Original Article

Efficacy of Orthosiphon aristatus (Cat's Whiskers) and an alpha-blocker for stone expulsion in patients with urinary tract calculi undergoing extra corporal shockwave lithotripsy

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Keywords:
Extra corporal shockwave lithotripsy, ESWL, treatment success rate, stone free rate; Orthosiphion aristatus, Cat's Whiskers, alpha-blockers

Abstract

Objective: To evaluate the efficacy of a herbal treatment, Orthosiphon aristatus (Cat's Whiskers) and alpha blockers with regard to stone free and treatment success rates in patients with urinary tract calculi undergoing extra corporal shockwave lithotripsy (ESWL).

Materials and Methods: Data pertinent to 84 patients who underwent ESWL for treatment of KUB stones were prospectively analyzed. Patients were randomized into two groups: Group 1: patients received the medicinal herb Orthosiphon aristatus post ESWL and Group 2: patients received an alpha-blocker (Doxazocin 2 mg) post ESWL. Both groups used the same medication throughout the 3-month period of the study. All patients were followed-up every 2 weeks after ESWL for 3 months with x-ray and blood tests and urine tests to evaluate results and complications.

Results: The stone free rate was 47.6% in the medical herb Orthosiphon aristatus group and 45.2% in the alpha-blocker group. Treatment success rates were 69.0% in the Orthosiphon aristatus group and 54.8% for alpha-blockers group. The differences in stone free rate and treatment success rate were not statistically significantly different ($p = 0.827$, 0.261) and the rate of complications in the Orthosiphon aristatus group was not statistically significantly different from the other group ($p = 1.000$)

Conclusion: Treatment with Orthosiphion aristatus medical expulsive therapy after ESWL give similar results of stone free rate as the group taking alpha-blockers. Both treatments are equally safe methods of medical expulsive therapy.

Insight Urol 2024;45(2):103-9. doi: 10.52786/isu.a.92

Introduction

Extracorporeal shock wave lithotripsy (ESWL) has been used as a treatment of urolithiasis since 1980.[1] As a minimally invasive procedure, the efficacy of ESWL is accepted worldwide especially in the treatment of small renal or ureteric calculi.[2] However, some patients require repeat ESWL treatment due to the failure

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Manuscript received: September 30, 2024
Revision received: November 26, 2024
Accepted after revision: December 9, 2024

or limitation of stone fragmentation. The success of ESWL treatment depends on several factors including stone size, stone number, stone composition, and renal function. The success rate of ESWL has a wide variation ranging from 46% to 91%.[3-8] The results of ESWL are measured by taking into consideration stone fragmentation and clearance, which have been found to be influenced by certain predicting factors such as stone size, stone location, skin-to-stone distance (SSD), stone composition, severity of obstruction, urinary tract anatomy, obesity, and ESWL machine type.[9-17] Greater success of ESWL was observed in cases of patients aged ≤ 40 years, with a stone size of ≤ 10 mm, a stone surface area of ≤ 50 mm and a location in the upper calyx.[18]

The main mechanism employed is the cavitation phenomenon. When a shock wave generated by an extracorporeal shock wave lithotripter interacts with a solid, it can produce cavitation bubbles at the interface between the solid and the surrounding liquid. The implosion of the cavitation bubbles plays an important role in the disintegration of the stone

Other studies related to Orthosiphon aristatus (Cat's Whiskers)

One study was carried out in patients with renal stones with patients taking an Orthosiphon aristatus (Cat 'Whiskers) infusion every day 3 times a day for 2-6 months. The results were promising. In 23 cases the size of stones reduced, 40% of the stones were expelled, and the symptoms improved by 20%.[19] Another study into the effect of cat's whisker grass in reducing the size of kidney stones in an area in the North-east of Thailand also showed promising results.[20] One report described a study into the treatment of kidney stones in patients who were given a decoction prepared from dried Cat's whisker grass leaves. The concentration of the solution was 0.5% and patients were given 300 ml once a day for 1-10 months. Nine cases were found to have a good clinical response. It was found that the patient's urine was more alkaline, which suggests that it should help to reduce the occurrence of uric acid stones. An increase in uric acid excretion was also noted after consumption of a tea prepared from Orthosiphon grandifloras.[21] Recently, a study showed a reduction in stone size in patients which was probably related to an increased excretion of calcium and uric acid.[22] In *in vitro* experiments it was shown that the antilithogenic activity of grandiflorus might be due to its diuretic activity.

It has also been demonstrated that methoxyflavonoids from Orthosiphon act as antagonists at adenosine Al receptors. Some studies revealed that adenosine Al receptor antagonists can induce diuresis and sodium excretion.[23] Since adenosine Al receptors are expressed in the afferent arterioles, glomerulus, proximal tubules, and collecting ducts adenosine antagonists could directly inhibit sodium reabsorption in the proximal tubules or indirectly by promoting afferent arteriole dilatation.[24]

Other studies related to alpha-blockers

The giving of an alpha-blocker after shock wave treatment to break up kidney stones appears to clear the fragments faster in more people and reduce the need for extra treatments. It has been shown that alpha-blockers might cause fewer unwanted events than usual care or a placebo.[25]

There is a modest increase in stone-free rates in those receiving alpha-blockers following ESWL, with a reciprocal modest risk reduction for steinstrasse (stone street), pain and auxiliary procedures. However, alpha-blockers do not reduce the risk of requiring retreatment.[26]

This study was the first study in patients with urinary tract stones who have taken Orthosiphon aristatus after treatment with ESWL. The aim of the study is to compare stone free rate, treatment success and prevalence of complications between treatment with the medicinal herb Orthosiphon aristatus and alpha blockers following ESWL. The hypothesis is that the herbal treatment in combination with ESWL improves the stone free rate to the same extent as alpha-blockers in combination with ESWL

Materials and Methods

A prospective, randomized, trial was conducted between July 2024 and September 2024 at Uttaradit Hospital. This study was approved by the Ethics Committee of Human Research (ECID: 4 /2567) and approved by the Ethics Committee for Research in Human Subjects in the Fields of Thai Traditional and Alternative Medicine (TAMEC)

From the original cohort 90 patients, 6 patients were excluded due to loss of follow up, the remaining 84 patients were enrolled in the study. All patients had radiopaque renal or ureteric

calculi. Written consent was given by all participants. Demographic data including age, sex, body mass index (BMI), stone size, and stone location were noted. As shown in Table 1, the patients were randomly divided into 2 groups. In the first group (Herbal Medicine group), the patients received Orthosiphon aristatus in the form of 500 mg capsules with 2 capsules being taken twice a day after the ESWL session and then the herbal treatment was continued to the end of the study. In the second group, the patients were given 2 mg Doxazocin before bed time after each ESWL session. Blood pressure, and oxygen saturation were monitored during the procedures.

All patients given ESWL were treated as outpatients under intravenous analgesia; pethidine 25 mg. A SEIMEN model MODULARIS machine was used for the ESWL, with 3,000 shots of shock waves given at the rate of 60-90 shockwaves/minute with the energy beginning at 8 and progressing up to 15 kilovolts. Patients were followed up at the outpatient department every 2-3 weeks after ESWL for 3 months with a plain film kidney ureter bladder (KUB) x-ray. ESWL was repeated if no stone fragmentation occurred or residual stone fragments were larger than 4 mm. Patients were permitted a maximum of 3 sessions of ESWL, 2-3 weeks apart. The primary outcome was stone free rate at 3 months after ESWL.

Stone free was defined as the complete clearance of stone or no visible stone seen on plain film KUB. Clinically insignificant residual fragments (CIRF) was defined as residual fragments of stone 4 mm or less on plain film KUB. The secondary outcome was the treatment success rate, defined as the complete clearance of stone (stone free) or CIRF on plain film KUB after 3 months. Inclusion criteria were patients above 18 years old, with a radiopaque renal or ureteric calculi size over or equal to 4 mm. The exclusion criteria were patients who were pregnant, suffered from uncontrolled coagulopathy, or urinary tract infection, and those with Diabetes mellitus and heart disease.

Statistical analysis was carried out using Statistical Package for Social Sciences STATA V 16.0 by Stata Corp. Categorial variables were compared using the Chi-square test. Continuous data are presented as mean and standard deviation (SD), which were compared using a Fisher's exact test

Results

A total of 84 patients were enrolled onto the study and randomly divided into two groups, 42 patients being allocated into each arm. There were no statistical differences between the 2 groups with regard to age, sex, BMI, stone size and stone location (Table 1).

The mean ages of the Orthosiphon aristatus group and the alpha-blocker group were 58.8 years and 55.9 years respectively, p-value 0.528. The mean BMI of the Orthosiphon aristatus group and the alpha-blocker group were 24.2 kg/m^2 and 24.9 kg/m^2 respectively, $p = 0.370$. The mean size of the stones in the Orthosiphon aristatus group and the alpha-blocker group were 1.61 mm and 1.32 mm respectively, $p = 0.248$. Fifty-two patients (61.90%) had a renal stone and thirty-two patients (38.09%) a ureteric stone. Patients with renal stones in the Orthosiphon aristatus group and the alpha-blocker group numbered 27 patients (64.9%) and 25 patients (59.5%) respectively. Patients with ureteric stone in the Orthosiphon aristatus group and the alpha-blocker group totaled 15 patients (35.71%) and 17 patients (40.47%) respectively.

There was no statistical difference between the stone free rate of the Orthosiphon aristatus group and the alpha-blocker group ($p = 0.227$). The overall treatment success rate in the Orthosiphon aristatus group was not significantly higher than in the alpha-blocker group (69.0% vs 54.8%, $p = 0.261$) (Table 2).

When we analyzed complications associated with treatment, it was found that there were no significant differences between the two sample groups as regards complications ($p = 1.000$). The specific complications in the Orthosiphon aristatus group were 13 (30.9%) gross hematuria and 7 (16.7%) colicky pain whereas in the alpha-blocker group they were 13 (30.9%) and 8 (19.1%) (Table 3).

Two patients (4.7%) in each group were treated with ureterorenoscopy to remove residual stones, 2 patients (4.7%) in the Orthosiphon aristatus group required a transurethral procedure for removal of a stone from the bladder after failure to pass spontaneously through their urethra, the same number required ureterorenoscopic lithotripsy in the alpha-blocker group. There were no significant differences in any of the auxiliary treatments (Table 4).

Table 1. Demographic data

General Data	Orthosiphion aristatus (n=42)	Alpha-blocker (n=42)	P-value
Gender			
Male n (%)	26 (61.9)	31 (73.8)	0.175
Female n (%)	16 (38.1)	11 (26.2)	
Age (years) (mean±SD)	(58.8±10.8)	(55.9±11.7)	
Body mass index (BMI) (kg/m^2) (mean±SD)	(24.2±3.9)	(24.9±3.6)	
Underlying disease			
Yes n (%)	25 (59.5)	24 (57.1)	1.000
No n (%)	17 (40.5)	18 (42.9)	
GFR (ml/min/1.73 m^2)			
<60 n (%)	7 (16.7)	1 (2.4)	0.188
60-89 n (%)	27 (64.30)	29 (69.0)	
>90 n (%)	8 (19.0)	12 (28.6)	
(mean±SD)	(74.9±17.5)	(91.2±75.9)	
Stone size (cm) (mean±SD)	(1.61±0.5)	(1.32±0.6)	0.248
Stone position			
Upper calyx n (%)	6 (14.3)	4 (9.5)	0.815
Middle calyx n (%)	4 (9.5)	2 (4.8)	
Lower calyx n (%)	8 (19.1)	10 (23.8)	
Renal pelvis n (%)	5 (11.9)	7 (16.7)	
Other n (%)	19 (45.2)	19 (45.2)	

SD = standard deviation

Table 2. Outcomes of the study

	Orthosiphion aristatus (n=42)	Alpha-blocker (n=42)	P-value
Stone free n (%)	20 (47.6)	19 (45.2)	0.827
CIRF* n (%)	9 (21.4)	4 (9.5)	0.227
Treatment success** n (%)	29 (69.0)	23 (54.8)	0.261

*Clinically Insignificant Residual Fragment (CIRF) is residual stone fragment less than or equal to 4 mm after treatment, **Treatment success defined as stone free and CIRF in combination

Table 3. Complications associated with treatment

Complications	Orthosiphion aristatus (n=42)	Alpha-blocker (n=42)	P-value
UTI n (%)	0 (0)	1 (2.8)	1.000
Persistent gross hematuria n (%)	13 (30.9)	13 (30.9)	1.000
Stone street with colicky pain n (%)	7 (16.7)	8 (19.1)	1.000
Serum potassium level n (%) (>5.0 ng/dl) (mean±SD)	0 (0.0)	0 (0.0)	1.000

SD = standard deviation

Discussion

ESWL is the treatment of choice for urolithiasis with small size stone, due to the minimally invasive nature of the procedure. The mechanisms involved in ESWL treatment for stone disintegration are compressive fracture, spallation, acoustic cavitation, and dynamic fatigue, of which cavitation is the most important.[27,28]

There were several factors found which could interfere with the success of ESWL treatment, for

Table 4. Auxiliary procedures

Procedures	Orthosiphion aristatus (n=42)	Alpha-blocker (n=42)	P-value
URSL n (%)	0 (0)	2 (4.7)	0.114
TUL n (%)	3 (7.1)	0 (0.0)	
PCN or ureteral stent indwelling n (%)	0 (0.0)	0 (0.0)	
Open surgery n (%)	0 (0.0)	0 (0.0)	

URSL = ureterorenoscopic lithotripsy, TUL = transurethral lithotripsy, PCN = percutaneous nephrostomy

example, in stone related factors stone size, stone number, stone composition, and in patient related factors intrarenal anatomy or stone location especially in the case of lower caliceal stones. Therefore, the choice of treatment which is the minimally invasive, while treating the condition effectively in each patient is an important issue that urologists should consider.

The findings of many studies currently being carried out will improve ESWL outcomes and promote a higher success rate of treatment for the maximum benefit for urolithiasis patients. This will ultimately mean that in more and more cases invasive surgery can be avoided.

The use of many medicinal herbs post-ESWL has resulted in improvements in outcomes of treatment. For example Andrographis paniculata tablets were shown to be beneficial in the treatment of post-ESWL urinary tract infection. In this study post-ESWL pyuria and hematuria in patients were significantly reduced after receiving Andrographis paniculata when compared to pre-ESWL values.[29]

Muangman et al. conducted a study on patients with Renal stones in Ramathibodi Hospital by having patients take an Orthosiphon aristatus infusion every day 3 times a day for 2-6 months. The results were promising. The size of 23 stones decreased, 40% of the stones fell off, and the symptoms improved by 20%. Premkamol et al. has studied the effect of Orthosiphon aristatus in reducing the size of kidney stones, and found that Orthosiphon aristatus can reduce the size of renal stones. Chronic symptoms including tightness of the stomach, waist pain, joint pain, fatigue, headache, lateral burning, and leg pain have all been alleviated in patients after treatment with Orthosiphon aristatus. From the results of the study, it was shown that Orthosiphon aristatus could contribute to the reduction of the size of kidney stones and that it was also good for patients with kidney stones who have suffered from physical torture and mental suffering, and also have insufficient money for medical expenses.[19]

Based on the current best evidence, this alpha-blocker may improve stone clearance and reduce auxiliary treatments and major adverse events after ESWL[29]

In our study, there was no statistically significant difference in overall stone free rate between the Orthosiphon aristatus group and the alpha-blocker group ($p = 0.827$), but the results did show that CIRF in the Orthosiphon aristatus group were closer to significance than in the control group ($p = 0.227$). It is reasonable to assume that if the period of follow up were longer, some CIRF may be passed and incidence of the stone free rate may increase over time.

The treatment success rate (stone free rate and CIRF) was not significantly higher in the Orthosiphon aristatus group than in the alpha-blockers group (69.0%: 54.8%, $p = 0.261$).

Conclusions

In this study treatment with Orthosiphon aristatus did not result in a significant difference in the improvement of the stone free rate or treatment success rate after ESWL in this study in comparison with the alpha-blocker.

Acknowledgement

The authors would like to thank Ratchaneekorn Jaikhamsuep, for assistance with the statistical analysis. We also wish to acknowledge the high level of cooperation within the team.

Conflict of Interest

The authors declare no conflict of interest.

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