



EVALUATION OF EFFICACY OF SILODOSIN VERSUS SILODOSIN WITH DEFLAZACORT IN EXPULSION OF LOWER URETERIC CALCULI

General surgery

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ABSTRACT

Objectives: To compare the efficacy of silodosin versus silodosin with deflazacort in expulsion of lower end ureteric calculi, in terms of episodes of pain,stone expulsion rate,stone expulsion time ,analgesic requirements and side effects

Introduction: Ureteric calculi represent 20% of urinary stones. Ureterscopy and Shock wave lithotripsy proven the method of treatments for lower ureteric stones; however, they are expensive and not risk free. A conservative approach is becoming more popular as a result of advances in pharmacological therapy which reduces the symptoms and helps in stone expulsion. We performed a randomized controlled prospective study to evaluate the efficacy of Deflazacort in combination with alpha blocker silodosin in medical management of symptomatic lower Ureteric stones of ≤ 8 mm size.

Material and methods: A prospective randomised controlled study was conducted on 60 patients, age ≥ 18 , who had unilateral lower ureteric stone of ≤ 8 mm. Patients were divided into three groups. Group 1 received silodosin 8 mg for 14 days,Group 2 received silodosin 8 mg plus deflazacort 30mg daily for 14 days and Group 3 (control) received diclofenac potassium (75 mg) when required. The patients were followed-up by ultrasonography ,plain radiograph KUB and computed tomography (in some cases).

Results: There was a higher stone expulsion rate of 95% in Group 2 as compared to Group 1(85%) and Group 3(35%) . Group 2 showed a significant advantage for stone expulsion time ,decreased pain episodes and analgesic use. Two patients, one in group 1 and group 2, reported retrograde ejaculation.

Conclusion: The results showed that silodosin with deflazacort , increases the stone expulsion rate, decrease the stone expulsion time, decreases the mean number of pain episodes and decreases the mean analgesic dosage requirement. But larger study is required to establish its efficacy for expulsion rate which will be statistically significant.

KEYWORDS

INTRODUCTION

Ureteric calculi represent 20% of urinary stones at the time of diagnosis, of which 70% of the stones are found in the distal third of the ureter [1]. Haematuria, pain and urinary tract infection are typical presentations in patients[2]. The treatment strategy depends on different factors including: stone location, size, and the anatomy of the urinary tract [3].

A conservative approach involving close monitoring can be used in most cases, and is becoming more popular as a result of advances in pharmacological therapy, which can reduce symptoms and facilitate stone expulsion [4]. For example, medical expulsive therapy (MET) using α -adrenoceptor antagonists has emerged as an alternative strategy for the initial management of small distal ureteral stones [5]. Silodosin is a novel highly selective $\alpha 1A$ -adrenoceptor ($\alpha 1A$ -AR) blocker: in vitro its $\alpha 1A$ -to-1B binding ratio is extremely high (162:1), suggesting that it has the potential to reduce dynamic neurally mediated smooth muscle relaxation in the ureter, while minimizing undesirable effects on blood pressure regulation[6]. Corticosteroid prevents the edematous reaction caused by the stone[7]. For this reason we performed a randomized controlled prospective study to evaluate the role of Deflazacort in combination with alpha blocker silodosin in medical management of symptomatic lower Ureteric stones of ≤ 8 mm size.

MATERIAL METHOD

A prospective randomized controlled study was carried out on all patients with lower ureteric calculus attending General Surgery OPD

and Emergency Department, SGT Medical college from Dec 2018 to May 2020. All patients with age of >18 yrs with a diagnosis of a symptomatic, solitary lower ureteric calculus, proved either on a plain Skiagram (X-ray) or Ultrasonography (USG) of the Kidney-Ureter-Bladder (KUB) or Non-Contrast Computed Tomography (NCCT) KUB with size less than or equal to 8mm were included in this study. Cases having active urinary tract infection, fever, acute renal failure, chronic renal failure, history of prior urinary surgery or endoscopic treatment, history of previous ureteric calculus and solitary functioning kidney were excluded from the study. A total of 60 symptomatic patients were randomized into three groups – group I, group II, group III, according to the computer generated randomization number sequence for three arm study with 20 patients in each group.

Group I patients were given tablet silodosin 8 mg for 14 days at night after dinner, group II patients were given tablet silodosin 8 mg and tablet deflazacort 30mg for 14 days at night after dinner and group III (control group) not receiving any medication other than analgesic whenever required (tablet diclofenac potassium 75 mg).

Patients were advised to take tablet diclofenac potassium 75mg whenever there was pain. In case pain was not controlled by oral analgesics, patients were given injection diclofenac potassium. Patients were reassessed after 2 weeks and 4 weeks. A skiagram & ultrasonography of kidney, ureter & bladder region were repeated to confirm whether stone had passed or not? The success rate of these three groups were compared & analyzed. Side effects like postural

hypotension, retrograde ejaculation, gastric upset and others were noted. Statistical analysis was done for expulsion rate of stone, days taken for expelling the stone, number of pain episodes during the treatment period and amount of analgesics required during the treatment period. Data were checked, entered and analysed using SPSS version 21.0 Data were presented as the mean for quantitative variables, and number and percentage for categorical variables; the chi-squared, Fisher's exact test, ANOVA test or t-test were used when appropriate. For statistical significance, p value of less than 0.05 was considered as significant.

RESULT:

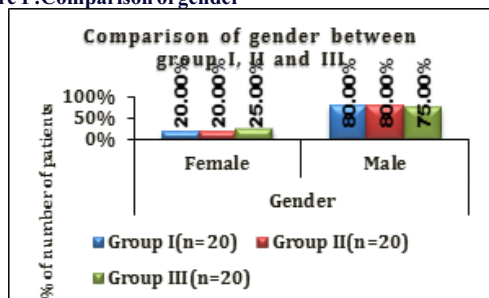
Majority of patients were in age group 31-40 years, in all groups. No significant difference was seen in the distribution of gender between group I, II and III. (p value>.05). Table

Table 1:-Comparison of age(years) between group I, II and III.

Age (years)	Group I (n=20)	Group II (n=20)	Group III (n=20)	Total	P value
<=20	1 (5%)	1 (5%)	4 (20%)	6 (10%)	0.767
21-30	5 (25%)	5 (25%)	5 (25%)	15 (25%)	I vs II:0.826
31-40	11 (55%)	8 (40%)	7 (35%)	26 (43.33%)	I vs III:0.607
41-50	2 (10%)	3 (15%)	3 (15%)	8 (13.33%)	II vs III:0.638
>50	1 (5%)	3 (15%)	1 (5%)	5 (8.33%)	
Mean ± SD	35.9 ± 10.94	35.45 ± 11.29	32.65 ± 10.61	34.67 ± 10.86	0.599
Median (IQR)	38.5 (27.25-40)	34.5 (25.75-45)	33 (22.75-37.25)	34.5 (25-40)	I vs III:0.346
Range	20-65	20-56	19-55	19-65	II vs III:0.424

Gender Distribution : Out of 60 patients males were 47 (78.3%) and females were 13(21.7%). No significant difference was seen in the distribution of gender between group I, II and III. (p value>.05)

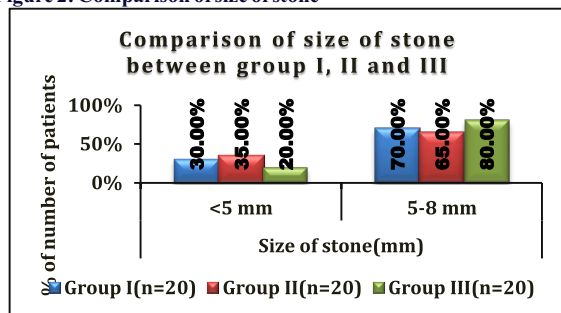
Figure 1: Comparison of gender



Size of Stone

Size of stone(mm) was 5-8 mm in majority of patients in all groups. Mean ± SD of size of stone(mm) in group I was 6 ± 1.44, group II was 5.92 ± 1.47 and group III was 5.76 ± 1.27 with no significant difference between them.

Figure 2: Comparison of size of stone



Pain episodes during treatment

In group II patients pain episodes score were zero and 1 in 30% and 25% patients respectively. In group I patients pain episodes score were zero and 1 in 0% and 10% patients respectively. In group II patient pain episodes scores were 2 and 3 in 20% and 25% in respectively. In group III patients pain episode score were >3 in 5% patients. Thus pain episode scores were highest in group III, least in group II patients with a significant (p value<.05).

Table 2:-Comparison of pain episode

Pain episode	Group I (n=20)	Group II (n=20)	Group III (n=20)	Total	P value
Zero	0 (0%)	6 (30%)	0 (0%)	6 (10%)	<.0001
1	2 (10%)	5 (25%)	1 (5%)	8 (13.33%)	I vs II:0.013
2	4 (20%)	3 (15%)	0 (0%)	7 (11.67%)	I vs III:0.029
3	5 (25%)	4 (20%)	2 (10%)	11 (18.33%)	II vs III:<.0001
>3	9 (45%)	2 (10%)	17 (85%)	28 (46.67%)	
Total	20 (100%)	20 (100%)	20 (100%)	60 (100%)	

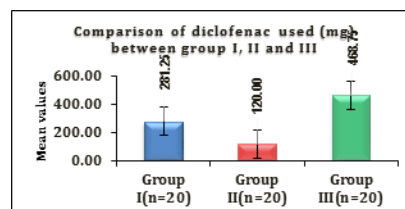
Amount of analgesia used :

Significant difference was seen in diclofenac used (mg) among groups I, II and III. Mean dose of diclofenac used in group III was (468.75) which was significantly higher as compared to group II (120) and group I (281.25). This is statistically significantly with p value<.05. Table 3

Table 3:-Comparison of diclofenac used (mg)

Diclofenac used (mg)	Group I (n=20)	Group II (n=20)	Group III (n=20)
Mean	281.25	120	468.75
Range	75-525	0-375	75-675

Figure 3:-Comparison of diclofenac used (mg) between group I, II and III.



Side effects

No significant difference was seen in the distribution of drug side effect between group I, II and III. (p value>.05) Drug side effect was nil in majority of patients in group I(95%), II(95%) and III(100%). Retrograde ejaculation was found 5% in group I and group II. Dizziness, postural hypotension and headache was not present in any of the patient.

Table 4:-Comparison of drug side effect.

Drug side effect	Group I (n=20)	Group II (n=20)	Group III (n=20)	Total	P value
Nil	19 (95%)	19 (95%)	20 (100%)	58 (96.67%)	1
Retrograde ejaculation	1 (5%)	1 (5%)	0 (0%)	2 (3.33%)	I vs II:1
Dizziness	0 (0%)	0 (0%)	0 (0%)	0 (0%)	I vs III:1
Postural hypotension	0 (0%)	0 (0%)	0 (0%)	0 (0%)	II vs III:1
Headache	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
Total	20 (100%)	20 (100%)	20 (100%)	60 (100%)	

Stone expulsion time

Significant difference was seen in the distribution of stone expulsion time among group I, II and III. (p value<.05) Proportion of patients who passed stones in 2 weeks was 95% of patients in group II which was significantly higher as compared to 55% of patients in group I and 20% of patients in group III. Proportion of patients who passed stones in 4 weeks was 25% of patients in group I which was significantly higher as compared to 0% of patients in group II and 15% of patients in group III. Proportion of patients who did not pass stones was 65% of patients in group III which was significantly higher as compared to 20% of patients in group I and 5% of patients in group II.

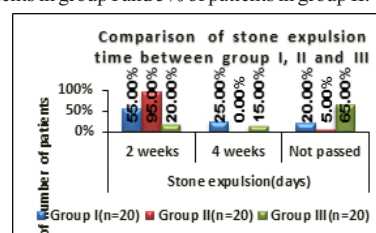


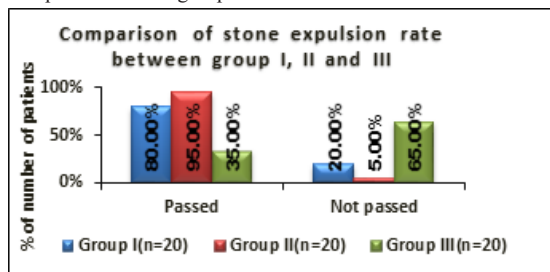
Figure 4: Comparison of stone expulsion time

Table 5:-Comparison of stone expulsion time between group I, II and III.

Stone expulsion (days)	Group I (n=20)	Group II (n=20)	Group III (n=20)	Total
2 weeks	11 (55%)	19 (95%)	4 (20%)	34 (56.67%)
4 weeks	5 (25%)	0 (0%)	3 (15%)	8 (13.33%)
Not passed	4 (20%)	1 (5%)	13 (65%)	18 (30%)
Total	20 (100%)	20 (100%)	20 (100%)	60 (100%)

Stone expulsion rate

Significant difference was seen in of stone expulsion rate between group I, II as compared to group III. (p value<.05) Stone expulsion rate was 80% in group I and 95% in group II which was significantly higher as compared to 35% in group I.

**Figure 5: Comparison of stone expulsion rate****Table 6:-Comparison of stone expulsion rate between group I, II and III.**

Stone expulsion	Group I (n=20)	Group II (n=20)	Group III (n=20)	Total
Passed	16 (80%)	19 (95%)	7 (35%)	42 (70%)
Not passed	4 (20%)	1 (5%)	13 (65%)	18 (30%)
Total	20 (100%)	20 (100%)	20 (100%)	60 (100%)

DISCUSSION

Ureteroscopy and Shock wave lithotripsy remain the most effective treatments for lower ureteric stones; however, they are expensive and not risk free. Spontaneous stone expulsion can occur in upto 50% of cases, nevertheless, many complications such as ureteric colic, UTI, and hydronephrosis, may occur. Recently, the use of various adjuvant medications as Medical expulsive therapy for lower ureteric stone has helped to reduce pain, complications, and increase the rate of stone clearance [4,18]. The alpha 1A- and alpha 1D-adrenoceptors are the most abundant subtypes in the distal ureter, stimulation of these alpha1-adrenoceptors leads to increases in both the frequency of ureteric peristalsis and the force of ureteric contractions. [9] However, blockade of these receptors decreases basal ureteric tone, decreases peristaltic frequency and amplitude, leading to a decrease in intraluminal pressure while the rate of urine transport increases, and thus increasing the chance of stone passage [9]. Highly selective alpha 1A-adrenoceptor blockers have been developed to minimise the cardiovascular adverse effects while maintaining their efficacy on the urinary tract [10]. Tamsulosin is a selective alpha1-blocker with a 10-fold greater affinity for the alpha1A- and alpha1D-adrenoceptor subtypes than for the alpha1B-adrenoceptor subtype, while the affinity of silodosin for the alpha1A-adrenoceptor subtype is 162- and 50-fold greater than its affinity for the alpha1B- and alpha 1D-adrenoceptor subtypes respectively, which explain the weak cardiovascular adverse effects of silodosin [10].

Steroids have also been used to aid stone passage. The rationale for this treatment is that it reduces stone induced edema and hence allows a calculus to pass. Recent studies have shown that corticosteroid drugs in association with tamsulosin seemed to induce more rapid expulsion.[11] Deflazacort is an anti-edema agent, which is a corticosteroid drug showing good efficacy and few side effects[12]. Dellabella and associates conducted similar study in 2004 and observed 96.7% expulsion rate when mean stone size was 6.9mm[11]. In 2004-05 , Porpiglia et al evaluated the efficacy of tamsulosin plus deflazacort and reported expulsion rate of 84.8% [13].

In a study conducted by dell Atti ,Tamsulosin 0.4 mg was given to group 1 patients and silodosin 8 mg to group 2 patients for a period of 3 weeks . The stone expulsion rate of 61.2% and 80.3% respectively showing that there was a significantly higher expulsion rates with silodosin[14]. After analyzing the above studies, it is clear that,

although tamsulosin and silodosin (alpha 1- A antagonist) is very effective in the expulsion of lower ureteral stones but expulsion rate improved significant when it is used in combination with deflazacort.

In the present study stone expulsion rate was higher in group II (95%) and 80% in group I and lowest in group III (35%). Thus we see that stone expulsion rate was significantly higher in group II as compared to group I & group III but statistically p value has been found to be (0.341) which is not significant ,probably a larger study is required to establish the statistically significant correlation. In a study conducted by Dellabella [11] and associates the mean time for stone expulsion was less in patients using combination of tamsulosin and deflazacort than patients using tamsulosin, statistically significant in terms of expulsion time. (p -0.036) In the present study Significant difference was seen in the distribution of stone expulsion(days) between group I, II and III. (p value<.05) Proportion of patients who passed stones in 2 weeks was 95% of patients in group II which was significantly higher as compared to 55% of patients in group I (p <.0001) and 20% of patients in group III (p <.0001).

Gupta et al in their study observed retrograde ejaculation in 2 patients of Silodosin group was significant[15]. Dell'Atti showed significant number of patients with retrograde ejaculation i.e. 4 (10.2%) in group A (n =39) and 10(22.7%) in group B (n=44)[14]. Retrograde ejaculation was seen in those patients who were given silodosin. No significant difference was seen in the distribution of drug side effect between group I, II and III. (p value>.05). Dellabella and associates conducted a study to compare the efficacy of tamsulosin alone with deflazacort for expulsion of lower ureteral stone. They showed that number of pain episodes were less in group using tamsulosin plus deflazacort as compared to group using tamsulosin alone[11].In the present study, pain episodes were less in group II . Significant difference was seen in the distribution of pain episodes between group I, II and III. (p value<.05). In the present study, significant difference was seen in diclofenac used (mg) between group I, II and III. (p value <.05). Mean $\pm$ SD of diclofenac used (mg) in group II was 120 ± 112.57 which was significantly lower as compared to group I (281.25 ± 139.52) and group III (468.75 ± 155.57).

CONCLUSION

The showed that silodosin with deflazacort decrease the stone expulsion time, decreases the mean number of pain episodes and decreases the mean analgesic dosage requirement. But larger study is required to establish its efficacy for expulsion rate ,which will be statistically significant.

Conflict of interest : No

Funding source :No

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