

A COMPARATIVE STUDY ON SAFETY AND EFFICACY OF TAMSULOSIN AND SILODOSIN AS MEDICAL EXPULSIVE THERAPY IN RENAL AND URETERIC STONES < 7mm

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ABSTRACT

Aim: To compare safety and efficacy of tamsulosin and silodosin in renal and ureteric stones as expulsive therapy and know the epidemiology.

Objectives:

- To determine the safety and efficacy of tamsulosin and silodosin in expulsion of renal Stones.
- To analyse the relation between predisposing factors with the help of a survey.
- To bring awareness on renal and ureteric calculus by changing their life style modifications.
- To compare the complication effect with use of the tamsulosin and silodosin.

Methodology: A Suitably designed data collection form was prepared for the patients which includes demographic details of the patients such as age, gender, weight, laboratory data of blood, biochemistry, USG of abdomen with PVR, CT-KUB, treatment pattern, follow up and Questionnaires on lifestyle changes occupation and side effects. Statistical analysis was performed by using mean, standard deviation two tailed paired T-test, class intervals and percentage in excel. The comparison between the study groups were performed with the use of two tailed t-test and class intervals was used for categorical measures

Results: In our study 250 patients with ureteric and renal stones were enrolled with 458 number of stones at the average of 2 stones in each patient and categorized into three groups such as tamsulosin, silodosin and control. According to gender wise distribution 143 were male and 107 were female. The maximum number of patients with ureteric and renal stones is in rural area (62%). The occupation that the patients does and the occurrence of stones as follows kuli (59), Farmers (52), housewives (41), students (36), business (27), employees (23) and drivers (12). According to the diet distribution, mixed type of diet people are more prone for cause of ureteric and stones in both urban and rural population. The maximum number of male patients are between the age group of 23-32 years where as female patients are 33-42 years. The maximum type of stone is calcium stones (167) followed by struvite stones (114), uric acid stones (102) and cystine stones (75).

Silodosin is more effective than tamsulosin and control group based upon the comparison of the significance t-value 1.264349, 1.400643 and 1.831018 respectively at p-value 0.05. So, silodosin is effect in the ureteric stone as the expulsive therapy whereas in renal stone, it is observed that silodosin effective than tamsulosin and control group based upon the comparison of the significance t-value 0.583305, 1.59962 and 1.913354 respectively at p-value 0.05. So, silodosin is effect in the renal stone as the expulsive therapy. the expulsive therapy is more effective in the ureteric stones than in renal stones. By above observation silodosin is more

effective than tamsulosin as expulsive therapy in both the renal and ureteric stones. Overall silodosin is effective as expulsive therapy than tamsulosin. By observation the effect of the drugs differs on the type of the stone. On calcium stone, silodosin (66.66%) is effective than the tamsulosin (60.18%) and control (0%), on cystine stone both silodosin and tamsulosin have same effect (100%) than control (72.72%), on struvite stone, silodosin(100%) is effective than tamsulosin (98.69%) and control(18.18%) and on uric acid tamsulosin (98.46%) is effective than silodosin (96%) and control (8.33%).

The mean time of expulsion of the ureteric stone is least in silodosin (5.958333± 2.475606 days) followed by tamsulosin (8.62962963± 2.904498 days) and control (10.8± 3.420526 days). By this silodosin have higher effective expulsion time than tamsulosin and control groups in ureteric stones. The mean time of expulsion of the renal stone is least in silodosin group (21.55932±4.235609 days) followed by tamsulosin group (22.16447±5.208811days) and control group (27.66665 ± 0.888844 days). By this silodosin have higher effective expulsion time than tamsulosin and control groups in renal stone. the mean time of expulsion of drug is least in expulsion of the ureteric stones than in the expulsion of the renal stones. By the above observation, it is identified that the silodosin has the greater rate of mean expulsion time.

The adverse drug reaction was reported in both Tamsulosin and silodosin groups. Orthostatic Hypotension was reported in 6 patients, 3 were tamsulosin taking patients and 3 Silodosin taking patients. Retrograde Ejaculation was reported in 7 patients, 4 were tamsulosin taking patients and 3 were silodosin taking patients.

Conclusion: In our study, mixed diet, rural area subjects, men and increasing age are more predisposed for formation of the kidney stones. Our results indicate that both tamsulosin and silodosin are effective drugs as the Medical Expulsive Therapy (MET) but we found that silodosin was more effective for ureteric calculi as well as in renal calculi of size < 7 mm. We conclude that silodosin is better than tamsulosin in terms of stone clearance rate and stone clearance time. Both the drugs show Adverse drug reaction like Orthostatic Hypotension and Retrograde Ejaculation at the same rate, hence the safety of the both drugs are similar. Large multicentre trials are required to prove the efficacy and safety of silodosin over tamsulosin especially in renal stone expulsion.

Keywords: renal stone, ureteric stone, silodosin, tamsulosin, Hounsfield unit (HU), expulsion time, orthostatic hypotension, retrograde ejaculation

INTRODUCTION

Obstruction in the urinary tract is common and important because it increases the susceptibility to infection and stone formation. An account of the most common and important cause of obstructive uropathy is **urolithiasis or Nephrolithiasis**. Nephrolithiasis or urolithiasis is formation of urinary calculi at any level of the urinary tract. Urinary calculi are worldwide in distribution but are particularly common in some geographic locations such as in parts of the United States, South Africa, India and South-East Asia. It is estimated that approximately 2% of the population experiences renal stone disease at some time in their life with male-female ratio of 2:1. The peak incidence is observed in 2nd to 3rd decades of life. Renal calculi are characterised clinically by colicky pain (renal colic) as they pass down along the ureter and manifest by haematuria ⁽¹⁾.

The epidemiology of urolithiasis differs according to geographical area in term of prevalence and incidence, age and sex distribution, stone composition and stone location ^(2, 8). Such differences have been explained in terms of area, diet and age distribution. The composition of the stones is classified based upon the Hounsfield unit (HU) is a relative quantitative measurement of radio density used by radiologists in the interpretation of computed tomography (CT) images. The absorption/attenuation coefficient of radiation within a tissue is used during CT reconstruction to produce a gray scale image and the values are given in the figure.1.

Stone groups	95% confidence interval for mean		Minimum	Maximum
	Lower bound	Upper bound		
HU				
Calcium oxalate	448.2	760.8	495	1250
Uric acid	260.3	348.7	274	401
Calcium phosphate	435	631	290	945
Struvite	282.5	373.6	225	396
Cystine	108.9	191.6	112	215
HD				
Calcium oxalate	49.94	68.19	53	179.8
Uric acid	23.63	41.2	15.8	43
Calcium phosphate	37.97	52.6	29.22	98
Struvite	20.29	38.2	14.87	39.9
Cystine	11.52	16.09	11.97	14.95

HU = Hounsfield unit; HD = Hounsfield density

Figure-1: Ranges of HU for different types of a kidney stones

Most small kidney stones won't require invasive treatment and can be passed out. The treatment of these stones can be done by Non- pharmacologically and pharmacologically. Passing a small stone can cause some discomfort. To relieve mild pain, pain relievers such as NSAIDS, acetaminophen or chlorzoxazone are used and drugs like silodosin and tamsulosin are used as the medical expulsive therapy. There is a large body of published data, which has shown the efficacy of such a therapy in increasing the expulsion rate and in decreasing the expulsion time of the stones. Tamsulosin, an $\alpha 1$ -adrenoceptor antagonist, is uroselective for $\alpha 1A$ and $\alpha 1D$ receptors. This is a very popular and effective medical agent used for Medical Expulsive Therapy (MET). But, recently it has been reported that the $\alpha 1A$ adrenoceptor is the main participant in phenylephrine-induced ureteral contraction in human isolated ureter. A newly introduced drug silodosin, more of an $\alpha 1A$ selective adrenoceptor antagonist has shown promising results with fewer side effects and better efficacy⁽³⁾. The use of these drugs in the treatment of distal ureteral stones arose from the concept that they could induce a selective relaxation of the ureteral smooth muscle, which could inhibit the ureteral spasms and result in dilatation of the urethral lumen and passage of ureteric stones⁽⁴⁾.

METHODOLOGY

The present study was conducted at **NEPHRON KIDNEY CENTER**, Hanamkonda. This centre is situated in the heart of the city with basic objectives of providing Pharmacological and Non pharmacological management of Urological and Andrological Diseases. A hospital based Ambispective (Retro-prospective) control Study. This study was carried out for 6 months (October – March) 2019-2020. The study was conducted on 250 patients with 458 stones at this centre. It includes Patients who are suffering with Renal Calculus of size < 7mm, patients who are suffering Hypertension renal and ureteric Calculus, child patients with size <5mm of renal and ureteric stones, patients who are suffering with BPH and Renal Calculus and patient with LUTS and Diabetics. We excluded patients with HIV and pregnant women. Patients visiting clinics will be reviewed. The patients who are meeting the study criteria will be enrolled in to the study. Patient demographics (age, gender, diet, and occupation), medical history, social history and diagnostic data of renal calculus especially the size were collected and follow-up will be conducted for next clinic visits. The Source of data is from patients, patient case reports, prescriptions and physician, patient relatives and Lab data. The statistical analysis was performed by using mean, standard deviation two tailed paired T-test, class intervals and percentage in excel. The comparison between the study groups were performed with the use of two tailed t-test and class intervals was used for categorical measures

RESULTS

In our study 250 patients with ureteric and renal stones were enrolled. They are divided into three groups i.e., Tamsulosin, Silodosin and control. These three groups are given analgesics for the pain relief. They are divided into three groups Tamsulosin (n=148), Silodosin (n=62) and control (n=40). In 250 patients, 143 were male and 107 were female. The maximum number of patients with ureteric and renal stones is in rural area (62%). The occupation that the patients does and the occurrence of stones as follows kuli (59), Farmers (52), housewives (41), students (36), business (27), employees (23) and drivers (12). The mixed type of diet people are more prone for cause of ureteric and stones in both urban and rural population. The above figure illustrates that the maximum number of male patients are between the age group of 23-32 years where as female patients are 33-42 years.

In our study patient with multiple stone is included. The total numbers of stones are 458 in 250 at the average of 2 stones in each patient. The figure illustrates the maximum type of stone is calcium stones (167) followed by struvite stones (114), uric acid stones (102) and cystine stones (75).

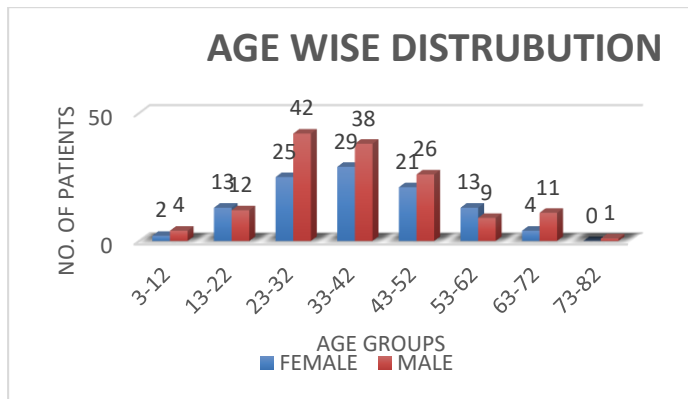


Figure-2: Age wise distribution of patients

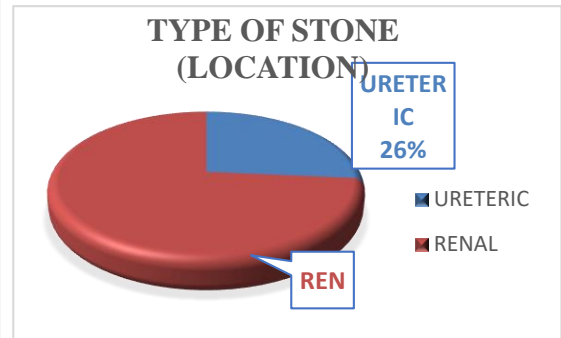


Figure-3: Type of stone based on location

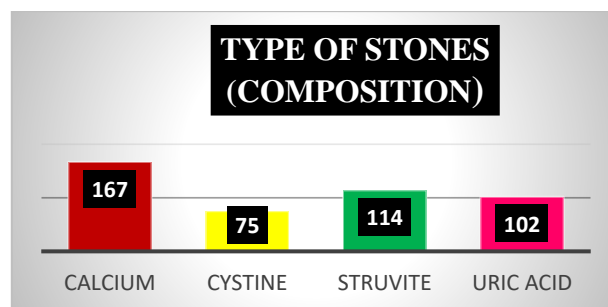


Figure-4: Type of stones based on composition

The pie chart illustrates that maximum number of patients are with renal stones 337 (74%) whereas the ureteric stones 121(26%).

A) Comparing the efficacy of the three groups by using the paired T-test:

In ureteric stones:

Table-1: Drug Effects on Ureteric stones

	TAMSULOSIN	SILODOSIN	CONTROL	TOTAL
EXPILED	81	24	5	110
NOT EXPILED	3	2	6	11
TOTAL	84	26	11	121

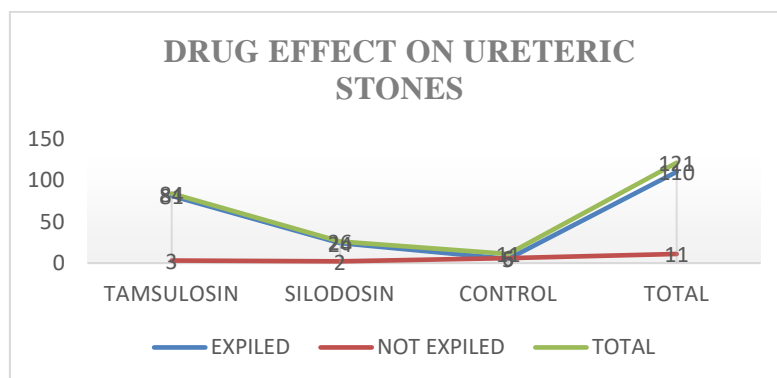


Figure-5: Drug effect on the Ureteric stones

Table-2: Comparing drug effect on the ureteric stone.

Drugs	Expulsion (Mean)	Significance(p value-0.05) t-value
Tamsulosin	56±45.92	1.400643
Silodosin	17.33333±13.3	1.264349
Control	7.333333±3.25	1.831018

Table-2 illustrates that silodosin is more effective than tamsulosin and control group based upon the comparison of the significance t-value. so silodosin is effect in the ureteric stone as the expulsive therapy.

In renal stone:

Table-3: Drug Effect on Renal stone

	TAMSULOSIN	SILODOSIN	CONTROL	TOTAL
EXPILED	152	59	16	227
NOT EXPILED	44	21	45	110
TOTAL	196	80	61	337

Table-4: Comparing drug effect on the renal stone.

Drugs	Expulsion (Mean)	Significance(p value-0.05) t-value
Tamsulosin	130.6667±78.21	1.59962
Silodosin	53.33333±29.905	0.583305
Control	40.66667±22.81	1.913354

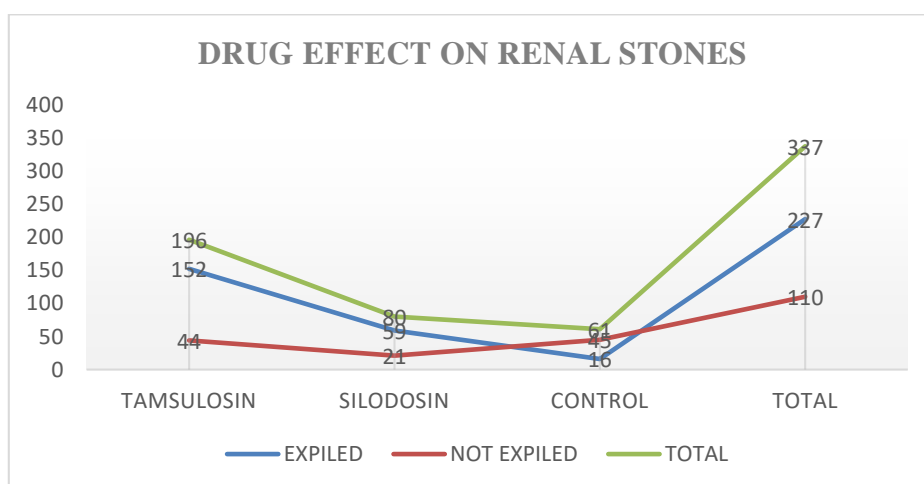


Figure-6: Drug effect on Renal stones

Table-4 illustrates that silodosin is effective than tamsulosin and control group based upon the comparison of the significance t-value. so silodosin is effect in the renal stone as the expulsive therapy.

B) Comparing the efficacy of the drugs as expulsive therapy in ureteric and renal stones.

Table-5: Comparing the effect of drugs between ureteric and renal stones

DRUG	URETERIC STONE Significance (p value-0.05) t-value	RENAL STONE Significance (p value-0.05) t-value
Tamsulosin	1.400643	1.59962
Silodosin	1.264349	0.583305
Control	1.831018	1.913354

Table-5 illustrates that the expulsive therapy is more effective in the ureteric stones than in renal stones. By above observation silodosin is more effective than tamsulosin as expulsive therapy in both the renal and ureteric stones.

C) Comparison of efficacy of the drugs on the type of renal calculus

Table-6: Percentage of the stone expelled

TYPE	TAMSULODSIN (%)	SILODOSIN (%)	CONTROL (%)
CALCIUM STONE	60.18519	66.6667	0
CYSTINE STONE	100	100	72.72
STRUVITE STONE	98.693	100	18.18
URIC ACID STONE	98.4615	96	8.33

Figure-7: Drug effect on the type of stone

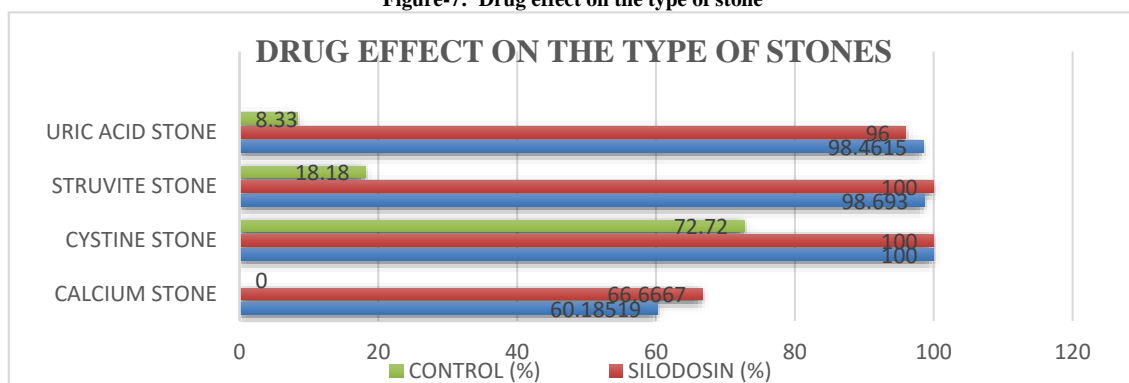


Table-6 and Figure-7 illustrates that overall silodosin is effective as expulsive therapy than tamsulosin. By observation the effect of the drugs differs on the type of the stone.

On calcium stone, silodosin (66.66%) is effective than the tamsulosin (60.18%) and control (0%), on cystine stone both silodosin and tamsulosin have same effect (100%) than control (72.72%), on struvite stone, silodosin(100%) is effective than tamsulosin (98.69%) and control(18.18%) and on uric acid tamsulosin (98.46%) is effective than silodosin (96%) and control (8.33%).

D) Comparison of the expulsion time of the drugs:

Table-7: comparing the mean expulsion time of drugs between ureteric and renal stones

DRUG	URETERIC STONE Mean expulsive time (DAYS)	RENAL STONE Mean expulsive time (DAYS)
Tamsulosin	8.62962963± 2.904498	22.16447±5.208811
Silodosin	5.958333± 2.475606	21.55932±4.235609
Control	10.8± 3.420526	27.5±5.46504

Table-7 illustrates that the mean time of expulsion of drug is least in expulsion of the ureteric stones than in the expulsion of the renal stones. By the above observation, it is identified that the silodosin has the greater rate of mean expulsion time.

SAFETY MEASURES:

Table-8: Reported adverse drug reactions in Tamsulosin and Silodosin group

ADR'S	Tamsulosin	Silodosin
Retrograde Ejaculation	4	3
Orthostatic Hypotension	3	3
Total	7	6

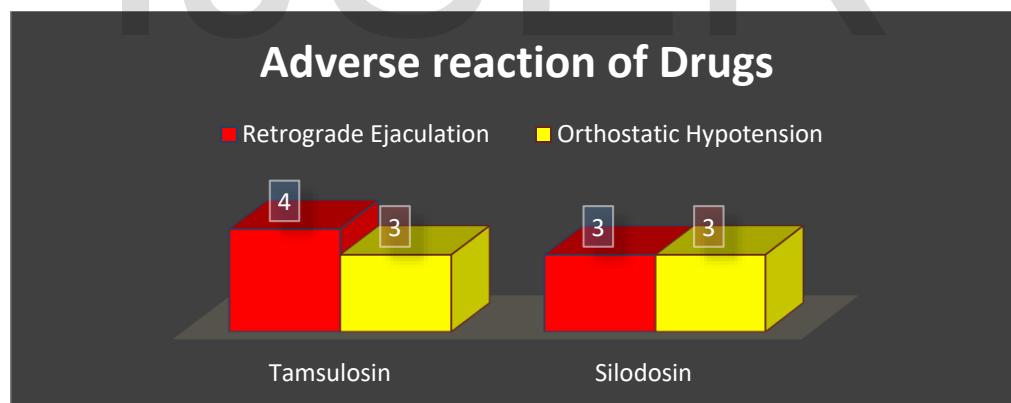


Figure-8: Adverse reaction of drugs

Table-8 and Figure-8 illustrate the adverse drug reaction were reported in both Tamsulosin and silodosin groups. Orthostatic Hypotension was reported in 6 patients, 3 were tamsulosin taking patients and 3 Silodosin taking patients. Retrograde Ejaculation was reported in 7 patients, 4 were tamsulosin taking patients and 3 were silodosin taking patients.

DISCUSSION

Nephrolithiasis or urolithiasis is formation of urinary calculi at any level of the urinary tract. Due to the family, social and dietary changes in the life style leads in the formation of the stones in the kidney. The treatment of this condition mainly depends on the size, location and the type of the stone. the diagnosis of this is mainly done by CBP, RFT, CUE, USG abdomen with PVR and CT scan. The life style modification and medication like NSAID's for pain relief, Medical expulsion therapy like alpha blocker (Tamsulosin, silodosin, Alfuzosin etc...)

and surgeries for the larger stone are used. The present study was conducted to evaluate the effect and safety in between the Tamsulosin and silodosin and predisposing factors of urban and rural patients of the Warangal district. In our study patient with multiple stone is included. The total numbers of stones are 458 in 250 at the average of 2 stones in each patient. The study is conducted about 6 months duration of the time. Our study results are comparable with other studies done in other parts of the world.

Our study results are comparable with study conducted by Amolr Dongre et al reported that they observed the incidence of the urinary tract stones increases with the age group of 20-40 years. Males are more predisposed to this condition, with male to female odds ratio 1.62:1. The odds of developing the renal stones was 2.29 times significantly greater than odds among the not working. The odds of developing renal stones among red meat consumer for \geq once a week and once a month had 18.3 times and 1.15 times higher risk respectively as compared to those who never consumed red meat. In our study the age group of 23-32 years in male and 33-42 years in female are most effected compared to other age groups in total population (250 patients) similarly to Yu Liu et al. study. The males 143(52%) are more predisposed than females 107(42.7%). The major population that is affected in rural area than in urban patients 155(62%) and 95(38%) respectively. The occupational distribution of patient kuli (59), Farmers (52), housewives (41), students (36), business (27), employees (23) and drivers (12). The mixed type of diet people is more affected than the vegetarian 238(95.2%) and 12(4.8%) respectively which is similar to the Shahida Banu Shamsuddeen et al. studies.

Diagnostic test are the proofs of finding the size, location and the type of the stones. In our study the main diagnostic test followed is NCCT and USG abdomen with PVR similar to the M. Alizadeh study. NCCT gives the information on the HU value and that helps in knowing the type of the stone. Our study is compared with the Parisa Sotoodeh Shahnani et al. study that they observed calcium stones of $HU > 448$, uric acid $HU > 348$, Struvite $HU > 225$ and cystine $HU < 215$. In our study the type of stones calcium $HU > 450$, Uric acid $HU > 274$, struvite $HU > 215$ and cystine $HU < 215$ are considered. The further analysis should be done for the identification of the type of stones. The type of stone considered in our study is the estimated type based on the HU values which is similar to the Parisa Sotoodeh Shahnani et al study.

In our study, Calcium stones 167(36.4%) are most frequent component of stone, followed by struvite stones 114 (24.8%), uric acid stones 102 (22.2%) and cystine stones 75 (16.3%) similar to the Haewook Han et al. study which observed calcium stones (75%), struvite stones (10-20%), uric acid stones (5-15%) and cystine stones (1%).

In our study both the renal 337(74%) and ureteric 121(26%) stones are considered in which they are divided into three groups tamsulosin group, silodosin group and control group. In our study the comparison of the effect of drug on ureteric stones and renal stones are compared separately and the compared in between them the both. Our study is compared with Sandeep Gupta et al. study in case of ureteric stones which they observed that A spontaneous stone expulsion was observed in 58% of the patients in group 1 and in 82% of the patients in Group 2, which was statistically significant. There was also a significant difference between the groups with regards to the mean stone expulsion time. A lower analgesic use was found in Group 2. Silodosin was found to be clinically superior to tamsulosin, both in terms of the stone expulsion rate and the stone expulsion time. In our study, there is significance difference between the groups where the t-values of tamsulosin group is 1.400643, silodosin group is 1.264349 and control group is 1.831018. As the t-value is lower for silodosin the rate of expulsion is higher than in the tamsulosin group and control group. In our study the rate of the expulsion in renal is done where the t- values of tamsulosin group is 1.59962, silodosin group is 0.583305 and control group is 1.913354 by t-values it is the silodosin have the higher expulsion rate than tamsulosin and silodosin even in the renal stones. By comparing the t-values between the ureteric and renal stones Medical expulsion therapy is more Significant and effective in the ureteric stone expulsion than the renal stone expulsion.

Our study is compared with Priyanka et al. study in which they observed that the 15 out of 27 cases in group tamsulosin and 23 out of 28 cases in group silodosin expelled the stones by the end of study. The mean time of expulsion in tamsulosin group was 19.1 ± 8.6 days, while silodosin group was 16.7 ± 6.8 days and it is the study on the ureteric stones. In our study at the end stone is expelled in tamsulosin group and silodosin group and control group are at 81 of 84, 24 of 26 and 5 of 11 respectively in case of the ureteric stone whereas in case of renal stones tamsulosin group 152 of 196, silodosin group 59 of 80 and control group 16 of 61 are expelled. The expulsion time of ureteric stones in silodosin group is 5.958333 ± 2.475606 days followed by tamsulosin group 8.62962963 ± 2.904498 days and control group 10.8 ± 3.420526 days. There is the significance difference between the group at p-value 0.05. by the observation silodosin group as the higher significance in expulsion time than tamsulosin group and control group. In renal stone the expulsion time as silodosin group (21.55932

± 4.235609 days) followed by tamsulosin group (22.16447 ± 5.208811 days) and control group (27.66665 ± 0.888844 days). Silodosin shows the highest level in expulsion time even in the renal stone expulsion.

Tamsulosin and silodosin have same mode of action and shows adverse effects such as priapism, orthostatic hypotension, retrograde ejaculation dizziness, visual impairment and hepatobiliary disorders which are the major side effects of both the drugs. In our study Adverse drug reactions were reported in both tamsulosin and silodosin groups. Orthostatic Hypotension was reported in 6 patients, 3 were tamsulosin taking patients and 3 Silodosin taking patients. Retrograde Ejaculation was reported in 7 patients, 4 were tamsulosin taking patients and 3 were silodosin taking patients. By the observation there is no significance difference in between the groups. The reported patients were followed by and the adverse effects have been reduced by providing the precautions to the patients.

In our study the risk factors for occurrence of urinary tract stones mainly based on the life style modification. We also reported the results of drug effect on the renal stones of size less than 7mm which requires the correlation with the studies conducted in other parts of the world. our study also shows the results of drug effect on the different type on stones , on calcium stone, silodosin (66.66%) is effective than the tamsulosin (60.18%) and control (0%), on cystine stone both silodosin and tamsulosin have same effect (100%) than control (72.72%), on struvite stone, silodosin(100%) is effective than tamsulosin (98.69%) and control(18.18%) and on uric acid tamsulosin (98.46%) is effective than silodosin (96%) and control (8.33%).

Our study is effective when compared with study conducted by Ravikumar R et al as they only reported the effect of tamsulosin and silodosin on ureteric stones as we also reported on renal stones and on type of stone. our study is compared with Hazem Elgalaly et al which shows that silodosin is more effective than tamsulosin in the management of DUS for stone clearance rates and stone expulsion times in ureteric stones.

CONCLUSION

In our study, Mixed diet, Rural area subjects, men and increasing age are more predisposed for formation of the kidney stones. Our results indicate that both tamsulosin and silodosin are effective drugs as the Medical Expulsive Therapy (MET) but we found that silodosin was more effective for ureteric calculi as well as in renal calculi of size < 7 mm. We conclude that silodosin is better than tamsulosin in terms of stone clearance rate and stone clearance time. Both the drugs show Adverse drug reaction like Orthostatic Hypotension and Retrograde Ejaculation at the same rate, hence the safety of the both drugs are similar. Large multicentre trials are required to prove the efficacy and safety of silodosin over tamsulosin especially in renal stone expulsion.

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REFERENCE

1. Text book of Pathology- Harsha Mohan, 6th edition pg.no. 690-693.
2. Yu Liu , Yuntian Chen , Banghua Liao , Deyi Luo Kunjie Wang , Hong Li , Guohua Zeng Epidemiology of urolithiasis in Asia [Elsevier... Asian Journal of Urology (2018) 5, 205-214]
3. Sasaki S, Tomiyama Y, Kobayashi S, et al. Characterization of $\alpha 1$ -adrenoceptor subtypes mediating contraction in human isolated ureters. *Urology* 2011;77(3):762.e13.
4. Priyanka, Ravikumar R. Jadhav Comparison between Tamsulosin and Silodosin in lower ureteric stone- a randomised controlled study [Journal of Evolution of Medicine and Dental sciences. Vol. 6/ Issue 93/ Dec. 11, 2017]
5. Sakip Erturhan, MD; Omer Bayrak, MD; Ahmet Mete, MD, Ilker Seckiner, MD; Gokhan Urgun, MD; Kemal Sarica, MD Can the Hounsfield unit predict the success of medically expulsive therapy? [Canadian Urological Association Journal • November-December 2013 • Volume 7, Issues 11-12 © 2013]
6. Parisa Sotoodeh Shahnnani, Mehdi Karami, Bahman Astane, and Mohsen Janghorbani The comparative survey of Hounsfield units of stone composition in urolithiasis patients [NCBI(PubMed).....Journal of Research in Medical Sciences, 2014 Jul; 19(7): 650–653]

7. Saba Fakhreddini, Ritty Sara Cherian Comparison of Therapeutic Efficacy and Safety of Combination Therapy of Antimuscarinic Drugs and Alpha Blockers Versus Mono Therapy in the Treatment of Urolithiasis in A Tertiary Care Hospital, Bangalore, India [Journal of Biochem Tech (2018) Special Issue (2): 127-131]
8. Shahida Banu Shamsuddeen, Dr. Rafia Bano, Dr. Eyad Al Shammari, Shamaah Huseen Al Enezi Risk Factors of Renal Calculi [ResearchGate..... Journal of Dental and Medical Sciences Volume 11, Issue 6 (Nov.- Dec. 2013), PP 90-95]
9. Hazem Elgalaly, Ahmed Sakr, Amr Fawzi, Emad A. Salem, Esam Desoky, Ashraf Shahin, Mostafa Kamel Silodosin vs Tamsulosin in the management of distal ureteric stones: A prospective randomised study [Science direct..... Arab Journal of Urology (2016) 14, 12–17]
10. Sandeep Gupta, Bijit Lodh, Akoijam Kaku Singh, Khumukcham Somarendra, Kangjam Sholay Meitei, Sinam Rajendra Singh Comparing the Efficacy of Tamsulosin and Silodosin in the Medical Expulsion Therapy for Ureteral Calculi. [Journal of Clinical and Diagnostic Research. 2013 Aug, Vol-7(8): 1672-1674]
11. Md Jawaid Rahman, M. Shazib Faridi, Naloh Mibang, Rajendra Sinam Singh Comparing tamsulosin, silodosin versus silodosin plus tadalafil as medical expulsive therapy for lower ureteric stones: A randomised trial. [Science direct..... Arab Journal of Urology (2018) 16, 245–249]
12. Chung-Jing Wang, M.D., Shi-Wei Huang, M.D., and Chien-Hsing Chang, M.D. Efficacy of an $\alpha 1$ Blocker in Expulsive Therapy of Lower Ureteral Stones. [JOURNAL OF ENDOUROLOGY Volume 22, Number 1, January 2008]
13. Sandeep Puvvada, Prasad Mylarappa, Kuldeep Aggarwal, Avinash Patil, Prarthan Joshi, Ramesh Desigowda Comparative efficacy of tadalafil *versus* tamsulosin as the medical expulsive therapy in lower ureteric stone: a prospective randomized trial [Central European Journal of Urology 2016; 69: 178-182 Published online: June 20, 2016]
14. Mustafa Yukse11, Serdar Yilmaz, Husnu Tokgoz, Soner Yalcinkaya, Serkan Bař, Tmy Ipekci, Ali Yildiz, Nihat Ates, Murat Savas Efficacy of silodosin in the treatment of distal ureteral stones 4 to 10 mm in diameter. [International Journal of Clinical and Experimental Medicine 2015; 8(10):19086-19092]
15. Hussein A. Aldaqadosi, Hossam Shaker, Mohammed Saifelnasr, Mohammed Gaber Efficacy and safety of tamsulosin as a medical expulsive therapy for stones in children [Arab Journal of Urology, Official Journal of the Arab Association of Urology]
16. M. Alizadeh & M. Magsudi The Effect of Tamsulosin in the Medical Treatment of Distal Ureteral Stones [Science direct...Global Journal of Health Science; Vol. 6, No. 7; 2014]
17. Jeremy S. Furyk, MBBS MPH&TM; Kevin Chu, MBBS MS; Colin Banks, MBBS; Jaimi Greenslade, PhD; Gerben Keijzers, MBBS PhD; Ogilvie Thom, MBBS; Tom Torpie, MBBS; Carl Dux, MBBS Distal Ureteric Stones and Tamsulosin: A Double-Blind, Placebo-Controlled, Randomized, Multicentre Trial [Elsevier.....American College of Emergency Medicine 2016;67:86-95]
18. A.S. Abdelaziz, A.M. Kidder Tamsulosin therapy improved the outcome of ureterorenoscopy for lower ureteral stones: A prospective, randomised, controlled, clinical trial [African Journal of Urology (2017) 23, 148–153]
19. Ralph C. Wang, MD, MAS; Rebecca Smith-Bindman, MD; Evans Whitaker, MD, MLIS; Jersey Neilson, BS; Isabel Elaine Allen, PhD; Marshall L. Stoller, MD; Jahan Fahimi, MD, MPH Effect of Tamsulosin on Stone Passage for Ureteral Stones: A Systematic Review and Meta-analysis [Volume 69, no. 3 : March 2017 Annals of Emergency Medicine pg no.352-367]
20. Wei Huang, Peng Xue, Huantao Zong, & Yong Zhang Efficacy and safety of silodosin in the medical expulsion therapy for distal ureteral calculi: a systematic review and meta-analysis [British Journal of Clinical Pharmacology / 81:1 /pg no. 13–22]
21. Andrew L. Schwaderer, Rupesh Raina, Anshika Khare, FayeZ Safadi, Sharon M. Moe and Kirsten Kusumi Comparison of Risk Factors for Paediatric Kidney Stone Formation: The Effects of Sex [Science direct... Frontiers in Pediatrics February 2019 | Volume 7 | Article 32]
22. Nagesha Shivanna, Abhishek Kumar Singh, Prateek Jugalkishore Laddha The Efficacy of Tamsulosin as Medical Expulsion Therapy in Ureteric Calculus of <8 mm Size [Science direct....Journal of Datta Meghe Institute of Medical Sciences University ,Volume 13, Issue 4,October-December 2018]
23. Michael Lipkin, MD, Ojas Shah, MD The Use of Alpha-Blockers for the Treatment of Nephrolithiasis [VOL. 8 SUPPL. 4 2006 REVIEWS IN UROLOGY]