Effect of Rowatinex on Calculus Clearance After Extracorporeal Shock Wave Lithotripsy

Hooman Djaladat,[1] Khatereh Mahouri,[2] Fatemeh Khalifeh Shooshtary,[1] Azadeh Ahmadieh[3]

Introduction: Our aim was to evaluate the effect of Rowatinex, an essential oil preparation of terpenic type, on kidney calculi clearance after extracorporeal shock wave lithotripsy (SWL).

Materials and Methods: A randomized controlled trial was performed at Hormozgan Hospital in Bandar Abbas, Iran, on 100 patients with 10-mm to 20-mm kidney calculi. They underwent SWL, and then, they were randomly assigned into 2 groups to receive either Rowatinex, 100 mg, 3 times per day, or placebo after SWL. The patients were followed up with plain abdominal radiography, ultrasonography, and excretory urography (if required), 2 and 4 weeks postoperatively.

Results: Two weeks following SWL, 6 (12%) and 9 (18%) patients in the Rowatinex and control groups had fragmented calculi without clearance, 26 (52%) and 24 (48%) had less than 50% clearance, 9 (18%) and 15 (30%) had more than 50% but not total clearance, and 9 (18%) and 2 (4%) patients were stone free, respectively. Rowatinex had a significant effect on the stone-free rate (P = .02). Four weeks post-SWL, 3 (7.3%) and 7 (14.6%) other patients in the Rowatinex and control groups became stone free, respectively. Overall, Rowatinex had no significant effect on the stone-free rate (P = .46). No complications or differences between the two groups in symptoms and signs were reported.

Conclusion: Rowatinex does not have a significant effect on clearance rate of kidney calculi after SWL. However, it can accelerate calculus passage after 2 weeks, and it does not have any significant adverse effects.

Keywords: urinary calculi, lithotripsy, therapy, terpenes, prospective studies

Urol J. 2009;6:9-13.
www.uj.unrc.ir

[1]Department of Urology, Mohammadi Hospital, Hormozgan University of Medical Sciences, Bandar Abbas, Iran
[2]Department of Community Medicine, Hormozgan University of Medical Sciences, Bandar Abbas, Iran
[3]Department of Oral Medicine, Beheshti University of Medical Sciences, Tehran, Iran

Corresponding Author:
Hooman Djaladat, MD
Mohammadi Hospital, Jomhoori Blvd, Bandar Abbas, Iran
Tel: +98 21 6671 7447
Fax: +98 21 6671 7447
E-mail: hoomanj@hums.ac.ir

Received March 2008
Accepted November 2008

INTRODUCTION

Urinary calculus is the most common disorder of the urinary tract after urinary tract infections and prostate disease. The challenge of urologists to treat patients with upper urinary tract calculi is to choose the best treatment option according to the characteristics of the patient and the calculus.[1-3] In the past 2 decades, extracorporeal shock wave lithotripsy (SWL) has revolutionized management of kidney calculi. However, the presence of calculus fragments after SWL is common and calculus clearance is not achieved immediately. Residual fragments larger than 5 mm usually indicate treatment failure.[4] Most of small fragments pass spontaneously and their clearance failure probably leads to further complications and subsequent interventions.[2]

Several studies have demonstrated

that medical management of residual fragments may improve the outcome of SWL.[4] Siller and colleagues[5] investigated the effect of Rowatinex, an essential oil preparation of terpenic type,[6] in the clearance of residual fragments after SWL and showed an 82% stone-free rate by day 28 in patients who used Rowatinex. This report, to our knowledge, is the only report available in the literature on the effect of Rowatinex on calculus clearance after SWL. To better address the issue, we performed a randomized single-blind clinical trial to determine the effect of Rowatinex on the clearance of kidney calculi after SWL.

MATERIALS AND METHODS

Participants

We performed a randomized single-blind clinical trial at Hormozgan Hospital in Bandar Abbas, Iran, between October 2005 and December 2006. Patients who were admitted to undergo SWL were approached and those with renal pelvis or caliceal calculi sized between 10 mm and 20 mm were selected. The exclusion criteria were ureteral and bladder calculi, drug hypersensitivity, history of kidney surgery or any urological interventions, pregnancy, and breast feeding. Calculus location and size were assessed using plain abdominal radiography and ultrasonography. Excretory urography was also used, if needed.

Study Design

The Review Board and Ethics Committee of Hormozgan University of Medical Sciences approved the study and all patients provided written informed consent before participation. Eligible patients were enrolled in the study and randomly assigned to receive either Rowatinex (Rowa Pharmaceuticals, Cork, Ireland) or placebo for 1 month after SWL. Rowatinex capsules, 100 mg, were administered 3 times a day in the study group. Rowatinex is a terpenic mixture is composed of pinene, camphene, anethol, borneol, cineol, fenchone, and olive oil.[6]

A Modulith SLK machine equipped with a cylindrical electromagnetic shock wave source (Storz Medical, Tuttlingen, Switzerland) was used to perform lithotripsy. All patients received a mean of 3400 ± 200 shocks (range, 2800 to 4000 shocks) with an energy level of 50.0 ± 3.5 kV (range, 40 to 60 kV) and a mean frequency of 2 shocks per second. The patients were followed up by history, physical examination, and radiological studies, 2 and 4 weeks postoperatively and whenever they would seek medical care. Plain abdominal radiography and ultrasonography results were reported by one expert radiologist. Also, excretory urography would be done if required. Results were compared in terms of patients' symptoms and signs such as renal colic, gastrointestinal problems, calculus passage, and clearance rate (fragmented, $< 50\%$ cleared (1% to 49%), $\geq 50\%$ cleared (50% to 99%), and totally cleared or stone free). Total calculus clearance was defined as undetectable calculi on plain abdominal radiography and ultrasonography or excretory urography in a symptom-free patient after SWL.

Statistical Analyses

Data were analyzed using the SPSS software (Statistical Package for the Social Sciences, version 13.0, SPSS Inc, Chicago, Illinois, USA). The chi-square test was used to compare categorical variables and the Student *t* test for continuous ones between the two groups. A *P* value less than .05 was considered significant.

RESULTS

Patients

From October 2005 to December 2006, a total of 545 patients were referred to undergo SWL in our lithotripsy center, of whom 255 met the study criteria and 100 accepted to be enrolled in the trial. They were randomly assigned to receive Rowatinex capsules (n = 50) or placebo (n = 50), and all of them completed the study course. The baseline characteristics were generally similar between the two groups (Table).

Efficacy

Two weeks following lithotripsy in the Rowatinex group, fragmented calculi without clearance were seen in 6 patients (12.0%), less than 50% clearance in 26 (52.0%), and 50% or higher clearance (but not total clearance) in 9

Baseline Characteristics of Patients With and Without Rowatinex After Shock Wave Lithotripsy

Characteristics	Rowatinex Group	Control Group
Number of patients	50	50
Mean age, y	38.3 ± 16.4	40.9 ± 14.0
Males	30 (60.0)	29 (58.0)
Calculus size, mm		
10	24 (48.0)	23 (46.0)
11 to 19	15 (30.0)	18 (36.0)
20	11 (22.0)	9 (18.0)
Calculus location		
Renal pelvis	19 (38.0)	28 (56.0)
Upper calyxes	6 (12.0)	2 (4.0)
Middle calyxes	10 (20.0)	9 (18.0)
Lower calyxes	15 (30.0)	11 (22.0)

patients (18.0%). Nine patients (18.0%) were stone free after SWL. In the control group, 9 patients (18.0%) had fragmented calculi without clearance, 24 (48.0%) had less than 50% clearance, 15 (30%) had 50% or higher clearance, and 2 (4%) had total calculus clearance (Figure 1). The stone-free rate was significantly higher in the Rowatinex group than the control group ($P = .02$)

In the Rowatinex group, calculus clearance correlated with age ($P = .03$), but not with sex, calculus size, or calculus location ($P = .16$, $P = .25$, and $P = .89$, respectively). In the control group, no significant correlation was seen between calculus clearance and age, sex, calculus size, or calculus location ($P = .64$, $P = .65$, $P = .08$, and $P = .92$, respectively).

Four weeks after SWL, we followed up 89 patients who were not stone free at the 2-week follow-up visit. In the Rowatinex group, fragmentation only, less than 50% clearance, 50% or higher clearance, and total clearance were seen in 5 (12.2%), 22 (53.7%), 11 (26.8%), and 3 (7.3%) patients, respectively. In the controls, 6 (12.5%), 19 (39.6%), 16 (33.3%), and 7 (14.6%) patients had fragmentation only, less than 50% clearance, 50% or higher clearance, and total clearance, respectively (Figure 2). Overall, there were no significant differences in the stone-free rate between the two groups ($P = .46$). Age, gender, calculus size, and calculus location had no significant effect on calculus clearance in neither of the groups (Rowatinex group: $P = .34$, $P = .28$, $P = .51$, and $P = .66$, respectively; control group: $P = .65$, $P = .22$, $P = .58$, and $P = .08$, respectively).

Tolerability

Two weeks post-SWL, 6 patients (12.0%) suffered from renal colic, while 21 (22.0%) had calculus passage without colicky pain in the Rowatinex group. None of the patients experienced significant gastrointestinal discomfort or any other side effects. In the control group, renal colic was reported by 2 patients (4.0%) and calculus passage without colicky pain by 24 (48.0%). After 4 weeks, 1 patient (2.4%) in the Rowatinex group experienced renal colic and 10 (24.4%) passed the calculi without colicky pain. There was no report of significant gastrointestinal or any other side effects during the second 2 weeks after SWL. In the control group, 1 patient (2.4%) had renal

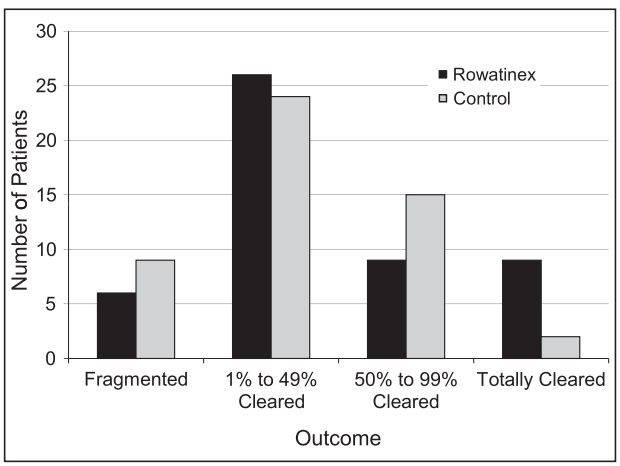

Figure 1. Outcomes 2 weeks after shock wave lithotripsy in patients with Rowatinex and controls.

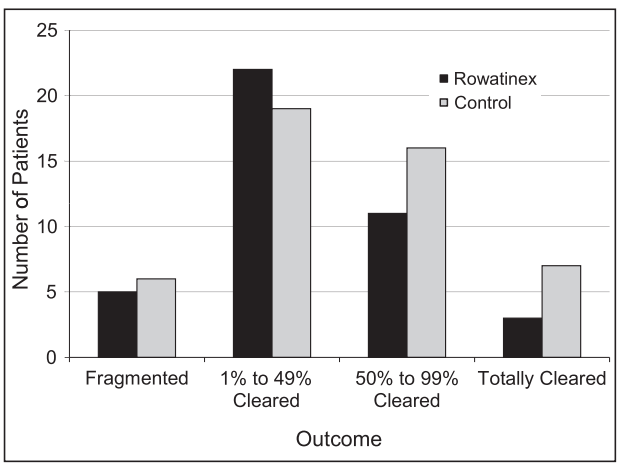

Figure 2. Outcomes 4 weeks after shock wave lithotripsy in patients with Rowatinex and controls.

colic and 15 (31.3%) had calculus passage without colicky pain. The differences were insignificant at 2 and 4 post-SWL weeks ($P = .32$ and $P = .77$, respectively).

DISCUSSION

The purpose of this study was to evaluate the effect of Rowatinex on clearance of kidney calculi after extracorporeal SWL. It has been generally assumed that SWL is the first-line management option for 10-mm to 20-mm kidney calculi. Although it is a less invasive procedure for treatment of such calculi, calculus clearance is not achieved immediately and most of fragments pass spontaneously during the first months after lithotripsy.[1,2] Residual fragments are important as they may lead to obstruction, recurrent infection, or calculus regrowth.

Medical therapy has been shown to be effective in prevention of calculus growth and recurrence.[4,7] Cicerello and colleagues showed the efficacy of alkaline citrate in the clearance of residual fragments after SWL in patients with calcium and struvite calculi.[8] They explained that persistence and regrowth are common in the natural history of residual calculus fragments. Citrate improved the outcome of these calculi by increasing the clearance of residual particles. Other medications, like tamsulosin and thiazides have been shown to enhance calculus clearance in patients with kidney calculus undergoing SWL.[12,13]

Rowatinex is an essential oil preparation of terpenic type composed of pinene (3%), camphene (15%), borneol (10%), anethol (4%), and cineol (3%) in olive oil, which has been suggested for the treatment of urolithiasis, nephrolithiasis, renal colic, and other urological problems.[6,9,10] To our knowledge, there is not much data in the literature to explain the exact mechanism of action of Rowatinex. However, it is assumed to improve renal blood flow, thus stimulating the kidneys and giving rise to increased urine excretion, and to have antispasmodic effect to facilitate passage of the calculi.

There are some studies that have evaluated the effect of Rowatinex in the treatment of urolithiasis. In an early study, Miller[11] reported 65% success in spontaneous expulsion of calculi in 40 patients with urolithiasis who received Rowatinex. This was a study on ureteral calculi in patients without a history of SWL. In our study, the total calculus clearance (stone-free rate) in the Rowatinex group was 24% in comparison with 18% in the control group, 1 month post-SWL ($P = .46$). The slight difference between these two studies might be due to various calculus locations. Also, the overall lower clearance rate in our study in comparison to the reports in the literature might be due to special climate conditions in our region (it is considerably hot and humid in Bandar Abbas), shorter period of follow-up assessments, and relatively higher frequency of lower caliceal calculi.

Mukamel and associates,[9] in a study on patients with renal colic, noted an insignificantly higher rate of calculus expulsion in the Rowatinex group when compared to a control group (61% versus 28%, respectively). They reported no serious side effects with Rowatinex. Engelstein and colleagues evaluated the effect of Rowatinex in patients with ureteral calculi in a case-control study.[6] They concluded that early treatment with Rowatinex might be helpful for patients with ureteral calculi before other invasive procedures are applied. The only study that evaluated the effect of Rowatinex on the clearance of kidney calculi after SWL was carried out by Siller and colleagues.[5] They administered Rowatinex on 50 patients with kidney calculi after SWL. They showed that 82% of patients were stone free 1 month after lithotripsy.

Reports on other drugs have also been relatively promising. Losek and Mauro[12] studied the effect of tamsulosin on calculus clearance after SWL. They showed that the 12-week kidney calculus clearance was 60% in the control group compared to 78.5% in the tamsulosin group ($P = .04$). Arrabal-Martin and coworkers evaluated the effect of thiazides on clearance of kidney calculi after SWL. The percentage of global expulsion of lithiasis was significantly greater in patients on thiazides in contrast to controls (72% versus 36%; $P = .03$).

In our study, 2 weeks following SWL, the stone-free rate was significantly different between

the patients on Rowatinex and the controls (18% versus 4%, $P = .02$). However, other SWL outcome measurements such as patients' symptoms and signs, renal colic, gastrointestinal problems, and calculus passage were not significantly different between the two groups. Four weeks post-SWL, Rowatinex did not show any significant effect on the overall calculus clearance rate or other outcome measures of the patients in comparison with placebo. Thus, we can conclude that Rowatinex might be effective in accelerating calculus passage, but it has no effect on the overall outcome. The weakness of our study is the limited number of studied patients. It is somehow due to the rigid inclusion and exclusion criteria we set. Also in our region, ureteral calculi that were not included in our study are much more common than kidney calculi.

CONCLUSION

Rowatinex has no significant effect on clearance rate of kidney calculi after SWL. However, early after therapy with Rowatinex, calculus clearance might be achieved in a greater number of patients, which means that Rowatinex can accelerate calculus passage, while having no significant side effects.

ACKNOWLEDGMENT

We wish to thank Dr Zare for his help with the manuscript.

CONFLICT OF INTEREST

None declared.

REFERENCES

1. Stoller ML, Bolton DM. Urinary stone disease. In: Tanagho EA, McAninch JW, editors. Smith's general urology. 15th ed. New York (USA): Lange Medical Books/McGraw-Hill; 2000. p. 291-320.
2. Pearl SM, Lotan Y. Urinary lithiasis: etiology, epidemiology and pathogenesis. In: Wein AJ, Kavoussi LR, Novick AC, Partin AW, Peters CA, editors. Campbell-Walsh urology. 9th ed. Philadelphia: Saunders; 2007. p. 1363-73.
3. Lingeman JE, Matlaga BR, Evan AP. Surgical management of upper urinary tract calculi. In: Wein AJ, Kavoussi LR, Novick AC, Partin AW, Peters CA, editors. Campbell-Walsh urology. 9th ed. Philadelphia: Saunders; 2007. p. 1431-58.
4. Tan YH, Wong M. How significant are clinically insignificant residual fragments following lithotripsy? Curr Opin Urol. 2005;15:127-31.
5. Siller G, Kottászs S, Pálfi Z. Rowatinex kapszula hatékonyságának vizsgálata ESWL-kezelés után keletkezett kõfragmentumokra. Magyar Urologia. 1998;10:139-46.
6. Engelstein D, Kahan E, Servadio C. Rowatinex for the treatment of ureterolithiasis. J Urol (Paris). 1992;98:98-100.
7. Fine JK, Pak CY, Preminger GM. Effect of medical management and residual fragments on recurrent stone formation following shock wave lithotripsy. J Urol. 1995;153:27-32.
8. Cicerello E, Merlo F, Gambaro G, et al. Effect of alkaline citrate therapy on clearance of residual renal stone fragments after extracorporeal shock wave lithotripsy in sterile calcium and infection nephrolithiasis patients. J Urol. 1994;151:5-9.
9. Mukamel E, Engelstein D, Simon D, Servadio C. The value of Rowatinex in the treatment of ureterolithiasis. J Urol (Paris). 1987;93:31-3.
10. Al-Mosawi AJ. A possible role of essential oil terpenes in the management of childhood urolithiasis. Therapy. 2005;2:237-47.
11. Miller R. [Experiences in the treatment of urolithiasis with Rowatinex]. Fortschr Med. 1967;85:39-42. German.
12. Losek RL, Mauro LS. Efficacy of tamsulosin with extracorporeal shock wave lithotripsy for passage of renal and ureteral calculi. Ann Pharmacother. 2008;42:692-7.
13. Arrabal-Martin M, Fernandez-Rodriguez A, Arrabal-Polo MA, Garcia-Ruiz MJ, Zuluaga-Gomez A. Extracorporeal renal lithotripsy: evolution of residual lithiasis treated with thiazides. Urology. 2006;68:956-9.