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Quantitative and qualitative scintigraphic measurement of Renal function in Persian cat using ^{99m}Technetium ethylenedicysteine and ^{99m}Technetium diethylenetriaminepentaacetic

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Abstract

Objective- To consider the use of renal scintigraphic evaluation of kidney function in Persian cat and make a comparison between ^{99m}Technetium ethylenedicysteine and ^{99m}Technetium diethylenetriaminepentaacetic in renal scintigraphy.

Design- Descriptive study

Animals- 6 male healthy adult Persian cats - no clinical sign of renal disorders and prior to presentation.

Procedure- The scintigraphy of right and left kidney using Gamma camera (Piker Model) and ^{99m}Tc-EC and ^{99m}Tc-DTPA as radiopharmaceuticals. Peak activity percentage (% PA), peak time (T_{max}), half emptying-time ($T_{1/2}$), total and individual GFR and flow and function time activity curves (TACs) are the determined parameters in this evaluation.

Results- % PA, T_{max} and $T_{1/2}$ in left and right kidney for ^{99m}Tc-EC and ^{99m}Tc-DTPA respectively, were 49/86 %, 50/1 %, 11/3 min, 11/5 min, 4/4 min, 4/6 min and 51/27 %, 49/05 %, 7/7 min, 8/3 min, 3 min, 3/43 min.

Moreover the quantities of total and individual GFR for left and right kidney measured by ^{99m}Tc-DTPA measured by modified Gates technique respectively, were 125/69 ml/min, 64/42ml/min (51/26 %), 61/24ml/min (48/73 %) and were in normal range defined by Gates technique.

Conclusion and Clinical Relevance- normal indices obtained for listed parameters and total and individual GFR quantities can play a major role in order to diagnose kidney disorder or function deterioration and can be a background and specialized knowledge conducive to future studies.

Also comparison of two radiopharmaceuticals ^{99m}Tc-EC and ^{99m}Tc-DTPA showed that ^{99m}Tc-DTPA scintigraphy has the superiority to assess the quantities of total and individual GFR so we can use ^{99m}Tc-DTPA to evaluate *Glomerular filtration rate in both kidneys.*

Key words- scintigraphy, kidney, cat.

Introduction

Nowadays, there is a greater need to utilize advanced techniques in the diagnosis of kidney abnormalities or function deterioration. The morphology of the kidneys can be assessed using radiology, ultrasonography, and, if necessary, computer tomography (CT) or Magnetic Resonance Imaging (MRI). An assessment of the kidney function is possible using excretory urography, scintigraphy, dynamic CT or MRI with contrast medium. However, the most commonly primarily applied and available technology is still the radiography[15].

In the past, CT was thought to be the first study of choice for a hospitalized patient in whom renal infection was suspected. CT demonstrates renal enlargement, poor corticomedullary definition and patchy areas of decreased density. Although, there may be some important drawbacks in the use of the technique in very young patients since sedation is required and respiratory movements are out of control[24].

Gamma scintigraphy is one of the modern diagnostic imaging methods similar to other methods such as radiography, ultrasound and endoscopy but in fact there is a major difference between this technique and the others which is the superiority of scintigraphy to perform physiological imaging. This technique is able to chart distribution of materials in a living organism determining the normal and abnormal processes of the target. These specifications have declared Gamma scintigraphy as a sensitive and specific method to confirm an accurate diagnosis[1].

A widespread range of renal abnormalities such as hydronephrosis, nephrolithiasis, polycystic degeneration of kidney, renal aplasia and hypoplasia, ureteral obstruction and kidney traumas can be easily diagnosed and distinguished by scintigraphic imaging technique[2].

The present study has been aimed to investigate value of dynamic renal scintigraphy with ^{99m}Technetium ethylenedicysteine and ^{99m}Technetium diethylenetriaminepentaacetic in 6 healthy male Persian cats in order to be a background conducive to future studies.

Materials and Methods

Animals

Six adult male persian cats were selected at first in order to obtain normal findings of renal scintigraphy. All cats were considered healthy based on a general physical examination, complete blood count, blood urea nitrogen, serum creatinine concentrations, routine urinalysis, radiology and sonography. All animals were held off feed 12 hours prior to scan but they had free access to water until the time of scan and they were in a moderately hydrated state before the examination because dehydration could lead to decrease in blood volume and as a result the radiopharmaceuticals will be washed out with a delay which is concerining with kidney function[5,18]. Every cat's height and weight were measured for scanning with ^{99m}Tc-DTPA.

Imaging technique

The cats were anaesthetized with a combination of Ketamin 10% (30 *mg/kg*) and Diazepam (0.2 *mg/kg*). Then they were positioned in dorsal recumbence with the gamma camera centred dorsal to the kidneys (figure 1). A catheter was placed in the saphenous vein of one of the back legs and flushed with 4 mci ^{99m}Tc-EC. The dynamic image acquisition, performed with a Gamma camera (Piker Model), was initiated simultaneously with the intravenous injection. Frames were acquired at 2 mins intervals and stored into a 128 × 128 digital matrix.

ROIs were drawn manually around both kidneys using the high count density-summed image of all frames, thereby avoiding overlap with the aorta, spleen, ureters or stomach.
The graphs of radiopharmaceutical activity in vessels until it's arrival to kidney (flow time activity graph) and then in kidney (function time activity graph) was drawn based on computer program for dynamic renal scan (figure 2)[11,12,13,14] and quantitative parameters including Peak activity percentage (% PA), peak time (T_{max}) and half emptying-time ($T_{1/2}$) were calculated for each kidney(table 1.)[14,20].
2-second and 2-minute films of ^{99m}Tc-EC radiopharmaceutical presence and activity in each kidney and bladder were provided by which we were able to observe radiopharmaceutical drainage from abdominal aorta to kidneys and from kidneys to the bladder (figure 3 and 4.)
Two weeks later the same cats were scanned with ^{99m}Tc-DTPA with the same dose. Frames were acquired at 3 mins intervals and stored again into a 128 × 128 digital matrix. ^{99m}Tc-DTPA superiority compared to tubular radiopharmaceuticals like ^{99m}Tc-EC was calculating some other parameters such as total and individual GFR for each kidney further than mentioned parameters in renal scan with ^{99m}Tc -EC (figure 5 and 6.).

Figure 1. Gamma scan camera device

Results

Average measured parameters of dynamic renal scan of 6 persian cats with ^{99m}Tc-EC and ^{99m}Tc-DTPA are shown in table 1 and 2.
Also, in dynamic renal scan with ^{99m}Tc-DTPA, quantitative results for individual GFR of each kidney, both left and right kidneys of every 6 cats (measured by *modified Gates method)*, were in normal range (45-55%) confirming clinical and para-clinical findings for kidneys health[6,21]. (table 2).
Also, according to provided graphs each radiopharmaceutical normally went through it's way in phases 1, 2 and 3, and in the part of graph corresponding to clearance phase or third phase, there was no sign of obstruction.
This study revealed that dynamic renal scintigraphy with ^{99m}Tc-EC can be an accurate and qualified technique for investigating renal function and abnormalities in Persian cats and a reliable method for future studies and researches.

And also comparison of tables 1 and 2 shows that ^{99m}Tc-DTPA scintigraphy has the superiority to assess the quantities of total and individual GFR for left and right kidney. So ^{99m}Tc-EC can be only used in investigating tubular function but ^{99m}Tc-DTPA can be used for total and individual GFR determination too.
Besides emptying half times for left and right kidney in scintigraphy with ^{99m}Tc-DTPA are shorter than with ^{99m}Tc-EC.

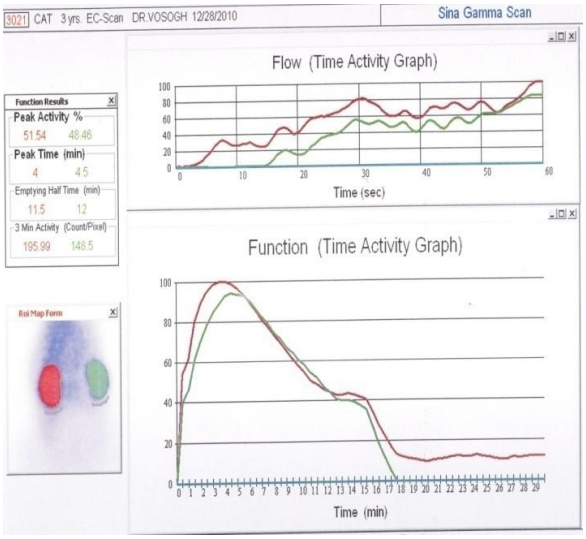

Figure 2. Dynamic renal scan with ^{99m}Tc-EC: Flow time activity and function time activity graphs.

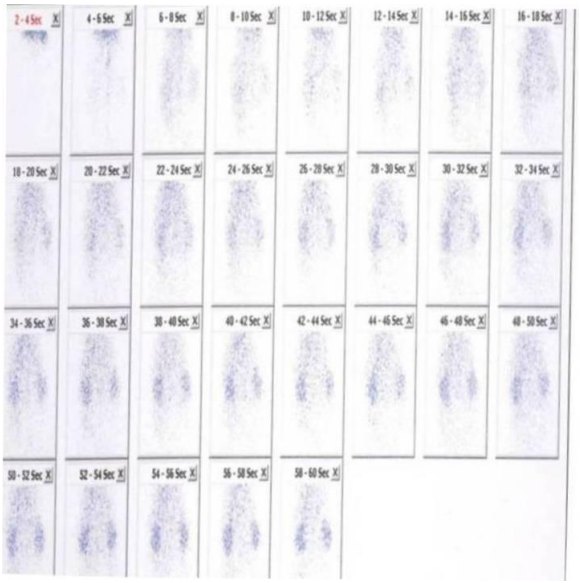

Figure 3. Dynamic renal scan with ^{99m}Tc-EC: 2-second films of radiopharmaceutical crossing from abdominal aorta to kidneys.

Figure 4. Dynamic renal scan with ^{99m}Tc-EC: 2-minute films of radiopharmaceutical crossing from kidneys and it's drainage to the bladder.

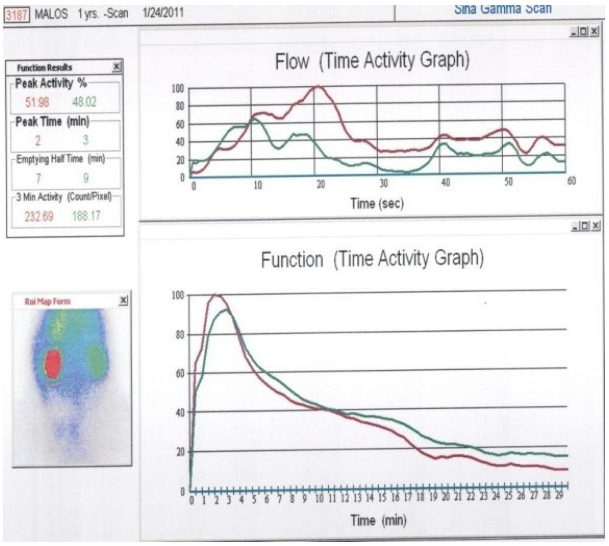

Figure 5. Dynamic renal scan with ^{99m}Tc-DTPA: Flow time activity and function time activity graphs

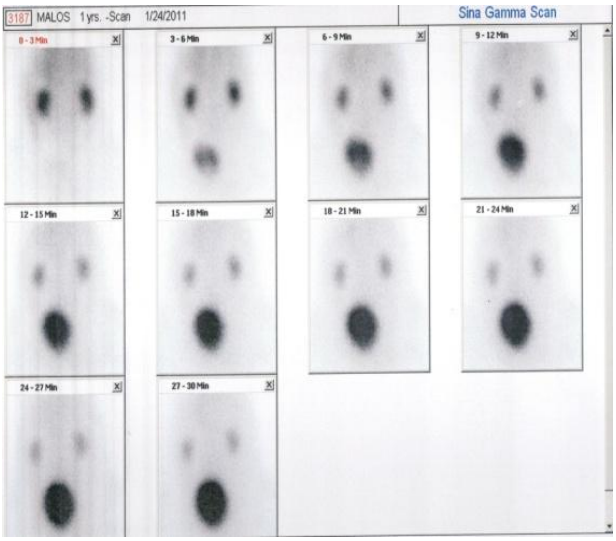

Figure 6. Dynamic renal scan with ^{99m}Tc-DTPA: 3-minute films of crossing from kidneys and it's drainage to the bladder

Table 1. average measured parameters of dynamic renal scan of 6 male healthy adult persian cats with ^{99m}Tc-EC

Parameters / samples	% peak activity	Time to peak activity(min) T_{max}	Emptying half time (min) $T_{\frac{1}{2}}$
Left kidney	49/86	4/4	11/3
Right kidney	50/1	4/6	11/5

Table 2. average measured parameters of dynamic renal scan of 6 male healthy adult persian cats with ^{99m}Tc-DTPA.

parameters / samples	Individua GFR (ml/min)	% Individual GFR (ml/ min)	% peak activity	Time to peck activity (min)	Emptying half time (min)	Total GFR (ml/min)
Left kidney	64/42	51/26	51/27	3	7/7	125/66
Right kidney	61/24	48/73	49/05	3/43	8/3	

Discussion

Nuclear medicine has been one of the modern and widespread medical fields for the last 30 years and now there are over 30 different techniques of nuclear medicine used as routine for patients in a modern hospital which many of them are practical methods of detecting cancer[1,6].

Uribe. D and et al. did some studies on GFR rate in cats at 1992 and thereby they investigated 6 healthy cats and 3 cats with clinical kidney disorders. This group induced lesions by nephrotoxic medications such as Gentamicin and Amphotericin B to ensure about the presence of renal lesions. They believe that by evaluation of obtained GFR rate and other datas, severity of subclinical kidney disorders can be determined[1, 21].

In 1996, westhoff et al investigated the presence of renal lesions such as hydronephrosis, polycystic degeneration of kidney, renal aplasia and hypoplasia and trauma in a study with ^{99m}Tc-MAG3 radiopharmaceutical on 11 animals including 5 cats and 6 healthy dogs and also 8 others including 7 dogs and 1cat[23]. Hecht et al in 2008 performed ^{99m}Tc-DTpA renal scintigraphy in 10 female healthy cats by which they evaluated the following parameters: global and individual glomerular filtration rate (GFR), shape of the time activity curve (TAC), $T_{1/2}$ and T_{max} curves. Besides they utilized a different kind of scan called Diuretic scan in which approximately 103 $\mp$ 6/2 mBq or 2/8 $\mp$ 0/2 mCi of radiopharmaceutical was injected intravenously into each cat[6].

We also injected about 4 mCi of ^{99m}Tc-DTpA radiopharmaceutical in our own study. This increase in dose of radiopharmaceutical will have wide effects on image resolution without intervention on final results but the negative and deleterious effects of this high dose on gonads should not be forgotten. These researchers obtained the total and individual amount of GFR according to Modified Gates technique[6,9,16,19] in which the normal total and individual GFR have been defined respectively: $\geq$ 2.5 ml/min and $\geq$ 1.25 ml/min1[6,22].

In 2003, Kibar. M et al performed a comparison of the estimates resulting from the renal scanning with 2 radiopharmaceutical ^{99m}Tc-EC and ^{99m}Tc-DMSA in which 29 children with various renal failures were investigated by dynamic scanning with with ^{99m}Tc-EC and after that static scanning with ^{99m}Tc-DMSA on the next day. According to the results of this study, a wider range of renal paranchymal lesions can be identified in static scanning with ^{99m}Tc-DMSA radiopharmaceutical[10]. Variation in results of GFR can be due to using different techniques, technical mistakes[8] or physiological homeostasis by kidneys[20] that in this study silimlar techniques and conditions were applied to perform all of the GFR measurements. The other technical factor that has the potential for error is the error before and after injection of the radiopharmaceutical, however this problem should be reduced to a minimum.

Time-interval and background region of interest (bg ROI) selection are also determining factors when calculating the glomerular filtration ratio (GFR) based on percentage uptake of $_{99m}$technetium-labelled diethylene triamine penta-acetic acid ($_{99m}$Tc-DTPA). In 2013, Debruyn and colleagues used three different time intervals (60–120 s, 120–180 s, 60–180 s) and three different bg ROIs (C-shape, caudolateral, cranial + caudal). In addition, in this study global GFRs based on percentage dose uptake of $_{99m}$Tc-DTPA for the different time-intervals and bg ROIs were compared with the global GFR based on $_{51}$chromium-ethylene diaminic tetra-acetic acid ($_{51}$Cr-EDTA) plasma clearance in nine healthy European domestic shorthair cats. Different time intervals seemed to cause significant variation (P <0.01) in absolute GFR values, regardless of the choice of bg ROI. Significant differences (P <0.01) between bg ROIs were only observed in the 120–180s time interval between the C-shape and cranial + caudal bg ROI, and between the caudolateral and cranial + caudal bg ROI. The caudolateral bg ROI in the 60–180 s time interval showed the highest correlation coefficient (r = 0.882)

between ^{99m}Tc-DTPA and ^{51}Cr-EDTA, although a significant difference (P <0.05) was present between both techniques[4].
The other effective factor on GFR is animal's water and dietary intake quality[3,6,7,13,14,17]. All the cats in this study received the same diet and were held off feed for 12 hours prior to the scan but they had free access to water until the time of scan. Anyhow we can't consider dehydration as a factor in decreasing GFR, however animal may not show none of the symptoms of decreased skin turgor, dry mucous membranes, long CRT, sunken eyes, tachycardia or cold extremities[17].
In comparison with other methods for GFR measurement which are time-consuming, scintigraphy is more helpful and we can have the result by it in a short time.

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چکیده

ارزیابی کمی و کیفی سینتی گرافی کلیه در گربه ایرانی با استفاده از دو رادیو داروی تکنسیوم اتیلن دی سیستئین و تکنسیوم دی اتیلن تریامین پنتاستیک

داریوش وثوق

گروه علوم درمانگاهی، دانشکده دامپزشکی، دانشگاه شهید باهنر کرمان، کرمان، ایران.

هدف- بررسی ارزش استفاده از سینتی گرافی کلیه در محاسبه میزان فیلتراسیون گلومرولی و عملکرد کلیه و مقایسه ی دو رادیو داروی ^{99m}Tc-EC و ^{99m}Tc-DTPA در سینتی گرافی دینامیک کلیه.

طرح مطالعه- مطالعه توصیفی

حیوانات- این مطالعه بر روی ۶ گربه سالم و بالغ ایرانی انجام گرفت. این گربه ها هیچ گونه علائم بالینی دال بر درگیری یا اختلالات کلیوی و قبل از ارزیابی نشان نمی دادند.

روش کار- جهت ارزیابی سینتی گرافی کلیه چپ و راست از دستگاه گاما اسکنر (مدل piker) و دو رادیو داروی ^{99m}Tc-EC و ^{99m}Tc-DTPA استفاده گردید.

پارامترهای درصد بیشینه فعالیت (PA ٪) ، نیمه عمر تخلیه دارو ($T_{1/2}$)، زمان بیشینه فعالیت (T_{max})، میزان فیلتراسیون گلومرولی کلی(total GFR) و میزان فیلتراسیون گلومرولی هر کلیه (individual GFR) و شکل نمودارهای زمان فعالیت (TAC) مورد بررسی و اندازه گیری قرار گرفت.

نتایج- درصد بیشینه فعالیت (PA ٪) ، نیمه عمر تخلیه دارو ($T_{1/2}$) و زمان بیشینه فعالیت (T_{max}) در کلیه چپ و راست برای رادیو داروهای ^{99m}Tc-EC و^{99m}Tc-DTPA به ترتیب، % 49/86، % 50/1، 11/3 min، 11/5 min، 4/4 min، 4/6 min و % 51/27، % 49/05، 7/7 min، 8/3 min، 3 min، 3/43 min بودند.

علاوه بر این، مقادیر GFR کلی و انحصاری کلیه چپ و راست که توسط رادیو داروی ^{99m}Tc-DTPA و طبق تکنیک گیت محاسبه گردیدند به ترتیب، ۱۲۵ /۶۶∓۵/۰۳ ml/ min، ۶۴/۴۲∓۴/۲۵ ml/ min (۵۱/۲۶∓۲/۲۹٪) و ∓۴/۳۲ml/min ۶۱/۲۴ (۴۸/۷۳ ∓۲/۷۵٪) بود که در رنج نرمال ارائه شده در این تکنیک قرار می گیرند.

نتیجه گیری و کاربرد بالینی- اندیسهای نرمال به دست آمده برای پارامترهای ذکر شده و نیز مقادیر کلی و انحصاری GFR

در این مطالعه می توانند معیاری برای تشخیص بیماری های کلیوی و یا اختلالات عملکردی کلیه و همچنین زمینه ای برای مطالعات آتی باشند.

همچنین مقایسه دو رادیو داروی ^{99m}Tc-EC و ^{99m}Tc-DTPA نشان می دهد که از رادیو داروی ^{99m}Tc-DTPA علاوه بر محاسبه پارامترهای مذکور میتوان در برآورد مقادیر کلی و انحصاری GFR نیز بهره جست.