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Role of Short Term Tamsulosin in Medical Management of Lower Ureteric Calculi in Today's Modern Era of Increasing Demand of Various Advancing Endo-Urological Procedures

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7 Abstract

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Introduction: The choice of ideal method like MET or URS to treat lower ureteric calculi 8 depends on the type of equipment available, type and size of stone, needs of the patient and 9 skills of the surgeon. The smooth muscle relaxant drug tamsulosin (an ?-adrenoceptor 10 antagonist) is a possible agent, its use being termed medical expulsive therapy (MET). The 11 disease spectrum in a developing country like ours is different from that of developed 12 countries, mainly because of delay in diagnosis, delay in investigations and lack of awareness 13 that tend to modify outcome in case of ureteral stones or for that matter any disease. More 14 so, advanced interventional facilities in this part of the world are not easily available. 15 Methodology: A prospective study was thus planned to compare the tamsulosin group with a 16 control group in our setup to evaluate the efficacy of tamsulosin for lower ureteric calculi 17 expulsion within a few days without the need for hospitalisation, common endoscopic 18

¹⁹ treatment or shock wave lithotripsy.

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21 22 Index terms— Role of Short Term Tamsulosin in Medical Management of Lower Ureteric Calculi in Today's Modern Era of Increasing Demand of Various Advancing Endo-Urological Procedures Introduction use being termed 23 medical expulsive therapy (MET) [4]. Meta-analyses of data from randomised controlled trials (RCTs) report a 24 statistically significant benefit fortamsulosin over controls for the outcome of spontaneous stone passage [5,6]. 25 Where a failed expectant treatment may well be complicated with hydro-nephrosis, deranged renal function 26 or urosepsis. Interventional techniques are not always free of complications and failures. Most of the work of the 27 efficacy of tamsulosin in lower ureteric calculi expulsion has been done in western affluent countries with variable 28 results. The disease spectrum in a developing country like ours is different from that of developed countries, 29 mainly because of delay in diagnosis, delay in investigations and lack of awareness that tend to modify outcome 30 in case of ureteral stones or for that matter any disease. More so, advanced interventional facilities in this part 31 of the world are not easily available. A prospective study was thus planned to compare the tamsulosin group 32 with a control group in our setup to evaluate the efficacy of tamsulosin for lower ureteric calculi expulsion within 33

a few days without the need for hospitalisation, common endoscopic treatment or shock wave lithotripsy.

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³⁶ 2 Methodology

After taking clearance/permission from the ethical committee of our hospital we did a Prospective randomised control study from feb 2014 to feb 2017 including 600 subjects in age group of 20-50 years with unilateral ureteric calculi of size 4mm-10mm. Patients having acute renal failure, chronic renal failure, urinary tract infection, fever & who have recently undergone surgery for ureteric calculi were not included in the study. The study group was given cap Tamsulosin 0.4mg& tablet Dytor 10mg once daily for a maximum of 2 weeks or till the stone was passed (whichever was earlier). Analgesic (table tdiclofenac 100mg) was given as needed. The control group was 43 given analgesic and diuretic tablets only for same period. During the study time a ultra sonography (KUB)was

done on day 0 of starting tamsulosin treatment followed by on day 7, day 14 and day 17. Results were compared between the Author: e-mail: aditya.yelikar@gmail.com he choice of ideal method like MET or URS to treat lower

46 ureteric calculi depends on the type of equipment available, type and size of stone, needs of the patient and skills

47 of the surgeon [1]. The stone burden remains the primary factor in deciding the appropriate treatment for a

⁴⁸ patient with ureteric calculi [2].

Expectantly managed patients who develop recurrent pain, sepsis, or compromised renal function need drainage if necessary followed by stone clearance using endoscopy or extracorporeal shock wave lithotripsy [3].

51 The smooth muscle relaxant drug tamsulosin (an ?-adrenoceptor antagonist) is a possible agent, its T

⁵² 3 III. Results & Observations

53 4 Consort Flow Diagram

All patients in our study were between the age group of 20-50 years. In our study the incidence of ureteric calculi was found to be more in males (81.44%) as compared to females (18.54%). We found incidentally that more stones were on the right side (51.61%) as compared to the left side (48.38%). No patient in group 1 had pain score in the range of 8-10 whereas 3.22% of patients in group 2 had a pain score in the range of 8-10. 83.87% of stones in group 1 & 62.90% stones in group 2 passed out successfully. 17.74% of patients in group 1 & 37.09% of patients in group 2 needed surgical intervention. However the need for surgical intervention for stone size up to 6mm was same in both the groups.

⁶¹ 5 IV . Discussion

Treatment modalities for ureteral stones have greatly changed during the last 20 years, especially following 62 the introduction of minimally invasive procedures such as extra-corporeal shock wave lithotripsy and uretero-63 renoscopy. The advantage of the medical expulsive therapy is important, because the risks which are related to a 64 surgical intervention are not trivial [7]. Studies have reported the overall complication rates after ureteroscopic 65 lithotripsies to be 10-20%, with major complications such as ureteral perforations, avulsions and strictures 66 occurring during 3-5% of the procedures [7]. Urinomas and sub capsular bleeds have been reported in15-32% of 67 the patients who are treated with shock wave lithotripsy [8]. Hollingsworth et al reported a 1.1% overall prevalence 68 of MET use between 2000 and 2006 in emergency departments in the USA, with a missed opportunity of sparing 69 approximately 260,000 individuals annually from stone surgery [9]. 70% of urolithiasisare located in the lower 70 71 third of the ureter. Determining factors for spontaneous passage of stones are their size, their configuration, and 72 the smooth muscle activity of the ureters. In the transport of stones, the greatest obstacle is usually the terminal part of the ureters, mainly in the intramural 'detrusor tunnel. Antagonists of the alpha-1-adrenergic receptor, in 73 particular, inhibit basal tone and decrease peristaltic frequency and amplitude with the consequences of increased 74 fluid transport and decreased intra-ureteral pressure; they also block the conduction of visceral referred pain to 75 the central nervous system, acting on C-fibres or sympathetic postganglionic neurons [10,11,12,13]. Both the 76 European (EAU) and American Urological Associations (AUA) outline the role of alpha-blockers as a viable 77 option in a select patient population who are comfortable with the approach and where there is no role for 78 immediate surgical stone removal [14,15]. The role of alpha-blockersin MET has been well described [14][15]. 79 The role of adrenergic receptors in the human ureter was first described in 1970 [16]. It was shown later, that 80 the alpha-adrenergic receptors were classified into three different subtypes & the distribution in the human ureter 81 was ?1D >?1A >?1B [17]. It was also shown that the alpha-adrenergic receptor agonists had a stimulatory effect 82 on the ureteral smooth muscle, whereas the beta-adrenergic receptor agonists had an inhibitory effect [18]. They 83 prevent the uncoordinated muscle activity which is seen in renal colic, while maintaining ureteral peristalsis, 84 which might facilitate a spontaneous stone passage [19]. The treatment effect on the expulsion rate was partially 85 lost, the sizes of the stones decreased, because of the high spontaneous expulsion rate of the small stones [2.20]. 86 Our study included only solitary ureteral calculi & located in the distal one third of the ureter. Current best 87 practice guidelines recommend alpha-blockers for the expulsion of distal ureteral stones. Meta-analyses have 88 demonstrated that patients treated with alpha-blockers are more likely to pass stones with fewer episodes of colic 89 [8,21]. Two recent randomized controlled studies by Al-Ansari et al [22] and Kaneko et al [23] validated the efficacy 90 of tamsulosin for distal ureteral calculi. However, a randomized control trial by Yilmaz et al demonstrated that 91 tamsulosin, terazosin, and doxazosin were equally effective in distal stone expulsion in comparison to the control 92 group [24]. There is no role of tamsulosin or watchful waiting in stones of size? 10mm & Surgical intervention 93 is the treatment of choice. In a recent study by Prof Robert Pickard et al [25] where they gave tamsulosin for 4 94 weeks they found that 95

96 6 V. Conclusion

In our study incidence of ureteric calculi was found to be more in males in the age group of 31-40 years& on the right side .Use of tamsulosin in MET for lower ureteric calculi upto 9mm helps in expulsion of stone, reduces the need for hospital admission, reduces pain, reduces the need for oral analgesics and reduces the need for surgical intervention. There was no significant difference in number of days required for expulsion of stones between two groups. There was no significant difference in mean size of stone passed in two groups. The possibility of expulsion of ureteric calculi spontaneously or with tamsulosin reduces as the stone size increases (maximum possibility with 5mm and minimum possibility with 9mm). There is no role of tamsulosin/watchful waiting in ureteric calculus of size ? 10mm. Most common Complications associated with tamsulosin are giddiness, retrograde ejaculation. Tamsulosin therapy is not cost effective than watchful waiting but cost effective than surgical intervention. However our study had only two groups, one study group and one control group. Adding two more groups simultaneously, one with some other alpha blocker drug and one with no drugs given at all, may show us the exact efficacy of tamsulosin Bibliography

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[Note: ? Not meeting inclusion criteria (n=30) ? Declined to participate (n=10) ? Other reasons (n=10) ? Received allocated intervention (n=314)]

Figure	1.	Table	1	•
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	Passed calculi in <14 days (%)	Not passed calculi	Mean no. of colic episodes	Mean pain score	Need for hos- pitali- sation during treat- ment	Need for surgical interven- tion
groups Tamsulosin 260 (83.87%)		50 (16.12%)	3 ± 1.7	$\begin{array}{rr} 4.1 & \pm \\ 1.7 \end{array}$	75	55 $(17.74%)$
WW	$195 \\ (62.9\%)$	115 (37.09%)	$\begin{array}{cc} 4.2 & \pm \\ 2.2 \end{array}$	$\begin{array}{rrr} 5.1 & \pm \\ 1.8 \end{array}$	135	115 (37.09%)
p value	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

NCCT was done in 70 (22.58%) cases in tamsulosin group and in 90 (29.03%) cases in WW group as USG calculus. most of the stones detected by CT were of 5mm.

Figure 2: Table 2 :

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6 V. CONCLUSION

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