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Randomized Controlled Trial

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Efficacy of cystone versus tamsulosin in treatment of stent-related lower urinary tract symptoms

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Abstract

Objective: Double-J stent is a common tool used in urological procedures that is inserted for 2–6 weeks, but it may induce abdominal and flank pain, incontinence and irritative urinary symptoms. Alleviation of such symptoms would be useful to improve the patients' quality of life. Accordingly, in this study, the efficacy of cystone versus tamsulosin in the treatment of double-J stent-related lower urinary tract symptoms was determined.

Materials and methods: In this randomised clinical trial, 128 patients who required double-J stent insertion after transureteral lithotripsy during 2018–2019 were enrolled. They were randomly assigned to receive either cystone, tamsulosin, both, or placebo. The international prostate symptom score and visual analogue score data were recorded at baseline, after 2 and 4 weeks across the groups.

Results: The international prostate symptom score and visual analogue score factors were statistically different across the case groups receiving cystone, tamsulosin and both drugs versus placebo (P=0.001). Two weeks after drug administration, the visual analogue score and international prostate symptom score were not statistically different in the tamsulosin, cystone and dual therapy groups; however, after 4 weeks the cystone group had the lowest symptoms.

Conclusion: Both tamsulosin and cystone are efficient drugs which would relieve stent-related lower urinary tract symptoms. The administration of cystone with or without tamsulosin for 4 weeks may have the best result in reducing the visual analogue score and international prostate symptom score.

Level of evidence: Level I, 1b, therapeutic study, randomised controlled trial

Keywords

Cystone, tamsulosin, double-J stent, IPSS (international prostate symptom score), VAS (visual analogue score)

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Introduction

Double-J is a useful stent for routine urological procedures which has been used for many years.[1] It is used to alleviate ureteral obstruction and should remain for 4–6 weeks. [2] It may induce some abdominal and flank pain, haematuria, lower urinary tract symptoms and urinary tract infections.[3] The main mechanisms related to stent symptoms is not yet clear but pain and lower urinary symptoms may be related to the double-J stent.[4] For symptom relief, different agents are administered.[5] Some drugs such as alfa-blockers (tamsulosin) and anti-cholinergics (solifenacin) are used for this matter.[5–7] Tamsulosin is a selective inhibitor of α1a/1d

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receptor, leading to fewer contractures. Hence, it may be conducive to less pressure at the bladder outlet.[6] Also, cystone is a herbal agent combined from didymocarpuspedicellata 65 mg, saxifragaligulata 49 mg, rubiacordifolia 16 mg, cyperusscariosus 16 mg, achyranthesaspera 16 mg, onosmabracteatum 16 mg, vernoniacinerea 16 mg, shilajeet (purified) 13 mg and hajrulyahoodbhasma 16 mg.[8] The efficacy of cystone is related to the removal of crystalurea and small stone passage besides the diuretic and anti-spasmodic effects.[7, 8] Determination of the best therapeutic method would require further studies.[9] Accordingly, in this study the efficacy of cystone versus tamsulosin in thhe treatment of stent-related lower urinary tract symptoms was determined.

Materials and methods

This double-blind, prospective, placebo controlled, clinical randomised trial was carried out on 132 patients requiring double-J stent after a transureteral lithotripsy (TUL) procedure during 2018–2019 in a tertiary urological centre. Inclusion criteria were the patients who underwent a unilateral TUL. All patients had an impacted 6–10 mm, middle or distal ureteral stone. However, patients with a bilateral ureteral stone, history of renal failure or urosepsis, anatomical or functional ureteral abnormality were excluded. The international prostate symptom score (IPSS) and visual analogue score (VAS) were fulfilled before stent insertion, after 2 weeks and after 4 weeks. IPSS included both voiding and storage symptom points with a total score of 0 to 35 points. The pain was also assessed by VAS ranging from 0 to 10 points by a single examiner. More VAS and IPSS indicate more severity in lower urinary tract symptoms.

After consulting with the methodologist, we allocated 160 applicants into four groups of 40 patients, using the random number table method (as simple randomisation) found in statistics books. However, 32 patients did not complete the study and the data of 128 patients were enrolled. These patients received tamsulosin (n=32), cystone (n=35), tamsulosin plus cystone (n=37) and placebo (n=24). Regarding concealment, the randomisation list was concealed from patients and all clinical investigators. An off-site person labelled the drug packages with coded numbers. The randomised controlled trial (RCT) study was approved by both the local ethical committee (registration ID: 1396.8923496021) and clinical trial registery (study ID: TCTR20200705001). The Declaration of Helsinki was respected, as well as an informed consent form was received.

The primary endpoint was to compare the study groups regarding the IPSS and VAS, 2 and 4 weeks after drug administration.

Statistical analysis

Mean ± standard deviation was used to describe quantitative variables; and categorical data were described using counts and percentages. An analysis of variance (ANOVA) repeated measure was used to compare quantitative variables and to study the trend. Statistical analysis was done using the Statistical Package for Social Sciences, version 21.0 (IBM SPSS Statistics Inc., Chicago, IL, USA).

Results

Finally, 128 patients including 84 men (65.5%) and 44 women (34.4%) completed the study. The patients had been randomely divided into four groups of tamsulosin (n=32), cystone (n=35), tamsulosin plus cystone (n=37) and placebo (n=24). Figure 1 shows the flowchart of study participants. The mean age was 45.2 ± 13.9 (ranging from 20 to 82) years. No significant side effects, such as gross haematuria and acute urinary infection and so on, were reported in this study.

The mean pain score of patients was evaluated based on the VAS at baseline, 2 and 4 weeks. The results showed that there was no significant difference in baseline pain score among the three groups before the stent was inserted (P=0.064); however, at 2 and 4 weeks, the mean pain score was significantly different among the three case groups and the placebo group (P<0.001). We depict the VAS results in Table 1 and Figure 2, as well as the IPSS results in Table 2 and Figure 3.

Table 1 shows the mean pain score of patients based on the VAS at baseline, 2 and 4 weeks. The results of *post hoc* LSD tests showed that the mean VAS in the placebo group at 2 and 4 weeks was significantly higher than the other groups (P<0.05). The mean pain score of the patients was evaluated at baseline, 2 and 4 weeks, in such a way that pain was significantly different during the three time points (P<0.001).

Figure 2 shows the trend, error bar, and mean pain at baseline, 2 and 4 weeks. The mean VAS score of patients at baseline, 2 and 4 weeks showed no significant difference in baseline among the three groups (P=0.989), but at 2 and 4 weeks the mean VAS score was significantly different among the three groups and the placebo group (P<0.001). *Post hoc* tests showed that the mean VAS score in the placebo group at 2 and 4 weeks was significantly higher than the other three groups (P<0.05). In addition, the mean VAS in the tamsulosin group was significantly higher than the cystone group at 4 weeks (P=0.017).

Table 2 shows that the mean IPSS trend of baseline patients at baseline, 2 weeks and 4 weeks was evaluated and the results showed that it was significantly changed during the three time points (P<0.001).

Figure 3 shows the trend, error bar and mean IPSS at baseline, 2 and 4 weeks. *Post hoc* tests showed that the mean IPSS in the placebo group was significantly higher than the other groups (P<0.05). Also, the mean IPSS in the tamsulosin group was significantly higher than the tamsulosin plus cystone group at 4 weeks (P=0.014).

Discussion

In this study, the efficacy of tamsulosin and cystone in an improvement of the urinary symptoms after double-J stent

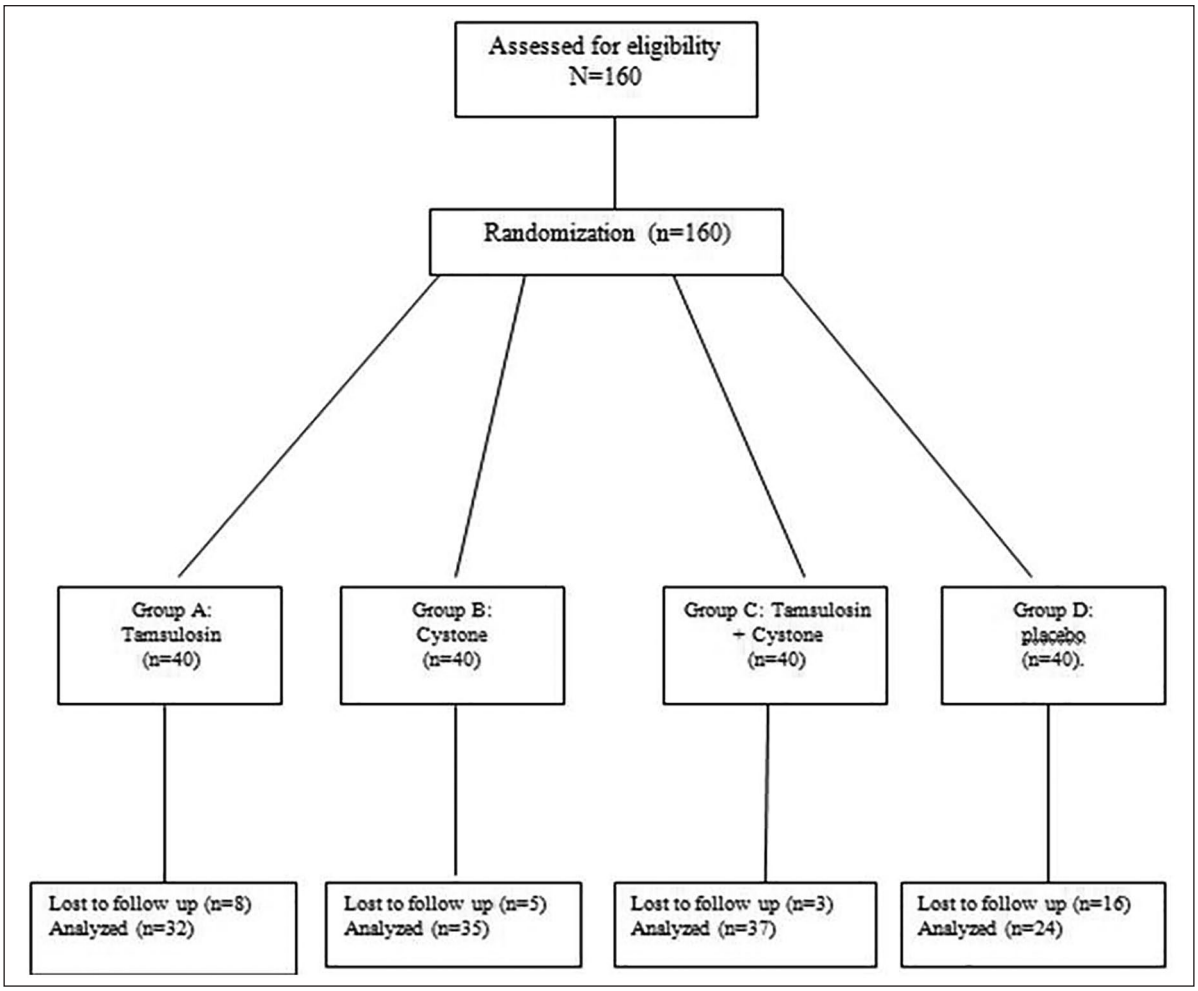

Figure 1. The flowchart of study participants.

Table 1. Comparison of the pain score of patients at baseline, 2 and 4 weeks.

Variable		*N*	Mean	SD	*P* value
Baseline	Tamsulosin	32	6.34	1.771	0.064
	Cystone	35	5.49	1.755	
	Tamsulosin & cystone	37	5.43	1.923	
	Placebo	24	6.25	1.359	
2 Weeks	Tamsulosin	32	8.81	1.378	<0.001
	Cystone	35	8.40	1.193	
	Tamsulosin & cystone	37	8.81	1.411	
	Placebo	24	9.83	0.381	
4 Weeks	Tamsulosin	32	7.44	1.134	<0.001
	Cystone	35	6.74	1.172	
	Tamsulosin & cystone	37	7.24	1.498	
	Placebo	24	9.75	0.442	

SD: standard deviation.

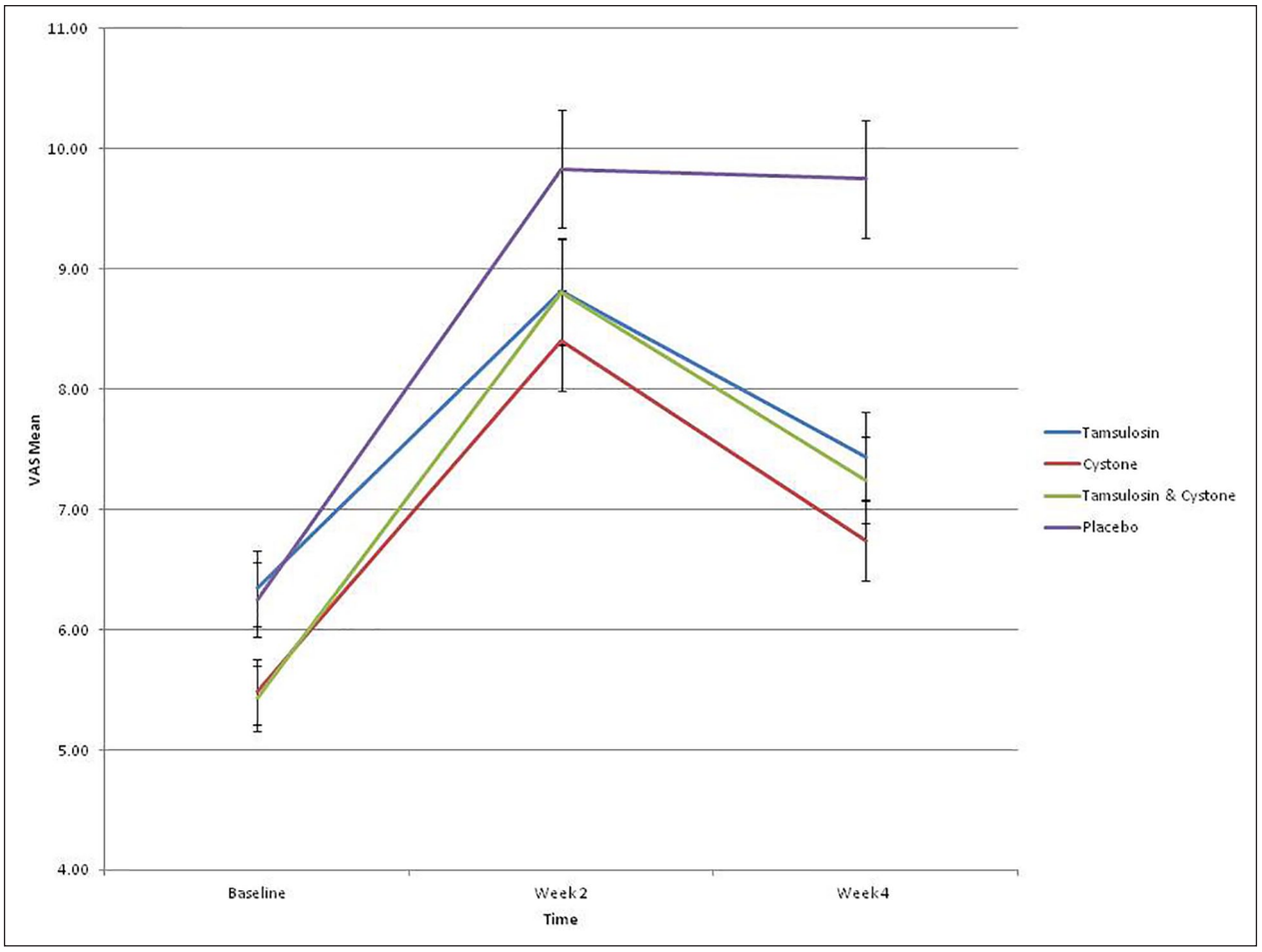

Figure 2. The trend, error bar, and mean pain at baseline, 2 and 4 weeks. VAS: visual analogue score.

Table 2. Comparison of the IPSS of patients at baseline, 2 and 4 weeks.

Variable		N	Mean	SD	*P* value
Baseline	Tamsulosin	32	9.78	2.406	0.989
	Cystone	35	9.51	2.954	
	Tamsulosin & cystone	37	9.62	4.146	
	Placebo	24	9.63	2.446	
2 Weeks	Tamsulosin	32	19.22	3.338	<0.001
	Cystone	35	18.26	4.559	
	Tamsulosin & cystone	37	18.54	4.388	
	Placebo	24	23.50	3.648	
4 Weeks	Tamsulosin	32	14.91	3.344	<0.001
	Cystone	35	14.06	3.472	
	Tamsulosin & cystone	37	12.76	3.578	
	Placebo	24	21.04	4.070	

IPSS, international prostate symptom score; SD: standard deviation.

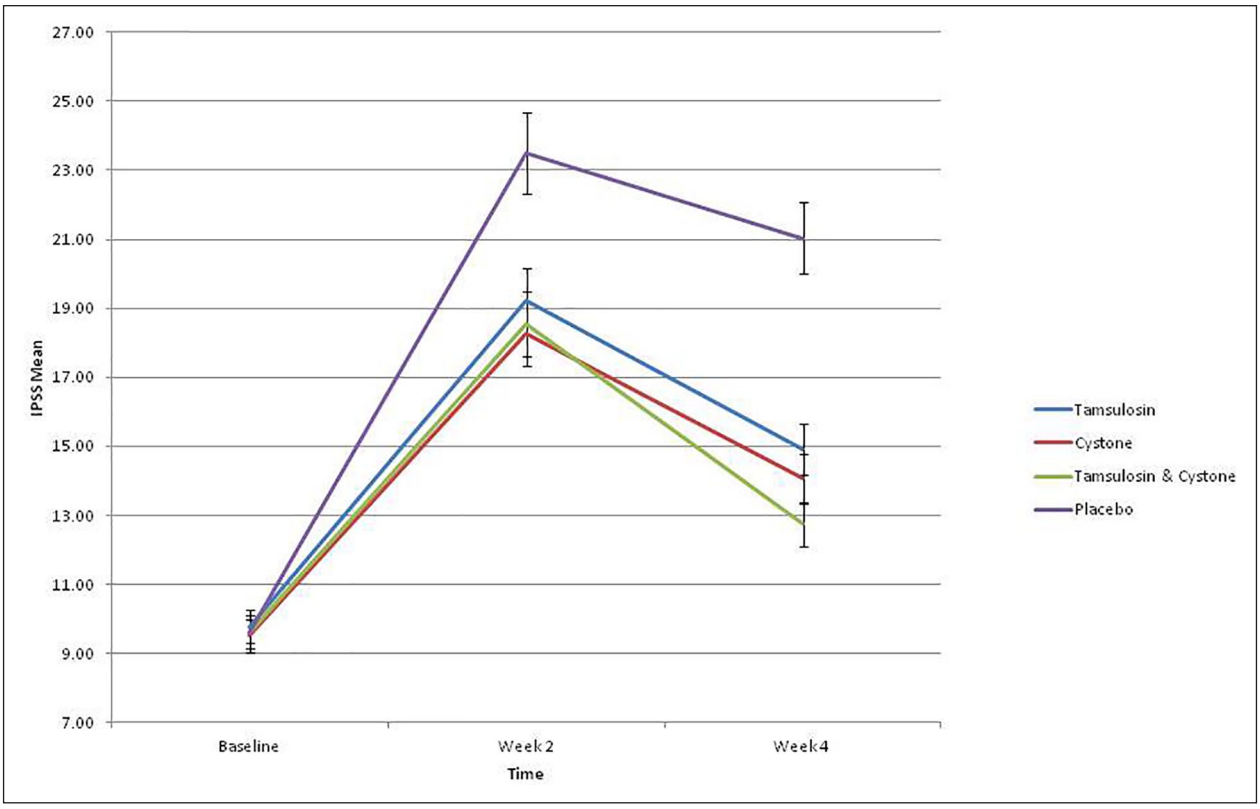

Figure 3. The trend, error bar, and mean international prostate symptom score (IPSS) at baseline, 2 and 4 weeks.

insertion was assessed among 128 patients. Two weeks after drug administration, the VAS and IPSS were similar in all case groups including tamsulosin, cystone and dual therapy; however, the cystone group had lower VAS scores after 4 weeks. The underlying mechanism may be that cystone is related to the removal of crystalurea, and small stone passage besides the diuretic and anti-spasmodic effects.[8]

The study by Shalaby et al.[9] in 338 patients with double-J stent insertion showed that the efficacy of tamsulosin, solifenacin and their combination was good for the relief of lower urinary tract symptoms. In addition, in their study, all groups had a significant difference with the control group.

Dellis et al.[10] assessed the efficacy of tamsulosin, solifenacin and their combination and similarly reported good efficacy in the control group and worse efficacy in the placebo group with a significant difference versus the other groups. Sengupta[8] reported good efficacy for cystone alone versus a combination of cystone and antibiotic (75% vs. 79.2%). This matter was due to some anti-microbial effects of cystone.

The study by Aggarwal et al.[11] compared tadalafil versus tamsulosin and found good similar efficacies for both groups. However the effects of tadalafil were better than tamsulosin to improve the sexual symptoms and body pain. Garg and Singh[12] reported good efficacy for cystone and 65.8% were improved in urinary symptoms after 5 days of treatment. Also, cystone alone was more effective than antiseptic alone in improving the symptoms, but their combination was more effective than each one alone. In our study the pain, quality of life and total IPSS were improved more in the intervention versus the placebo group.[12–16]

Our study is the first research in the literature, which determines the efficacy of cystone in double-J-induced lower urinary tract symptoms. Moreover, the results of this study demonstrated that despite the painful status of double-J stent insertion, the voiding and storage symptoms were improved by cystone or tamsulosin or their combination, leading to better improvement in the total IPSS and VAS. Also, the administration of each one of these drugs led to decreased pain and increased quality of life in patients. It was found that in all patients, the urinary symptoms and pain were intensified after 2 weeks but they were decreased after 4 weeks in the drug versus placebo groups.

The small sample size and difficulty in follow-up of the patients were the major limitations of our study. Further studies on the other clinical symptoms and side effects with a larger sample size are required to attain more definite comparative results.

Conclusions

Both tamsulosin and cystone are efficient drugs which would relieve stent-related lower urinary tract symptoms. The administration of cystone with or without tamsulosin for 4 weeks may have the best results in reducing the VAS and IPSS.

Conflicting interests

The author(s) declare that there is no conflict of interest to declare.

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Ethical approval

The RCT study was approved by both the local ethical committee (registration ID: 1396.8923496021) and the Declaration of Helsinki was respected.

Informed consent

An informed consent form was received from all patients included in the study.

Guarantor

MAG, RR.

Contributorship

RR, AS and RM researched the literature and conceived the study.
MAG and RR wrote the first draft of the manuscript.
AS and RM were involved in the data analysis.
All authors reviewed and edited the manuscript and approved the final version of the manuscript.

Trial registration

Clinical Trial Registry (study ID: TCTR20200705001)

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