Biological and Clinical Sciences Research Journal
eISSN: 2708-2261; pISSN: 2958-4728
www.bcsrj.com
DOI: https://doi.org/10.54112/bcsrj.v2023i1.193
*Biol. Clin. Sci. Res. J., Volume, **2023**: 193*
Original Research Article

COMPARATIVE ANALYSIS OF TAMSULOSIN AND TADALAFIL AS MEDICAL EXPULSIVE THERAPY FOR URETERAL STONES

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(Received, 7th September 2022, Revised 25th January 2023, Published 28th January 2023)

Abstract: *This study was designed to compare the efficacy of placebo, tamsulosin and tadalafil as expulsive medical therapy for removing distal ureteral stones. The prospective study was conducted in Multan, DI Khan & Lahore, from November 2021 to November 2022. The study included 129 subjects with distal ureteral stones sized ≤10mm. Subjects were randomly categorized into 3 groups, A, B and C, with 43 subjects each. Group A was administered tamsulosin 0.4 mg O.D., Group B was administered tadalafil 10 mg O.D. Subjects underwent therapy for 4 weeks. Duration and rate of stone expulsion, time and dose of NSAIDs, adverse effects and analgesic use of medication were recorded. The frequency of expulsion in groups A, B and C was 72.09%, 62.7% and 56.0%, respectively; this difference was statistically insignificant (p=.294). The mean expulsion time in groups A, B, and C was 17.65±1.2 days, 21.23±1.15 days and 22.35±1.16 days, respectively (p=.46). Frequency of endoscopic intervention after unsuccessful MET in groups A, B and C was 14 (32.5%), 18 (41.8%) and 20 (46.5%) respectively, the difference in frequency of endoscopic treatment among all groups was not significant (P=.294). Tamsulosin is a more effective MET for distal ureteral stones than tadalafil.*

Keywords: Medical expulsive therapy, Tadalafil, Tamsulosin, Distal ureteral stones

Introduction

Nephrolithiasis is a common urological disease; its prevalence in men is about 12%, and in women, about 6%. It is most prevalent in individuals aged between 20 to 40 years(Liu et al., 2020). Ureteral stones account for 22% of nephrolithiasis, and 68% of ureteral stones are located distally (Kızılay et al., 2019). Stones are clinically present in the form of urinary symptoms and colic pain. Management of ureteric stones depends upon technical, anatomic, clinical and stone factors. Sometimes more than one procedure is done to reduce side effects and achieve a high stone-free rate(Schlomer, 2020; Tzelves et al., 2021). Currently, ureteral stones are treated using pharmaceutical or surgical interventions. Studies report that for proximal ureteral stones larger than 10 mm, different surgical procedures like percutaneous nephrolithotomy (PCNL), laparoscopic ureterolithotomy (LU), ureteroscopic lithotripsy (URSL) and extracorporeal shock wave lithotripsy (ESWL)(Lim et al., 2022; Wang et al., 2020).

European and American guidelines suggest that Medical expulsive therapy (MET) is an effective method for increasing stone passage. MET includes prostaglandin inhibitors, calcium channel blockers, alpha adrenoreceptor antagonists and Phosphodiesterase type 5 inhibitors (PDE5-Is)(Pricop et al., 2020). Alpha-blockers, preferably tamsulosin, are the most commonly used MET drugs. Tamsulosin increases stone passage and reduces expulsion time by selective ureteral muscle relaxation. Different studies reported that tamsulosin effectively increases stone passage. Although some studies(De Coninck et al., 2019; Hsu et al., 2018) show positive evidence for tamsulosin's effectiveness, another study(Kava et al., 2019) has not confirmed its positive effects.

It has been found recently that tadalafil (a PDE5-Is) is effective for managing lower urinary tract symptoms (LUTS). It causes relaxation of prostate smooth muscles, thus improving LUTS. Recent studies have shown PDE5-Is, along with tamsulosin, lead to the increased stone passage and reduced stone expulsion time(Marconi et al., 2019). Currently, limited comparative studies have been done to

[Citation: Seerwan, M., Ahmad, I., Adnan, M., Shafi, H., Saifullah., Hussain, M. (2023). Comparative analysis of tamsulosin and tadalafil as medical expulsive therapy for ureteral stone. *Biol. Clin. Sci. Res. J.*, **2023***: 193*. doi: https://doi.org/10.54112/bcsrj.v2023i1.193]

analyze effective of tamsulosin and tadalafil for the treatment of ureteral stones. Thus, this study aims to compare the efficacy of placebo, tamsulosin and tadalafil as expulsive medical therapy for removing distal ureteral stones.

Methodology

The prospective study was conducted in Multan, DI Khan & Lahore, from November 2021 to November 2022. The study included patients aged 18 to 65 years who had a single distal ureteral stone < 10 mm and renal colic. Distal ureteral stones and colic were diagnosed using ultrasound or CT scan. Patients who were candidates for surgical intervention, had resistant renal colic pain, multiple ureteric stones, single kidney, GFR ≤30, history of gastric ulcer, diabetes, ureteral surgery and usage of nitrates, calcium channel blocker and alpha-blocker drugs were excluded. The study included 129 subjects with distal ureteral stones sized ≤10mm. The informed consent of patients was recorded. The ethical board of the hospital approved the study.

The medical history of the subjects was recorded. All subjects' serum creatinine and blood urea nitrogen (BUN) were measured. A total of 129 topics were randomly categorized into 3 groups, A, B and C, with 43 subjects each. Group A was administered tamsulosin 0.4 mg O.D., Group B was administered tadalafil 10 mg O.D., and Group C received placebo treatment O.D. Drugs were continued for up to 4 weeks. Subjects were advised to report any complications and pass urine in a filter. They were instructed to note the time of stone expulsion and report it. Duration and rate of stone expulsion, duration and dose of NSAIDs, adverse effects and use of analgesic medication were recorded. Stone expulsion was confirmed through a CT scan after 4 weeks. If stones persisted, the endoscopic intervention was done.

Data were analyzed using SPSS version 23. The chi-square test was used to compare the frequency of variables. T-test was used for diagnosing variance. The therapeutic impact of interventional variables was determined using the regression model. P-value< 0.05 was considered statistically significant.

Results

The demographic data of the subjects are summarized in Table I. The age in group A was 36±11.45 years, in group B 36.24±11 years, and group C 36.7±11.33 years. The difference between sex, age, BMI and stone size among the three groups was not statistically significant (Table I). 94 (72%) subjects underwent CT scans to diagnose ureteral stones.

Table I Demographic data of study sample

Variables	Group A (n=43)	Group B (n=43)	Group C (n=43)	P value
Female/male	20/23	21/22	20/23	0.97
Age (years)	36±11.45	36.24±11	36.7±11.33	0.98
BMI (kg/m^2)	26.88±1.75	26.41±1.82	26.12±1.84	0.286
Stone size (mm)	6.94±1.56	6.85±1.64	6.89±1.47	0.978

The frequency of expulsion of stones in groups A, B and C was 72.09%, 62.7% and 56.0%, respectively; this difference was statistically insignificant (p=.294). The mean time of expulsion in groups A, B, and C was 17.65±1.2 days, 21.23±1.15 days and 22.35±1.16 days, respectively (p=.46). Mean dose of NSAIDs in groups A, B and C was 819.19±619.04mg, 1057.01±502.2mg and 1094±502.2mg respectively. The tamsulosin group had significantly lower usage than other groups (p=.038); however, the difference between groups B and C was insignificant (Table II).

8(18.6%) patients in the tadalafil group complained of headache; it was significantly higher in tamsulosin group 3 (6.9%) and placebo group 0 (0%) (p=.011). In group A, 2(4.6%) subjects had retrograde ejaculation, and 3 (6.9%) had orthostatic hypotension; none of these complications occurred in group B (P=.106). A total of 6 subjects had backache, of which 2(4.6%) were in group A and 4(9.3%)in group B (p=.126). A total of 8 subjects reported dizziness, of which 5 were in group A and 3 in group B (P=.069). Frequency of endoscopic intervention after unsuccessful MET in groups A, B and C was 14 (32.5%), 18 (41.8%) and 20 (46.5%), respectively; the difference in frequency of endoscopic treatment among all groups was not significant (P=.294).

Table II Clinical outcomes

Outcome	Group A (n=43)	Group B (n=43)	Group C (n=43)	P value
Frequency of stone expulsion (n (%))	31(72.09%)	27(62.7%)	24(56.0%)	0.294
Time of stone expulsion (days)	17.65±1.2	21.23±1.15	22.35±1.16	0.46
Dose of NSAID required (mg)	819.19±619.04	1057.01±502.2	1094±502.2	0.038

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Duration of analgesic requirement (days)	9.6±5.09	14.5±7.7	12.4±21.27	0.004
Side effects (n(%))	13(30.2%)	13 (30.2%)	1(2.3%)	0.002

Discussion

Distal ureteral stones are quite symptomatic. MET is the highly recommended procedure for stone expulsion. In this study, the frequency of stone expulsion in groups A, B and C was 72.09%, 62.7% and 56.0%, respectively. However, some studies show that tadalafil more effectively facilitates stone expulsion than tamsulosin (Gnyawali et al., 2020; Ouyang et al., 2020). Another study showed that compared to a placebo, tadalafil significantly improves stone expulsion(Parikh et al., 2019).

Regarding stone expulsion time, the mean time of expulsion in tamsulosin, tadalafil and placebo were 17.65±1.2 days, 21.23±1.15 days and 22.35±1.16 days, respectively. A previous study showed that stone expulsion time in tadalafil is significantly higher than in tamsulosin(Parikh et al., 2019).

In this study, the tamsulosin group had a lower analgesic requirement than the tadalafil group.

Interestingly, this finding contrasts with previous studies(Gnyawali et al., 2020; Kızılay et al., 2019), which showed that tadalafil reduces analgesic requirements. However, a recent study showed that the tadalafil group had a significantly higher analgesia requirement than the tamsulosin group(Li et al., 2019). In the current study, side effects were well tolerated, transient and mild to moderate in all groups. It may be because of the young study population. The placebo group had a lower rate of side effects than the tadalafil and tamsulosin groups, which had an equal incidence of adverse effects. Another study shows that the tadalafil group has more negative effects like orthostatic hypotension, backache, dizziness, and headache than tamsulosin(Sun et al., 2018) as headaches may result in different types of pain, which limits the prescription of tadalafil. However, due to its effectiveness in stone expulsion, it has been increasingly used. A study showed that though tadalafil cannot completely replace tamsulosin, combining both yields very beneficial results(Sebastianelli et al., 2020). Our study has some limitations. It was a single-centred study; therefore, further broader research is required to validate the results.

Conclusion

Though tamsulosin and tadalafil are well tolerated, effective and safe, tamsulosin has higher efficacy than tadalafil as MET.

Conflict of interest

The authors declared no conflict of interest.

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