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EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY AND ITS EFFECT ON RENAL FUNCTION

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ABSTRACT

Extracorporeal shock wave lithotripsy has become a major treatment modality for symptomatic upper tract renal stone disease. Although proved to be effective in disintegrating stones the short-term and long-term effects on renal function are not yet known.

We evaluated several basic physiological parameters, namely creatinine clearance, fractional sodium excretion, protein excretion and urine osmolality before and after extracorporeal shock wave lithotripsy in 26 consecutive patients in an attempt to quantitate changes in renal function. In addition, a 3 to 6-month followup study of patients showing excessive protein excretion with extracorporeal shock wave lithotripsy also is reported.

Our data suggest that with extracorporeal shock wave lithotripsy transient nephrotic range proteinuria occurs immediately after treatment, returning to normal values within 3 to 6 months after treatment without a change in the glomerular filtration rate. The glomerular filtration rate increases after successful extracorporeal shock wave lithotripsy in patients with kidneys obstructed by the treated stone before the start of the procedure, and the kidney appears to maintain its ability to dilute urine and to conserve sodium after treatment. (*J. Urol., 139: 482–485, 1988*)

Extracorporeal shock wave lithotripsy (ESWL*) has become a major treatment modality for symptomatic upper tract renal stone disease. Pressure waves greater than 10,000 pounds per square inch are delivered to a focal point whose treatment volume is approximately 1.5 cc. However, although proved to be effective in disintegrating stones the short-term and long-term effects on renal function are not yet known. To date only radionuclide renography has been used in an attempt to quantitate renal function with either ^{99m}technetium-dimercaptosuccinic acid[1] or ^{131}iodine (^{131}I)-hippurate.[2] These studies, however, have not considered the effect of stone size or location, or the presence or absence of obstruction on renal function. Although serum electrolyte levels have been recorded[1] no systematic evaluation of glomerular or tubular function has been done. We report our prospective study designed to evaluate and to quantitate the acute changes in renal function that occur during and after ESWL.

Excretory urography (IVP) was used to delineate stone burden and we systematically evaluated several basic physiological parameters, namely creatinine clearance, fractional sodium excretion, protein excretion and urine osmolality before and after ESWL.

METHODS

All patients undergoing ESWL during the 3-month study period were eligible for inclusion in the study. Criteria for inclusion of patient data in this series were 2-fold: 1) urine creatinine greater than or equal to 5 mg./kg./12 hours for collections obtained before and after ESWL,[3] and 2) an IVP performed within 1 month of treatment. Data from 26 patients satisfied these criteria and, therefore, they were used in this study. The primary reason for exclusion was the inability to perform technically adequate collections for creatinine clearance, in particular collections after ESWL that were difficult to obtain secondary to catheter manipulations.

At hospitalization a 12-hour collection of voided urine was begun for evaluation of total volume, electrolytes, creatinine (alkaline picrate method), osmolality and protein concentration (sulfosalicylic method). A standard urinalysis and culture were performed. A complete blood count and SMA-6 (serum electrolytes, blood urea nitrogen and creatinine) on a peripheral blood sample also were obtained at hospitalization. These collections were repeated for 12 hours after completion of ESWL. All patients were hydrated after treatment for the study period with a solution containing 5 per cent dextrose and 0.25 normal saline at a rate of 150 cc per hour. Urine collections before and after ESWL were of pooled bladder urine.

The IVP obtained before ESWL in all patients was used to determine stone size (maximum diameter) and location, and the presence or absence of obstruction. Infundibular, pelvic or ureteral stones with associated hydronephrosis, hydroureter or delayed function on the IVP were considered to be obstructive. No attempt was made to differentiate incomplete from complete obstruction.

The ESWL parameters of voltage (kV.) and the number of shocks delivered (parameters directly related to the force generated) were tabulated.

The estimated glomerular filtration rate was calculated with the empiric formula developed by Cockcroft and Gault.[3] The formula was based upon 2, 24-hour urine collections for creatinine clearance in 534 consecutive admissions to a medical ward at a Veterans Administration hospital (96 per cent male patients). The correlation coefficient found between their formula and the measured creatinine clearance was 0.84. This correlation coefficient was identical to that found between the measured creatinine clearance on the 2, 24-hour urine collections, which suggests that the predictive error in measuring creatinine clearance depends upon biological variation as well as urine collection errors. The results of Cockcroft and Gault also were confirmed and extrapolated upon by Sawyer and associates.[4]

The equations used to estimate creatinine clearance were

$$[(140 - A) \times W]/(72 \times SCr) \text{ for men and}$$

$$([(140 - A) \times W]/[72 \times SCr]) \times 0.85 \text{ for women,}$$

where A is the age at hospitalization (years), W is the weight

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at hospitalization (kg.) and SCr is the serum creatinine (mg./dl.).[3]

Our data were expressed as the mean ± standard error of the mean. The appropriate t statistic was calculated and compared to the critical values from standard tables for determination of level of significance.

RESULTS

The study group was comparable to the total population of ESWL patients described in a previous study from our institution.[5] A total of 26 patients fulfilled the criteria for inclusion in our study (8 women and 18 men). Mean patient age was 53 years, with a range of 24 to 74 years. Mean operating voltage was approximately 20 kV. with minimal variation. The mean number of shocks used was 1,600, with a median of 1,697 and a mode of 2,000. The mean weight of our patients was approximately 80 kg. There was no significant change in serum creatinine within 24 hours after ESWL.

To compare our functional data we divided our 26 patients into 2 groups based upon the presence (10) or absence (16) of obstruction on a pre-ESWL IVP. Data for glomerular filtration rate (ml. per minute) are shown in table 1 and figure 1. Of note is that the estimated glomerular filtration rate is not significantly different from the pre-ESWL glomerular filtration rate in either the obstructed or nonobstructed series. However, there was a significant increase in glomerular filtration rate after ESWL of approximately 30 ml. per minute in patients with previously obstructed kidneys. This increase in glomerular filtration rate after ESWL did not occur in the nonobstructed group.

There was a significant increase in the urinary protein excreted (gm./dl.) after ESWL in patients with obstructed and nonobstructed kidneys (table 2 and fig. 2). The difference in excreted protein (gm./dl.) after ESWL between the 2 groups was not significantly different ($p > 0.05$). Of 12 patients whose 24-hour post-ESWL protein excretion was greater than 1.5 gm. 5 were studied again 3 to 6 months after treatment and the 24-hour urine specimen no longer revealed significant proteinuria. In addition, in these 5 patients glomerular filtration rate was not significantly different from pre-ESWL studies (fig. 3).

Table 3 demonstrates the functional data other than glomerular filtration rate obtained when the patients were grouped according to the presence or absence of obstruction before ESWL. There was no significant change in the fractional excretion of sodium in either group with ESWL. Fractional sodium excretion remained less than 1 per cent after ESWL.

Urine osmolality decreased from 484 to 246 mOsm./kg. water in patients with nonobstructing calculi and from 294 to 183 mOsm./kg. water in patients with obstructing calculi. The difference in pre-ESWL osmolality in patients with obstructing versus nonobstructing calculi (484 compared to 294) was significant ($p < 0.05$), while that for post-ESWL osmolality (246 compared to 183) was not ($p > 0.05$, table 3 and fig. 4).

Blood hematocrit and hemoglobin (gm./dl.) values decreased significantly after ESWL (table 4). The mean hematocrit and hemoglobin values after ESWL still were within normal limits for patient age.

TABLE 1. *Glomerular filtration rate before and after ESWL treatment*

	Glomerular Filtration Rate (ml./min.)			
	Estimated	Before ESWL	After ESWL	Change
Pts. without an obstructed kidney before treatment				
Mean value	92.13	105.24	99.09	6.15
Standard error	5.71	7.71	11.37	8.18
Paired t test				0.75
No.				16
P value				Not significant
Pts. with an obstructed kidney before treatment				
Mean value	87.97	88.68	121.49	32.81
Standard error	6.31	9.83	12.62	11.28
Paired t test				2.91
No.				10
P value				<0.01

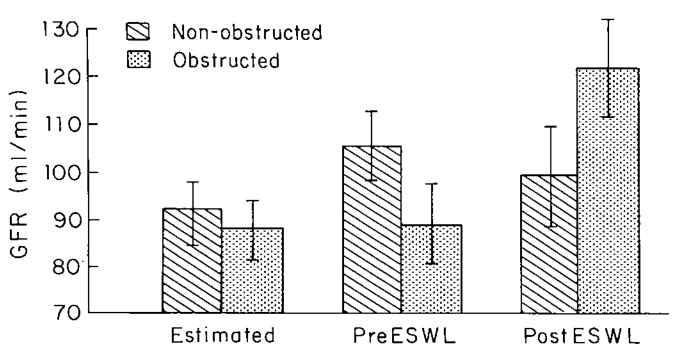

FIG. 1. Estimated glomerular filtration rate (*GFR*), and rates before (*PreESWL*) and after (*PostESWL*) treatment. Glomerular filtration rate increases significantly after ESWL in patients with kidneys obstructed before therapy. Estimated rate is in agreement with measured values. Values are mean ± standard error.

TABLE 2. *Protein concentration and excreted load before and after ESWL treatment*

	Protein Concentration (gm./dl.)			Protein Excreted Load (mg./min.)		
	Before	After	Change	Before	After	Change
Pts. without an obstructed kidney before treatment						
Mean value	0.010	0.095	0.085	1.5	22.7	22.7
Standard error	0.004	0.037	0.038	0.37	7.89	8.32
Paired t test			2.25			2.73
No.			16			14
P value			<0.01			<0.01
Pts. with an obstructed kidney before treatment						
Mean value	0.008	0.132	0.124	1.4	44.9	48.0
Standard error	0.004	0.046	0.046	0.56	17.3	18.5
Paired t test			2.69			2.61
No.			10			12
P value			<0.05			<0.05

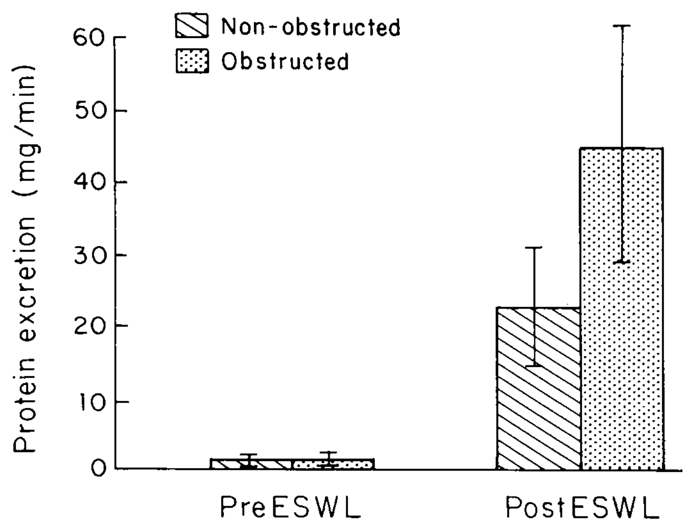

FIG. 2. Protein excretion in urine increases significantly after ESWL treatment (*PostESWL*) in patients with or without obstructed kidneys. Values are mean ± standard error. *PreESWL*, before treatment.

DISCUSSION

Our study attempts to measure several basic physiological parameters to assess the changes in renal function with ESWL. The significant decreases in serum hematocrit and hemoglobin that occurred after ESWL most likely reflect the patient's state

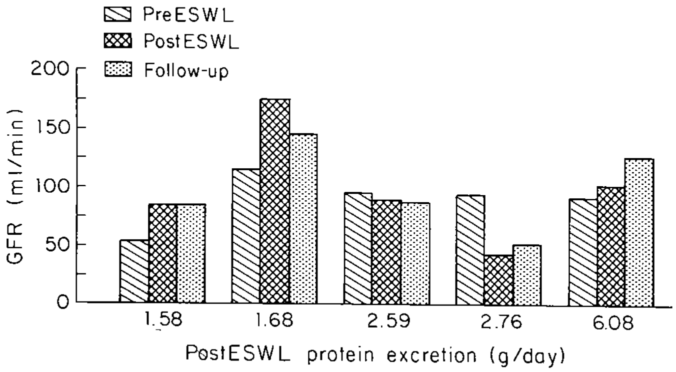

FIG. 3. Glomerular filtration rate (*GFR*) before (*PreESWL*), within 24 hours after (*PostESWL*) and 3 to 6 months after treatment in 5 patients with marked (greater than 1.0 gm. per 24 hours, abscissa) proteinuria after ESWL shows no significant change.

TABLE 3. *Fractional sodium excretion and osmolality before and after ESWL treatment*

	Fractional Sodium Excretion			Osmolality (mOsm./kg.)		
	Before ESWL	After ESWL	Change	Before ESWL	After ESWL	Change
Pts. without an obstructed kidney before treatment						
Mean value	0.011	0.008	−0.003	484.13	246.14	273.17
Standard error	0.004	0.001	0.005	51.68	31.18	65.88
Paired t test			−0.90			4.15
No.			14			11
P value			Not significant			<0.01
Pts. with an obstructed kidney before treatment						
Mean value	0.007	0.010	0.003	294.50	183.11	109.29
Standard error	0.001	0.003	0.002	31.07	15.53	20.61
Paired t test			1.60			5.30
No.			8			6
P value			Not significant			<0.01

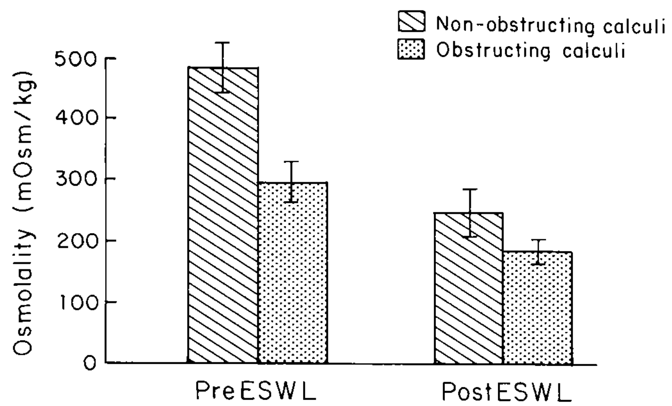

FIG. 4. Osmolality before (*PreESWL*) and after (*PostESWL*) treatment is compared in patients with obstructing and nonobstructing calculi. Osmolality decreases to significantly greater extent with obstructing calculi. Values are mean ± standard error.

of hydration rather than blood loss resulting from urothelial damage,[1] subcapsular hematoma[6] or interstitial bleeding,[2] since these patients are vigorously hydrated after ESWL. Although not quantified, Chaussy and Schmiedt observed subcapsular hematoma in 0.6 per cent of 896 patients,[6] while Kaude and associates, using almost twice the number of shocks in their treatments (mean 1,800, range of 800 to 2,400 compared to an average of 978 as reported by Chaussy and Schmiedt) found abnormal images, possibly hemorrhage, in 29 per cent of their 38 treated kidneys as evaluated by computerized tomography or magnetic resonance imaging.[2]

Although the decrease in hemoglobin and hematocrit might be statistically significant it does not appear to be clinically

TABLE 4. *Hemoglobin and hematocrit before and after ESWL treatment*

	Hemoglobin (gm./dl.)			Hematocrit (%)		
	Before	After	Change	Before	After	Change
Mean value	14.65	13.41	1.25	42.48	38.95	3.52
Standard error	0.30	0.48	0.40	0.93	1.42	1.15
Paired t test			3.12			3.05
No.			13			13
P value			<0.01			<0.01

significant. In our previous series only 1 of 518 consecutive patients required a blood transfusion.[5]

Serum osmolality before and after ESWL is affected by many factors other than fluid (salt and water) intake. In our study no attempt was made to regulate salt and water consumption. However, if we assume that the integrity of tubular function is demonstrated adequately by the maintenance of a normal fractional excretion of sodium (less than 1 per cent, table 3), then the decrease in urine osmolality after ESWL may be partly owing to the physiological response to volume loading. However, in experimental animals concentrating ability is greatly impaired for prolonged intervals following relatively transient elevations of ureteral pressure.[7] Our data are consistent with these experimental findings. Urine osmolality before ESWL was significantly less in patients with obstructed than with nonobstructed kidneys (p <0.01, table 3). Although this decreased osmolality might in fact be owing to the increased oral fluid intake in patients who are symptomatic from obstructing calculi, we would have expected to find a less than isosthenuric urine osmolality. In addition, it is known that proximal and distal reabsorption of glomerular filtrate is depressed in obstructed kidneys.[8] Therefore, to equate urine osmolality with total body fluid hydration alone is simplistic. However, our data suggest that the kidney treated with ESWL retains its ability to dilute urine and does not appear to have measurable salt wasting.

Two studies using radionuclide renography have not found any adverse effects of ESWL on renal function.[1,2] Another study with ^{131}I-iodohippurate evaluated effective renal plasma flow and the "post maximum renal clearance half time" before and 3 months after ESWL. No significant difference was found.[9] For kidneys obstructed (as determined by a pre-ESWL IVP) before treatment there was a 20 per cent decrease in the mean post-treatment half-time suggestive of expected improvement with ESWL treatment.

When our data were subdivided into 2 groups based upon the presence or absence of obstruction on a pre-ESWL IVP, several interesting results were obtained. Glomerular filtration rate increased significantly after ESWL when kidneys were obstructed before treatment, which suggested an immediate functional benefit of ESWL. Whether this effect was owing to the relief of obstruction with a concomitant increase in the net driving forces for glomerular filtration across the glomerular membrane or to an increase in the hydraulic conductivity of the glomerular membrane itself, or whether it was related to a redistribution of blood flow after relief of obstruction is difficult to delineate from these data.

Significant proteinuria also occurred with ESWL. Conceivably, the measured proteinuria might be the result of excreted hemoglobin occurring with hemolysis, plasma protein in urine resulting from urothelial or endothelial disruption, or altered glomerular membrane permeability.

In their original study Chaussy and associates showed a direct (linear) relationship between plasma hemoglobin and the number of shocks given to 10 ml. of blood.[1] However, they did not find any systematically demonstrable hemolysis in their animal studies. The stated reason was that the focus zone of the shock wave was too small in comparison to the whole volume for the effect to be noted.

Naturally, the hematuria universally found after ESWL might contribute to the over-all protein measured in urine. However, if one assumes that the 3-unit hematocrit decrease occurs via bleeding from the urothelium after ESWL (unlikely in light of the data presented but for our purposes a "worse case" assumption), then we can calculate the approximate urine protein owing to blood loss. Since the mean urine output after ESWL is approximately 4,200 cc/24 hours a 3-point hematocrit decrease (table 4) would represent a blood loss of approximately 1 unit or 200 cc plasma. This value translates (with a measured mean serum albumin concentration of 4.6 gm./dl.) to a protein concentration of 0.022 gm./dl. Since our measured post-ESWL urine protein concentration was 0.095 gm./dl. for patients without obstructed kidneys and 0.132 gm./dl. for patients with obstructed kidneys, the possible artifact owing to urothelial bleeding after ESWL could account for at most 20 per cent of our measured urinary protein. This still would not affect the significance of the observed results.

Glomerular filtration is determined by the driving forces of oncotic and hydrostatic pressure as delineated by the relationship $Jv = k\ (HP - COP)$, where Jv is the fluid flux from glomerular capillary to Bowman's space, k is the effective hydraulic permeability of the capillary wall, HP is the hydrostatic pressure gradient across the glomerular capillary and COP is the capillary oncotic pressure gradient across the glomerular capillary. The effective hydraulic permeability (k) of the capillary membrane is known to vary with pore size, ratio of total pore cross-sectional area to pore length and charge selectivity of the glomerular capillary wall.[10] Whether pore size or total pore cross-sectional area to pore length varies with ESWL treatment cannot be evaluated by this study. It is known that increases in hydrostatic pressure tend to decrease k.[11] Also, loss of fixed negative charges appear to be responsible for the enhanced filtration of polyanions.[12] Thus, we might speculate that the proteinuria observed in our study might be related to an effect of ESWL on the fixed negative charge of the glomerular capillary membrane and/or an increase in Bowman's space pressure. Conceivably, this increase in Bowman's space pressure might be the result of retrograde pressure waves generated in the pelviocaliceal system during ESWL or as a direct result of electromechanical energy on the glomerular membrane. However, it is noteworthy that the occurrence of proteinuria is transient, with recovery to baseline levels within 3 to 6 months.

The data presented represent pooled urine from the treated as well as the untreated kidneys. Ideally, an animal model should be used to collect split function data. Until these data are obtained one can only assume that the treated kidney is the only one affected by ESWL. Nonetheless, a rational protocol for long-term followup of patients undergoing ESWL should include a routine urinalysis with particular emphasis on urine protein.

In summary, our results suggest that the urinary protein concentration increased with ESWL to a greater extent than can be accounted for by the hematuria that was present. However, this abnormality appears to resolve spontaneously within 3 months after treatment. Glomerular filtration rate increases after ESWL in patients whose kidneys were obstructed before the start of the procedure. Treated kidneys appear to maintain the ability to dilute urine and to conserve sodium.

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