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RADIONUCLIDE EVALUATION OF RENAL FUNCTION IN PATIENTS WITH RENAL STONE TREATED BY EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY

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Summary. *Radionuclide studies were made in 13 patients with renal stone within one week before and after ESWL treatment. GFR was estimated by measuring ^{99m}Tc-DTPA clearance, while ^{99m}Tc-DMSA renal uptake ratio was determined as an indicator of tubular function. Urine excretion was evaluated on residual renal activity value obtained from renogram. Pre-ESWL and post-ESWL mean values of ^{99m}Tc-DTPA clearance and ^{99m}Tc-DMSA renal uptake ratio showed no significant difference, neither for global kidney function nor for separate function of treated and untreated kidney. However, after ESWL individual values of treated kidney were found slightly changed in certain patients. Excretory parameter indicated urine flow improved in 4 patients and a delay in 3 patients. Pre-ESWL studies by ^{99m}Tc-DTPA detected decreased renal function in 4 patients, and by ^{99m}Tc-DMSA in 3 patients. Post-ESWL study with ^{99m}Tc-DTPA demonstrated the increase of glomerular function in one patient and the decrease in 2 patients, while ^{99m}Tc-DMSA showed the decrease and the increase of tubular function, each in 3 patients. Diverging responses to ESWL treatment reflect multifactorial mechanism of renal function outcome. This finding points the need to evaluate renal function before as well as after ESWL treatment in order to assess treatment success or complication occurrence. Radionuclide methods, providing quantitative information on specific function of each kidney separately, are particularly suitable for this follow up.*

Key words: *Radionuclide studies, renal function, renal stone, ESWL*

Introduction

Urolithiasis is a very common problem leading often to the progressive loss of renal function (1). Therefore, stone has to be eliminated from the kidney collecting system or ureter as soon as possible. The choice of the appropriate treatment modality is important to provide the efficacy and to lessen the morbidity. Extracorporeal shock wave lithotripsy (ESWL) was introduced as non-invasive, effective method and became very widely accepted management of renal stone disease. However, bioeffects of shock waves on renal tissue manifested with the impairment of kidney structure and function were reported (2,3). Experimental studies with various animal models showed histological changes of renal tissue after ESWL treatment (4). These findings point the need of the follow-up of patients treated by ESWL. The evidence of stone elimination and detection of structure damage involve various techniques, such as abdominal plain radiography, excretory urography, ultrasonography, computerized tomography and magnetic resonance. On the other hand, radionuclide methods provide information on kidney functions, which are often non available by other techniques.

The present study was aimed to assess the early outcome of glomerular filtration rate and tubular function by radionuclide methods in patients with renal stone disease treated by ESWL.

Patients and Methods

Thirteen patients with one side renal stone were involved in the present study. Patients were of both sexes, 8 women and 5 men, aged 26-48 years, and none of them had ureteral stent or nephrostomy. The location of the treated stones was renal pelvis in l0 patients, while 3 patients had calyceal stone. Stone size ranged from 6 to 21 mm. All patients studied had serum creatinine values within normal limits. Renal stone presence, location and size were evidenced by plain X-ray, excretory urography and ultrasonography.

Electrohydraulic lithotripsy device, Lithostar of Siemens was used for stone fragmentation. Mean equipment voltage was approximately 20 kV, while the number of shock waves varied from 1600 to 2500 de-

pending on the stone type suspected and the size measured. Shock waves were focused to the target areas determined by ultrasound probe.

Radionuclide studies were performed in all patients within one week, both before and after ESWL treatment. Glomerular filtration rate (GFR) was estimated by determination of ^{99m}Tc-DTPA clearance, renal uptake of ^{99m}Tc-DMSA was used to evaluate tubular function, while urine excretion was estimated by ^{99m}Tc-DTPA dynamic scintigraphy. Dynamic scintigraphy was performed by a Siemens Pho Gamma V camera linked to Scintiwiev computer, after i.v. injection of ^{99m}Tc-DTPA in a dose of l.85 MBq/kg b.w. Data acquisition was made in 16 seconds frames for 1216 s using 64×64 matrix. Renal time-activity curves were processed to obtain residual activity (RA) as an index of the rate of urine elimination from the kidney. Residual activity was expressed as a percentage of renal activity at the end of the study related to maximal renal activity. Total ^{99m}Tc-DTPA clearance was measured from a single blood sample drawn l80 minutes after radiotracer administration (5) and normalized to body surface 1.73 m^2. The single kidney function was calculated from the net counts accumulated by each kidney during 64-128 s with attenuation and background correction (6). These values were used to calculate relative kidney function, as a contribution of each kidney to total function, and to calculate absolute clearance of the single kidney.

Renal uptake of ^{99m}Tc-DMSA for individual kidney was measured from posterior image obtained 4 hours after iv injection of 1.85 MBq/ kg b.w. Absolute uptake of each kidney was presented as a percent of the radiotracer bound to the kidney related to the injected dose (7). The sum of both kidneys uptake was expressed as absolute value of total uptake, while the participation of each kidney to total uptake was presented as relative kidney uptake. Renal activity was corrected for the kidney depth, background activity and radionuclide decay.

Our previous studies showed the following normal values for parameters used: ^{99m}Tc-DTPA clearance 119±4.3 ml/min, RA 49±1.1%, ^{99m}Tc-DMSA renal uptake 48.8±1.9% and relative kidney function ranged 45-55% (8, 9).

Group values obtained for parameters analyzed were expressed as the mean±S.E.M., while Student t-test was applied to determine the significance of differences between pre-ESWL and post-ESWL values.

Results

Absolute values of ^{99m}Tc-DTPA clearance presented in Fig. 1 show no difference between pre-ESWL and post-ESWL glomerular filtration rate. The change was not found either for both kidneys (116.8±4.6 and 116.2±6.6 ml/min), or for treated (55.9±3.4 and 56.1±4.4 ml/min) and untreated (60.8±5.3 and 60.1±5.7 ml/min) kidney separately.

The corresponding values of ^{99m}Tc-DMSA renal uptake rate in both kidneys (45.5±2.6% and 44.3±2.3%), treated (23.3±2.2% and 21.6±1.7%) and untreated (20.1±1.7)% and 20.3±1.7%) kidney were also without a significant change after ESWL application (Fig. 2).

Mean values of 99mTc-DTPA clearance and 99mTc-DMSA renal uptake ratio were found within the normal range, while the comparison of ESWL-treated kidney values with those of contralateral kidney did not reveal a significant difference both before and after treatment (Fig. 1 and Fig. 2).

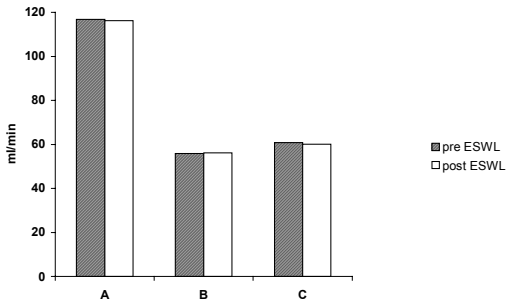

Fig. 1. ^{99m}Tc-DTPA clearance in patients with renal stone treated by ESWL.
A-total clearance; B-clearance of treated kidney; C-clearance of untreated kidney.

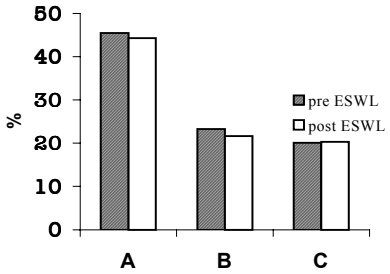

Fig. 2. ^{99m}Tc-DMSA renal uptake rate in patients treated by ESWL.
A-total uptake; B-uptake of treated kidney; C-uptake of untreated kidney.

Table 1. Urine elimination rate and relative ^{99m}Tc-DTPA and ^{99m}Tc-DMSA uptake values of ESWL treated kidney

Patients	RA (%)		^{99m}Tc-DTPA uptake (%)		^{99m}Tc-DMSA uptake (%)	
	Pre	Post	Pre	Post	Pre	Post
1. R.T.	100	100	38	40	49	50
2. S.S.	56	55	45	46	54	59
3. Z.V.	73	65	55	55	53	43
4. G.S.	57	75	46	46	49	54
5. V.I.	69	57	58	62	46	49
6. R.N.	51	50	48	45	49	47
7. D.K.	47	47	34	35	40	41
8. K.R.	59	58	83	84	88	89
9. A.J.	63	64	54	52	51	47
10.D.S.	62	69	50	46	51	50
11.J.A..	61	69	40	38	40	34
12.S.T.	84	79	30	32	30	32
13.Lj.P.	57	53	52	54	51	53
Means	64.5	64.7	48.7	48.8	50.1	49.8
S.E.M.	3.9	3.9	3.7	3.8	3.7	3.9

Table 1 shows individual excretory parameters and relative uptake rates of ^{99m}Tc-DTPA and ^{99m}Tc-DMSA in the treated kidney. Pre-ESWL and post-ESWL mean values of all parameters presented did not differ significantly, but individual values showed variations in several patients. The analysis of these parameters was made with the assumption that only changes of 3% or more could reflect the alteration of renal function by ESWL, while less variations may be due to method mistake. Considering as normal renal residual activity under 55%, urine excretion before ESWL was found normal in 2 patients and decreased in 10 patients, while one patient had a complete obstruction. ESWL treatment resulted in improvement of urinary excretion in 4 patients, but a delay in 3 patients also was observed. Complete obstruction was not resolved by ESWL, 9 patients had urinary elimination delayed, while in 3 patients a normal rate was recorded.

The presentation of relative function of the kidney on the stone side pointed decreased DTPA uptake in 4 patients and lower DMSA uptake in 3 patients. High value in one patient was caused by a very poor function of the opposite kidney. After ESWL treatment relative uptake of both radionuclide studied was found increased only in one patient. In summary, the study with ^{99m}Tc-DTPA showed glomerular function improved moderately in one patient and worsened in 2 patients, while tubular function estimated by ^{99m}Tc-DMSA was recorded as increased in 3 patients and decreased in 3 patients, too.

Discussion

Radiopharmaceutical application does not disturb physiological processes, since only tracer amounts of compounds are used. The use of radiopharmaceuticals with specific renal handling enables the separate estimation of different renal functions. Radionuclide studies provide semiquantitative or quantitative informations on renal perfusion, parenchymal function and urine flow. Glomerular filtration rate can be evaluated by ^{99m}Tc-DTPA, because its elimination has almost exclusively this pattern (10). On the other hand, renal uptake of ^{99m}Tc-DMSA was shown to represent an index of tubular function, due to high percentage binding to tubular epithelial cells (11). Hippurate labeled with radioactive iodine has a very high extraction rate from the blood followed by kidney elimination mostly by tubular secretion (12). These properties determine its use to measure effective renal plasma flow (ERPF).

The advatanges of radionuclide studies in the menagement of patients with urinary system obstruction involve the estimation of obstruction degree and parenchymal function to predict potential recovery as well as the evaluation of the recovery after treatment applied. Several options are available for the removal of renal stone, including open nephrolithotomy, percutaneous lithotomy and ESWL. The last method is based on stone fragmentation by shock waves to the size which allow passage through ureter. It is introduced in the treatment of stone disease due to less morbidity related to open surgery. The safety of ESWL was suggested by some studies which did not reveal any direct influence of shock waves on renal function. However, other clinical reports (2,3) and studies on animal models (4) established the occurrence of renal morphology changes secondary to ESWL. The harmful effect could be expected as a consequence of local contusion due to high energy shock waves propagation trough renal tissue. The study on rabbits showed histological renal damage after ESWL, including glomerular destruction, capsular thickening, tubular atrophy, and interstitial fibrosis (4). Free radicals and cellular membrane disruption were considered to have an important role in subcellular mechanism of injury and some pretreatments were attempted to lessen the incidence of complications (13, 14). The impairment of renal function was demonstrated obviously by some laboratory findings, such as transient nephrotic range proteinuria (15) and altered level of urinary marker proteins and serum enzymes (16, 17). Apart from renal contusion, obstruction of ureters by stone fragments is another major type of ESWL complication.

Plain abdominal radiography, excretory urography and ultrasonography are essential methods in the evaluation of the success in stone fragmentation and clearance of fragments from the kidney and ureter. On the other hand, radionuclide methods were showed particularly suitable for renal function evaluation in patients treated by ESWL. Goel et al. studied functional renal outcome in children after ESWL and showed no change in total or ipsilateral GFR within the mean follow-up of 31.7 months (18). Gilbert et al. found GFR increased after ESWL only in patients with kidney obstructed before the start of the procedure (15). Split renal function was proposed as more sensitive parameter to estimate renal function impairment. Gupta et al. found no significant change in total GFR at one and 3 months post-ESWL, while at the same time individual function of the treated kidneys was lower (19). A significant decrease in the mean split GFR was also found by Bomanji et al. 48 to 72 hours and 3 weeks after ESWL (20).

Similar findings were obtained in the investigation of ERPF. Thomas et al. reported total ERPF significantly decreased immediately after ESWL (20). However, Kaude et al. did not found total ERPF change following ESWL, while at the same time relative function of the treated kidney was shown diminished more than 5% in 30% of cases (22).

Tubular function was also estimated by determination of ^{99m}Tc-DMSA renal uptake. Matsura et al observed neither renal uptake rate nor uptake ratio rate of ^{99m}Tc-DMSA significantly changed one week after ESWL treatment (23). The follow-up of children by Lottman et al. up to three months after ESWL demonstrated a decrease of function and heterogeneous accu-

mulation of DMSA on the treated side (24). In the study of Lechevallier et al. a loss of local renal uptake of radiotracer was observed in all patients, but parenchymal scars were developed later only in some patients (25). All patients followed by Dumont et al. presented some anomalies of ^{99m}Tc-DMSA study after 48 hours of ESWL with an improvement after one month (26). Groshar et al found significantly lower value of absolute kidney uptake rate of ^{99m}Tc-DMSA in the treated than in normal kidney, but there was no significant difference between pre- and post-treatment values (27). In no patient of Munk et al. parenchymal scars were recorded by ^{99m}Tc-DMSA 5 weeks after ESWL (28).

The evaluation of renal function by measuring renal transit times of ^{99m}Tc-DTPA and ^{131}I-hippurate showed significantly prolonged parenchymal and shortened pelvic transit time in the kidney exposed to ESWL (29). This finding indicates parenchymal function worsened and urine drainage improved. However, the majority of ESWL treated patients followed by Michaels et al. had abnormal image finding demonstrating pelvocaliceal stasis (30).

Diverging findings on the effect of ESWL on renal function in rewieved radionuclide studies are probably due to the lack of ESWL parameters standardized or criteria defined for patients selection. For instance, it is known that renal injury is directly proportional to the number and energy of shock waves, being also dependent on the stone type, size and location. The second generation lithotriptors are proved to be more safe devices using lower energy and smaller focal target area.

In the present study, in patients with mostly maintained or slightly impaired renal function various early response to ESWL treatment was recorded. This difference in the outcome of glomerular filtration rate and tubular function appears to have multifactorial origin. Pre-ESWL factors influencing renal function include the state of renal function, existence of urinary infection and the presence of obstruction. Potential bioeffects of shock waves on renal tissue, and the relief of obstruction or, on the contrary, eventual occurrence of new ureter obstruction by stone fragments are postreatment factors affecting renal function. Greater number of patients with altered renal uptake rate of ^{99m}Tc-DMSA than that of ^{99m}Tc-DTPA may be due to higher sensitivity of tubular function to factors involved in urine drainage or to ESWL bioeffects.

This study favors radionuclide methods use in renal stone patients before ESWL treatment as well as in the follow-up. The assessment of the kidney functional status by radionuclide methods could be important for the choice of the treatment, because poor function is a limitation factor for ESWL use. The follow-up of patients treated by ESWL enables the insight in the success of the treatment and also in the occurrence of complications. Information on urinary flow available by dynamic scintigraphy is useful in detection of ureteric obstruction by stone fragments. Finally, quantitative measurement of specific function of the individual kidney makes radionuclide methods favorable for the evaluation of renal function and suggests their performance combined with other renal imaging techniques in the management of patients treated by ESWL.

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PROCENA FUNKCIJE BUBREGA RADIONUKLIDNIM METODAMA U PACIJENATA SA RENALNOM KALKULOZOM LEČENIH VANTELESNOM LITOTRIPSIJOM UDARNIM TALASIMA

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Kratak sadržaj. *Renalna kalkuloza dovodi do progresivnog gubitka funkcije bubrega. Ranim uklanjanjem kamena sprečava se dalje oštećenje i omogućuje oporavak reverzibilno oštećene funkcije. Vantelesna lipotripsija udarnim talasima (ESWL) je neinvazivna metoda lečenja sa manjim morbiditetom u odnosu na hirurške metode. Medjutim, uočeno je da i ESWL može izazvati komplikacije, usled kontuzije bubrežnog tkiva udarnim talasima ili opstrukcije uretera fragmentima razbijenog kamena. Nasuprot dezobstrukciji, kojom se popravlja bubrežna funkcija, nastale komplikacije mogu dovesti do njenog oštećenja.*

U ovom radu, u 13 bolesnika sa kalkulozom, bubrežna funkcija je ispitivana radionuklidnim metodama unutar jedne nedelje pre i posle podvrgavanja bolesnika dejstvu ESWL. Procena brzine izlučivanja urina vršena je na osnovu analize radiorenograma. Jačina glomerulske filtracije je odredjivana merenjem klirensa ^{99m}Tc-DTPA, a tubulska funkcija je procenjivana iz vrednosti 4-časovne fiksacije ^{99m}Tc-DMSA. Iz broja impulsa akumuliranih u jednom bubregu i broja impulsa oba bubrega izračunavana je relativna funkcija za svaki bubreg posebno.

Uporedjivanje dobijenih srednjih vrednosti pre i posle lečenja sa ESWL nije pokazalo postojanje značajnih razlika u klirensu ^{99m}Tc-DTPA i fiksaciji ^{99m}Tc-DMSA. Medjutim, pojedinačne vrednosti relativne funkcije tretiranog bubrega pokazale su lako smanjenu glomerulsku filtraciju u 4 bolesnika i smanjenu tubulsku funkciju u 3 bolesnika, pre lečenja sa ESWL. Posle lečenja, primenom ^{99m}Tc-DTPA u 2 bolesnika nadjeno je smanjenje, a u jednog povećanje funkcije, dok je primenom ^{99m}Tc-DMSA u po 3 bolesnika, u suprotnom smeru bila izmenjena funkcija. Ispitivanje brzine eliminacije urina pod dejstvom ESWL pokazalo je ubrzanje u 4, a usporenje u 3 bolesnika.

Različit odgovor na ESWL je posledica kompleksnog mehanizma uticaja na bubrežnu funkciju, a radionuklidne metode su vrlo pogodne za njenu procenu, radi provere uspešnosti lečenja, kao i za otkrivanje komplikacija.

Ključne reči: *Radionuklidne metode, bubrežna funkcija, renalna kalkuloza, ESWL*

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