The Egyptian Journal of Hospital Medicine (January 2019) Vol. 74 (6), Page 1377-1386

Evaluation of Silodosin in Comparison to Tamuslosin in Treatment of Benign Prostatic Hyperplasia with lower Urinary Tract Symptoms: A Prospective Study

Mohammed H. M Mousa, El Sayed M. Salih, El Sayed M. Mousa.
Department of Urology, Faculty of Medicine, Al-Azhar University**,** Cairo, Egypt
*Corresponding author: Mohammed H. M Mousa, E-mail: mohammedhassan8181@Gmail.com

ABSTRACT

Background: benign prostatic hyperplasia represents one of the main fields of urology.

objective: aim of the study to verify the efficacy and safety of the alfa one adrenoreceptor blocker silodosin compared with tamsulosin in patients with lower urinary tract symptoms associated with bph.

patients and methods: outcomes were assessed by change from baseline in ipss, quality of life (qol), qmax, pvr. responders to the treatments on the basis of ipss decrease ≥ 25% and qmax increase ≥ 30% were calculated.

results: silodosin and tamsulosin significantly improved ipss total score in (p=0.625). both no statistically significant difference. improved qol (p<0.505) both no statistically significantly difference between both improved qmax (p<0.633). silodosin and tamsulosin no statistically significantly. improved pvr; there no statistically significantly difference between both (p<0.0001). in silodosin group, a retrograde ejaculation was reported in 25 patients from 40 patients were sexually active (62.5%). while in tamsulosin group, a retrograde ejaculation was reported in 1 patient from 41 patients sexually active (2.4%).

conclusions: silodosin is not only comparable to tamsulosin in treatment of luts/bph, with safety. however, retrograde ejaculation troublesome for sexually active patients.

keywords: silodosin, tamsulosin, benign prostatic hyperplasia, lower urinary tract symptoms, quality of life, α-1a adrenergic receptors.

INTRODUCTION

Lower urinary tract symptoms (LUTS) are a common problem of aging males. Benign prostatic hyperplasia (BPH) is the most common cause of LUTS in elderly men over 70 years of age. BPH, usually, starts in men in their 50s; by the age of 60 years, 50% of men have histological evidence of BPH and 80% of men in their 70s suffer from BPH-related LUTS **(1).**

Symptomatic BPH is characterized by a mix of obstructive and irritative symptoms, collectively known as prostatism. The former include difficulty in initiation of micturition (hesitancy), poor or interrupted flow, post-void dribbling, and sensation of incomplete voiding that can manifest (urge to revisit the toilet immediately after voiding). The latter includes frequency of micturition, nocturia, dysuria and urgency or even urge incontinence **(1).**

The former category is expected to provide relatively rapid symptom relief starting within 2-6 weeks, while the latter acts more slowly restricting the hyperplasia, and taking 6 months or longer to produce symptom relief **(1).**

Alfa-blockers are now considered as first-line drugs in the medical management of BPH. Silodosin; an α_{1A}-adrenoceptor blocker is said to be highly selective for this receptor subtype. Our objective is to compare the effectiveness and safety of silodosin in elderly men with BPH, in comparison to the older *established α_1-blockerTamsulosin* **(1).**

The definitive management of symptomatic BPH is surgery to relieve the obstruction imposed by the enlarged portion of the prostate. However, apart from invasiveness, there are potential complications of surgery, including the unfortunate development of permanent urinary incontinence **(2).**

AIM OF THE STUDY

The aim of the study is to verify the efficacy and safety of the Alfa one adrenoreceptor selective antagonist silodosin compared with tamsulosin in patients with lower urinary tract symptoms associated with Benign prostatic hyperplasia (BPH)**.**

PATIENT AND METHODS

- Prospective Randomized Study.

Study population patient's selection: patient with lower urinary tract symptoms (LUTS) associated with BPH attending to our urological department at Al-Hussin University hospital and Al Harm hospital with type patients Men ≥50 with BPH

- Target sample is 100 patients
- Patients included in this study were introduced into two group :

Group A: patients were treaetd by silodosin 8 mg for 3 months.

Group B: patients were treated by tamsulosin 0.4 mg for 3 months.

Received:23/10/2018
Accepted:12/11/2018

Inclusion criteria:

1) Men ≥50 with BPH with LUTS
2) IPSS ≥ 8
3) QoL ≥ 3
4) Prostate size ≥25 ???
5) Qmax ≤ 15 voided volume ≥ 120 ml
6) PSA < 4 ng/dl

Exclusion criteria

1) Urethral stricture
2) Antiandrogen therapy patients must stopped 1 year ago
3) Post prostatectomy
4) Prostatic cancer
5) Bladder cancer
6) Stone bladder
7) Neurogenic bladder

Patient Evaluation:

1. patients were randomized to receive oral silodosin 8 mg/day, tamusulosin 0.4 mg/day for 12 week,
2. At 2, 4, 12 weeks during the treatment period subjective symptoms (IPSS) and QOL score and medication compliance were recorded and physical examination.
3. Uroflowmetry and urine analysis were done at 4 and 12 weeks of treatment
4. All patients provided written informed concent to participate before study entry.

Clinical Assessment:

Full medical history, including the International Prostate Symptom Score (IPSS) questionnaire and question 8 about quality of life related to urinary symptoms (IPSS-QoL), was used. The IPSS is a validated instrument widely used for the assessment of symptom severity in patients with BPH. The total score was taken as the sum of 7 individual symptom scores of questions (1-7), the score of ≥13 was used as a cut off point for inclusion in the study. Also history of concomitant conditions and medications was taken. Sexual history was taken, the patients were asked about if either ejaculatory dysfunction (EjD) or erectile dysfunction (ED) already present before the study, or not.

Clinical examination including:

General examination was done; systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured as a pretreatment baseline with the subject supine at rest for at least 5 minutes before measurements. A test for postural hypotension (measurements of SBP and DBP during supine position and after standing) was performed (orthostatic test). Abdominal examination was done to detect any scares, swellings or tenderness. A digital rectal examination (DRE) was done to assess the prostate size and consistency, and assess anal tone to exclude any accompanying neurological diseases affecting the normal bladder filling and emptying.

- **Laboratory Investigation:**

A. Urinalysis was done to exclude concurrent infection.

B. PSA was done to exclude malignancy or acute prostatitis, and also recorded as a pretreatment baseline.

- **Radiological & Imaging studies:**

A. U/S Abdomen & pelvis to assess the upper urinary tract and estimation of PVR as a pretreatment baseline (volume of >120ml were excluded).

- **Uroflowmetry Assessment:**

Uroflowmetry illustrating peak urine maximum flow rate (Q_{max}) and voided volume was done, using standard calibrated devices and a voided volume of at least 120ml needed to be obtained for a valid assessment. Patients with Qmax less than 4ml/sec or more than 15ml/sec were excluded.

Subjects who met the selection criteria were randomized to two groups; A and B in a ratio of 1:1. They took either silodosin 8mg capsule, tamsulosin 0.4mg capsule, respectively, all of medications taken once daily after breakfast for 12 weeks.

The capsules were removed from their commercial blister strip packaging and repackaging in air-tight, screw cap containers and suitably labeled and coded as trial medication. Repackaging was done with the help of residents not otherwise involved in the study. Capsule identity was not revealed to the patients, or the investigators, for the entire duration of the study.

Follow up:

Patients were followed up at 2 and 8-week from the start of the treatment, with the final study visit being at 12-week.

2nd visit (2weeks after treatment):

A. Reassessment of IPSS total score, IPSS-QoL score, and changes from pretreatment baseline were reported.

B. SBP, DBP, and, and changes from baseline were reported. Orthostatic test was performed to detect the presence of postural hypotension or not, after 4weeks from receiving the treatment.

C. The appearance of new unfavorable and unintended signs, symptoms, or diseases or worsening of conditions already present at baseline before the study (like retrograde ejaculation, dizziness, headache, gastric upset, etc.) were considered as treatment-emergent adverse events (TEAEs) and reported at each visit.

D. PVR was assessed by U/S Abdomen & pelvis done to all patients; changes from pretreatment baseline were estimated.

E. Q_{max} was assessed by Uroflowmetry done to all patients; changes from pretreatment baseline were estimated.

3rd visit (4weeks after treatment):

The same clinical, radiological and uroflowmetry assessments done in the 2nd visit were done again to all patients 4weeks after treatment. With regard to assess Q_{max} 2-6 hours postdose.

4th visit (12weeks after treatment):

The same clinical, radiological and uroflowmetry assessments done in the 3rd visit were done again to all patients 12weeks after treatment. Besides to all laboratory investigations

At endpoint of the study, the patients who showed a decrease from baseline ≥25% of total score of IPSS were considered treatment responders by IPSS, and their percentages were calculated in each group. Also the patients who showed an increase from baseline ≥30% in Q_{max} were considered treatment responders by Q_{max}, and their percentages were calculated in each group.

The study was approved by the Ethics Board of Al-Azhar University.

Statistical analysis

The overall patient's data of the entire study were collected in special Excel sheet. Data entry and analysis were all done with IBM compatible computer using software SPSS version 21. Graphics were done using Excel.

Quantitative data were presented as mean and standard deviation, while qualitative data were presented as frequency distribution. Independent samples t-test was used.

The probability (p value) of less than 0.05 was used as a cut off point for all significant tests.

RESULTS

A total 100 patients were randomized to two groups, 50 patients received silodosin 8 mg (**A**) and the other 50 patients received tamsulosin 0.4 mg (**B**). No statistically significant difference between the two groups with regard to age, as shown in table (1):

Table (1): Ranges of ages in the two groups total 100 patients.

GROUP		No.	Minimum	Maximum	Mean	Standard Deviation
A (silodosin group)	Age	50	50	80	62.77	6.22
B (tamsulosin group)	Age	50	50	73	62.97	5.82

Half of the patients of the two groups have ages ranging from 60yrs to 70yrs,

At screening, 14 patients from the total 100 were known as hypertensive patients and on concomitant antihypertensive medications from history taking. And on assessment, 4 patients from the total subjects presented with elevated blood pressure (≥ 145 mmHg).

Table (2): Summary of the baseline characteristics of the total 100 patients screened in the two study groups

Parameter	Silodosin group	Tamsulosin group
IPSS		
Mean	18.18	18.10
Range	16-21	15-22
IPSS-QoL		
Mean	4.8	4.7
Range	2-7	1-7
Qmax(ml/sec)		
Mean	9.6	10.6
Rang	5-14	6-14
PVR (cc)		
Mean	72.75	87.8
Range	25-145	45-145
Diabetes mellitus		
N. (%)	7 (17. 5%)	6 (15%)
Sexually active	45	47
Sexually inactive	5	3

EFFICACY RESULTS

The International Prostatic Symptom Score (Ipss)

International prostatic symptom score **IPSS** was assessed for all patients (100 patients) came to this study in the two groups throughout four visits, and the results were as follows in table (3):

Table (3): The overall four visits records of IPSS among total 100 patients in the two groups A, B

GROUP		No.	Range	Mean	Std. Deviation
A	IPSS1 (baseline)	50	16-21	18.18	1.430
	IPSS2 (2 weeks)	50	9-20	13.45	2.855
	IPSS3 (4 weeks)	50	7-- 19	12.30	2.972
	IPSS4 (12 weeks)	50	6--18	11.15	3.25
B	IPSS1 (baseline)	50	15--22	18.10	1.692
	IPSS2 (2 weeks)	50	9-- 20	13.35	3.270
	IPSS3 (4 weeks)	50	8--19	12.18	3.265
	IPSS4 (12 weeks)	50	6--17	11.40	3.485

P. Value 0.625

- There was a decrease in the total **IPSS** in two groups, with the largest decrease in the **IPSS** total score occurred rapidly, within the first 2 weeks of treatment chart (1).

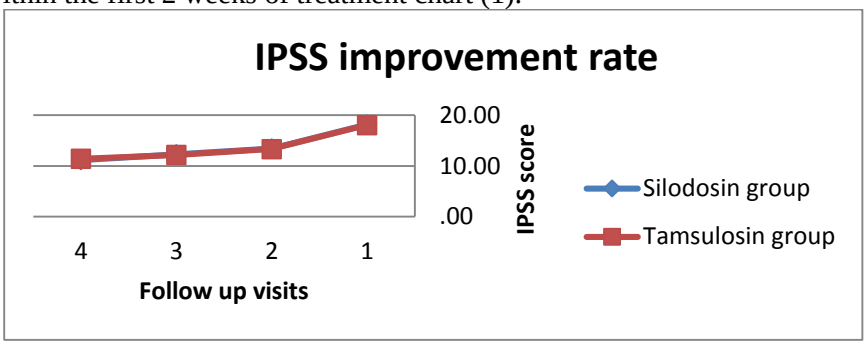

Chart (1): IPSS improvement rate in the two group total 100 patients

- The adjusted mean changes from baseline to endpoint of the study in the total IPSS of the patients in each group, the differences between both active treatments groups were estimated.
- The mean change from baseline to endpoint in IPSS for patients of silodosin group (A) was [-7.025], while was [-6.7] for tamsulosin group (**B**), with statistically non-significant difference (p=0.625).

Table (4): Comparison of IPSS changes from baseline to endpoint of the study between the total 100 patients groups A and B (based on adjusted means).

Items	Group A (silodosin)	Group B (tamsulosin)
Patients no.	50	50
Change from baseline to endpoint(adjusted means).	-7.025	-6.7
Standard Deviation.	3.1	2.7
Mean Difference (between the two groups) (95% CI)	-0.325 (-1.64, 0.99)	
Significance (p-value)	0.625*	

*Non-significant [**Equivalency sign**] CI = Confidence Interval

The percentage of **IPSS** treatment responders (defined by decrease ≥25% from baseline) at study end, were67.5%and 62.5%of the patients receiving silodosin or tamsulosin, respectively, the comparison between silodosin and tamsulosin didn't show a statistically significant difference.

Table (5): Responder rates according to total IPSS in the two group total 100 patients

Group	esponders no. (Decrease from baseline≥25%)	n- responders no. (Decrease from baseline <25%)	Percentage of responders
Silodosin group)	33	17	**67.5%**
Tamsulosin group	32	18	**62.5%**

P value 0.888 (Non significant)

Quality of life related to urinary symptoms (IPSS-QoL)

The question 8 of IPSS questionnaire about quality of life related to urinary symptoms (IPSS-QoL) were assessed for all patients in the two groups total 100 patients throughout **at 4week and 12 weeks**, and the results were as follows in:

Table (6): The overall at4week and 12 week visits records of IPSS-QoL among patients of the two groups A, B total 100 patients

	GROUP	No.	Range	Mean	Std. Deviation
A	**QoL 3 (4 weeks)**	**50**	**1-5**	**3.36**	**1.388**
	QoL 4 (12weeks)	**50**	**1-5**	**2.53**	**1.377**
B	**QoL 3 (4 weeks)**	**50**	**1-6**	**3.26**	**1.485**
	QoL 4 (12 weeks)	**50**	**1-6**	**3.63**	**1.599**

P. value 0.505

There was a decrease in the **IPSS-QoL** in two groups, but there was no plateau in response. Chart (2):

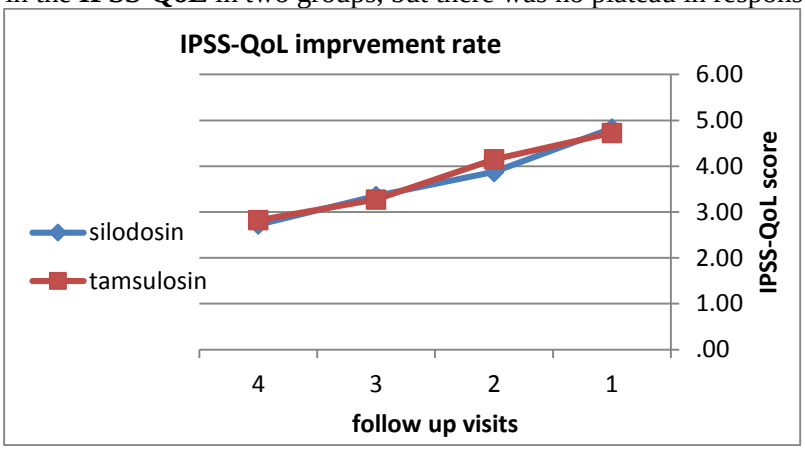

Chart (2): IPSS-QoL improvement rate in the two groups.

The adjusted mean changes from baseline to endpoint of the study in the **IPSS-QoL** of the patients in each group.

- The mean change from baseline to endpoint in **IPSS-QoL** for patients of silodosin group **(A)** was [-2.1], while was [-1.9] for tamsulosin group (**B**), with no statistically significant difference (p=0.505). Table7):

Table (7): Comparison of IPSS-QoL score changes from baseline to endpoint of the study between total 100 patients the two groups A and B (based on adjusted means)

Items	Group A (Silodosin group)	GroupB (Tamsulosin group)
Patients no.	50	50
Change from baseline to endpoint (adjusted means).	-2.1	-1.9
Standard Deviation.	1.335	1.335
Mean Difference (between the two groups)(95% CI)	-0.2 (-0.79, 0.39)	
Significance(p-value)	0.505*	

* Non-significant [**Equivalency sign**] CI = Confidence Interval

The maximum flow rate (Qmax)

The maximum flow rate **Qmax** (milliliters per second) for all patients of the two groups were measured throughout **at 4 weeks and 12 weeks**, and the results were as follows in table (8):

Table (8): The overall at4week and 12 week measurements of Qmax among total 100 patients of the two groups of the study A, B.

	GROUP	N	Range	Mean	Std. Deviation
A	**Qmax 1 (4w eeks)**	50	6-16	11.65	2.597
	Qmax 2 (12weeks)	50	6-20	13.48	3.266
B	**Qmax 1(4weeks)**	50	9-18	12.43	2.571
	Qmax 2 (12weeks)	50	10-20	14.15	3.026

P. value 0.633

There was an increase in Qmax in the two active treatment groups the increase was more prominent and rapid. Chart (3):

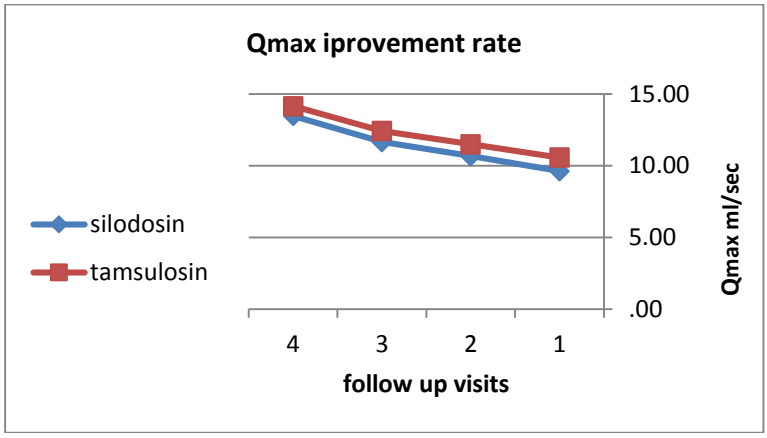

Chart (3): Qmax improvement rate in the two groups total 100 patients

The adjusted mean changes from baseline to endpoint of the study in the **Qmax** for the patients in each group, the differences between both active treatment groups were estimated. A large increase from baseline in **Qmax** was observed for both active treatment groups and there was no statistically significant.

The mean change from baseline to endpoint in **Qmax** for patients of silodosin group (**A**) was [3.75], while was [3.575] fortamsulosin group (**B**), with non-significant difference (p=0.633). Table (9):

Table (9): Comparison of Qmax changes from baseline to endpoint of the study between the two groups A and total 100 patients B (based on adjusted means)

Items	Group A (Silodosin group)	roup B (Tamsulosin group)
Patients no.	50	50
Change from baseline to endpoint(adjusted means)	3.75	3.57
Standard Deviation.	1.78	1.46
Mean Difference (between the two groups) (95% CI)	0.17 (-0.55, 0.9)	
Significance (p-value)	0.633*	

*Non-significant **[Equivalency sign]** CI = Confidence Interval

The percentage of **Qmax** treatment responders (defined by increase ≥ 30% from baseline) at study end, were 52.5% and 50% of the patients receiving silodosin and tamsulosin, respectively, whereas the comparison between both active groups didn't show a statistically significant difference. Table (10):

Table (10): Responder rates according to Qmax in the two study groups A, B total 100 patients

Group	Responders no. (Decrease from baseline≥30%)	Non- responders no. (Decrease from baseline < 30%)	ercentage of responders %
A (Silodosin group)	26	24	**52.5%**
B (Tamsulosin group)	25	25	**50%**

p value < 0.633.

The post-void residual urine (PVR)

The post-void residual urine (PVR) was assessed for all patients in the two groups throughout **at 4 weeks and 12 weeks**, and the results were as follows in table (11):

Table (11): The overall at 4 week and 12 weeks assessment of PVR among total 100 patients of the two groups of the study

GROUP		No.	Range	Mean	Std. Deviation
A	**PVR 1(4weeks)**	50	5-75	27.50	19.987
	PVR 2(12weeks)	50	5-60	20.33	16.381
B	**PVR 3(4weeks)**	50	35-125	73.88	19.398
	PVR 4(12weeks)	50	30-120	70.75	19.662

There was a decrease in PVR in all groups, but the largest decrease in PVR was in silodosin group and occurred rapidly, within the first 6 weeks of treatment. Chart (4):

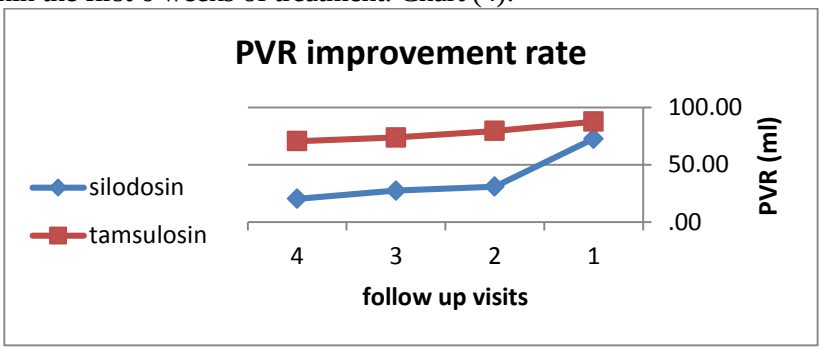

Chart (4): PVR improvement rate in the two groups total 100 patients

Safety results

Treatment-emergent adverse events (TEAEs)

The most frequently reported treatment-emergent adverse events TEAEs were retrograde ejaculation, headache and postural hypotension.

Retrograde ejaculation

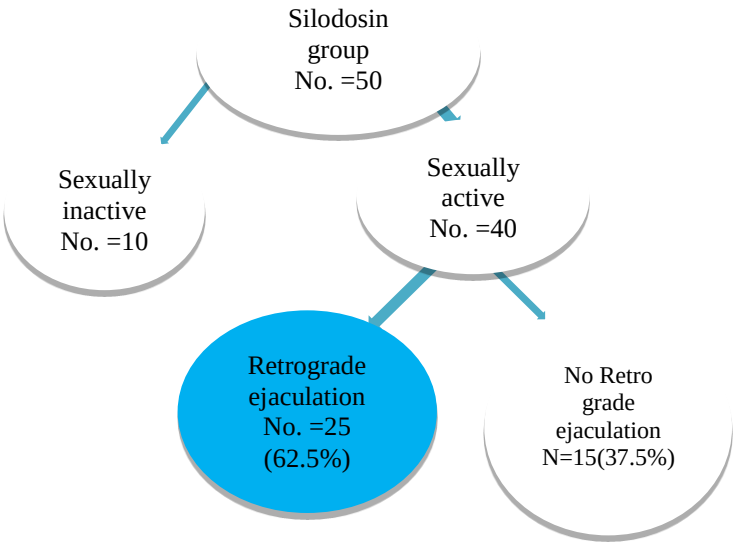

Figure (1): Retrograde ejaculation

The term retrograde ejaculation covers a broad spectrum of patients reported events of abnormal ejaculation, including the absence seminal emission, reduced ejaculate volume, and reduced ejaculation force. Relaxation of the bladder neck muscle secondary to α_{1A}-adrenoreceptor blockade leads to backflow of seminal fluid from the prostatic urethra into the bladder**.**

- In silodosin group, a retrograde ejaculation was reported in 25 patients from 40 sexually active patients (62.5%).
- In tamsulosin group, a retrograde ejaculation was reported in 1 patient from 41 patients were sexually active (2.8%).
- There was a statistically significant difference in the incidence of retrograde ejaculation emergence between both active treatment groups A and B (*p Value* =0.002).

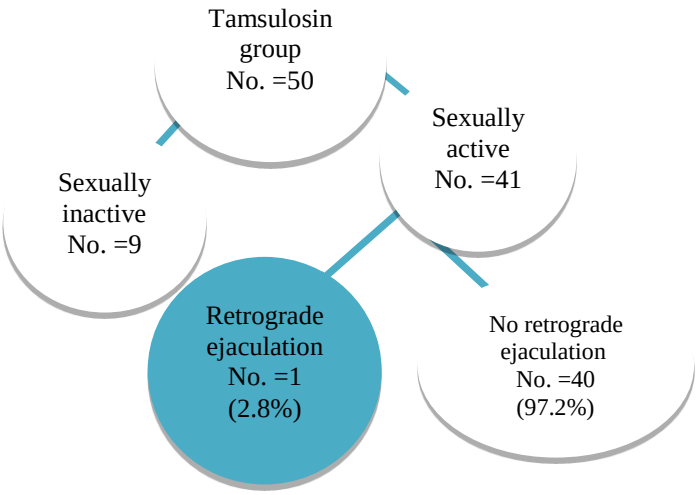

Figure (2): Retrograde ejaculation

DISCUSSION

Benign prostatic hyperplasia (BPH) contributes to, but is not the single cause of, bothersome lower urinary tract symptoms (LUTS) that may affect quality of life [(1)].

In clinical practice, patients are treated for LUTS suggestive of bladder outlet obstruction (BOO) due to BPH, often called ʹLUTS/BPHʺ[(1)].

Recetor binding studies show that the affinity of silodosin for the α_{1A}-adrenergic receptor is 162 times higher than that for the α_{1B}-adrenergic receptor, and 55 times higher than that for the α_{1D}-adrenergic receptor [(3)].

Although safety and efficacy of drugs are expected to be established prior to marketing, there is a concern about evaluating drugs further in the post-marketing phase. Since silodosin has been introduced into the Egyptian market recently and is reported to be highly selective for the α_{1A}-adrenoreceptor blocker, we sought to assess whether a newly introduced drug is offering any clinical advantage compared to the older drug tamsulosin regarding the safety and the efficacy or not.

Published studies from other countries reported that silodosin is comparable to tamsulosin in the management of BPH [(4)]. A large, international, randomized, double-blind, placebo- and active-controlled clinical trial performed in 72 European centers was conducted by [(4)], a total of 955 patients were randomized (2:2:1) to silodosin 8 mg (no.=381), tamsulosin 0.4 mg (no.=384), or placebo (no.=190) once daily for 12 weeks. Regarding the efficacy in the European study, it was found that the change from baseline in the **IPSS** total score with both silodosin and tamsulosin was significantly superior to that with placebo. Difference between two drug was [-2.3] with silodosin and [-2] with tamsulosin, almost the same of our study **IPSS** changes. Responder rates according to total **IPSS** (in European study) were significantly higher with silodosin (66.8%) and tamsulosin (65.4%), compared to (67.5%), (62.5%), in our recent study.

Also it was found that the changes from base line in the **QoL** due to urinary symptoms (question 8 of IPSS) with silodosin, tamsulosin were (-1.1, -1.1, respectively), with no statistically significant differences between two treatments at all weeks (at endpoint $p = 0.002$) in**.** [(4)] study's, whereas our study revealed the changes in **IPSS-QoL** with silodosin, tamsulosin were (-2.1, -1.9 respectively), with highly statistically significant differences more than that in the European study, which is explained by the tendency of our Egyptian patients to the medical treatment rather than other invasive interferences making them highly sensitive to any positive effects on their life.

In the European study by [(4)], there was a large increase from baseline in the maximum flow rate (**Qmax**) for both active treatment groups compared with placebo but, unlike our study both active treatment groups compared without placebo, was not statistically significant. The percentage of **Qmax** responders was larger for the silodosin and the tamsulosin treatment groups but, also unlike our study, was not statistically significant (46.6% for silodosin,), (46.5% for tamsulosin). The lack of significant difference as compared with placebo in European study could be explained by a higher than expected placebo response**.**

While in our study, a large increase from baseline in **Qmax** was observed for both two treatment groups and was statistically significant. The mean change from baseline to endpoint of the study was [3.75 ml/s] for patients of silodosin group **(A),** with highly statistically significant difference ($p< 0.633$). The mean change from baseline to endpoint in **Qmax** for patients of tamsulosin group (**B**) was [3.57 ml/s with highly significant difference ($p < 0.633$). The percentage of $\mathbf{Q_{max}}$ treatment responders at study end,

were 52.5% and 50% of the patients receiving silodosin and tamsulosin, respectively.

Our study results in Qmax were compatible with the results described from two phase studies which were performed by [6] in the United Sates on the safety and efficacy of silodosin, these results similar to our results of Qmax changes. The two 12-week studies were identically designed, parallel grouped, multicenter, randomized, double-blind and placebo-controlled. in this study, 923 patients (mean age=65 years) included, 466 patients received silodosin, and 457 patients received the placebo. The primary endpoint was a change in the IPSS.

From baseline at the last observation; the secondary endpoint was a change in Qmax. The mean change from baseline in the Qmax at 2-6 hours after the initial dose was greater ($p < 0.0001$) with silodosin (2.8±3.4) than with the placebo (1.5±3.8). Differences remained significant ($p< 0.001$) for the 12 weeks [6].

Also, our Qmax changes were compatible with what revealed by [7] who performed the first phase ш randomized, study at 88 Japanese centers, 457 patients were randomized into two groups as179 patients received silodosin 4mg twice daily, 192 patients received tamsulosin 0.2 once daily, and 89 patients received the placebo for 12 weeks. According to the **Qmax** changes in the original study, silodosin did not show a significant improvement in the **Qmax** compared to the placebo. The authors have speculated that the great changes in voiding volume before and after treatment in some men may have affected the results owing to the fact that Qmax depend on the voided volume at measurement. Therefore, a subsequent analysis was conducted in subgroup of patients whose difference of voided volume between pre- and after treatment was less than 50%. In this analysis the improvement in Qmax from baseline was significantly greater in the silodosin group compared with the placebo group ($P= 0.005$), with mean changes from baselineof 1.7, 2.6, and 0.26 mL/sec in the silodosin, tamsulosin, and placebo groups, respectively [7].

These findings are confirmed by our study's results in **PVR** changes, as there was a significant decrease in sliodosin group (A) was greater than that in tamsulosin group (B). The mean change from baseline to endpoint in **PVR** for patients of silodosin group (A) was [-52.32], while the mean change from baseline to endpoint in **PVR** for patients of tamsulosin group(B) was [-17.05], [1]concluded that the overall efficacy of silodosin is not inferior to tamsulosin, whereas our results in the recent study revealed the superiority of silodosin to tamsulosin in most of the efficacy parameters.

In our study, silodosin proved to be an effective drug for the treatment of LUTS/PBH because a statistically significant and potentially clinically relevant was observed in the IPSS total score, **QoL-IPSS**, **Qmax**, and **PVR**. The improvement became evident soon after the initiation of therapy and remained for the 12 weeks.

This treatment effect with silodosin appeared to be not only equivalent to, but also greater than that seen with tamsulosin in most of efficacy results.

Regarding safety in our study, no clinically meaningful changes or unfavorable effects were recorded for any of (silodosin or tamsulosin).

The most frequently reported treatment-emergent adverse event (TEAE) was retrograde ejaculation, the percentages were (62.5.%) in silodosin group and (2.8%) in tamsulosin group, and it is not perceived as particularly bothersome leading to discontinuation of our current study, as confirmed by [1]whose results were very low discontinuation rates in silodosin group and comparable with placebo, only 1.3% of silodosin-treated patients discontinued treatment due to retrograde ejaculation [4].

Although 25 patients from of the 40 patients who reported retrograde ejaculation in our current study discontinued the treatment, some patients experienced frustration with this symptom. Therefore, patients should be educated on the adverse effects of silodosin treatment.

A subsequent analysis to results of the two studies conducted by [6] suggested that Ejaculatory dysfunction may be a predictor of the efficacy of the α_{1A}-adrenoreceptor blockade. Roehrborn and colleagues found that 62.5% of patients in these studies experienced Ejaculatory dysfunction and reported that these patients experienced a greater improvement in symptoms and a clinically meaningful greater improvement in flow rate than those who did not experience Ejaculatory dysfunction [1].

Another similar analysis was conducted to evaluate improvement in symptoms in the Japanese study by [7], suggested that the existence of ejaculatory disorder was correlated with the magnitude of symptom improvement in the patients treated with silodosin [8].

The second most frequently treatment-emergent adverse event (TEAE) reported in our current study was headache, with percentages of 2.5% for silodosin (only one patient) and 7.5% for tamsulosin (three patients). These results were similar to that recorded by [4], which were 2.9% for silodosin and 5.5% for tamsulosin.

Also postural hypotension reported in 3 patients from 50 patients in tamsulosin group, and none in silodosin group.

CONCLUSION

- Overall the study, all the efficacy parameters used, the International Prostate Symptom Score (**IPSS**), Quality of life due to urinary symptoms (**IPSS-QoL**), maximum urinary flow rate ($\mathbf{Q_{max}}$), and post-void residual urine (**PVR**) seemed to be significantly improved with silodosin. The improvements with silodosin treatment were at least equivalent to and numerically greater than that seen with tamsulosin treatment. A major advantage of silodosin was the lack of clinically relevant or statistically changes in blood pressure or heart rate. Silodosin and tamsulosin were well tolerated. However, retrograde ejaculation may be troublesome for sexually active patients received silodosin.

REFERENCES

1. **Roehrborn CG and McConnell JD (2009):** Etiology, pathophysiology, epidemiology and natural history of benign prostatic hyperplasia. In: Walsh PC, Retik AB, Vaughan ED Jr, Wein AJ, editors. Campbell's Urology. 8th ed. Philadelphia: WB Saunders Co, p: 1279-1336.
2. **Reznicek SB (2000):** Common urological Problems in the elderly. Prostate cancer, outlet obstruction, and incontinence require special management. postgrad Med.,107: 163-167.
3. **Yoshida M, Kudoh J, Homma Y and Kawabe K (2011):** Safety and efficacy of silodosin for the treatment of benign prostatic hyperplasia. Clinical Interventions in Aging ,6:161-172.
4. **Tatemichi S, Kobayashi Y, Maezawa A, Kobayashi M, Yamazaki Y, Shibata N (2006):** Alpha1-adrenoceptor subtype selectivity and organ specificity of silodocin . Yakugaku zasshi,126:209-216.
5. **Chapple CR, Montorsi F,TammelaTL, Wirth M, Koldewijn E, Fernandes Fernandes E, European Silodosin Study Group (2011):** Silodosin therapy for lower urinary tract symptoms in men suspected benign prostatic hyperplasia: results of an international, randomized, double-blind, placebo- and active-controlled clinical trial performed in Europe. European Urol., 59:342-352.
6. **Marks LS, Gittelman MC, Hill LA, Volinn W, Hoel G (2009):** Rapid efficacy of the highly selective alpha 1A-adrenoreceptor- selective antagonist silodosin in men with signs and symptoms of benign prostatic hyperplasia: pooled results of 2 phase3 studies. J Urol., 181:2634-40.
7. **Kawabe K, Yoshida M, Homma Y (20060):** Silodosin clinical study group. Silodosin, a new alpha 1A-adrenoreceptor –selective antagonist for treating benign prostatichyperplasia: results of phase ш randomized, placebo-controlled, double-blind study in Japanese men. BJU Int.,98:1019-24.
8. **Homma Y, Kawabe K, Takeda M, Yoshida M (2010):** Ejaculation disorder is associated with increased efficacy of silodosin for benign prostatic hyperplasia. Urology, 76:1446-50.