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# EFFECT OF EXTRACORPOREAL SHOCKWAVE LITHOTRIPSY (ESWL) ON ENZYMATIC AND ELECTROLYTIC LEVELS IN RENAL STONE PATIENTS

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**ABSTRACT**

OBJECTIVE : *To study the effects of Extracorporeal Shockwave Lithotripsy (ESWL) on Enzymatic and Electrolytic level in renal stone patients.*
STUDY DESIGN : *Observational study*
PLACE AND DURATION : *Department of Biochemistry, Basic Medical Sciences Institute (BMSI) , Jinnah Postgraduate Medical Centre (JPMC), with collaboration of Sindh Institute of Urology and Transplantation (SIUT) Karachi, from Feb. 2007 to March 2008.*
PATIENTS AND METHODS : *Twenty males and ten female patients, mean age (35± 9.6 years) with kidney stones 2.0 cms in diameter were investigated for serum Alkaline Phosphatase (ALP), Lactate Dehydrogenase (LDH), Glutamic Oxaloacetic Transaminase (GOT), Glutamic Pyruvate Transaminase (GPT), Electrolytes ($Na^+$,$K^+$,$Cl^-$), Calcium and Phosphorous. 24 Hrs. urine specimens were collected to be tested for urinary Sodium, Potassium, Chloride, Calcium and Phosphorous. Blood and Urine samples were collected before ESWL and Day-1 and Day-5 after ESWL. All serum and urinary parameters were run by commercially available kits from Stanbio Diagnostic, USA using Hitachi system 704 model autoanalyzer. Serum and urinary electrolytes were measured by Ion Selective Electrode (ISE) technology method using "EasyLyte" automated microprocessor controlled analyzer. Data analysis including paired and correlation analysis were computed using SPSS software version 10.0 for windows. P value upto 0.05 was considered significant for all comparisons.*
RESULTS : *Significant increments ($p<0.001$) in serum levels of ALP, LDH, SGOT, SGPT,and urinary levels of sodium, potassium, chlorides were noted on 1st Post-ESWL day, which reached the highest value on first post-ESWL day and then decreased to the pre-treatment level on 5th Post-ESWL day as the number of shocks increased from 2000-3500 shockwaves.*
CONCLUSION : *The results suggested that ESWL is not devoid of side-effects. The significant acute trauma to the kidneys and adjacent tissues such as liver, skeletal muscles induced by shockwaves exposure were exhibited by significant increase in cell escaped enzymes and electrolytes and that the extent of damage depends on energy and number of shockwaves exposure.*

**KEY WORDS :** Extracorporeal Shockwaves Lithotripsy (ESWL), serum enzymes, serum electrolytes, urinary electrolytes, renal function, energy level.

## INTRODUCTION

Kidney stone disease is a major problem in Pakistan as this country belongs to the so-called stone belt. Urolithiasis is common in all regions of Pakistan[1]. The highest incidence of kidney stone is in the age group of 31-40 years. Stones are more frequent in males than in females, with a ratio 2:1, and the most common stone is the "infection stone", consisting of calcium phosphate or magnesium ammonium phosphate[2]. Majority belongs to poor socioeconomic strata. A large number of subjects were either labourers or farmers and had a positive family history of stones[3].
Extracorporeal shock wave lithotripsy (ESWL) is the preferred modality for the treatment

of renal and upper ureteric calculi. ESWL is a technique by which stones can be broken by shockwaves generated outside body and focused on the stone[4]. Shockwaves are focused to disintegrate kidney stones which are frequently being voided through urine[5]. Shockwaves cause fragmentation of stone by erosion and shattering. Erosion at the entry and exists sites of the shockwaves result from cavitational force. Shattering results from energy absorption with stress, strain and shear force[6]. The importance of traditional factors in predicting ESWL success, such as stone size, location, composition and renal anatomy, are well known[7]. More recently, authors have created nomograms to predict stone-free outcome after ESWL. Others have used the information obtained from computed tomography to predict stone comminution. In addition, modifications in shock wave delivery by altering shock rate and voltage have been researched in an effort to improve shock wave efficacy[8].

Increased risk of cellular injury occurs at energy levels of greater than 2000 shockwaves at 20 kilo volt (kV), thus causing increase level of enzymes in the serum. The low energy treatment has only mild increase in enzyme level including less cellular injury. In general, as the shocks increase from 2000 to 3500 shockwaves, lesion size increases. The most profound functional change, noted was a 70% decrease in renal function and protein excretion exceeding 1.5 gm. one hour after 2000 shockwaves at 24 kilo voltage[9]. A majority of shockwaves lithotripsy (SWL) patients have elevated serum enzymes, implying significant acute trauma to the kidney and adjacent tissues such as liver and skeletal muscles[10]. Elevation of alkaline phosphatase (ALP) has been shown to sensitive and specific marker of proximal tubular damage. The number of shock waves that can be delivered at each session depends on the type of lithotripter and shock-wave power. There is no consensus on the maximum number of shock waves. However, as the shock-wave frequency increases, tissue damage increases, stone disintegration improves at lower frequencies[11]. The aim of our study was to evaluate the effects of ESWL on enzymatic and electrolytic level in renal stone patients by measuring blood and urine chemistry as well as to investigate the degree of severity of shockwave induced renal damage.

## PATIENTS AND METHODS

It was a descriptive observational study, carried out in the Department of Biochemistry, Basic Medical Sciences

**TABLE – 1**

**CHANGES IN SERUM ENZYMES BEFORE AND AFTER ESWL**

***Number of observation and units are given in parenthesis***
***Individual values are expressed as mean ± s.e.m.***

| Parameters | | ESWL Effect | | |
|---|---|---|---|---|
| | Post – ESWL (n=30) | Pre – ESWL (n=30) | | |
| | | 1st Day | 5th Day | D5-D1 |
| ALP (U/L) | 159.63 ±9.38 | ** 190.17 ±10.29 | †† 161.50 ±8.77 | 28.67 ±6.03 |
| LDH (U/L) | 363.07 ±10.16 | ** 403.03 ±8.67 | **†† 354.73 ±10.01 | 48.30 ±5.46 |
| SGOT (U/L) | 33.97 ±2.86 | ** 44.23 ±3.07 | **†† 31.37 ±2.65 | 12.87 ±2.12 |
| SGPT (U/L) | 21.70 ±1.94 | ** 29.70 ±2.07 | *†† 19.90 ±1.92 | 9.80 ±1.78 |

* P<0.01; ** P<0.001 : Significant when compared to Pre-ESWL
† P<0.01; †† P<0.001: Significant when compared to 1st Post-ESWL day
Pre-ESWL = Before exposure to Extracorporeal Shockwave Lithotripsy
1-Day Post-ESWL = First Day after Extracorporeal Shockwave Lithotripsy
5-Day Post-ESWL = Fifth Day after Extracorporeal Shockwave Lithotripsy
D5-D1 = Difference between fifth and first Post-ESWL Day.

**TABLE – 2**

**COMPARISON OF SERUM ENZYMES BEFORE AND AFTER EXPOSURE TO ESWL BETWEEN RIGHT AND LEFT KIDNEYS**

***Number of observation and units are given in parenthesis***
***Individual values are expressed as mean ± s.e.m.***

| Parameter | Right Kidney (n=14) | | | Left Kidney (n=16) | | |
|---|---|---|---|---|---|---|
| | Pre-ESWL | Post – ESWL | | Pre-ESWL | Post – ESWL | |
| | | 1-Day | 5-Day | | 1-Day | 5-Day |
| ALP (U/L) | 162.69 ±11.55 | ** 198.38 ±13.52 | 168.62 ±10.93 | 157.63 ±14.58 | 185.38 ±15.59 | 163.38 ±13.93 |
| LDH (U/L) | 360.00 ±14.77 | 396.85 ±12.34 | 349.62 ±14.27 | 368.56 ±14.40 | ††† 408.88 ±12.60 | ††† 362.00 ±14.27 |
| SGOT (U/L) | 29.46 ±3.86 | 41.92 ±5.80 | 27.23 ±3.77 | ††† 36.94 ±3.66 | 45.56 ±3.19 | ††† 34.06 ±3.69 |
| SGPT (U/L) | *** 22.69 ±2.66 | *** 32.38 ±3.33 | *** 21.23 ±2.82 | 19.38 ±2.43 | 26.25 ±2.23 | 17.44 ±2.32 |

* P<0.05; ** P<0.01; *** P<0.001 : Significant when compared to Right Kidney
† P<0.05; †† P< 0.01; ††† P<0.001: Significant when compared to Left Kidney
Pre-ESWL = Before exposure to Extracorporeal Shockwave Lithotripsy
1-Day Post-ESWL = First Day after Extracorporeal Shockwave Lithotripsy
5-Day Post-ESWL = Fifth Day after Extracorporeal Shockwave Lithotripsy

**TABLE - 3**

**CHANGES IN SERUM AND URINARY ELECTROLYTES BEFORE AND AFTER ESWL**

***Number of observation and units are given in parenthesis***
***Individual values are expressed as mean ±s.e.m.***

| Parameter | ESWL EFFECT ON ELECTROLYTES | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | SERUM | | | | URINE | | | |
| | Pre-ESWL (n=30) | Post-ESWL (n=30) | | | Pre-ESWL (n=30) | Post-ESWL (n=30) | | |
| | | 1st Day | 5th Day | D5 -D1 | | 1st Day | 5th Day | D5 -D1 |
| | | ** | ** †† | | | ** | ** †† | |
| Na+ (m Eq / L) | 140.33 ± 0.54 | 142.83 ± 0.73 | 137.10 ± 0.64 | 5.70 ± 0.66 | 164.90 ± 1.09 | 171.03 ± 1.45 | 162.13 ± 1.24 | 8.90 ± 1.19 |
| | | * | ** †† | | | ** | ** †† | |
| K+ (m Eq / L) | 3.96 ± 0.07 | 4.11 ± 0.08 | 3.65 ± 0.08 | 0.46 ± 0.08 | 14.98 ± 0.49 | 16.14 ± 0.57 | 14.01 ± 0.44 | 2.31 ± 0.31 |
| | | * | **†† | | | ** | ** †† | |
| Cl? (m Eq / L) | 102.50 ± 0.42 | 103.40 ± 0.45 | 99.27 ± 0.60 | 4.13 ± 0.53 | 129.80 ± 1.35 | 134.00 ± 1.43 | 128.03 ± 1.38 | 5.97 ± 0.64 |

* P <0.01; ** P <0.001 :Significant when compared to Pre-ESWL
† P <0.01; †† P <0.001 : Significant when compared to 1st Post-ESWL day
Pre-ESWL = Before exposure to Extracorporeal Shockwave Lithotripsy
1-Day Post-ESWL = First Day after Extracorporeal Shockwave Lithotripsy
5-Day Post-ESWL = First Day after Extracorporeal Shockwave Lithotripsy
D5-D1 = Difference between fifth and first Post-ESWL day

Institute (BMSI) , Jinnah Postgraduate Medical Centre (JPMC), Karachi, from Oct. 2007 to March 2008. The cases that were included presented as out-patient from the "Stone Clinic" of Sindh Institute of Urology and Transplantation (SIUT) Karachi, were examined, evaluated and were qualified for the study having following criteria :-

(a) X-ray or ultrasound evidence of unilateral or bilateral urinary lithiasis.
(b) Absence of acute infection.
(c) Adult patients age less than 60 years.
(d) All patients have normal blood chemistry findings.

All patients with other systemic illness were excluded . Thirty patients, twenty males and ten females, mean age (35± 9.6 yrs) range (22-58 yrs) with unilateral and bilateral renal stones 2.0 cms in diameter were included in the study. Sixteen patients were treated for stones in the Left kidney, thirteen for stones in Right kidney and one for stones in both kidneys. Nine calculi were located in the pelvis, four in the upper calyx, sixteen in the middle calyx and one in lower calyx of the kidney.

Data were collected along with physical and systemic examination using a questionnaire comprising of socio-demographic features, medical history, present, past and family history of stone disease. Blood and 24 hours urine sample (n=30) were collected before treatment ( Pre-ESWL ) and on $1^{st}$ and $5^{th}$ Post-ESWL Days of treatment. Instruments used were "Hitachi" System 704 Model Autoanalyzer and "EasyLyte" Automated Microprocessor Controlled Analyzer. All serum and urinary parameters except serum and urinary electrolytes were run by commercially available kits for alkaline phosphatase (ALP), lactate dehydrogenase (LDH), glutamic oxaloacetic transaminase (GOT), glutamic pyruvate transaminase (GPT) using Hitachi system 704 model autoanalyzer. Kits were obtained from Stanbio Diagnostic, USA. Serum and urinary electrolytes ($Na^{+,}$ $K^{+}$, $Cl^{-}$) were measured by Ion Selective Electrode (ISE) Technology method using 'EasyLyte' automated, microprocessor controlled analyzer. ESWL was performed with the Dornier HM-4 lithotriptor. The mean number of exposure was 2944 ± 67.61 shockwaves delivered at 20 kV. We studied patients with kidney stones in three groups using same voltage but different number of shockwaves to identify the severity of renal damage .Each group received shockwaves (GROUP – I : Range 2000 – 2500, mean 2355 ± 61.22), (GROUP – II : 2600 - 3000, mean 2827 ± 48.33 ) and (GROUP – III :Range 3100 - 3500, mean 3247 ± 51.03 ) delivered at 20 kilo volts .

STATISTICAL ANALYSIS :

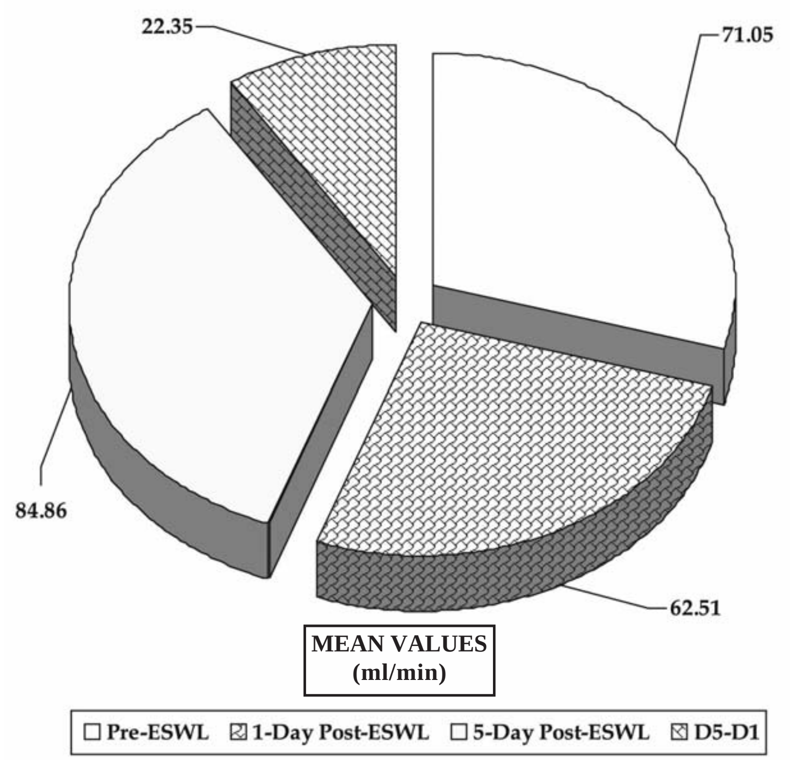
Data analysis including paired and correlation analysis were computed using SPSS software version 10.0 for windows. Paired 't' test were used to determine the significance of changes in all parameters after ESWL. P (probability) value of 0.05 or less was considered to indicate statistical significance.

## RESULTS

Total thirty patients with renal stones treated by Extracorporeal shockwave lithotripsy (ESWL) were assessed in the study. Results of serum enzymes level of ALP, LDH, SGPT and SGOT (table-1) were found significantly (p<0.001) increased on $1^{st}$ Post-ESWL Day returning to pre-treatment value on $5^{th}$ Post-ESWL Day. Whereas ALP, LDH, SGOT and SGPT were also found significantly decreased (p<0.001) on $5^{th}$ Post-ESWL Day when compared to $1^{st}$ Post-ESWL Day . Right kidney treatment shows (table-2) the highly significant ($p<0.01$ and $p<0.001$) elevation in serum SGPT and ALP after $1^{st}$ and $5^{th}$ Post-ESWL Day treatment respectively when compared to the value of Left sided treated kidney. Whereas Left kidney treatment shows highly significant ($p<0.01$ and $p<0.001$) elevation in serum GOT and LDH after Day 1 and Day 5 of ESWL treatment respectively. Regarding electrolytes our results shows (table-3) significant ($p<0.01$, $<0.001$ & $<0.001$) increased serum level of $Na^+$, $K^+$, and $Cl^-$ on $1^{st}$ Post-ESWL Day respectively which gradually returned to Pre-treatment value until the end of $5^{th}$ Post-ESWL Day. Also a significant ($p<0.001$) increase in Urinary $Na^+$, $K^+$ & $Cl^-$ excretion on $1^{st}$ Post-ESWL Day respectively, with gradual return to Pre-treatment value on $5^{th}$ Post-ESWL day were observed. Serum Creatinine level increased highly significantly ($p<0.01$) on $1^{st}$ Post-ESWL Day which returned below to pre-treatment level on $5^{th}$ Post-ESWL Day. However, creatinine clearance (Cr-C) ml/min decreased markedly on $1^{st}$ Post-ESWL Day with significant increase on $5^{th}$ Post-ESWL Day ($p<0.001$) (figure-1). In our study we have observed non-significant but positive correlation between the number of shockwaves versus serum (ALP, LDH, SGOT and SGPT) and serum potassium.

**FIGURE – 1**

**CHANGES IN CREATININE CLEARANCE BEFORE AND AFTER ESWL**




| | | |
|---|---|---|
| ESWL | = | Extracorporeal Shockwave Lithotripsy |
| Pre-ESWL | = | Before exposure to Extracorporeal Shockwave Lithotripsy |
| 1-Day Post-ESWL | = | First Day after exposure to Extracorporeal Shockwave Lithotripsy |
| 5-Day Post-ESWL | = | Fifth Day after exposure to Extracorporeal Shockwave Lithotripsy |

## DISCUSSION

Management of urinary stones has been revolutionized by the induction of ESWL. ESWL is a superior modality of treatment; however it is not devoid of side effects as it causes severe untoward effects and damage to renal parenchyma[12] . Our study attempts to assess the side effects of ESWL by measuring the blood and urine chemistry including cell escaped enzymes before and on Day-1 and Day-5 after ESWL as well as to investigate the relationship between the numbers of shock waves and the degree of renal damage in an attempt to search for upper limit of shock wave energy. It is generally agreed that cell damage soon after ESWL correlates well with the changes in cell escaped enzymes, increase in serum enzyme activities and excretion of proteins, indicating tubular and glomerular damage of kidney[12,13]. We evaluate the impact of a slow gated treatment rate on the efficacy of extracorporeal shockwave lithotripsy and with a minimal increase in procedure time, greater efficacy can be obtained for the treatment of stones with a slower shock-delivery rate[14]. In particular, upper-ureteral calculi and calculi <10 mm benefit from a slower treatment rate, those patients undergoing shockwave lithotripsy treatment with ESWL having low morbidity and high effectiveness[15]. The number and location of stones and a history of urolithiasis significantly influence recurrence.

In our study there were significant ($p<0.001$) increase in serum level of ALP, LDH, GPT and GOT on $1^{st}$ Post-ESWL Day returning to pre-treatment value on $5^{th}$ Post-ESWL Day, except in case of ALP where no significant change was observed on the $5^{th}$ Post-ESWL Day. Whereas ALP, LDH, SGPT and SGOT were also found significantly decreased ($p<0.001$) on $5^{th}$ Post-ESWL Day when compared to $1^{st}$ Post-ESWL Day. Our observations are in consistent with many others studies[16,17,18]. Our results slightly deferred with Sen S et al[19], who reported no change in serum LDH level on $1^{st}$ Post-ESWL Day. This discrepancy could be explained in the difference of number of shockwaves applied in two studies. Our result also showed that the ALP, LDH, SGOT and SGPT increase significantly ($p<0.01$) on $1^{st}$ Post ESWL Day when compared to Pre-ESWL as the number of shocks increased from 2000-3500 shockwaves[20]. Our results also demonstrate similar findings as reported by other studies[21,22,23] that Right side kidney treatment shows highly significant ($p<0.01$ and $<0.001$ ) elevation in serm

GPT and ALP respectively before and after Day- 1 and Day-5 of ESWL when compared to the value of left sided treated kidney. Similarly left side treatment shows highly significant ($p<0.001$ and $p<0.001$) elevation in serum GOT and LDH respectively before and after Day-1 and Day-5 of ESWL when compared to the values of right side treated kidney. These findings clearly indicate that ESWL is capable to induce injury both to kidney as well as liver cells in patients whose right kidneys were treated. In a study of Krambeck *et al.,*[24] revolutionized effect of ESWL during the management of nephrolithiasis at 19 years of follow up ESWL for renal and proximal ureteral stones was associated with the development of hypertension and diabetes mellitus.

Our results also shows significantly (p<0.01, <0.001, <0.001 repectively) increased serum and urinary conc. of $Na^+$, $K^+$and $Cl^-$ on 1st Post-ESWL Day respectively which gradually returned to pretreatment value until the end of 5th Post-ESWL Day. It is believed that elevated concentration of serum $Na^+$, $K^+$and $Cl^-$ and their increased excretion in early phase is an indicator of tubular dysfunction. Serum creatinine level increased highly significantly (p<0.01) on 1st Post-ESWL Day which returned below to pre-treatment level on 5th Post-ESWL Day. Similarly the creatinine clearance (ml/min) decreased markedly on 1st Post-ESWL Day with significant increase on 5th Post-ESWL Day (p<0.001) when compared to Pre-ESWL Day. This finding indicates decrease in renal function after ESWL treatment. Lee C *et al.,* [25] states that the efficacy of ESWL is decreased in patients with serum creatinine concentrations of 2.0 to 2.9 mg/dL, and the complication rate is higher in patients with serum creatinine >4.0 mg/dL. Preoperative counseling may include a discussion of the impact of renal insufficiency on success and complication rates associated with ESWL. Earlier Cevik *et al*.[26] study demonstrates that ESWL performed by either a single-shot or twin-shot shockwave technique has a transient detrimental effect on renal function in their study observed that although there was no statistically significant difference in the results between the groups, urinary levels of alanine and aspartate aminotransferases, >-2-microalbumin, >-glutamyltranspeptidase, $Na^+$, $K^+$, and $Ca^{++}$ rose acutely after ESWL, reaching maximum levels on the 3rd day, and returned to the baseline by the 7th day following the treatment in both groups.

## CONCLUSION

Shockwaves induce significant damage to the renal and adjacent tissues as indicated by significant increase in cell escaped enzymes and electrolytes and the extent of damage depends on energy and numbers of shockwaves exposure. The most profound functional change noted was a 70% decrease in glomerular filtration rate (GFR ) within one hour of ESWL treatment. Our study also demonstrated that in order to avoid serious kidney damage it is suggested to restrict the patients to 2500 shocks/kidney/day on the electro-hydraulic lithotripter.

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