Early Detection of Bacteremia and Bacteriuria after Extracorporeal Shock Wave Lithotripsy By C-Reactive Protein Measurements

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ABSTRACT :

BACKGROUND:

Extracorporeal shock wave lithotripsy (ESWL) has long been accepted as the least invasive and reliable method in the treatment of urolithiasis. The success rates have been very high in renal and upper ureteral stones .

OBJECTIVE:

Is early detection of bacteriuria and bacteriemia after extracorporeal shock wave lithotripsy (ESWL) of calcium and infection stones by measurement of plasma C-reactive protein (CRP) levels.

METHODS:

A total of 150 patients who had infection stones (n 54) and calcium stones (n 96) were included in the study. All patients had sterile urine before ESWL. The mean age was 41.6+_ 4.85 and male/female ratio was 2.12. Blood cultures were obtained within 1 hour post-ESWL period. Urine cultures were obtained 3 times just after and on the first and seventh day of ESWL.

RESULTS:

Post-ESWL evaluations showed 6 positive blood cultures with 4(5.32%) patients in infection stone and 2 (2.66%) patient in calcium stone groups, whereas urine cultures revealed 12 (16%) positive results in infection stones and 8(10..66%) in calcium stones. The patients who had positive cultures also had elevated plasma CRP levels when compared to the levels in patients with negative cultures (p 0.000).

CONCLUSION:

Bacteriuria and bacteriemia after ESWL have been well-identified entities and may be responsible from some of the post-ESWL complications. CRP can be useful for early detection of such complications.

KEYWORDS: CRP, bacteriemia , bacteriuria, early detection, ESWL

INTRODUCTION:

Extracorporeal SWL has revolutionized the treatment of urinary stones. The concept of using shock waves to fragment stones was noted in the 1950s in Russia. However, it was during the investigation of pitting on supersonic aircraft that Dornier, a German aircraft corporation, rediscovered that shock waves originating from passing debris in the atmosphere can crack something that is hard. It was the ingenious application of a model developed in hopes of understanding such shock waves that extracorporeal (outside the body) SWL emerged.

The first clinical application with successful fragmentation of renal calculi was in 1980. [1]

The least invasive method of stone removal is extracorporeal shock wave lithotripsy(ESWL), and this is a suitable first-line treatment for stones up to approximately 1cm in diameter.[2]

Many patients have benefited from this technology, but the energy that causes this stone fragmentation may result in trauma to the targeted tissue and surrounding structures. This trauma usually has limited clinical impact, but there is potential for serious acute and chronic complications. In addition, other untoward events may occurs, such as peritreatment infections and renal obstructive complications, which may lead to adverse sequelae.[3]

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Complications of SWL include skin bruising, subscapular and perinephric hemorrhage, pancreatitis, urosepsis, and Steinstrasse ("street of stone," which may accumulate in the ureter and cause obstruction). [4]

Definitive stone treatment should be undertaken only in the setting of sterile urine, although a negative urinalysis may be an applicable surrogate to negative culture. [5]

Bacteriuria, bacteriemia and septic shock may be seen even after apparently uneventful ESWL sessions [6-8].

Since post-ESWL infections generally develop gradually without prominent distinct symptoms and may cause sudden disrupt changes in health status, early diagnosis and treatment have been crucial .[7]

The clinical diagnosis of bacteriemia and bacteriuria is based on urine analysis, and cultures [8]. Safety and efficacy of erythrocyte sedimentation rate (ESR) and white blood cell (WBC) count are limited. C-reactive protein (CRP) is considered to be a method, which is as efficient as urine and blood cultivating.

CRP is an acute phase reactant, which increases rapidly and dramatically, and proportional to the level of tissue damage, following an acute inflammatory stimulus [9]. CRP enables a direct and quantitative measurement of the acute phase reaction [10]. Addition- ally, it enables the distinction of disease exacerbation and bacterial infection such as in systemic lupus erythromatosis (SLE). Following sequential CRP levels is also valuable in evaluating the effects of the treatment [11].

Diagnosis of the bacteriuria and bacteraemia, which can occur after ESWL, before the culture results are obtained, and initiation of an empiric therapy would be an important advantage for the patient. In this study, the value and the efficacy of CRP were examined, as well as the possibility of early diagnosis of these complications by following CRP levels in ESWL patients.

PATIENTS AND METHODS:

From Jaunary 2014 to October 2016, 150 patients ,aged 18-60 year old(mean age 41.6+_ 4.85 years) referred to AL-YARMOUK TEACHING HOSPITAL in BAGHDAD,IRAQ, were involved in a randomized controlled trial.

One hundred fifty patients with renal calculi were included in this study. Routine blood examinations, CRP, ESR and WBC measurements of the patients were carried out prior to the procedure. Patients with bacterial growth in urine samples were excluded. Patients ages were between 18 years and 60 years (mean 41.6+_ 4.85) and male to female ratio was 100/50. Stone composition identified with infrared spectroscopy by evaluating stone particles obtained after ESWL. No patient received antibiotic prophylactic treatment.

Patients with nonsterile urine cultures before ESWL,congenital renal diseases(e.g,horseshoe kidney), previous urological interventions(open or endoscpic surgery), malignancy, and immune comprised patients were excluded.

Mean calculus size of the patients was found to be 1.02+_ 0.42 cm. The procedure was carried out using a third generation lithotripter, electrohydralauic, Stone Litho3pter (PCK^{TM}). A mean shock number of 2854.40+ 106.45 was applied to the patients. Mean power was 19.62 +1.12 kV.

Blood samples to be cultured were collected immediately after ESWL. The blood samples were transferred into ready BACTEC plus+ aerobic culture mediums in the ESWL room. These mediums were placed into a BACTEC 9050 system (Becton, Dickenson and Company Sparks, MD Benex Limited, Bay K 1a/d, Shannon Indutrial Estate, Shannon, County Clare, Ireland). Negative or positive results were observed in 7 days.

Further urine samples to be cultured were collected on 1st and 7th days of the procedure. Urine samples were examined microscopically under Thoma slide and cultured in eosin methylene blue agar culture media including sheep blood, using a swab with a diameter of 0.001 ml. Samples incubated at 35±37 C were evaluated after 18±24 hours.

CRP levels were measured daily for the first 7 days and on the 15th day. CRP levels were evaluated using Beckman synchronic CX 7 clinical system. Values below 0.2 mg/dl were accepted as normal.

When bacteriuria and bacteriemia confirmed, we started antibiotic treatment. Antibiotics were started to the patients on post-ESWL 4th day with elevated CRP levels, who also had positive cultures.

Statistical analysis was performed by using Mann-Whitney U- test. A p-value less than 0.05 was considered to be statistically significant.

RESULTS:

All patients were evaluated after ESWL. Stone analyses showed 54 infection and 96 calcium calculi. Bacterial growth was detected in the urine cultures of 20 patients within the first week. Microorganisms were detected in 4 of the patients immediately after the procedure (5.32%), 1 day after the procedure in 14 patients (18.66%) and 7 days after the procedure in 2 patient (2.66%). Bacterial growth was detected in blood samples, taken immediately after the procedure, in 6 of the patients who showed growth in their urine cultures as well (8%). Four of blood culture positive patients had infection stones and 2 patient had calcium stone. Twelve patients whose urine cultures were positive after the procedure were in the infection group (44.44%) and 8 in the calcium group (16.66%). The microorganisms, isolated from the urine and blood cultures within the first week, are shown in Tables 1 and 2.

Table 1 : Demographic parameters and ESWL variables in the patients(data are mean+_S.E.).

	Aa	Bb	p-value
Number	150	20	
Sex(M/F)	102/48	14/6	
Age(Year)	41.6+_4.85	41.92+_4.92	0.897
Weight(Kg)	72.54+_3.12	72.12+_3.08	0.865
Height(cm)	168.54+_2.98	167.89+_3.17	0.763
SWL duration(min)	30.40+_0.78	29.68+_0.86	0.726
Stone size(cm)	1.02+_0.42	1.01+_0.45	0.789
Number of shocks	2854.40+_106.45	2888.12+_110.56	0.854
Voltage(kV)	19.62+_1.12	19.84+_1.26	0.767
Stone location:			
Right Kidney	72	10	
Left Kidney	78	10	

a All patients.
b Patients with bacteriuria and bacteriemia.

Table 2 :The microorganisms, isolated from the urine and blood cultures.

	Just after	1 day after ESWL	7 days after ESWL
Escherichia coli	2	4	2
&-hemolytic streptococcus	2	2	_
Klebsiella pneumonia	_	2	_
Staphylococcus aureus	_	2	_
Pseudomonas auruginosa	_	4	_

There were no differences between the patients with regards to ESR, WBC and fever in follow-up studies. Serum CRP levels of 20 patients, who were found to have bacterial growth in their urine and blood cultures, measured after the ESWL, were significantly higher, when compared to those who showed no growth. Serum CRP levels of these patients reached their maximal levels especially on the 3rd day (0.09 +_0.02 mg/dl; 11.27 +_1.74 mg/dl; p 0.000) and decreased rapidly after the 4th day (0.09 +_0.02 mg/dl; 8.36 +_0.98 mg/dl). Daily measurement of CRP levels for the first 7 days

were significantly higher compared to the group with no bacterial growth (7.46 +_1.04 mg/dl; 0.42 +_0.11 mg/dl; p 0.000). CRP levels of the patients, who had positive blood cultures, were higher compared to those who had positive urine cultures within the first 7 days (9.22+_ 1.13 mg/dl; 6.71+_ 0.98 mg/dl; p 0.008).

Serum CRP levels were higher in patients, who showed growth in their culture immediately after the procedure, compared to the group of patients, who showed no growth in their culture immediately after the procedure (5.97+_ 0.82 mg/dl; 0.32 +_0.08 mg/dl; p 0.000). CRP levels of the patients, who were detected to have growth, were found to be close to the pre-procedure basal values, on the 15th day (0.61 +_0.15 mg/dl; 0.09 0.02 mg/dl; p 0.678).

CRP values decreased after antibiotics, however, in general, in acute infectious disease, it is well known that the decrease of CRP level started after a peak on 4th day .

DISCUSSION:

ESWL is most effective for stones <2 cm in diameter, in favorable anatomical locations. It is less effective for stones >2 cm diameter, in lower-pole stones in a calyceal diverticulum (poor drainage), and those composed of cystine or calcium oxalate monohydrate (very hard).[12]

Most patients with uncomplicated kidney stones can be successfully treated with SWL. Shock waves break stones via multiple different mechanisms, including both compressive and tensile forces.[13]

ESWL causes a certain amount of structural and functional renal damage (found more frequently the harder you look). [14]

Sepsis-occurs in < 3% of patients and is more likely to occur in the presence of UTI or struvite stones. Treat a UTI adequately prior to ESWL. Preoperative antibiotics reduce the risk of sepsis.[15]

The risk of sepsis after ESWL is higher in patients who have had previously treated or untreated urinary tract infections (UTI) and especially those with infection stones.Li and colleagues reported that the urine in patients with larger stones more frequently contained endotoxin,which was associated with a higher risk of sepsis.A study by Yilmaz and associates compared bacteraemia risks of 75 patients with either calcium or infection stones;all of these patients had sterile urine cultures before SWL.Bacteraemia developed in 2.6% of those with struvite stones after SWL as compared with 1.3% of those with calcium stones after SWL.An elevation of the inflammatory mediatory,C-reactive protein(CRP),also has been identified as a predictor of bacteraemia.

Controversy exists regarding whether or not to administer prophylactic antibiotics at the time of SWL to patients who had sterile pre-treatment urine.A meta-analytic study by Pearle and Roehrborn demonstrated that there was a significant decrease in the development of Post-SWL UTI in patients who received prophylactic antibiotics.

Patients with UTI should receive appropriate antibiotic therapy before SWL.Those suspected of harboring infection stones should receive broad spectrum antibiotic therapy because there may be discordance between stone and urine cultures.These prophylactic measures lessen the risk of sepsis.[3]

The relation between urinary system calculi and bacteriuria has been emphasized in various studies [6-8,16]. It has been established that, urinary system infections are seen more often in cases of infection calculi, compared to those of other types of calculi (17.2% versus 2.1%) [17]. Therefore, the need for prophylactic antibiotics in these patients has also been stated, although bacteriuria was not detected prior to the procedure [18,19].

In a multi-centric study, regarding ESWL, 5% of the patients, who had non-struvite calculi and showed no growth in urine samples prior to treatment, were detected to have positive urine samples after lithotripsy [20]. Silber et al. asserted that, bacteria were released after the lithotripter broke the calculi into pieces in patients whose urine samples were sterile prior to treatment [6]. In a series of 124 patients with negative urine cultures prior to treatment, Tonitz and Heinz reported a post-ESWL bacterial contamination incidence of 16% [21]. In our study, bacteriuria and bacteraemia were detected in 20 of the 150 patients (26.66%) a week after ESWL.

If bacteriuria and bacteraemia could be detected using a diagnostic method, which could give earlier results compared to urine and blood cultures, these serious complications could be prevented by anti-microbial chemotherapy before it leads to sepsis.

Various diagnostic methods are used in order to detect post-ESWL bacteriuria and bacteraemia. The symptoms experienced by the patients, ESR, WBC, urine and blood cultures are all helpful in diagnosis. Shigeta et al. in a study where they examined the relation between bacteriuria and fever, emphasized that bacteriuria in cases of

calculi larger than 2 cm lead to resistant fever. It has been reported that bacteriuria is seen more often in cases of kidney calculi larger than 2 cm compared to that of ureter calculi [22].

CRP was first obtained as a precipitin, which was formed in the serum of patients with pneumococcal pneumonia, acute joint rheumatism and streptococcal infection, and which reacted with the C and somatic polysaccharides of pneumococci [9-11]. Serum CRP levels reach a maximal level in 2-3 days after the acute stimulus and start to decrease rapidly from this level [23,24]. Its half-life is 18 hours. CRP level can constantly stay at a high level in chronic inflammatory diseases such as pulmonary tuberculosis and acute rheumatoid arthritis [10]. CRP measurement is of a higher value than erythrocyte sedimentation rate in determining the activity of the illness in inflammatory rheumatic diseases. ESR is an indirect indicator of the acute phase reaction. It responds more slowly to the changes in inflammatory activity and can be affected by other factors. However, CRP provides us with a direct and quantitative measurement of the acute phase reaction [11].

Planz et al. used CRP in order to detect the tissue damage caused after ESWL and reported that it could be advantageous [25]. Mladenov et al. emphasized that serum CRP levels increased in post-ESWL renal parenchymal damage [26]. Wolff et al. also reports that CRP is more useful than BC, ESR and fever follow-up in infective ureteral obstructions and in detecting tissue damage [27]. It is also used in urinary system infections with other diagnostic methods. Biggi et al. reported that, CRP sensitivity and specificity in children, who had their first urinary infections with a positive DMSA, were 64% and 69%, respectively. CRP level was found to increase with the increasing amount of damage in kidneys [28]. Pulliam et al. also emphasized that CRP sensitivity and specificity in detecting urinary system infections in children, who were 1-36 months old, were 79% and 91%, respectively [29]. CRP was considered to be a more valuable laboratory test compared to BC and neutrophil count. Serum CRP concentration was detected to be high in children with bacteraemia [30]. Addition- ally, it has been emphasized that CRP is a test that can be useful in the follow-up of urinary system infections in combination with pro-calcitonin [31]. Fornara showed that, CRP increased more in open nephrectomy, compared to laparoscopic nephrectomy, together with IL-6 [32].

In our study, of the 150 patients, evaluated after ESWL, 20 were detected to have bacteriuria and 6 of these 20 patients were detected to have growth in their blood cultures, as well. In all of these 20 patients daily, serum CRP levels during the first week were significantly higher than in those who showed no growth in their cultures (p 0.000).

CRP levels of the patients who showed growth in blood cultures were especially high (p 0.008).

CRP levels, which reached a peak level on the 3rd day, started to decrease from the 4th day onwards and reached the basal values on the 15th day.

CONCLUSION:

These results convinced us that CRP follow-up on the 1st and the 3rd days after ESWL will be useful for early diagnosis of the complications, bacteraemia and bacteriuria. The disease can be prevented from advancing, especially by means of early diagnosis of asymptomatic bacteriuria and hence, empiric therapy.

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