

The Effect of Tamsulosin and Combination of Terpenes (Rowatinex) on the Clearance of Renal Stone Gravels After Single Session of Extracorporeal Shock Wave Lithotripsy (ESWL)

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Abstract

Background: Extracorporeal shock wave lithotripsy (ESWL) is currently considered one of the main lines of treatments for urolithiasis. The effectiveness of pharmacologic therapies in facilitating stones expulsion after ESWL has been reported.

Objectives: To evaluate the effect of Tamsulosin and terpenes combination (Rowatinex) on the clearance of stone gravels after extracorporeal shock wave lithotripsy (ESWL) of renal stone.

Methods: From May 2010 to June 2011 (84) patients with single radio opaque renal stone presented to urologic consultation department at Al-Ramadi teaching hospital/Iraq were included in this prospective, case-control study. All patients were examined by ultrasonography, and intravenous urography. Their age ranged from 19 to 62 years. All patients underwent ESWL and randomly divided into three groups, group A, of 28 patients, received conservative medical therapy alone and served as the control group, group B, of 28 patients, received tamsulosin 0.4 mg once daily in addition to conservative medical treatment and group C, of 28 patients, received Rowatinex capsules, 1 capsule before food 3 times daily in addition to conservative medical therapy. All patients were followed up by clinical examination, urine analysis, ultrasonography and abdominal radiograph (KUB) at 4 and 8 weeks and the number of patients with clinical success was recorded. Clinical success defined as stone-free status or clinically insignificant stone .

Results: The age of patients ranged from 19 to 60 years in group A (mean 35.7 ± 6), 20-62 years in group B (mean 36.6 ± 13.25) and 20-61 years in group C (mean 36.2 ± 13.02), there was no significant statistical difference between the age, gender and site and size of renal stones among the three groups (p value > 0.05). The percentage of patients with clinical success after ESWL at 4 weeks was 23% in group A, 44% in group B and 40% in group C and increased to 46%, 80% and 76% in group A, B and C respectively at 8 weeks. The clinical success was statistically more significant in group B and C compared to group A at both 4 and 8 weeks (p value < 0.05). There was no statistically significant difference in the clinical success between group B and C (p value > 0.05). Although the incidence of drugs side effects in group B and C occurred more than in group A, but no significant side-effect was detected so as to require exclusion of a patient from the study and medical intervention was not performed in any of the patients because of side-effects.

Conclusion: The use of medical expulsion in this study by tamsulosin or terpenes combination (Rowatinex) was well tolerated and it demonstrated that it is clinically meaningful and statistically it has significant improvement in the clearance of stone fragments after ESWL of renal stone. The effect on tamsulosin and terpenes combination (Rowatinex) is comparable.

Key Words: ESWL; Renal stone; Tamsulosin ; Terpenes combination (Rowatinex).

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Introduction:

Urolithiasis shows a worldwide increasing prevalence and incidence.^[1] Extracorporeal shockwave lithotripsy (ESWL) is considered the standard of care for renal calculi less than 20 mm, the major goal in treating patients with renal stones is to achieve a stone-free state.^[2] Medical expulsive therapy (MET) may improve stone-free rates and symptoms during stone passage. In particular, α -adrenergic blocking agents and calcium-channel antagonists have proven efficacy in randomized controlled studies^[3-9]

Terpen combinations derived from naturally occurring essential oils have been suggested to improve stone-free rates and symptoms during stone passage in patients with urolithiasis^[10-14]

It would be reasonable to assume that MET is effective after ESWL for renal stones because the fragments have to pass the ureter. Pooled data for α -blocker after SWL suggested a treatment benefit for ureteral stones.^[15]

Tamsulosin hydrochloride is an alpha 1A antagonist, each Tamsulosin capsule for oral administration contains tamsulosin HCl 0.4 mg.^[16]

Rowatinex is Capsules of combination of terpenes: anethol 4 mg, borneol 10 mg, camphene 15 mg, cineole 3 mg, fenchone 4 mg, pinene 31 mg with dose 1–2 capsules 3–4 times daily before food to dissolve and expulse the stone; and it is not recommended for children. Rowatinex can be used for increasing the elimination-rate of stones and lowering the adverse effects in the first three months after SWL.^[11,17]

This study was carried out to evaluate the effect of tamsulosin and Rowatinex on the clearance of stone fragments after ESWL and to compare both effects.

Patients and Methods:

From May 2010 to June 2011 (84) patients, Their age ranged from 19 to 62 years, with single radio opaque renal stone presented to urologic consultation department at Al-Ramadi teaching hospital were included in this prospective, case controlled study. All patients were examined by ultrasonography, and intravenous urography. Inclusion criteria were single radio opaque stone with size of 10-20 mm located in the renal pelvis or upper pole calyces, mid calyceal and lower pole stones were excluded because they have less success rate compared with pelvic and upper pole stones. Patients with multiple stones, urinary tract obstruction, renal function impairment, and radiolucent stones were excluded from this study. All patients underwent ESWL (Karl Storz Modulith SLX-F2 electromagnetic lithotripter). Post ESWL the patients were randomly divided into three groups, group A, of 28 patients, kept on conservative therapy alone and served as the control group, group B, of 28 patients, received tamsulosin 0.4 mg capsule once daily in addition to conservative treatment and group C, of 28 patients, received Rowatinex capsules 1 capsule before food 3 times daily in addition to conservative therapy.

The conservative therapy was good hydration, diclofenac suppositories 100 mg on demand and ciprofloxacin tablets 500mg twice daily for 2 week after ESWL to prevent urinary tract infection.

The lithotripter used in this study was the Karl Storz Modulith SLX-F2 electromagnetic lithotripter. Treatment then began with very low power shocks.

The power of shocks then gradually increased every 250 shocks; however, the maximum limit of number of shocks given were 3000shocks/session and the maximum limit of power of shocks were 5 kilo voltage with frequency of 60-90/min. All patients were followed up by clinical examination, urine analysis, ultrasonography and abdominal radiograph (KUB) at 4 and 8 weeks and the number of patients with clinical success was recorded. Eight patients (two in group A, 3 in group B and 3 in group C) were excluded from this study because of loss of follow up.

Statistical tests used in our analysis were ANOVA and Chi-square (χ^2) in addition to Graphical presentation by (bar - charts). Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS version 17.0) software. All P values less than 0.05 were considered to indicate significance.

Results:

The age of patients ranged from 19 to 60 years in group A (mean 35.72 ± 5.32), 20-62 years in group B (mean 36.6) and 20-61 years in group C (mean 36.2). There was no significant statistical difference between the age, the distribution of men and women, the size of stones and the distribution of upper and pelvic renal stones among the three groups (p value > 0.05). Table (1)

Table (1) The distribution of age, sex and size and site of renal stones.

Variable	Groups						P value	
	A		B		C			
Mean age/years ± SD	35.71±13.14		36.66±13.25		36.22±13.02		0.967	
Mean stone size/mm± SD	15.41±3.50		16±3.67		15.80±3.54		0.838	
Sex	Number	%	Number	%	Number	%		
	Men	17	65.3	18	72	16	64	0.753
	Women	9	34.6	7	28	9	36	0.562
Site	upper pole	13	50	12	48	13	52	0.923
	Pelvic	13	50	13	52	12	48	0.923

Clinical success defined as stone-free status or clinically insignificant stone. Clinically insignificant residual fragments were defined as asymptomatic fragments 4 mm or less in diameter.

The percentage of patients with clinical success after ESWL at 4 weeks was 23% in group A, 48% in group B and 44% in group C and increased to 46%, 80% and 76% in group A, B and C

respectively at 8 weeks (Fig 1). The clinical success was statistically more significant in group B compared to group A at both 4 and 8 weeks (p value < 0.05). The clinical success was statistically more significant in group C compared to group A at both 4 and 8 weeks (p value < 0.05). There was no statistically significant difference in the clinical success between group B and C (p value > 0.05). Tab. 2

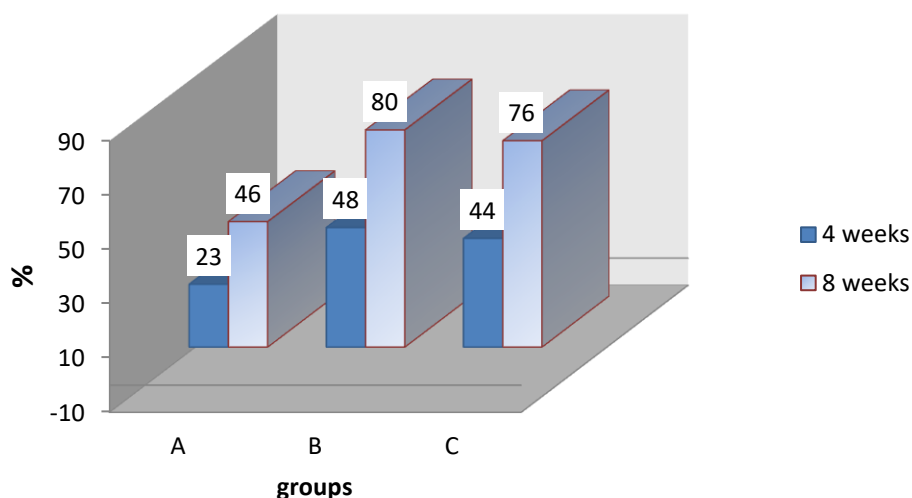


Table (2): Comparison of clinical success among the three groups.

Four weeks	Total number	Clinical success		P value
		Number	%	
Group A	26	6	23	0.003
Group B	25	12	48	
Group C	25	11	44	
Group B	25	12	48	0.677
Group C	25	11	44	
Eight weeks				
Group A	26	12	46	0.002
Group B	25	20	80	
Group C	25	19	76	
Group B	25	20	80	0.749
Group C	25	19	76	

There was no significant complication apart from slight hematuria which occurred in all patients of all groups and resolved within 48 hours, steinstrasse occurred in 7(26%) patients in group A, 2 patients (8%) in group B and 3 patients (12%) in group C, it resolved spontaneously in 2 patients (28%) in Group A, 2 patients (100%) in group B and 2 patients (66.6%) in group C.

All patients who did not achieve clinical success at 2 months where treated by another session of ESWL for the renal and upper ureteric fragments and ureteroscopic removal for nonprogressing lower ureteric fragments. The second session of ESWL was needed in 8 patients (30.7%) in group A, 3 patients (12%) in group B and 4 patients (16%) in group C and ureteroscopy for lower ureteric fragments in 6 patients (23%) in group A, 2 patients (8%) in group B and 2 patients in

group C but because the end point of this study is the 2 months of follow up, so their response after the 2nd session of ESWL had not been included in this study.

The incidence of side effect of drug in group B (Tamsulosin) such as headache, abnormal ejaculation, and dizziness occurred more than in group A, no significant side-effects was detected so as to require exclusion of a patient from the study, and medical intervention was not

performed in any of the patients because of side-effects. The incidence of side effect in group C (Terpenes combination) such as nausea, headache, and diarrhea occurred more than in group A, no significant side-effects was detected so as to require exclusion of a patient from the study, and medical intervention was not performed in any of the patients because of side-effects. Table(3)

Table (3): Side effects among three groups.

Side effects	Headache/%	Abnormal ejaculation/%	Dizziness/%	Nausea/%	Diarrhea/%
Group A	7.6	0	0	3.80	3.8
Group B	20	28	16	8	4
Group C	16	0	4	12	8

Discussion

Revolution in the treatment of urolithiasis is achieved since the introduction of extracorporeal shock wave lithotripsy at 1982.^[18] From that time, ESWL has been used as the 1st line of modality for treatment for renal calculi because of its non-invasiveness and high success rate.^[19]

Eighty percent of urinary tract calculi is treated with ESWL with success rate varies from 70% – 90%.^[19,20] Once the calculus bulk is disintegrated into smaller fragments to pass within the ureter, various factors like ureteral lumen, edema, infection and fragments size determine their spontaneous descent through the ureter. It means that management at this stage is similar to conservative treatment of ureteral calculi. However, use of some drugs can control symptoms and facilitate stone expulsion like anti-inflammatory and anti-edematous, alpha adrenergic blockers, calcium channel blockers or terpenes combination.^[21-23]

Micali et al,[6] reported that medical therapy with nifedipine or tamsulosin following ESWL to facilitate ureteral stone expulsion results in increase 1- and 2-

month stone-free rates and in a lower percentage of those needing re-treatment.

Losek et al,^[9] suggested that adjunctive tamsulosin therapy combined with ESWL is safe and effective in enhancing stone clearance in patients with renal stones 10-24 millimeters in diameter.

Pooled analyses by Seitz et al, suggested that MET with α -blockers or calcium channel blockers augments stone expulsion rates, reduces the time to stone expulsion, and lowers analgesia requirements for ureteral stones with and without ESWL for stones ≤ 10 mm, renal stones after ESWL also seemed to profit from MET.^[15]

In the present study, the use of tamsulosin was safe and effective in enhancing the clearance of stone gravels after ESWL of renal stones with clinical success of 44% and 80 % compared to 23% and 46% in the control group at 4 and 8 weeks, respectively. So our results are comparable with the above mentioned studies regarding the use of tamsulosin after ESWL of renal stones.

Dellabella et al ^[24] proposed that tamsulosin induces an increase in the

intraureteral pressure gradient around the stone by: (1) increasing the urine bolus above it (thus increasing intraureteral pressure above the stone), and (2) decreasing peristalsis below the ureter (thus decreasing intraureteral pressure below the stone). These actions are in addition to a decrease in basal and micturition pressures. As a result, there is a stronger effect to expel the stone.

Terpenes were reported to have diuretic anti-inflammatory analgesic and spasmolytic properties. Among the reported properties, the anti-inflammatory effect is achieved by the suppression of arachidonic acid metabolism and cytokine production.^[25] Rowatinex is a combination of seven naturally appearing essential oils (terpenes). The pharmaceutical effects of the included terpenes are diuretic, spasmolytic, antibacterial, and hyperemic. Due to the pharmacologic nature of the utilized terpenes, Rowatinex is used as a supportive drug in conservative stone management and stone expulsive therapy.^[26]

Siller et al.^[27] were the first to evaluate the effect of Rowatinex on stone-free rates in patients who received ESWL and suggested increased rate of stone fragments clearance after ESWL but their study was uncontrolled. Djaladat et al.^[28] reported a series of 100 patients after uncomplicated SWL who were randomized into a Rowatinex group and a placebo group. The authors concluded that despite missing advantages in overall stone-free status after 4 wk, the treatment with Rowatinex may lead to accelerated stone expulsion.

Romics et al.^[23] published a prospective randomized trial of >200 patients receiving ESWL and postoperative expulsion supportive therapy with either Rowatinex or placebo. They found significantly higher rates of stone-free patients in the Rowatinex group within a 12-wk interval.

The use of terpenes combination (Rowatinex) in this study was safe and

effective in increasing the number of patients with stone free status at 4 and 8 weeks of follow up compared to the control group. This result is compatible with the results of previous studies.

The use of medical expulsion in this study by tamsulosin or terpenes combination (Rowatinex) was well tolerated and demonstrated clinically meaningful and statistically significant improvement in the clearance of stone fragments after ESWL of renal stone. This improvement is probably due to the effect of these drugs on the possible causes of stone retention, spasm, edema, and ureteral infections, which are modifiable factors.^[29]

This study also compared the effect of tamsulosin on the clearance of stone to that of terpenes combination at 4 and 8 weeks and despite the relatively small number of patients. There was no statistically significant difference between the 2 groups.

Large-scale randomized trials comparing the effect of Rowatinex versus tamsulosin and calcium-channel antagonists are pending.^[26]

It had been observed that the clinical success increase with increasing duration of observation so it may be wealthy to prlong the interval between the sessions of ESWL in order to decrease the burden on the kidney.

Although the incidence of side effect in tamsulosin group or terpenes combination group occurred more than in the control group, no significant side-effect was detected so as to require exclusion of a patient from the study, and medical intervention was not performed in any of the patients because of side-effects.

Conclusion:

The use of medical expulsion in this study by tamsulosin or terpenes combination (Rowatinex) was well tolerated and it demonstrated that it is clinically meaningful and statistically it has significant improvement in the clearance of stone fragments after ESWL of renal stone.

The effect of tamsulosin and terpenes combination (Rowatinex) on the clearance of stone fragments after ESWL of renal stone was comparable.

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