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EFFECT OF TAMSULOSIN IN TREATMENT OF URETERIC CALCULI

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ABSTRACT

Current therapeutic options for ureteral stone include active intervention as well as conservative "watch and wait" approaches. Endoscopic treatment of ureteral stones has a high success rate and reliably results in immediate stone removal. However, surgical as well as anaesthetic risks are not negligible and serious complications are possible. Küpeli *et al.*, (2004), studied that "whether tamsulosin facilitate expulsion of distal ureteric calculus following lithotripsy or not (Küpeli *et al.*, 2004). They found it to be effective in the treatment of ureteric calculi. Resim *et al.*, (2005) studied the effect of tamsulosin on the number and intensity of ureteral colic in patients with lower ureteral calculus (Resim *et al.*, 2005) studied was done to determine whether tamsulosin as an alpha-1 blocker was effective in ureterolithiasis located in the lower part of the ureter. Sayed *et al.*, (2008) studied the efficacy of tamsulosin in medical expulsive therapy for distal ureteral calculi (Sayed *et al.*, 2008). They evaluated the potential role of tamsulosin in the medical treatment of distal ureteral stones. Their study reveals that tamsulosin is effective for the treatment of distal ureteral stones. Beach and Mauro (2006) studied the Pharmacologic expulsive treatment of ureteral calculi (Rajpathy *et al.*, 2008). They evaluated the role of nifedipine and the alpha-1-adrenoreceptor antagonists tamsulosin, terazosin, and doxazosin in treatment of ureteral calculi. Their result also shown that Nifedipine, tamsulosin, terazosin, and doxazosin are safe and effective options in enhancing ureteral stone expulsion in selected Patients. Effect of tamsulosin in the management of ureteric calculi, a prospective type of study, conducted in SSG Hospital, Baroda, from June 2007 to December 2009. Total 50 patients are selected. Patients selected are those, who came with pain in abdomen on OPD basis. All Patients where USG KUB or X-RAY KUB findings are suggestive of ureteric calculi of size less than 9 mm. In present study total 50 patients were taken, all patients were given TAMSULOSIN 0.4 mg, daily. Stone expulsion rate were noted. Out of 25 patients, in whom the size of stone was less than 5 mm, 20 patients were found to passed stone that comprises approx 80%; but only in 10 patients out of those 25, in whom the stone size was more than 5 mm; comprises approx 40%. This study reveals the efficacy of tamsulosin for the treatment of distal ureteral stone. Finally concluded that tamsulosin should be added to the standard medical approach for treating these stones.

Keywords: Tamsulosin, Ureter, Stone, Expulsion Rate, Pain

INTRODUCTION

The urologists have been defined for ever as Surgeons because of their methods of dealing with urinary Lithiasis. Anthropologic history provides evidences that Urinary Calculi existed as long as 7000 years ago. The specialty of urologic surgery was even recognized by Hippocrates, who in his famous oath for the physician stated:

"I will not cut even for the stone but leave the procedure to the practioners of the craft".

Until the end of 17th century the majority of stones were operated upon by itinerant "Stone Cutters", (Joly, 1929), and the physician considered themselves bound by the dictum of Hippocrates, the result was that surgery of stone was entirely in hands of barbers and wise women of district. As far as hindu writings are concerned it is not until we came to writings of 'Charaka', 'Shshruta' and 'Vagbhatta', who lived in 2nd, 5th and 7th century respectively. We find real discription of disease or indication for treatment. Rufus of ephesus recommended diet of cock or sparrow as curative measures. Renal lithiasis constitutes one of the major problems of urology. Many still labour under the stone. It is strange "TETaTIEe" stories attracted relatively little investigative attention in view of their importance in morbidity and occasionally in the mortality. Sir Henry Thompson became famous for his interest in medical therapy of stone and suggested

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the possibility of treatment by dissolution. After this period significant amount of attention turned to medical treatment of Urolithiasis. Surgery continues to be important as one aspect of treatment of urinary calculi, but it is now one step in total therapeutic plan for patients of urinary lithiasis. Urinary lithiasis represents a realm of sharing between the urologist and his medical colleague. In some instances medical specialists with training in endocrinology perform non-surgical evaluation and treatment of urinary stone disease.

Aims

- 1) To evaluate the effect of Tamsulosin (α -1 receptor antagonist) used for medical management in ureteric calculi-
- 2) Frequency of colicky pain,
- 3) Stone expulsion rate.
- 4) Adverse effect of Tamsulosin on patients.

MATERIALS AND METHODS

Patients and Methods

- Effect of tamsulosin in the management of ureteric calculi, a prospective type of study, conducted in SSG Hospital, Baroda, from June 2007 to December 2009.

Patient Selection

- Patients selected are those, who came with pain in abdomen on OPD basis.

Inclusion Criteria

- All Patients where USG KUB or X-RAY KUB findings are suggestive of ureteric calculi of size less than 9 mm.

Exclusion Criteria

- Associated renal calculus.
- History of ureteric surgery,
- Evidence of associated UTI.
- Previous History of disease in opposite kidney, severe hydronephrosis,
- Multiple stones,
- Nonopaque stones,
- A solitary kidney,
- Medical diseases- diabetes mellitus, hypotension or hypertension on α adrenoceptor blocker or calcium-antagonists, severe obesity, kidneyfailures, pregnancy.
- Total 50 patients are selected.
- **All Patients were Signed Written and Informed Consent after Explaining the Potential Side Effects & Complications in Detail**
- All patients are given tamsulosin 0.4 mg once daily for 4 weeks.
- Additionally, from day of treatment, all patients received conventional treatment with-
 - 2500 ml oral hydration daily,
 - Levofloxacin (100 mg, BD) for 1st 7 days.
- During 4-week treatment period, analgesic (Diclofenac sodium, IM) was given, SOS.

Follow-Up

- All patients were followed up every week for 4 weeks.
- On each follow-up visit, Routine examination performed-
 - X-rays (KUB),
 - USG (KUB),
 - Urinalysis,
 - Serum urea & creatinine.

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- At each follow-up-
 - Stone-free condition noted.
 - Complete absence of any stone on plain KUB X-rays and in USG KUB.
 - Dose of analgesic injections,
 - Any side effects & complications noted.

Patients Noted for

Positive cases- positive cases are those patients who passed the stone.

Negative cases- negative cases are those patients who failed to pass the stone.

RESULTS AND DISCUSSION

Results

In this study 50 Patients were selected & evaluated the effect of tamsulosin in the management of ureteric calculi, of less than 9 mm.

- The study is conducted in SSG Hospital, Baroda, from June 2007 to December 2009.

The Variables Studied

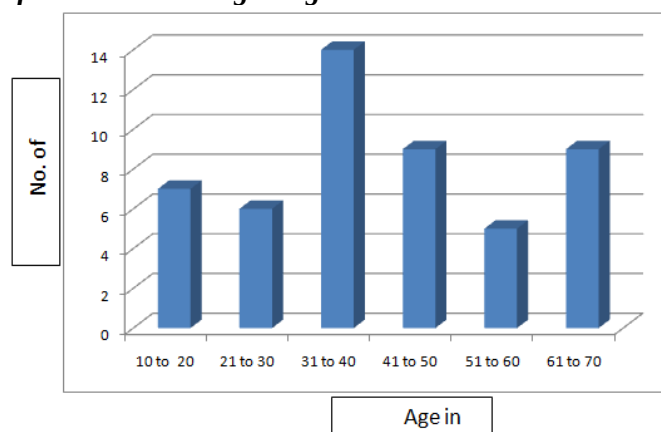
- Age distribution.
- Size of stone.
- Duration of symptoms.
- Period of observation (period between induction of treatment and results).
- Presence of UTI.
- Colicky pain in abdomen during observation period.
- Observation for morbidity and complications.

Frequency distribution of patient according to age

AGE (YEARS)	No. OF PATIENTS
10 to 20	7
21 to 30	6
31 to 40	14
41 to 50	9
51 to 60	5
61 to 70	9

From study it is noted that stone incidence is seen in all age group, but incidence is more common in 30-50 years of age group.

Frequency Distribution of Patient according to Age



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From study it is noted that stone incidence is seen in all age group, but incidence is more common in 30 to 50 years age group.

Correlation of age incidence

Age group	
Maximum age	70 years
Minimum age	10 years
Average age	35 years

From study it is noted that stone incidence is seen in all age group, from 10 year to upto 70 years. Average incidence is seen in middle age.

Data description of duration of symptoms

Symptom duration	
Maximum duration	60 days
Minimum duration	1 day
Average duration	7 days

Range is from 1 – 60 days. Average duration is 7 days. It is observed that patient usually present with complaints within a short period of time. So the presentation of symptomatic patient usually not delayed.

Data description of relation of size of stone

Stone size	
Maximum size	9 mm
Minimum size	3 mm
Average size	6 mm

Maximum size of stone is 9 mm and minimum size is 3 mm.

Correlation of duration of period of observation

Observation period	
Maximum days	28 days
Minimum days	7 days
Average days	16 days

Maximum number of days of observation is 28 days and minimum number of days of observation is 7 days. Observation period is not very long hence trial for medical management can be given.

Data description for pain and UTI

Observation for pain and UTI	No. of patients
Colicky pain in abdomen	08
Microscopic presence of pus cells	09

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The table shows that 8 patients out of 50 experienced episodes of colicky pain, constituting 16%. Microscopic presence of pus cells present in 9 patients out of 50 patients.

Result table

Number of patients	Expulsion	No expulsion
Less than or equal to 5 mm, (25)	20 (80%)	5 (20%)
More than 5 mm but less than 9 mm, (25)	10 (40%)	15 (60%)

The table shows that stone expulsion rate is 80% if size of stone is less than 5 mm; but it is only 40% for stone size more than 5mm.

The overall rate of expulsion is 60%.

Observation made are

Positive cases- those cases that passed the stone,

Negative cases- those cases that do not passed stone.

The graph shows that stone expulsion rate is 80% if size of stone is less than 5 mm; but it is only 40% for stone size more than 5mm, the direction of the graph shows that expulsion rate gradually decrease with increasing size of stone.

Observation for Morbidity and Complication

- It is observed that the size of stone is not affected by tamsulosin.
- The size of stone remains constant in those patients who failed to pass the stone.
- None of the patients in this study develop any morbidity or complications related to ureteric calculi like hydroureter, hydronephrosis and infective complications (pyonephrosis).
- None of the patients develop any side effect of tamsulosin, like-
- Headache, infection, asthenia, back pain & chest pain.
- Dizziness, somnolence, insomnia, libido decreased.
- Rhinitis, pharyngitis, coughs increased, sinusitis.
- Diarrhoea, nausea, tooth disorder.
- Abnormal ejaculation.
- Amblyopia.

Discussion

An in vitro study on human ureteric smooth muscle with the α_1 -adrenoceptor subtype blocker, tamsulosin have demonstrated that peristaltic activity in human ureteric smooth muscle is inhibited by tamsulosin (Küpel *et al.*, 2004).

It is suggested that α -adrenergic stimulation reduces the volume of urine flow passing through the ureter. In contrast, α -adrenergic antagonists result in decreased ureteral peristaltic amplitude and frequency. Based on the evidence that α_1 -receptors have an important role in the expulsion of lower ureteral physiology, some urologist have more recently proposed the use of α_1 -blockers with the aim of facilitating lower ureteral stone expulsion.

We investigated whether tamsulosin, as an α_1 -blocker drug, induced the relaxation of ureteral smooth muscles and thus would increase the spontaneous passage of stones and relieve colic pain.

The majority of small ureteral calculi can pass spontaneously and intervention is usually not required. Other published studies provide a variety of results regarding the spontaneous passage of ureteral stones. If the stone diameter is less than 4 mm, spontaneous passage is generally possible, Ureteral calculi >6 mm have a 5% or less chance of spontaneous passage (Margaret and Yair).

Ureteral calculi located at the distal ureter have a 50% chance of spontaneous passage with only conservative observation. The majority of stones generally pass spontaneously within a 6-week period

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after the onset of symptoms. Therefore, it is difficult to make a decision between interventional therapy (shock wave lithotripsy or ureteroscopy) and conservative therapy.

The downward transport of stones in the ureter is affected by factors such as the spasm of smooth muscles, submucosal edema and pain.

Holmlund reported the first experimental and clinical studies on the passage and arrest of ureteral stones. According to Holmlund's study, a stone in the ureter passes when the force that tends to move it down the ureter exceeds the friction between the stone and the ureteral wall. Ureteral relaxation in the region of the stone is considered to be an important factor promoting stone passage. The factors that affect the spontaneous passage of ureteral calculi are the size and shape of the stone, intrinsic areas of narrowing within the ureter, ureteral peristalsis, hydrostatic pressure of the column of urine proximal to the calculus and edema, inflammation, and spasm of the ureter at the site at which the stone is lodged. If the friction between the intraureteral wall and stone decreases, ureteral relaxation occurs and promotes stone passage at the site of obstruction. Two factors that appear to be most useful in facilitating stone passage are an increase in hydrostatic pressure proximal to a calculus and relaxation of the ureter in the region of the stone.

The primary functional anatomic unit of the ureter is the ureteral smooth muscle cell. The sympathetic nervous system appears to modulate ureteral activity as evidenced by the demonstration of adrenergic receptors in the ureter. The ureter contains excitatory α -adrenergic and inhibitory β -adrenergic receptors. In this study of 50 cases, the role of tamsulosin in management of ureteric calculi, are studied in detail and discussed as follows.

Symptomatology and Clinical Presentation of Ureteric Calculi

In present study, most of the patients present with pain in abdomen, in almost 100% of patients.

Associated Symptoms are

Nausea- present in 17 patients (34%), more if duration of symptom is less than 10 days and with the mean stone size of 7 mm.

Hematuria- present in 15 patients (30%), more in stone size of more than 5 mm.

Burning micturition- present in 17 patients (34%), and more common in stone size of more than 5 mm.

Age Distribution

In this study, number of patients in age group 30-40 is 14 and in age group 40-50 are 9. Most patients are in age group of 30-50 year, constitute about 46%.

Sex Distribution

In this study, the incidence of symptomatic stone is much less in female than males. Total percentage of female patients in the study is only 12% and 88% are male patients.

Size of Stone

The result of successful spontaneous passage of stone depends on-

- **Duration of Symptoms**
- **Size of the Stone**

Duration of Symptoms

Maximum duration of symptom is 60 days and minimum is 1 days, mode is 7 days.

Symptoms present for less than 14 days have expulsion rate in 16 out of 21, constituting approx 76%.

Symptoms present for more than 14 days have expulsion rate 18 out of 29 patients, constituting approx 62%.

Stone Size

It is important criterion for spontaneous passage of stone. Generally the maximum size permitted is 5 mm. Maximum size is 9 mm and minimum size is 3 mm, mean is 6.17 mm. Rate of expulsion is highly dependent upon size of stone. This study can be compared with study of Sefa *et al.*, (2005) they studied the effect of tamsulosin on the rate of expulsion in patients with lower ureteral calculus (Kazunari *et al.*, 2009). In this studied they took 30 patients of ureteric calculi, all patients were given TAMSULOSIN 0.4 mg, daily. Spontaneous passage was observed in 26 of the 30 patients in (86.6%). In present study total 50 patients were taken, all patients were given TAMSULOSIN 0.4 mg, daily. Stone expulsion rate were

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noted. Out of 25 patients, in whom the size of stone was less than 5 mm, 20 patients were found to passed stone, that comprises approx 80%; but only in 10 patients out of those 25, in whom the stone size was more than 5 mm; comprises approx 40%. Therefore present study result is comparable with result of Sefa *et al.*, (2005), study. The present study can also be compared with Sayed MA, Abolyosr A, Abdalla MA, El-Azab AS, they Studied the efficacy of tamsulosin in medical expulsive therapy for distal ureteral calculi 45 patients with symptomatic distal ureteral calculi were enrolled. All patients received tamsulosin 0.4 mg/daily for 4 weeks. Abdominal ultrasound scans and KUB X-rays were performed weekly. Stone expulsion rates, time to expulsion, pain episodes and analgesic usage were determined. The result of this study revealed stone expulsion rate 88.9%. Only 5 patients of 45 failed to pass stone. This study reveals the efficacy of tamsulosin for the treatment of distal ureteral stone. Finally concluded that tamsulosin should be added to the standard medical approach for treating these stones.

In present study total 50 patients were taken, all patients were given TAMSULOSIN 0.4 mg, daily. Stone expulsion rate were noted. Out of 25 patients, in whom the size of stone was less than 5 mm, 20 patients were found to passed stone, comprises approx 80%; but only in 10 patients out of those 25, in whom the stone size was more than 5 mm; constituting approx 40%. Therefore again present study result is comparable with result of Beach and Mauro (2006) study.

Duration and Frequency of Colicky Pain in Abdomen

An ureteral stone usually causes severe colic pain as a result of an increase in intraureteral pressure above the site of ureteral obstruction. The goals in the treatment of renal and ureteral colic are to relieve the pain and release the ureteral obstruction. This aspect is important for result to be successful. The study shows that duration of sickness is necessary attribute in the conservative management of ureteral stone. Present study can be compared with study of Sefa *et al.*, (2005), they studied effect of tamsulosin on the number and intensity of ureteral colic in patients with lower ureteral calculus (Margaret and Yair). Again they selected total 30 patients of ureteric calculi. All patients were given TAMSULOSIN 0.4 mg, daily. Result of this study revealed that total number of patients that suffered episodic attack of pain was 4 out of 30 patients, constituting about 13.33%. In my study total 50 patients were taken, all patients were given TAMSULOSIN 0.4 mg, daily. Total number of episodes of colicky pain was noted. In my study colicky pain is present in 8 out of 50 patients, in about 16% of patients. Our results are in agreement with the result of Sefa *et al.*, (2005) study. Spontaneous passage was observed in 26 of the 30 patients (86.6%). 7 patients out of 30 suffered from colicky episodes of pain. Results of the study revealed that the treatment of alpha (1)-blockers decreased the number of ureteral colic episodes and the intensity of pain during spontaneous passage of lower ureteral calculi. Also, it will be beneficial to patients' quality of life. Beach and Mauro (2006) evaluated the role of alpha (1)-adrenoreceptor antagonists tamsulosin, terazosin, and doxazosin in the treatment of ureteral calculi. In 28 day trials, the rates of ureteral stone passage were 79.3-100% in patients treated with tamsulosin. The number of pain episodes was significantly lower. They concluded that, tamsulosin is safe and effective options in enhancing ureteral stone expulsion in selected patients with uncomplicated presentations and in reducing the number of pain episode. In present study total 50 patients were taken, all patients were given TAMSULOSIN 0.4 mg, daily. Total number of episodes of colicky pain was noted. In my study colicky pain is present in 8 out of 50 patients, in about 16% of patients. Our results are in agreement with the result of above mentioned study. The percentage of expulsion rate and episodes of colicky pain is significantly beneficial with the use of TAMSULOSIN. The result from study of Kazunari *et al.*, (2009); Sefa *et al.*, (2005); Davenport *et al.*, (2006); Kim *et al.*, (2007); Gaurav *et al.*, (2008); Naja *et al.*, (2008) also revealed that in the management of ureteric calculi tamsulosin has a significant effect.

Conclusion

The treatment of ureteric calculi with α 1-blockers has significant effect on the number of ureteral colic episodes and the intensity of pain during spontaneous passage of ureteric calculi.

- ❖ Tamsulosin also has significant effect on the rate of spontaneous expulsion of ureteric calculi.
- ❖ Also, it will be beneficial to patients' quality of life.

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REFERENCES

- Davenport K, Timoney AG and Keeley FX (2006).** A comparative in vitro study to determine the beneficial effect of calcium-channel and alpha (1)-adrenoceptor antagonism on human ureteric activity. *BJU International* **98**(3) 651-5.
- Gaurav G, Karthikeyan A and Nitin S Kekre (2008).** Does tamsulosin facilitate expulsion of distal ureteric calculus following lithotripsy? *Indian Journal of Urology* **24**(2) 274–275.
- Kazunari O, Yoshihiro O and Kazuhiro S (2009).** The investigation of ureteral sympathetic innervation, using semi-serial sections: why does the α 1-adrenergic receptor antagonist work well for ureteral stones? *International Urology and Nephrology* (Springer Science+Business Media) B.V. 10.1007/s11255-009-9592-3 Urology - Original Paper, Published online.
- Kim D, Anthony G Timoney and Francis X Keeley (2007).** Effect of smooth muscle relaxant drugs on proximal human ureteric activity in vivo: a pilot study. *Urological Research, A Journal of Clinical and Laboratory Investigation in Urolithiasis and Related Areas* (Springer-Verlag) 10.1007/s00240-007-0100-x Original Paper, Published online.
- Küpelı B, Irkilata L, Gürocak S, Tunç L, Kiraç M, Karaoğlan U and Bozkirli I (2004).** Does tamsulosin enhance lower ureteral stone clearance with or without shock wave lithotripsy? *Urology* **64**(6) 11115.
- Margaret S Pearle and Yair Loton (No Date).** Campbell-walsh, ureteric calculi, 9th edition, *Urology* **2** 1363- 1373.
- Naja V, Agarwal MM, Mandal AK, Singh SK, Mavuduru R, Kumar S, Acharya NC and Gupta N (2008).** Tamsulosin facilitates earlier clearance of stone fragments and reduces pain after shockwave lithotripsy for renal calculi: results from an open-label randomized study. *Urology* **72**(5) 1006-11.
- Rajpathy J, Aswathaman K, Sinha M, Subramani S, Gopalakrishnan G and Kekre NS (2008).** An in vitro study on human ureteric smooth muscle with the alpha1-adrenoceptor subtype blocker, tamsulosin. *BJU International* **102**(11) 1743-5..
- Resim S, Ekerbicer H and Ciftci A (2005).** Effect of tamsulosin on the number and intensity of ureteral colic in patients with lower ureteral calculus. *International Journal of Urology* **12**(7) 615-20.
- Sayed MA, Abolyosr A, Abdalla MA and El-Azab AS (2008).** Efficacy of tamsulosin in medical expulsive therapy for distal ureteral calculi. *Scandinavian Journal of Urology and Nephrology* **42**(1) 59-62, Epub 2007.
- Sefa R, Hasan E and Ahmet C (2005).** Effect of tamsulosin on the number and intensity of ureteral colic in patients with lower ureteral calculus, *International Journal of Urology* **12**(7) 615-20.