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COMPARISON OF ETHYLENE DICYSTINATE(EC) AND DIETHYLENE TRIAMINE PENTA ACETIC ACID (DTPA) DIURETIC RENOGRAPHY IN EVALUATION OF HYDRONEPHROSIS

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ABSTRACT

Aim: To Compare use of EC and DTPA for diuretic renography in evaluation of hydronephrosis. **Methods:** All patients with hydronephrosis on ultrasound during the period October 2009 to May 2012 were included in the study. They underwent DTPA diuretic renogram with F-0 protocol. Repeat renogram with EC was done after 48 hours. Parameters studied were isotope uptake, differential function, time activity curves with region of interest (ROI) over the kidney, T1/2, status of drainage in delayed images. **Results:** 32 children were studied during this period. They were aged 1 month to 11 years with a median age of 8 months). In 14 patients DTPA showed obstructive parameter/s while EC scan showed non obstructive parameter/s excluding obstructive hydronephrosis. In addition EC scan was more accurate in determining differential function in 6 patients in whom DTPA overestimated the function. EC scan also picked up other anomalies like duplex system, ectopic kidney, horseshoe kidney which were not noticed in DTPA. **Conclusion:** This study demonstrates that EC is more specific in diagnosing obstruction than DTPA, better at calculating split function and in addition detects certain associated anomalies.

KEYWORDS: hydronephrosis, EC, DTPA, diuretic renography.

INTRODUCTION

Hydronephrosis is the most common urinary tract anomaly in children, most of them being detected prenatally. Pelviureteric Junction (PUJ) obstruction requiring surgical intervention account for 15-20% of all hydronephrosis detected antenatally.[1]

The postnatal management of fetal hydronephrosis is more or less standardized, the only point of debate being how to deal with those patients having likelihood of PUJ obstruction, investigations to use and indications for surgery.

Technetium tagged Diuretic renography is the standard investigation for evaluating patients with hydronephrosis, in diagnosing obstuction and evaluating split renal function on which decisions regarding surgery are usually based.[2] Various molecules with different handling by the kidney have been used in this test and include, Diethylene Penta acetic acid(DTPA), Mercapto acetyl triglycine(MAG3) and Ethylenedicysteine(EC).[3] Gordon1, Piepsz A, Sixt R, Guidelines for standard and diuretic renogram in children, Eur J Nucj Med Mol Imaging 2011 Jun; 38(6): 1175-88.

The main problem of 99mTc-MAG3 is its high costs, which may hinder its use in the clinical practice in many countries.

The most used radiopharmaceutical for diuretic renography in many countries is 99mTc-DTPA. The main advantages of 99mTc-DTPA are ease preparation of the kit, availability and low cost, but it is a slow, filtered agent with an increasingly poor target-to-background ratio in decreasing renal function that can make processing difficult, with curve forms and diuretic responses less immediate. The main practical problem of using 99mTc-DTPA is the high rate of indeterminate or possible false-positive results for obstruction attributable to reduced renal function or severe kidney dilation.

99mTc-EC is a renal tubular radiopharmaceutical based on the diaminodithiol ligand (N2S2) recently available. This radiopharmaceutical is a diacid derivative of the brain tracer 99mTc-ECD (ethylenedicysteine diethyl-ester labeled with technetium-99m).

99mTc-EC has been used as a substitute for 99mTc-DTPA, with apparently more accurate results.

However, it is not clear if there is real clinical advantage of using 99mTc-EC instead of 99mTc-DTPA in obstructive renal disease, especially in patients with reduced renal function or severe kidney dilation in which there is a higher probability of indeterminate or false-positive results for obstruction.

The aim of this study is to compare the excretion of 99mTc-EC and 99mTc-DTPA after furosemide injection, using exactly the same image protocols in patients with indeterminate or possible false-positive results for obstruction attributable to reduced renal function or severe dilation.

MATERIALS AND METHODS

PROCEDURE[6]- Patient Preparation-If the patient is not going to receive intravenous fluids, oral hydration is encouraged before arrival and while in the department. Oral fluids in the range recommended for intravenous administration are appropriate.

Preparation before injection of the radiopharmaceutical-The procedure is explained to parents and all children old enough to understand. Parents can remain and help with the examination if their presence is beneficial. Continual communication and reassurance with explanation of each step is essential for cooperation and successful intravenous injection of the radiopharmaceutical and catheterization of the bladder.

An indwelling venous catheter is inserted to maintain sufficient hydration for a good diuretic effect. For the administration of the diuretic at the time of tracer injection (F0), a 21- or 23-gauge butterfly needle is used for the simultaneous injection of the radiopharmaceutical and the diuretic and may be removed after the injection. Sterile urethral catheterization should be performed with the largest sized Foley or feeding catheter that will comfortably pass the meatus French 8 for most patients and French 6 for infants. A French 8 feeding catheter may also be used for continual bladder drainage.

Continual drainage by catheterization of the bladder may be required in patients with hydroureter, vesicoureteral reflux, a neuro- pathic bladder, a small-capacity bladder, a dysfunctional bladder, or posterior urethral valves.

The review of available past radiographic, ultrasound and radionuclide studies adds to the accuracy of interpretation of the current study.

Precautions

The examination table is covered with plastic-lined absorbent paper to contain spilled tracer and reduce contamination of the table during drainage and catheterization.

Radiopharmaceutical

99mTc-diethylene triamine pentaacetic acid (99mTc-DTPA) is a glomerular agent. The biologic half-life is less than 2.5 h and 95% of the administered dose is cleared by 24 h. The recommended administered dose is 3.7 MBq (100 mCi) per kilogram of body weight (minimum, 37 MBq [1 mCi]).

EC is a tubular agent. Renal scintigraphy was performed after the intravenous injection of 4.2 MBq/kg (0.12 mCi/kg) of 99mTc-EC.

Acquisition Protocol of the Renal Scintigraphy- scintigraphy was performed using a scintillation camera equipped with a low-energy all-purpose collimators. Posterior view dynamic images for 25 minutes (matrix 64 □ 64, with variable zoom depending on the patient size, ranging from 1 to 3) in the supine position were acquired immediately after the bolus intravenous injection of the radiopharmaceutical (The dose of furosemide is 1.0 mg/kg, F 0 method is used where there is simultaneous injection of the radiopharmaceutical and the diuretic).

Processing and Analysis

1. From the dynamic renal study, careful evaluation of the parenchymal phase reveals renal function, size and position. Cortical transit time and dilatation of the collecting system may be examined in the excretory phase (initial 2–4 min).
2. Baseline images of the diuretic phase are used for assessment of the diuretic effect.
3. Cinematic viewing of the diuretic phase assesses patient movement. If there is considerable patient motion, regions of interest around the collecting systems of individual frames will have to be compared at various intervals of the study to assess drainage.
4. Regions of interest are drawn around the dilated pelvicalyceal system for curve analysis and calculation
5. The diuretic T1/2 is the time at which the time–activity curve decreases to half its maximal activity.

Interpretation Criteria

1. The diuretic effect usually begins within 1–2 min after the administration of the diuretic.
2. In the absence of obstruction, rapid and almost complete washout of the radiotracer occurs before injection of diuretic. However, if function is decreased, there may be slow emptying of the kidneys.
3. Obstructed systems can result in delayed drainage from the collecting system. The amount of activity proximal to the obstruction can also increase over time.

With the injection of the diuretic after the radiopharmaceutical, a T1/2 less than 10 min usually means the absence of obstruction and a T1/2 greater than 20 min usually identifies obstruction. A T1/2 with a value between 10 and 20 min is an equivocal result. These T1/2 measurements are applicable to neonatal hydronephrosis. The natural history of neonatal hydronephrosis is variable. Drainage may gradually improve or worsen. Therefore, follow-up examinations are usually necessary. These T1/2 values refer to kidneys with normal or near-normal function. Kidneys with reduced function may have prolonged T1/2 values without obstruction.

With the simultaneous injection of the radiopharmaceutical and furosemide (F0), a T1/2 greater than 20 min is compatible with obstruction. In cases, however, of extrarenal pelvis, nonobstructing pelviectasis and megaureters of long standing and particularly post- operative patients with residual dilatation of the collecting system, the possibility of obstruction is studied mainly by observing the cortex and the cortical graphs. When the cortical graphs are normal and the cortices appear empty, then there is no obstruction, even if the curves of the total kidneys have a T1/2 greater than 20 min. The F0 study should therefore be interpreted not only for the behavior of the collecting system but also for the behavior of the cortex of the kidney in question.

If the renogram of the entire kidney is upsloping continuously, such patients often require surgery. Patients with a downsloping curve usually compensate and do not need an immediate operation, but follow-up. Patients with a horizontal graph need close observation because some of them require surgery.

Reporting

1. The procedure, date of the study, activity and route of administration of the radiopharmaceutical and a previous study for comparison are included.
2. The history includes symptoms or diagnosis.
3. The technique includes catheter size and type if implemented, amount and kind of intravenous fluid if administered, the imaging sequence, the amount and time of diuretic administration and the urine volumes before and after the diuretic, if measured.
4. The findings may include renal perfusion, split renal function, transit times and the T1/2 of collecting system emptying after the diuretic.

All patients with hydronephrosis on USG were subjected to DTPA and EC renogram with a gap of 48 hours

- Prospective study
- Period-Oct 2009 to Aug 2011

RESULTS

- N=32
- M:F-28:4
- Age: 1 month to 12 yrs
- Median age- 2 months

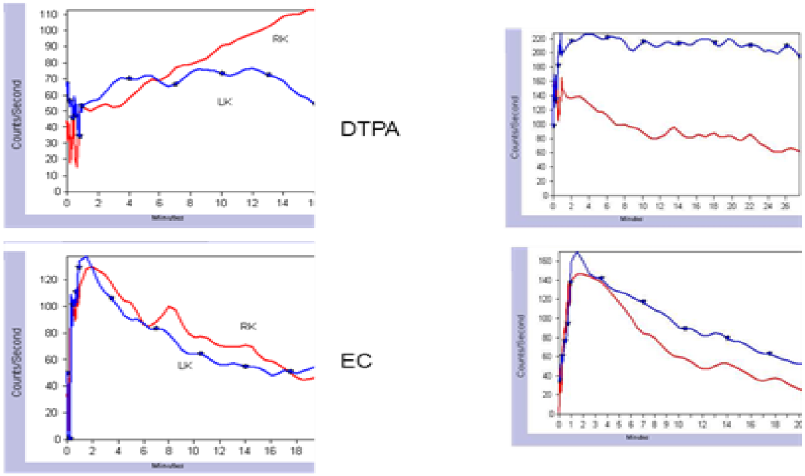
MASTER CHART

Sr no.	Age/sex	diagnosis	Differential function-DTPA LK RK	Differential function-EC LK RK	Advantages of EC
1	1yr/boy	b/l HDN	49.8 50.2 pujo pujo	48 52 pujo no obstruction	Clearance not documented on DTPA images on RK EC ruled out obstruction
2	9yr/boy	R(HDN)	62.9 37.1	65.1 34.9	
3	1m/boy	L(HDN)	50 50 pujo pujo	49 51 pujo non-obstructive	EC rules out obstruction on Rt
4	1.5m/m	L(HDN)	50 50 pujo	45 55 delayed, non obstructive	EC ruled out obstruction
5	1.5yr/m	b/l(HDN)	59.8 40.2 pujo pujo	49.2 50.8 (49+51) pujo pujo	EC picked up duples on Lt side. DTPA overestimated LK function
6	10m/boy	R(HDN)	50 50 pujo	53 47 delayed/non-obstr	EC ruled out obstruction
7	11yrs/boy	L(HDN)	49 51 pujo	49 51 delayed excretion	EC ruled out obstruction. DTPA image clearance is not well documented.
8	1m/m	R(HDN)	58 42 pujo	76 24 pujo	RK overestimated in DTPA. Images are better with EC despite less administered dose
9	2m/m	R(HDN)	49 51 pujo	49 51 non obstructive	EC picked up horse shoe kidney(lower poles medially rotated)
10	1yr/m	L(HDN)	47.9 52.1	54 46	Picked up duplex on LK,

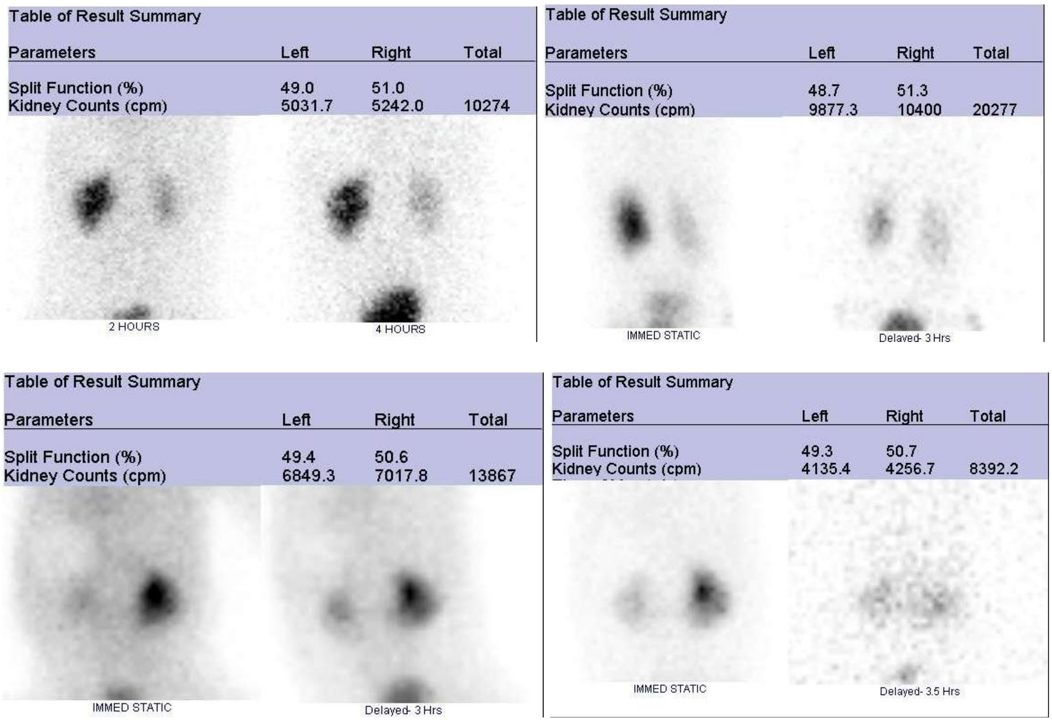
			pujo	60+40 and non obstructive	upper moiety functioning, hydronephrotic lower moiety. Puj non obstructive.
11	6m/f	b/l(HDN)	38.3 61.7 pujo no pujo	35 65 pujo no pujo	
12	1m/m	L(HDN)	58 42 pujo	48 52 non obstructive	EC showed reduntant pelvis, and delayed clearance
13	1m/m	R(HDN)	53 47 redundant pelvis	53 47	EC clearance prompt and no redundant pelvis
14	7yr/f	R(HDN)	60 40 pujo	65 35 pujo	EC more accurate in split function and showed thinned out parenchyma.
15	2m/m	L(HDN)	47.8 52.2 pujo	42 52 pujo	EC-more accurate split function
16	1m/m	L(HDN)	46.3 53.7 pujo	45.4 54.6 no pujo	EC ruled out obstruction
17	2m/m	b/l(HDN)	41 59 pujo	40 60 pujo	
18	2y/m	L(HDN)	44 66 pujo	45 55 pujo	EC picked up horseshoe kidneys(lower ends fused)
19	2yr/m	R(HDN)	94.9 5.14 pujo	95 5 pujo	Rt gross HDN, thinned out parenchyma
20	11m/m	R(HDN)	59 41 pujo	54 46 (62+38)pujo	Upper moiety functioning, lower pujo
21	6m/m	b/l(HDN)	50 50	51 49	EC picked up VUR on left side
22	2m/m	b/l(HDN)	44 56 pujo pujo	40 60 pujo partial pujo	LK function overestimated. RK redundant pelvis
23	12yr/m	R(HDN)	44 55 pujo	47 53 no obstruction	EC ruled out obstruction
24	4m/m	L(HDN)	17 83 pujo	12 88 pujo	
25	6m/m	L(HDN)	50.3 49.7	55 45	EC detected horse shoe kidneys
26	1.5yr/m	L(HDN)	48.7 51.3 pujo	49 51 no obstruction	EC ruled out obstruction
27	8m/m	L(HDN)	55 45 pujo	50 50 (51+49) no obstruction	LK-duplex. Upper moiety functioning. Lower moiety delayed clearance
28	8m/m	R(HDN)	48.2 51.8 pujo	53 47 no obstuction	Delayed clearance in RK. EC ruled out obstruction
29	3.1yr/m	L(HDN)	36.2 63.8 pujo	36 64 pujo	
30	1yr/f	L(HDN)	Not seen 100	8 92 pujo	LK not seen in DTPA.
31	13m/f	R(HDN)	94 6 pujo	95 5 pujo	Thinned out parenchyma with minimal function
32	6m/m	L(HDN)	42.2 57.8 pujo	36 64 pujo	LK function overestimated on DTPA

Comparative graphs of DTPA and EC scan in respect to time activity curve, delayed static images, split function of some patients are shown below.

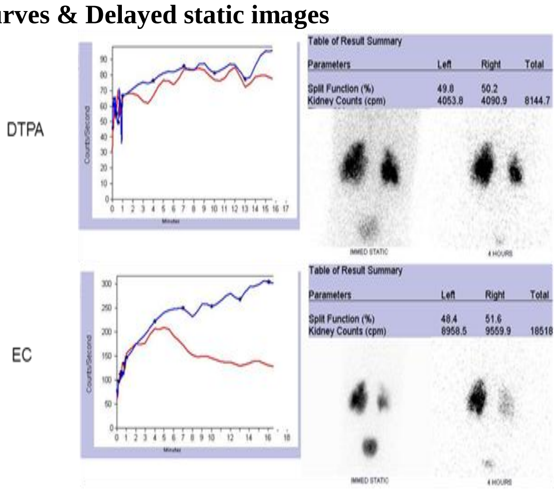
Time Activity Curves.



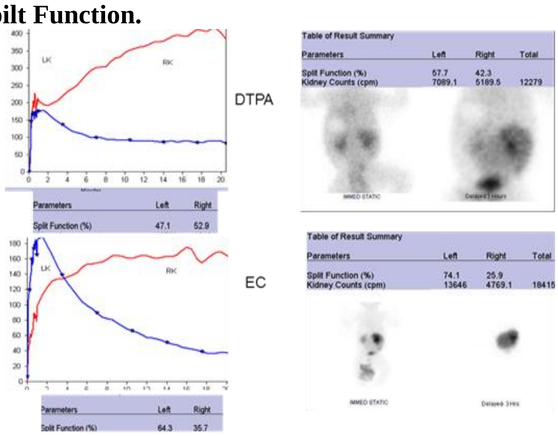
Delayed static images.



Curves & Delayed static images



Spilt Function.



In our study EC, showed following findings

- Ruled out obstruction -14 patients
- Detected duplex - 4 patients
- Detected horseshoe kidney in 2 patients
- More accurate function(over estimated in DTPA) -6 patients
- Showed kidney in one patient wherein DTPA failed to show in early images(megahydronephrosis)
- Better depictment of images in all patients

DISCUSSION

- L,L-ethylenedicysteine (EC) is a new carrier of technetium Tc 99m (99mTc) with a lower affinity to plasma albumin in comparison with diethylenetriamine pentaacetic acid (DTPA).[7]
- Renal clearance half life was shorter
- Results were similar in uraemic patients(s.creat>2mg)
- Less radiation-useful in children
- Better depictment of image
- EC is better in excluding obstruction presenting less false positive and indeterminate results.
- EC lyophilized kit is that its labelling with Tc99 is easy and rapidly obtained at room temp, remains stable upto 6 hrs
- High renal to background contrast and more accurate delineation of cortex to pelvis is possible
- Accurate assesment of split function
- Clearance can be commented when function is moderately impaired (split function is 20-35%)
- Can be done in gross hydronephrosis and kidneys with poor renal function where other radionucleide scans are contraindicated.
- Extraction efficiency is good(>50%)
- Information on cortical outline is possible

PHARMACOKINETICS:COMPARISON

	DTPA	MAG3	EC
Plasma clearance	>95% Renal	60% renal 40% liver	>95% Renal
Renal Handling	> 95% Glomerular Filtrn	95% tubular 5% Glomerular	85% tubular 15% Glomerular
Clearance	Around 100 ml/min	(300-350 ml/min, 50-65% of OIH)	(450-500 ml/min, 70-80% of OIH)
Extraction efficiency	15%	50%	>50%
Protein Binding	5%	70-90%	24%
Renal to background Ratio	Low, bad when function is impaired	fair	Very good
Information on cortical outline	Not possible	To some extent	possible

CONCLUSIONS

In this study, EC was more effective than DTPA[8] in

- Excluding obstruction
- Better depiction of split function and images
- Detecting associated anomalies
- Helpful in gross hydronephrosis

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