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Are There Any Changes in Serum Renal Parameters in Patients Undergoing ESWL Therapy?

ESWL tedavisi gören hastalarda serum böbrek fonksiyon değerlerinde herhangi bir değişiklik olur mu?

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ÖZET
Amaç: Bu çalışmanın amacı, ESWL(Extracorporeal Shock Wave Lithotripsy) tedavisinin böbrek fonksiyon değerleri üzerine olan etkilerini incelemektir.
Materyal ve Metot: Kasım 2019 ve Ekim 2020 tarihleri arasında, böbrek taşı nedeniyle ESWL tedavisi yapılan ve çalışma kriterlerine uyan 50 erişkin hasta ile gerçekleştirildi. Ürogenital anomalisi olan ve soliter böbrekli hastalar çalışmaya alınmamıştır. Hastaların ortalama yaşı 37,2(26-67) idi. Hastaların 31'i(%62) erkek, 19'u(%38) kadındı. Hastalara 3 seans ESWL yapıldı ve seanslar arası süre 7 gün olarak belirlendi. İlk ESWL seansından bir gün önce rutin serum değerleri (Rutin I) alındı, ilk ESWL seansından bir gün sonra (Rutin II) ve 3. ESWLseansından bir gün sonra (Rutin III) tekrarlandı**.**
Bulgular: Kan serumu elektrolit değerleri, serum kreatinin değeri, glomerül filtrasyon hızı (GFR) ve bikarbonat değerlerinin rutinler arasında istatistiksel olarak farklı olmadığı görüldü.
Sonuç: Çalışmamızda elde ettiğimiz bulgulara göre, ESWL'nin üst üriner sistem taşlarının tedavisinde kullanımının hastalarda böbrek tübüllerinde disfonksiyona yol açmadığı, böbrek fonksiyon değerlerinin takibine gerek olmadığını göstermektedir.

Anahtar Kelimeler: Extracorporeal Shock Wave Lithotripsy, Böbrek taşı, Renal fonksiyon ve glomerüler filtrasyon hızı.

ABSTRACT
Objective: The goal of this research was to explain the effects of ESWL on renal function (Extracorporeal Shock Wave Lithotripsy)..
Material and Method: This study was carried out retrospectively between November 2019 and October 2020, with 50 adult patients scheduled to perform an ESWL treatment because of a diagnosis of kidney stone and to completed the study protocol. In all of these patients, there was no urogenital abnormality, and none had a solitary kidney. Patients' mean age was 37.2 (between 26 and 67 years of age). Of patients, 31 (62%) were male and 19 (38%) were female. Three ESWL sessions were carried out in the patients and the time between sessions was set at 7 days. The routines collected one day before the ESWL (Routine I) protocol were repeated one day after the first session (Routine II) and one day after the end of all ESWL (Routine III) sessions.
Results: There wasn't any statistically significant difference among routines in terms of the ratio of serum electrolytes, serum creatinine, GFR and spot urine/protein.
Conclusion: The findings indicate that the renal function tests do not need to assess whether ESWL leads to a tubular functional dysfunction in patients when treating upper urinary system stone disease.

Keywords: Extracorporeal Shock Wave Lithotripsy (ESWL), Renal stone, Renal function and glomerular filtration rate (GFR).

INTRODUCTION

Urolithiasis is one of the most common urinary diseases and its incidence tends to increase with age (Akinci et al., 1991). Although ESWL treatment has been an effective treatment since 1980, great progress has been made in the treatment of urinary tract stones. It is accepted as an important treatment option in upper, lower and middle calyx, renal pelvis and upper ureteral stones. Also, it is known that the success of ESWL is high, especially in small stones. Pregnancy, uncorrected coagulopathy and active urinary tract infection are considered absolute contraindications. The experience of the urologist and patient preference are also very important in the selection of treatment. The high success rate of ESWL in upper ureteral stones and

the potential undesirable side effects of other alternative treatments make ESWL the primary treatment modality in this group. This method of urolithiasis treatment is accepted because it offers non-operative treatment (Turna et al., 2005).

With this study, we aimed to estimate the possible side effects of ESWL on the group of patients with nephrolithiasis. Between November 2019 and October 2020 in our clinic, 50 adult patients who were diagnosed with a kidney stone and were underwent an ESWL treatment was enrolled into this study. We retrospectively investigated the effect of ESWL on kidney stones and discussed the subject by comparing it with the previous studies in the literature.

MATERIAL and METHOD

In our study, the data of 82 patients who were diagnosed with kidney stones and were scheduled for ESWL procedures who applied to our outpatient clinic between November 2019 and October 2020 were analyzed. Thirty-two of the patients were excluded from the study because they didn't comply with the study protocol.

Patients' mean age was 37.2 (between 26 and 67 years of age). Of patients, 31 (62%) were male and 19 (38%) were female. None of these patients suffered from a urogenital abnormality or had a solitary kidney. We examined patients with nephrolithiasis in our study. Patients with ureterolithiasis, cystolithiasis and urethrolithiasis were excluded from the study. Four of the patients, two male and two female (8%) was determined in an upper calyx stone, a mid calyx stone in 8, five male and three female (16%), a lower calyx stone in 9, six male and three female (18%) and a pelvis stone in 29, eighteen male and eleven female (58%).

The device employed in this procedure was an ELMED brand fluoroscopy focusing lithotripter. A maximum of 3000 shock-wave, accompanied with a 7-18 kv power was applied at each session. Three ESWL sessions were carried out in the patients and the time between sessions was set at 7 days. All patients who met the study criteria were included in a single group. The remaining 32 patients failed to complete the study protocol due to various reasons such as pain, non-compliance with the treatment, and inability to start the treatment because of acute infection. The routines collected one day before the ESWL (Routine I) protocol were repeated one day after the first session (Routine II) and one day after the end of all ESWL (Routine III) sessions. Fifty patients were able to complete this study protocol.

Before initiating the ESWL procedure, total blood count, serum BUN and creatinine levels, prothrombin time and partial thromboplastin time, total urine analysis and urine culture of all patients were evaluated. Antibiotic treatment was applied for patients who have bacterial reproduction in their urine culture, ESWL procedure was initiated to patients without reproduction in their urine culture. Creatinine (Cr), Na, K, Cl, Ca, P, Mg and venous blood gases of in blood serums were studied one day before the patients underwent a ESWL procedure. A total urine analysis was conducted. Protein and creatinine levels were studied in spot urine, plus a 12-hours urine was collected to calculate GFRs. This was the completion of Routine I. The next day patients underwent a first session of ESWL.15 days later the second session of ESWL and 30 days later the third session of ESWL were performed. Routine II was completed one day after the first session of ESWL while Routine III was completed one day after the end of the sessions of ESWL. GFRs of patients were calculated by the aid of the creatinine clearance formula [Clearance = U/PXV; U: Content of creatinine in urine (mg/dl); p: Plasma creatinine (mg/dl), and V: Amount of urine (ml)]. The biochemical tests of patient serums, venous blood gases and the protein/creatinine content in spot urine were measured by repeated measured variance analysis and the level of significance was considered 5% ($p<0.005$).

IBM SPSS Statistics ver. 22.0 (IBM Co., Armonk, NY, US) were used for the statistical analysis. Descriptive statistics were provided as mean for continuous

variables, and as percentage for categorical variables. Differences between more than two dependent groups were examined by Repeated measures analysis of variance. A p value of <0.05 was considered statistically significant.

RESULTS

No major complications were observed in any of the patients during the ESWL procedure. However, a stone path (strain strasse) developed in three patients and endoscopic ureteral stone-removing procedure was applied. Additionally, fever was noticed in two patients (mean 38 C degree) and this finding improved after appropriate antibiotic therapy. One patient was hospitalized for a single day due to severe pain. To understand whether ESWL affected renal functions, we measured the glomerular filtration rate (GFR), blood creatinine level and the bicarbonate level in venous blood gas. Calculated GFR values were found 86.06 ± 16.45 ml/min in Routine I, 88.42 ± 17.80 ml/min in Routine II and 90.16 ± 17.62 ml/min in Routine III. Alterations in GFR were within physiological limits and there was no any significant difference (p>0.05). The blood creatinine level was 1.06 ± 0.15 mg/dl at Routine I, 1.03 ± 0.13 mg/dl at Routine II and 1.03 ± 0.10 mg/dl at Routine III. Similarly, there was no any significant difference in blood creatinine level (p>0,05). Blood bicarbonate levels in blood samples collected from venous blood vessels without using a tourniquet was determined as 26.10 ± 1.27 mmol/L for Routine I, 25.21 ± 1.59 mmol/L for Routine II and 24.64 ± 1.47 mmol/L for Routine III. Also there was no any significant difference between bicarbonate levels in groups (p>0.05). The relationship between parameters related with renal functions and repeated routines are summarized in Table 1.

Table 1. Before and after ESWL, changes of GFR, bicarbonate and serum electrolytes

	I. Routine	II. Routine	III. Routine	p*
GFR (ml/min)	86.06 ± 16.45	88.42 ± 17.80	90.16 ± 17.62	0.400
Creatinine (Blood) (mg/dl)	1.06 ± 0.15	1.03 ± 0.13	1.03 ± 0.10	0.108
Bicarbonate (Blood gas) (mmol/l)	26.10 ± 1.27	25.21 ± 1.59	24.64± 1.47	0.302
Phosphorus (mg/dl)	3.15 ± 0.30	3.12 ± 0.27	3.14 ± 0.33	0.613
Calcium(mg/dl)	9.52 ± 0.31	9.55 ± 0.27	9.57 ± 0.25	0.788
Chlorine (mmol/l)	102.59± 1.81	102.91 ± 1.70	102.25 ± 1.41	0.732
Magnesium (mmol/l)	2.06± 0.15	2.07 ± 0.14	2.08 ± 0.16	0.658
Sodium (mmol/l)	138.98 ± 1.99	140.19 ± 2.40	139.45 ± 1.45	0.636
Potassium (mmol/l)	4.03 ± 0.29	3.97 ± 0.24	3.96 ± 0.25	0.561

* Repeated measures analysis of variance.

(I) : Routines obtained one day before ESWL

(II) : Routines obtained one day after the first ESWL session

(III) : Routines obtained one day after the end of all ESWL sessions.

DISCUSSION

ESWL is a less invasive method in the treatment of urinary system stone disease when compared to alternative operative methods. The procedure is also considered as one of the first in the treatment options of urinary system stone disease because it is easy to apply and in general, does not require hospitalization of the patient and plus has lower morbidity ratios. After it's wide spread use in urinary

system stone disease, miscellaneous studies related with the impact of ESWL on renal functions and different results were obtained in the acute and chronic term.

In animal model studies, a positive correlation has proven to be between histological renal tubular damage and urinary enzyme excretion generated by the shock wave energy (Weichert-Jacobsen et al., 1997; Weichert-Jacobsen et al., 1998). In different studies which were carried out, after the ESWL treatment, it has been shown that acute histological damage took place in structures including renal parenchyma, renal vessels and renal tissues and also led renal morphological changes such as subcapsular hematoma and focal parenchymal damage (Gunasekaran et al., 1989; Evan et al., 1991; Preminger, 1993). However, it was displayed that even though these damages in the renal units which were exposed to ESWL complied with the area to where shock wave energy spreads (Gunasekaran et al., 1989; Karlsen et al., 1991). Also they were closely associated with ESWL treatment parameters such as the number of shock waves, shock wave energy and host factors like renal immaturity, the presence of pyelonephritis and intact renal nerve (Evan et al., 1998; Evan et al., 1999; Connors et al., 2000; Connors et al., 2003; Willis et al., 2005). Especially in animal studies had shown that ESWL treatment did not have any effect on the renal development or animal growth. In addition, when the impacts of ESWL on renal function parameters were studied, in the treated renal unit it was demonstrated that reduction in renal plasma flow (RPF) and glomerular filtration rate (GFR) were acute and temporary. Also, this decline returned to baseline level within 24 hours (Connors et al., 2000, Evan et al., 1998, Willis et al., 1996). In a study conducted in the pediatric population, it was found that the long-term follow-up after ESWL for treatment of renal stones no effect on renal growth and no development of chronic diseases (El-Nahas et al., 2013). Of course, we also do not consider that at the microscopic level, ESWL is harmless or innocent in morphological, histological and physiological damage caused by its mechanical power and energy in stone fragmentation and comminution. However, we believe that in a way which supports our study this damage is transient and has no long-term effects on patients, who were selected according and treated with the appropriate protocol to the literature.

Literature data about the effects of ESWL treatment is more limited in human kidney. In physiological studies related to urinary enzymes and other markers indicating urinary injury, temporary increase related to those markers has been shown to return to normal levels within a few days or weeks after the treatment ESWL (Assimos et al., 1989; Recker et al., 1992; Rutz-Danielczak et al., 1992). Some researchers have evaluated urinary enzyme excretion and renal function parameters before and after ESWL treatment. In studies carried out by Karlsen et al., 1991; Rutz-Danielczak et al., 1992; Gupta et al., 1995; Goel et al., 1996; Ilgın et al., 1998 and which were related with GFR, it was reported that GFR values returned to baseline after the sudden temporary reduction or remained stabil after ESWL. In studies conducted by Pienkny et al., 1999 and Perry et al., 2000, in patients undergoing simultaneous bilateral ESWL treatment, even after their long follow-up period (mean, 3,5 years and 21 months) not any deterioration or impairment in renal function was shown. In our study, we found no any significant difference between GFR values which were calculated before the treatment was started, one day after the end of the first and third session. Findings obtained from our study, demonstrate a parallelism with the findings of investigators mentioned above. However, in a study carried out by Sheir et al., 2003, in the literature, showed a significant increase in GFR values after ESWL, but in a study carried out by Saxby, 1997, a significant decrease was observed and finally, in a study carried out by Cass, 1994, some patients displayed a decrease while some displayed an increase. When compared, findings obtained in our study demonstrate some differences with the findings of the investigators mentioned

above. We suggest that ESWL does not have an effect on GFR. Patients who were included in the study had bilateral kidneys and their biochemical parameters were within normal limits. Routines were not calculated separately, and total GFR was estimated. Therefore, even though GFR was altered in a kidney which was subjected to ESWL, we think that this variation was compensated by the aid of the other kidney.

Commonly, in the literature, serum creatinine is assessed together with GFR. In a study carried out by Greenstein et al., 1990; Karlsen et al., 1991; Gupta et al., 1995 and El-Assmy et al., 2008, the investigators presumed that ESWL was not capable to change serum creatinine values. The findings we have obtained from our study is compatible with the findings as mentioned in the literature above, regarding serum creatinine levels. No any significant difference was determined in serum creatinine levels before and after ESWL therapy. In a study conducted by Saxby, 1997, serum creatinine levels appeared to increase after a ESWL procedure. However, the result obtained from this study does not show parallelism with our study and other studies. We assume that ESWL does not alter serum creatinine levels.

In a study carried out by Saxby, 1997, it was shown that ESWL procedure caused an increase in serum calcium levels when compared with serum calcium levels prior the procedure. In our study, findings obtained with serum calcium levels does not show a parallelism with the findings obtained from the above study of the investigator. Accordingly, we assume that ESWL does not affect serum calcium levels. We also assume that, the reason that serum calcium levels were not altered, could rely on the fact that ESWL does not have an effect on tubular reabsorption. In a study carried out by Villany et al., 2001, it was determined that ESWL caused no any difference in serum sodium and serum potassium levels. In our study, we also found that there was no any significant difference between serum sodium and serum potassium levels, before and after ESWL. This data shows a similarity when compared with the data obtained from Villany.

No any studies were found in the literature related with serum phosphor and magnesium. In our study there is no any significant difference in serum phosphor and magnesium levels and the results obtained are within normal physiological limits.

Consequently, ESWL serum electrolytes, does not generate a significant difference on serum GFR and creatinine and serum bicarbonate studied in venous blood gas. ESWL treatment did not affect GFR, proteinuria and serum electrolytes in kidneys. The number of cases is extremely few in this study.

According to our opinion, ESWL which is used in the treatment of renal stones did not have a negative effect on GFR, proteinuria and electrolyte balance, when used in a short-term period, as the procedure is considered to be a safe method, but principally advanced studies related with the renal tubular function must be conducted.

Conflicts of Interest

The authors report no actual or potential conflicts of interest.

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