RENAL STONES "BIOEFFECTS AND FREQUENCIES OF SHOCK WAVE LITHOTRIPSY (SWL)"

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Aim Of The Work: Our primary end point of this prospective study was to evaluate the bioeffects of SWL for treatment of renal stones using different frequencies of shock wave lithotripsy to determine the optimal frequency required, not only for stone fragmentation, but also for safety concerning its bioeffects.

Patients And Methods: This prospective study was conducted upon 100 patients (64 male and 36 female) aged 17- 60 years with mean age 35.92 years. All patients had symptomatic renal calculi at the SWL unit, Urology Depart, Minia University Hospital, in the period between July 2008 and Aug. 2009. Extracorporeal shock wave lithotripsy (SWL) was used as primary treatment option for all patients. All patients subjected to complete history taking, clinical examination, laboratory and imaging studies. Patients were randomly classified into 3 groups according to the frequency of shock waves used: Group 1 included 30 patients in whom we used 60 shock waves per minute. Group 2: included forty patients in whom we used 90 shock waves per minute. Group 3: included thirty patients using shock waves 120 shock per minute. All patients were followed up within the first week, 3 months after SWL for the above mentioned laboratory and imaging study to assess the bioeffects of SWL in this group of patients.

Results: This study included 100 patients presented with symptomatic renal stones, in those group of patients in this work we noticed some degree of transient renal damage had occurred as a result of stone disintegration by SWL in the first week in the form of a varying degree of intra and peri-renal edema and hemorrhage as well as some degree of impaired renal function, also, there is a decreased in the intra renal blood flow within the first 24 hours after SWL which evidenced by increased renal vascular resistive index. Shock wave lithotripsy (SWL), not only produce renal damage but also has extra renal damaging effects to other organs such as liver (transient rise in the liver enzymes as well as bilirubin), pancreas (rise in the blood glucose level in the first 24 hours following SWL) and cardiovascular system (decrease pulse rate in the first 24 hours after SWL). These bioeffects of ESL not affected by the change in the frequency of shock waves between 60, 90, 120 shock/min except for hematuria which is markedly significant using high frequency shock waves? All of these bio effects produced by SWL disappeared three month after SWL.

Conclusion: All the bioeffects produced by SWL either physical and/or chemical are not influenced by changing the frequency of shock waves used for disintegration of renal calculi between 60, 90, 120 shock/min except for hematuria which was markedly significant with the use of higher frequency shock waves. All the bioeffects produced by SWL disappeared three months after SWL.

Key Words: Extracorporeal, Shock waves lithotripsy, bioeffects, frequency, renal calculi, resistive index.

INTRODUCTION

Shock wave lithotripsy since its first presentation in West Germany in the early 1980,1 has revolutionized the treatment of urinary tract stones. SWL has gained rapid acceptance worldwide because of its ease of use, noninvasive nature, and high efficacy in treating kidney and ureteral stones, and wide availability of lithotripters. SWL acts through a number of mechanical and dynamic forces on stones disintegration such as cavitations bubbles, shear forces, and spalling mechanism.2 The most important force is thought to be cavitations bubbles.2 The destructive forces generated when the cavitation bubbles collapse are responsible for the ultimate stone fragmentation. However, they can also generate trauma to thin-walled vessels in the kidneys and nearby organs,3 which result in haemorrhage, release of cytokines, inflammatory cellular mediators, and infiltration of tissue by inflammatory...
response cells. These may lead to short-term complications and to formation of renal scar and possible chronic loss of tissue function, the efficacy of lithotripsy is dependent on the interval between the shock waves, the success rate of lithotripsy decrease by decreasing the time between shock waves. Thus, the efficacy of lithotripsy is reversely proportional to the frequency of shock waves used.3

PATIENTS AND METHODS

This study included 100 patients (64 male and 36 female) aged 17-60 years old, with the mean age 35.92 years. Presented at out patients clinics of urology departments of Minia University Hospital, in the period from May 2007 to June 2009. All patients were presented with symptomatic renal calculi. Extracorporeal shock wave lithotripsy was used as primary treatment option for all patients. Our inclusion criteria in this study included patients with Solitary renal calculi either pelvic stone or calyceal stone less than 2.5 cm with no or mild back pressure changes in imaging studies. Our exclusion criteria include Patients with previous SWL, Diabetes mellitus, Liver diseases, medical diseases of the kidney and Patients with any previous history of coronary heart diseases and/or hypertension. All the patients in this study were subjected to complete history taking focusing on previous SWL sessions, any medical illness such as bleeding tendency, hypertension, diabetes mellitus and medical disease of the kidneys. Complete clinical Examination and laboratory work up such as complete urine analysis, culture and sensitivity when indicated, complete blood coagulation profile, renal functions tests, liver functions, fasting blood sugar, and 24h protein in urine were done for all patients in this study, and all patients had the following imaging studies in the form KUB plain films, Intravenous urography, abdominal ultrasonography and renal Doppler ultrasonography to assess renal resistive index at the level of inter lobar artery at the stone bearing area.

Patients in this series classified into three groups: Group 1 included 30 patients; in this group SWL has been done using frequency of 60 shocks waves per minute, group 2 included 40 patients; SWL has been done using frequency of 90 shock per minute and group 3 included 30 patients in whom SWL of 120 frequency per minute was used. Electromagnetic Siemens Lithostar lithotripter with Focal zone: 4 x 40 mm and Peak focal pressure: 650 bar. The voltage we used ranged between: 3:5 which equals (14.9:16.4 k.v.). All patients were followed up within the first week after therapy, 3 months later to assess the bioeffects of SWL in this group of patients.

RESULTS

This study were conducted upon one hundred patients with renal calculi (64 males &36 females) aged from 17-60 years (mean age = 35.92 years). Right side renal stones were found in 56 patient (56%) however left side renal stones were found in 30 patients (30%) and 14 patients presented with bilateral renal stones stone (14%). The patients were randomly classified into three groups according to the frequency of shock waves used for stone disintegration. Fifty two patients were presented by right renal colic, 38 patients presented with left renal colic, hematuria either microscopic/or macroscopic were seen in 28 patients (20 microscopic and 8 macroscopic hematuria) and only 2 patients were presented with bilateral renal pain.

Table (1): Number of sessions in each group.

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<tr>
<th>Number of sessions</th>
<th>Group 1</th>
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<th>Group 3</th>
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The mean duration of sessions in group 1 was 49.56 ± 4.312 minutes, 37.02 ± 4.13 in group 2 and 31.54 ± 1.71 in group 3. We found a statistically significant difference between group 1 and group 3 (p = 0.002) and between groups 2 and 3 (p = 0.022), we didn’t find statistically significant difference between group 1 and 2 (p = 0.256) fig. (1).
Fig. (1): The mean duration of sessions in the studied groups
Pethidine was given as analgesic in 46.07% of patients in group 3, 19.8% of patients in group 2 and 17.03% of patients in group 1 this summarized in figure (2). We found a statistically significant difference in the analgesic requirement between groups 1 and 2 (P = 0.029) and between groups 1 and 3 (P = 0.014). However, no statistically significant difference was noted between groups 2 and 3.

Fig (2): Patients received analgesia in each group

In table (2) RI significantly increased within the first 24 hours following SWL from 0.646 ± 0.054 to reach 0.681 ± 0.057 this rise in RI occurred in the three groups of patients, this rise in the RI returned to a level lower than the pre SWL one (0.628 ± 0.053). The changes in the RI were insignificant between the three groups of patients (p = 0.427).

We found a statistically significant correlation between the age of patients and changes in the resistive index following SWL (p = 0.041). There was higher basal level of resistive index in patient aged >40 years old (mean RI = 0.665 ± 0.062) than the age <40 years old (mean RI = 0.648 ± 0.058) fig. (3).

Regarding to the renal function in this study we found a statistically significant rise in blood urea and serum creatinine within the first week after SWL in the three groups of patients with a statistically significant decrease in their levels on follow up period after three months to reach the pre-SWL levels fig.(5,4). The difference in between the groups was statistically insignificant (P = 0.263 & P = 0.682 respectively).

Fig. (3): Changes in resistive index in relation to age

Table (2): Changes in the resistive index following SWL
Group 1 (30)

Group 2 (40)

Group 3 (30)

Total (100)

RI

Mean

SD

Mean

SD

Mean

SD

Pre SWL

0.637
3 month

0.620

0.042

0.635

0.045

0.622

0.051

0.628

0.053

![Graph](image.png)
Fig. (6): Changes in AST following SWL.
Fig. (7): Changes in ALT following SWL.
Fig (8): Correlation between the changes in liver enzymes after SWL and stone side.

Fig. (9) Changes in 24h protein in urine following SWL.
Table (3): Changes in the total and direct Bilirubin levels after SWL

<table>
<thead>
<tr>
<th>Group 1</th>
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<tr>
<td>Total</td>
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Bilirubin

Mean

Mean

Mean

Mean
Pre SWL

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<td>0.770</td>
<td>0.825</td>
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1 week
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<th>T.BILI</th>
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<th>0.768</th>
<th>0.856</th>
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<td>0.270</td>
<td>0.258</td>
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3 month

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<tr>
<th>T.BILI</th>
<th>0.767</th>
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Table (4): The changes in total bilirubin, ALT urinary RBCs in relation to total number of shock waves

Parameter

Total bilirubin

ALT

Urinary RBCs

Pre ESWL
Liver enzymes (AST & ALT) both of them showed a significant rise in the first week following SWL. These changes involved the two enzymes at the same patient or one of these enzymes. The levels of these enzymes statistically decrease to pre SWL level after 3 month fig. (6&7). In Three patients the liver enzymes levels decline but not reaching the pre SWL level. One case showed three folds rise in both enzymes, after 3 month the level dropped to levels slightly higher than the pre SWL one. The difference in between the groups was statistically insignificant.

We found a statistically significant correlation between the changes in the liver enzymes (Ast & Alt) in relation to stone side fragmented by SWL. (p = 0.014 & p = 0.019 respectively) as shown in fig. (8). The rise in liver enzymes more in the right sided stones more than the left sided ones (p = 0.034).

We also found a statistically significant rise in the total and direct Bilirubin in the three groups of patients one week after SWL. The
levels of total and direct bilirubin returned to pre-SWL values 3 month after SWL. The difference in total Bilirubin and direct Bilirubin between the groups was statistically insignificant (P = 0.319 & P = 0.221 respectively). see table (3).
There was a significant change in levels of total Bilirubin, Alt and urinary RBCs after SWL. These changes significantly correlate with the total number of shock waves (P = 0.014 & P = 0.047 & P = 0.005 respectively) see table (4).
The twenty four hours protein was significantly increased from 0.114 gm to 1.07 gm in the first 24 hours following SWL (p = 0.030) then it dropped to reach 0.115 gm after 3 month fig.(10). The difference in between the groups was statistically insignificant.
A significant rise in urinary RBCs during the first 24h following SWL (p = 0.032) in comparison TO pre SWL this rise significantly returned to levels lower than that of pre SWL after 3 month (p =0.002). A significant difference was found between group 1 and 3 (p =0.025). The difference between group 2 and 3 was statistically insignificant (p =0.430).

DISCUSSION
In this prospective study that conducted upon 100 patients (64 male and 36 female), we evaluated the renal bioeffects of SWL using different shock waves frequencies. The mechanism of disintegration of renal calculi by SWL produced by three mechanisms: pressure gradients formed by waves, spalling, and cavitation bubbles effects. Air bubbles form as a result of changes in pressure. The bubbles that are not reflected on the stone surface decrease the shock wave energy by spreading and absorbing it. For this reason, very little energy load is present when the next wave arrives. As the frequency of shock waves increase, no time is left for the spreading of the created cavitation bubbles, and they form bubble piles by joining with each other.
Intrarenal parenchymal hemorrhage produced in the renal tissue of canine kidney when a rapid frequency shock waves was used, similarly, acute histologic changes detected in the rabbit kidney at a rapid frequency; so that renal parenchyma damage, intravenous analgesia, and the sedation requirement are decreased with the use of a low frequency was also shown in human studies.
Many studies revealed significant deterioration in the renal functions after SWL this deterioration became more evident with post SWL renal obstruction, these changes in the renal functions return to normal values after three month following SWL and this similar to the results of our study.
In this study at the 1-week evaluation for our patients, we found a significant deterioration of the renal function in the form of rise in mean blood urea from 27.6 mg/dl pre SWL to 32.35 mg/dl within one week after SWL. Also mean serum creatinine level showed rise from 0.88 mg/dl pre SWL to 1.14 mg/dl within 1 week after SWL these values returned to pre SWL level after three month. The changes in the renal functions not related to changes in the frequency of shock waves. Other authors stated that the functional deterioration may last longer and require at least 90 days to return to the normal range, after SWL and this match with results gained in this study. We found a significant heamaruria evidenced by rise in mean urinary RBCs from 22.2 RBCs pre SWL to 40.1 RBCs in the first week after SWL in the three studied groups of patients. This rise returned to level lower than the pre SWL level after three month (mean 2.7 RBCs). The rise in urinary RBCs following SWL more with the use of frequency 120 shock/min than with frequency 60 shock/min and 90 shock/min.
There was no statistical difference on using frequency 60 shock/min or 90 shock/min. The rise in urinary RBCs after SWL was due to the various extent of reno-parenchymal damage with venous rupture particularly of the arcuate veins, occurring during SWL or due to passage of stone fragments following SWL. The adverse Effects of SWL on renal function are still to be identified. In a number of animal studies done after SWL which resulted in interstitial hematomata and/or hemorrhage. Interstitial hemorrhage was found in all kidneys immediately after SWL. Large extrarenal hematomas were found in up to 0.2% of post-SWL patients.
In our series of 100 patients Perirenal hematoma diagnosed by real time renal ultra sonography occurred in 2 patients in group 3 and was not found in group 1 & 2. Each one measured about 3 X 4 X 3.5 cm that completely disappeared after 2 weeks with the conservative treatment.
In 1999 Robert observed that administration of intravenous sedation and analgesia during SWL decreased as the frequency of shock waves decline he reported also Kidney damage and renal function decrease due to SWL have been shown to be directly proportional to the application of a rapid frequency.
In 2005 Erdal Yilmaz reported that the use of intravenous pain killer and sedative decreased on using low frequency of shock waves. In his prospective study, patient who treated with frequency 120 shock/min twenty three out of fifty six received analgesic and sedatives, with frequency 90 shock/min, nine out of fifty seven and with frequency 60 shock/min eight out of fifty seven received sedatives and analgesics.
In the present study non steroidal anti inflammatory medication and Pethidine was given as pain killer in 46.07% of patients with frequency 120 shock/min, 19.8% of patients with frequency 90 shock/min and 17.03% of patients with frequency 60 shock/min which delineated that with high frequency shock waves there was increased analgesic and sedative requirements.
Regarding to the interval between shock waves in 2005 Wiksell has reported that in patients who received shock waves at 0.4-second intervals, the stones disintegrated into minute particles, but they split into even more smaller one in those who received shock waves at 2-second intervals.14 In 1999 Greenstein conducted a cohort randomized a study upon 118 ceramic stones patients, he noticed that a greater disintegration rate of the calculi produced when he used a high energy levels and at a low frequency. He and co-workers observed that the best shock waves frequency for effective fragmentation was 60 shock waves per minute.15 Paterson et al. (2002) similarly asserted that decreasing the frequency in animal models increased the efficacy of SWL. Furthermore, although the total duration of therapy was significantly longer at a low frequency, its high success rate and decreased number of repetitive therapy sessions were evaluated as important advantages.16

For single renal calculus sizable between 1 and 2 cm a slower rate (SR) results in a better treatment outcome than faster rate (FR) for SWL. However, when stone diameter is less than 1 cm, stone free rate differences in the SR and FR treatment groups become less significant.17

The stone free rate in our study was 84.6% in group 1, 83% in group 2 and 80.1% in group 3. A statistically significant difference between the groups were found, Higher stone free rate was found in group 1&2 than in group 3 and this results similar to what obtained by Erdal Yilmaz et al. (2005).13 The efficacy of the process has also been shown to increase at lower frequencies in pediatric patients with stones.18

Studies showed that the mean duration of session was 25.54 ±1.51 min with frequency 120 shock/min, 31.02 ±3.13 min with frequency 90 shock/min and 48.56 ±5.312 min with frequency 60 shock/min.13 However, duration is an important problem in SWL performed at a low frequency. As the duration increases, the number of patients treated may decrease. Thus, it is clear that the optimal frequency should be determined in terms of time and success rate to find the answer to the question regarding the optimal frequency.13

In our present study the mean duration of sessions in group 1 was 49.31 ± 4.112 min, 37.02 ±4.13 in group 2 and 31.54 ±1.71min in group 3. We observed that the reduction of frequency from 120 to 60 shock/min increased the rate of successful treatment. However, we also noted that the SWL duration at frequency 60 shock waves per minute was prominently greater. As a result the frequency of 90 shock/min appeared to be a preferable frequency because of the high rate of successful treatment and the shorter duration.

Gilbert et al. (1988) found a significant proteinuria following SWL and he explained this proteinuria by the excreted hemoglobin occurring with haemolysis, and plasma protein in urine resulting from endothelial disruption or altered glomerular permeability.19 On the other hand, (Mumtaz A., 1990) explained the proteinuria by structural and functional changes that lead to an increase in permeability across the renal tubule.20

The current study revealed significant proteinuria within the first 24h following SWL in the three groups of studied patients with significant normalization of the protein concentration in urine was found after 3 month following SWL in the three groups of patients these results similar to Gilbert et al. (1988). There was no correlation between the change in the frequency of shock waves and proteinuria.19

The resistive index (RI) has proved to be a sensitive tool for monitoring vascular and tubulo-interstitial diseases of the kidney. It is widely used to detect intrarenal edema, which occurs in transplant rejection, acute tubular necrosis and obstructive pyelocaliectasis. In all of these conditions, RI levels greater than 0.7 are considered to indicate pathologic change.21

In our study we measured the vascular resistive index of the interlobar arteries in the stone bearing area pre SWL, within the first 24 hours following SWL and after three month. We found that the RI significantly increased within the first 24hours following SWL from 0.646 ± 0.054 to reach 0.681± 0.057 this rise in RI occurred in the three groups of patients, this rise in the RI returned to a level lower than the pre SWL one (0.628 ± 0.053). The changes in the RI were insignificant between the three groups of patients, so the RI changes not related to the frequency of shock waves.

In our study Patients > 40 years old had higher RI baseline levels (mean RI = 0.665 ± 0.062) than patients <40 years old (mean RI= 0.648 ± 0.058). This may be attributed to a loss of elasticity of renal tissue and sclerosis of intrarenal vessels. The rise in the RI following SWL not related to the age of the patients.

Other studies showed that elderly patients had significantly a higher basal RI (0.657 ± 0.068) than younger patients (0.640 ± 0.047) and reported the presence of a significant changes in the RI following SWL by using piezoelectric shock wave generator.21 Beduk et al. (1992) reported that no significant difference was recorded in RI of the renal vessels before and after treatment with Dornier MPL 9000 lithotripter.22 Kataoka et al(1993) reported that significant increase in RI were observed in 23 patients immediately after treatment with the Dornier MPL 9000 lithotripter. In another study reported a positive correlation between patient age and post-SWL changes in RI, they evaluated RI in 76 patients within 3 h after SWL with a Dornier HM5 lithotripter.23

Our study revealed a significant affection of the liver function in the form of significant rise in liver enzymes (AST & ALT) as well
as total and direct Bilirubin in the first week following SWL, there was a significant correlation between the stone side and the changes in liver functions, the rise was more prominent on right sided stones. These changes in the liver function returned to pre-SWL levels after three month following SWL, there was one patient in the study showed three folds rise in both AST & ALT in the first week following SWL with rise in total and direct bilirubin, hepatitis markers showed negative results. After three month the liver function normalized and became near to the pre SWL levels. In three patients on follow up after three month, the liver enzymes didn’t reach the pre-SWL levels and on follow up after 6 month returned back to the pre-SWL level.

Brian W. Goodacre et al. (1990) studied the effects of biliary lithotripsy on liver functions and reported that a significant affection of liver functions occurred following SWL which may be due to direct tissue damage or obstruction of the biliary passages by the stone fragments. Padilla Valverde et al. (2001) described a case presented with the presentation of a hepatic subcapsular hematoma as a complication following an extracorporeal renal shock wave lithotripsy. In our study the changes in the liver functions due to direct cellular injury caused by shock waves and these injurious effects more at the right which may attributable to close anatomic relation of liver to the right kidney.

CONCLUSION
The efficacy of lithotripsy is dependent on the interval between the shock waves, the success rate of lithotripsy decrease by decreasing the time between shock waves. Thus, the efficacy of lithotripsy is reversely proportional to the frequency of shock waves used. Using a low frequency of shock waves decreases the number of sessions required for stone disintegration in addition to angesics and sedatives requirement. However, the reduction in frequency will result in prolongation of the session duration. The effects produced by SWL not affected by the change in the frequency of shock waves between 60, 90, 120 shock/min except haematuria which is marked with the use of higher frequency shock waves. All of these effects produced by SWL disappeared three month after SWL.

REFERENCES


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