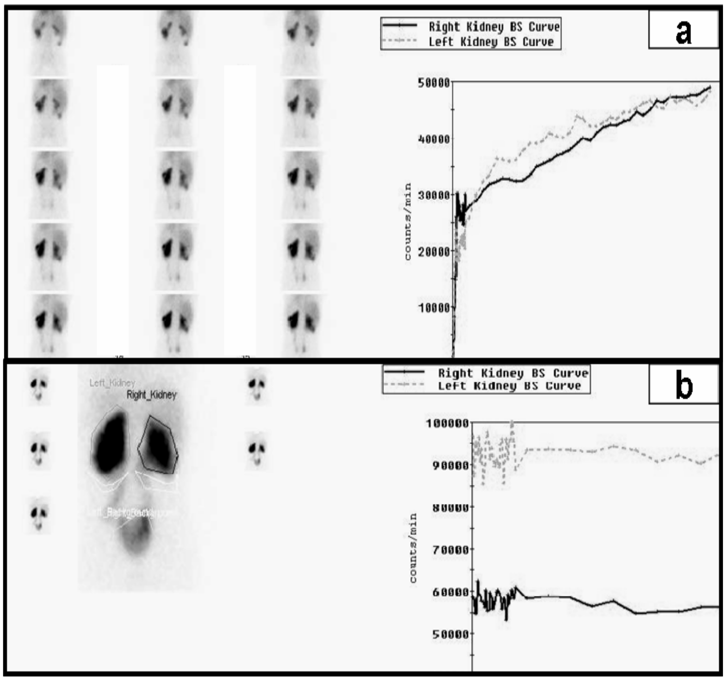

Fig. 5: Seven years old boy with neurogenic bladder, bilateral hydronephrosis and hydroureters. First time renogram (a) shows bilateral obstructive renograms patterns, while second time renogram (b) shows flat renograms with no drop of renal activity compared to first time renogram (false positive obstructive patterns)

with certainty without a waiting period for the development of measurable progressive renal injury.[1,9]

Diuretic renography was indicated in situations of suspected renal obstruction. Several protocols for diuretic renography have been described based on variation in timing of diuretic administration relative to the radiopharmaceutical.[1,10-13] Accepted protocols for Furosemide injection during renography are the F+20 and F-15 methods described by O'Reilly *et al.*[12] Several groups have reported the utility of early Furosemide administration, either at F+ 0 (i.e. at the same time as radiopharmaceutical administration)[13,14] or 2–3 minutes after radiopharmaceutical administration.[15, 16]

The maximal effect of Furosemide is 15-18 minutes after intravenous injection,[1,2,17] which can justify using F-15 variation of diuretic renography in our study. It has also been emphasized that use of the F-15 protocol would be better for avoiding false-negative or equivocal results, particularly in cases of intermittent obstruction. Foda *et al*,[18] in a prospective randomized trial, studied 88 children according to the F-15 or F+20 protocol (44 children in each group) and showed that the number of positive results was significantly higher with the F-15 protocol. Turkolmez *et al.*[19] found that F+0 and F-15 protocols allow clarification in cases of equivocal F+20 studies, although the F+0 and F-15 protocol were more practical and shorter, makes them well tolerated by most of the patients.[17,19]

The fundamental hypothesis underlying diuretic renography is that increased urine flow, as produced by the diuretic, will result in prompt washout of activity in a dilated nonobstructed system. In cases of obstruction, washout after diuretic remains slow and there will be prolonged retention of radiopharmaceutical proximal to the obstruction.[1,3] The renogram pattern is usually related to the degree of obstruction;[1,7] an non-obstructed system is easily assessed by prompt tracer washout, whereas a rising curve will be highly suggestive of true obstruction. Simple parameters such as time to peak and time to obtain a washout of 50% of tracer from the kidney allow one to quantify the response.[1] However, equivocal and even obstructive patterns on diuretic renography are frequently encountered during diuretic renograms for non-obstructed hydronephrotic kidneys. Causes of such finding can be due to severe dilatation of pelvicalyceal system, post pyeloplasty, dehydration, renal function impairment, immature kidneys in neonates, vesicoureteric reflux, tubular necrosis, neurogenic bladder and full bladder

Table I. Age distribution, second time scan patterns including: obstructive (O), non obstructive (N.O) or equivocal and final diagnoses within our study group

No.	Age	Second time Scan	Final Diagnosis	No	Age	Second time Scan	Final Diagnosis
1	3 Weeks	N.O(a)	N.O	28	3 years	O (a)	N.O
2	3 weeks	N.O (b)	N.O	29	3 years	O (b)	O
3	3 weeks	O (b)	O	30	3 years	N.O (a)	N.O
4	4 weeks	O (a)	N.O	31	3 years	O (b)	N.O
5	4 weeks	Equivocal (b)	O	32	4 years	O (a)	O
6	4 weeks	O (a)	N.O	33	4 years	Rt: O (b)	N.O
7	4 weeks	N.O (a)	N.O			Lt: O (b)	N.O
8	4 weeks	N.O (b)	N.O	34	4 years	Equivocal (a)	O
9	6 weeks	O (a)	N.O	35	5 years	O (b)	N.O
10	6 weeks	O (b)	O	36	5 years	Equivocal (a)	O
11	2 months	N.O (a)	N.O	37	5 years	N.O (a)	O
12	3 months	O (b)	O	38	5 years	O (b)	O
13	3 months	N.O (b)	N.O	39	5 years	O (a)	N.O
14	4 months	O (a)	N.O	40	6 years	O (b)	O
15	6 months	O (b)	O	41	7 years	E (a)	N.O
16	9 months	O (a)	O	42	7 years	Rt: N.O (b)	N.O
17	9 months	Rt: O (b)	N.O			Lt: N.O (b)	O
		Lt: O (b)	N.O	43	7 years	O (b)	N.O
18	9 months	N.O (a)	N.O	44	8 years	Equivocal (a)	N.O
19	9 months	O (b)	O	45	8 years	O (b)	N.O
20	9 months	N.O (b)	N.O	46	8 years	N.O (a)	N.O
21	1 year	N.O (b)	N.O	47	10 years	O (b)	O
22	1 year	Equivocal (b)	N.O	48	10 years	Equivocal (b)	N.O
23	1 year	Equivocal (b)	O	49	10 years	O (a)	N.O
24	1 years	O (b)	O	50	11 years	O (b)	O
25	2 years	N.O (b)	N.O	51	11 years	N.O(b)	O
26	2 years	O (b)	O	52	12 years	O (b)	O
27	2 years	O (a)	N.O	53	12 years	Equivocal (a)	N.O

Table II. Distribution of patients according to dual-time ^{99m}Tc-MAG3 diuretic renography results and clinical outcome

Final diagnosis	Down sloping renogram with drop in kidney counts by ≥30%/10 minutes (Kidney)	Flat renogram with drop of activity by ≥ 50% (Kidney)	Progressive raising renogram (Kidney)	Flat renogram with drop of activity By < 30% (Kidney)	Equivocal patterns (Kidney)
Non obstructed	6	7	3	8	5
Obstructed	1	2	7	13	4
Total	7	9 (8 patients)	10	21 (19 patients)	9

effect,[1,4-8] which are compatible with our experience in this regard.

Gravity assisted drainage was recommended to increase the accuracy of diuretic renography and to overcome most diagnostic problems related to full bladder and its resultant back pressure.[20,21] During our study gravity assisted drainage was somehow not helpful since 15 kidneys did not show gravity assisted drainage and only six of them were found to be obstructed.

Because renal function, especially glomerular filtration, is immature at birth, some authors recommend waiting until at least four weeks after birth before performing diuretic renography,[12,14] while there is still much debate over how hydronephrosis in neonates is best managed. Some authors recommend conservative management and close follow-up, whereas others prefer early surgery.[22,23] Our study group included eight neonates with obstructive patterns during diuretic renography, and only two were found to have significant obstruction.

Our study included 56 kidneys with variable degrees of hydronephrosis. All had obstructive patterns during routine diuretic renography, while only 27 were found to have significant obstruction. Excluding obstruction in such patients is critical to avoid unjustified surgical interventions. Our study was able to rule out obstruction in 13 (43%) of non obstructed kidneys. Although our new criteria on dual-time renography misinterpreted three obstructed kidneys as non-obstructed, we still think that patients with non-obstructed criteria according to dual-time renography can be safely managed by follow up scan to avoid unjustified surgical interventions.

Our new protocol and criteria were of clear benefit in ruling out obstruction, even in neonates with immature kidneys and post pyeloplasty children who had obstructed or equivocal routine diuretic renography. False positive results were noted in patients with neurogenic bladder and severe hydronephrosis.

Although our new protocol would extend the duration of diuretic renography study, which can affect patients' throughput in busy departments, still the improvement in the efficiency can justify this modification. Also, gravity assisted static view will not be necessary and will be replaced by the second time renogram. This can compensate for the duration of second time renogram with further improvement in the efficiency.

Although this study was set up prospectively, still our applied new criteria were set retrospectively depending on second time imaging findings and final clinical diagnosis. This factor can be considered a limitation in our study, and further prospective studies on larger number of patients are necessary before establishing the diagnostic value of this protocol.

Conclusion

Our data and results show the potential advantage of dual-time ^{99m}Tc-MAG3 renography to differentiate between obstructed and non-obstructed hydronephrosis. This method may reduce unjustified surgical interventions and the need for frequent follow up scanning.

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