# COMPARISON OF THE EFFICACY OF TAMSULOSIN AND NIFEDIPINE IN THE EXPULSION OF LOWER URETER STONE WITH SIZE BETWEEN 5MM TO 9MM

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## ABSTRACT

**Objectives:** Ureteric stones management makes a large part of urological practice. In our study we have compared efficacy of Tamsulosin and Nifedipine in the expulsion of lower ureter stone with size between 5mm to 9mm.

**Material and Method:** 168 patients with distal ureter stone were allocated in two groups, 84 in each, at Department of Urology, Institute of Kidney Diseases, Hayatabad Medical Complex, Peshawar from June 2014 to May 2015. Patients in group A received 0.4mg Tamsulosin daily and group B receiving 30mg daily of long acting formulation of Nifedipine. Oral analgesics were prescribed to all patients and were followed after 6 weeks to study the stone expulsion.

**Results:** There were 118 male and 50 female patients with male to female ratio of 2.36:1. Their age ranged from 15 to 68 years with the mean age of 35.4 years, with the mean age in Group A was 31.6 years and that in Group B was 39.1 years. Adverse effects of the drugs in the form of transient hypotension was observed in 6 patients in Group A while one patient in Group B, but there was no drop outs because of this effect. The mean size of the stone was 6.7mm in Group A and 7.2mm in Group B. Sixty eight patients (80.9%) in Group A achieved complete stone expulsion while the rate of stone expulsion in Group B was 59 out of 84 (70.2%) patients with P value of 0.106.

**CONCLUSION:** There are conflicting data in literature regarding the superiority of Nifedipine and Tamsulosin .Our study shows that none of them is superior to the other in the expulsion of moderate sized lower ureter stones.

**Key Words:** Ureter, Urinary Tract Stone.

## INTRODUCTION

Urolithiasis is an ancient disease with global distribution and has perplexed human beings and physicians for many centuries. The existence of kidney stones was first recorded thousands of years ago, and procedures for the removal of urinary tract stones are of the earliest known surgical procedures[1].

The lifetime risk of urinary stone disease is established to be 5%-10% in the industrialized countries[2], afflicting 13% of men and 7% of women[3]. The Afro -Asian stone belt stretches from Egypt through the Middle East, India and Pakistan[4]. Poor nutritional status and inadequate health facilities are common in these countries. Against this background, urolithiasis constitutes 40 to 50 % of the hospital workload[5]. Calculus disease is the commonest urological ailment in Pakistan. Urinary stones in its different forms are the third most common affliction of the urinary tract[5]. The established prevalence in this country is 10 to 15%[6].

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Urolithiasis is a chronic disease with substantial economic consequences and is of great public health importance through out the world. In USA alone, nearly two million patients were affected in the year 2000, with expenditures for inpatient and outpatient claims totaling around US $ 2.1 billion[8].

Treatment options for dealing with ureteric stones include, MET, Extracorporeal Shockwave Lithotripsy(ESWL), Minimally invasive and open surgical techniques. Minimally invasive procedures have revolutionized treatment for ureteric calculi, never the less, these procedures are expensive, not uniformly available and even not without risks[9].

Studies have established that MET should be the first line treatment for patients with ureteric stones not requiring emergency surgical intervention[10]. Various drugs including alpha blockers e.g. tamsulosin and calcium channel blockers e.g. nifedipine have been studied to assist the process of spontaneous stone expulsion, thereby reducing the need for surgical intervention[11].

Calcium channel blockers decrease the intracellular calcium concentrations, thereby inhibiting ureteral spasm caused by stone, but do not inhibit the normal peristaltic activity necessary for the expulsion of stone. Additionally, these drugs have a known antihypertensive affect, so are particularly benificial for the hypertensive patients with ureter stones. On the other hand, the alpha adrenergic recepter blockers have the effect of relaxing the lower ureter by inhibiting the alpha recepters

which are particularly abundant in this segment of the ureter[12].

Success rates with these two drugs is varied in different stidies randomizing patients into groups using tamsulocin and nifedipine, acheiving upto 96% versus 74% complete stone expulsion rate, respectively[13]. Several other studies have compared these two drugs with placebo groups observing variable success rates, i.e. from 53% vs 20% upto 90% vs 46% in case of Tamsulocin and from 83% vs 56% to 91% vs 64% in case of nifedipine[11].

Since Medical Expulsive Therapy(MET) is the recommended first line treatment in the management of patients having lower ureter stones of size that can be spontaneously expelled from the ureter, adequate emphasis must be put on its promotion so that patient may not be unnecessarily subjected to surgery or shock wave lithotripsy for dealing with such stones. tamsulosin, an alpha-adrenergic receptor blocker and nifedipine, a calcium channel blocker, are drugs recommended for this purpose but no national studies with adequate sample size are present which compare the effectiveness of these two drug classes. The rationale of this study is to compare the effectiveness of these two drugs in the stone expulsion in our population and as both these drugs are found to be more effective, we recommend their routine use in all patients with lower ureter stones with size between 5mm to 9mm.

## MATERIALS AND METHODS

This study was conducted at Department of Urology, Institute of Kidney Diseases, Hayatabad Medical Complex, Peshawar. Study design was randomized controlled trial and the duration of the study was 1 year (from June 2014 to May 2015) in which 168 patients were observed by taking 84 in each group keeping 96%[13] efficacy of Tamsulosin and 74%[13] efficacy of Nifedipine in expelling lower ureter stones, 95% confidence interval and 90% power of the test under WHO sample size calculations. More over lottery technique was used for sample collection. All patients of both genders having single unilateral lower ureter stone of size from 5 to 9 mm, 14 years or above were included while patients having multiple stones on X-ray KUB, patients having urinary tract infection diagnosed on urine culture, having deranged renal functions with creatinine level above 1.1mg/dl, having solitary functioning kidney and patients with history of previous endoscopic or open surgery were not included in the study.

The collected information was analyzed on SPSS. Frequencies and percentages were calculated for categorical variables like gender and efficacy while mean $\pm$ SD was calculated for numerical variables like age and baseline size of the stone. Efficacy was stratified among age, gender and baseline size of the stone to see the effect modification. All results were presented in the form of tables and graphs.

## RESULTS

A total of 168 patients were included in the study who were distributed randomly into two groups making a total of 84 in each group. The mean age of patients included in my study was 35.4 years and median age was 33years, age ranged from 14 to 68 years, with the mean age in Group A of 31.6 $\pm$11.7 years and that in Group B was 39.1$\pm$13 years. The highest age representation was between 20 to 30 years, a total of 70 patients representing 41.7% of the whole sample. There were 57 male and 27 female patients in the group receiving Tamsulosin and 61 male and 23 female patients in the group receiving Nifedipine (figure2).

The stone size ranged from 5 to 9mm, with the mean stone size of 6.99 $\pm$ 1.16mm. Applying the statistical test of significance on the comparison of the overall efficacy of the two drugs, it was found that the difference of efficacy was not statistically significant with P. value = 0.0106.

In establishing the efficacy of drugs in both groups, it was found that both the drugs were more effective in the moderate sized stones i.e. in the size range from 5 to 7mm. In the Tamsulosin group all 13 patients with stones of 5mm passed the stones, while efficacy was recorded in 28 out of 32(87.5%) and 11 out

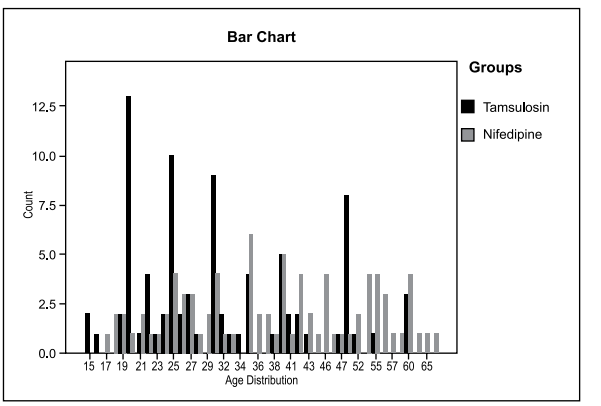


Figure 1

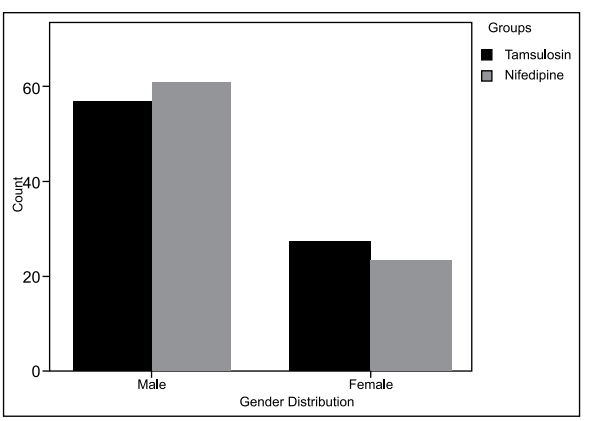


Figure 2

**Table1: Efficacy of Drugs in Two Groups**

| Efficacy | Groups | | Total | p-valve |
|---|---|---|---|---|
| | Tamsulosin | Nifedipine | | |
| Effective | 68 | 59 | 127 | 0.016 |
| Not Effective | 16 | 25 | 41 | |
| Total | 84 | 84 | 168 | |

**Table2: Effect of Size on Drug Efficacy**

| Groups | | | Efficacy | | Total |
|---|---|---|---|---|---|
| | | | | | |
| Tamsulosin | Baseling | 5 | 13 | 0 | 13 |
| | Size of | 6 | 28 | 4 | 32 |
| | the stone | 7 | 11 | 2 | 13 |
| | | 8 | 10 | 3 | 13 |
| | | 9 | 6 | 7 | 13 |
| | Total | | 6 | 7 | 13 |
| Nifedipine | Baseling | 6 | 20 | 3 | 23 |
| | size of | 7 | 22 | 4 | 26 |
| | the stone | 8 | 14 | 15 | 29 |
| | | 9 | 3 | 3 | 6 |
| | Total | | 59 | 25 | 84 |

of 13(84.6%) patients with stones of 6 mm and 7 mm sizes respectively. Similarly in the Nifedipine group, the drug was found to be efficacious in 20 out of 23(86.9%) patients and 22 out of 26(84.6%) patients with stone sizes of 6mm and 7mm respectively. Applying the statistical test of significance on the effect of variation in stone size on the efficacy of the individual drug, it was found that a statistically significant difference occurred as the stone size varied in the groups using either of the drugs with P. value=0.006 for Tamsulosin and 0.004 for Nifedipine.

## DISCUSSION

Symptomatic ureteral stones represent the most common emergency condition treated by urologists[14]. Management of stones is usually conservative in the first instance because of the high spontaneous passage rate. When stones are not expected to pass, do not pass spontaneously, or become problematic, more invasive treatment is recommended. The American Urological Association and the European Association of Urology guidelines for the treatment of ureteral stones recommend appropriate evidence-based use of shock wave lithotripsy (SWL), percutaneous nephrolithotomy, or ureteroscopy depending on stone size and location within the ureter[15,16]. However, these minimally invasive procedures are not risk-free and they require some experience and imply high costs [17, 18].

If ureteral stones could be expelled with pharmacotherapy, these procedures and associated costs could be avoided. Additionally, if the efficacy of these procedures could be improved pharmacologically, the cost of further and repeat procedures could be reduced. Besides, the accurate prediction of stone passage may prevent unnecessary intervention and therefore possible complications. In the uncomplicated patient, the probability of spontaneous passage is based on a number of factors including stone size, stone position, degree of impaction and obstruction[19].

In my study, the most common stone size was 6mm i.e.55 patients (29.8%), followed by 8mm i.e. 42 patients (25%) and 7mm (23.2%). In different international studies on the MET for the distal ureter stones, the mean size of stone studied has been 5.21mm with the size ranging from 3.6mm to 6.7mm[20]. Due to the high likelihood of spontaneous passage for stones up to about 4 mm, one would expect that the efficacy for MET would decrease because of the high spontaneous expulsion rate. The same applies for the study of Vincendeau *et al,* including distal ureteral stones with a mean stone size of 2.9 mm and 3.2 mm for the treatment and control groups, respectively[21]. Similar results are observed in my study, where both the drugs are most effective in the moderate size range i.e. 6 to 7mm, and the efficacy of both the drugs decreases as the stone size further increases. The change in the efficacy with

the variation of stone size is statistically significant in my study.

In my study, the stone expulsion rate is not significantly different statistically between the groups using tamsulocin and nifedipine. There are conflicting results by different investigators working on the beneficial effect of expulsive treatment of ureteral stones with either nifedipine or tamsulosin. Keshvary *et al;* found no statistical difference in expulsion rates between tamsulosin and nifedipine[22]. Porpiglia *et al*; evaluated the effectiveness of tamsulosin versus nifedipine in combination with deflazacort for stones <10 mm. Expulsion rates and expulsion time were in favor of the tamsulosin group, although differences were not significant[23]. Dellabella *et al;* compared the efficacy of tamsulosin and nifedipine in combination with phloroglucinol for stones >4 mm and found a significantly higher expulsion rate ($p = 0.001$) and shorter expulsion time ( $p < 0.0001$) in the tamsulosin group. The same trial demonstrated lower rates of hospitalization and ureteroscopy and fewer work days lost with tamsulosin than with nifedipine[24]. But, since phloroglucinol has significant antispasmodic effects, there was no true control group in this trial. In my study, although, both the drugs are effective in expelling the distal ureter stones, the efficacy of each drug over the other is not statistically supported by my study.

Stratification of the efficacy among age and gender to see the effect modification does not show any statistically significant effect as shown in the results of my study. To the best of our knowledge based on the internet based review of literature on this subject, no investigator has so far studied the effects of these variables on the MET of ureter stones.

The practical implications of this study applies not only on the urologists practicing in the tertiary care urological centers like ours but also on the physicians and the general surgeons who are sharing the load of dealing with the urological stone disease in the primary and secondary setups. The application of the MET for properly selected stones disease patients will avoid unnecessary referrals and will help saving precious government resources and lesson the patient's sufferings not only from the pain of the disease but also in terms of saving the logistics and poor patient's meager resources.

## IMITAIONS

Certain other parameters like requirement for analgesia in case of individual drugs, the type of analgesia required and the time to stone expulsion were not studied for each drug, which would have thrown more light on the utility of each drug and superiority of each drug over the other based on these parameters.

## CONCLUSION

Stone disease comprises a major bulk of the urologic workload globally. Alpha receptor blockers exemplified by Tamsulosin and calcium channel blockers exemplified by Nifedipine form the well-known drugs for the MET of Lower Ureter Stones. The results of my study shows that both Tamsulosin and Nifedipine are equally effective in the expulsion of moderate sized Lower Ureter Stones

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