Does symptomatic improvement in IPSS & IIEF Scores correlates with objective changes in urodynamic parameters amongst patients with symptomatic BPH following tamsulosin/tadalafil monotherapy or combination of both? : A Prospective Study.



Does symptomatic improvement in IPSS & IIEF Scores correlates with objective changes in urodynamic Materials and methods combination of both? : A Prospective Study.

Introduction and objective

Erectile dysfunction (ED) and LUTS are highly prevalent and often coexist in the elderly with BPH. Recent studies have shown the The three groups were comparable. The mean age was 61.82 ± 8.794 years with mean duration of LUTS were 2.51 ± 1.576 efficacy of phosphodiesterase5 (PDE5) inhibitors alone and in combination with alpha-adrenergic blockers in managing lower years. A statistically significant change in IPSS score $[7.93 \pm 6.90 (p = .001)$ in Group A, $7.00 \pm 5.59 (p = .000)$ in Group B and urinary tract symptoms. Although clinical benefit of PDE5 inhibitors has been shown, urodynamic data regarding the effect of 5.80 ± 5.51 (p = .001) in Group C] was observed. However, there was no significant difference on intergroup comparison PDE5 inhibitors is sparse. This study was designed to assess the efficacy of tamsulosin, tadalafil or a combination of the two in (p=0.628). Significant improvement in the QOL Index in Group A (p=.000) and B (p=.003) was noted. terms of improving LUTS, urodynamic parameters and sexual function in patients with BPH.

INTRODUCTION

- The incidence of LUTS/BPH and ED increase parallel with age, physicians need to be in a position to effectively treat both these conditions simultaneously. Moreover treatment of one condition can improve the other too.
- Recent large-scale epidemiological studies have reported a statistically significant association between the two conditions, independent of age and cardiovascular co-morbidities

(McVary K.et al, BJUI. 2006;97 Suppl 2:23-8.)

- A growing body of evidence suggests the efficacy of phosphodiesterase5 (PDE5) inhibitors alone and in combination with alpha-adrenergic blockers in managing lower urinary tract symptoms related to BPH.
- Although clinical benefit of PDE5 inhibitors has been shown, urodynamic data regarding the effect of PDE5 inhibitors is sparse.

AIMS & OBJECTIVES

- To evaluate the efficacy of Tamsulosin and Tadalafil alone or in combination in improving symptoms and pressure flow urodynamic parameters in patients with symptomatic BPH.
- To evaluate the effects of Tamsulosin and Tadalafil as monotherapy or in combination in terms of improvement in sexual function.

MATERIALS & METHODS

We conducted a prospective, randomized open label trial on 45 men with symptomatic BPH

Inclusion Criteria

Men 45 years of age or more with LUTS/BPH

Exclusion Criteria

- Contraindication to investigational drugs. • Patients with known allergy to drugs under study.
- Bladder outlet obstruction due to cancer, calculi or stricture.
- Previous prostate surgery.
- Any neurological disease affecting storage and voiding functions.
- Prostatic diseases like prostatitis and prostate cancer.
- An episode of acute urinary retention within weeks of the study initiation.
- Untreated urinary tract infection.
- Uncontrolled diabetes or hypertension.
- Indication for surgical management of BPH

Selected patients were randomly assigned to three treatment groups.

- GROUP A : Tamsulosin 0.4mg once daily • GROUP B : Tadalafil 10mg once daily GROUP C: Tamsulosin 0.4mg + Tadalafil 10mg
- as combination once a day
- Computer generated random number table was used for allocation of treatment group

ABSTRACT

Statistically significant improvement of ED was noted only in patients who received Tadalafil (Group B and C). The mean change parameters amongst patients with symptomatic BPH following tamsulosin/tadalafil monotherapy or 45 symptomatic BPH patients were prospectively randomized to receive tamsulosin (Group A), tadalafil (Group B) in Qmax, Pdet Qmax and PVR were insignificant and similar in all the three groups. The bladder outlet obstruction index (BOOI) and combination (Group C). Patients were assessed at the start of the study and at the end of 3 months. Outcome was measured in bladder contractility index (BCI) failed to show any significant change following therapy (Table2). Adverse events (headache and terms of change in IPSS, QOL, IIEF-5 and urodynamic parameters including change in Qmax, Pdet Qmax, BOOI, BCI and PVR. body aches) were noted more frequently in Group C although none discontinued treatment.

<u>Results</u>

- Patients were assessed at the start of the study and at the end of 3 months.
- Outcome was measured in terms of change in IPSS, QOL, IIEF-5 and urodynamic parameters including change in Qmax, Pdet Qmax, BOOI.BCI and PVR.

Statistical analysis

• Statistical analysis was performed using commercially available statistical analysis software (SPSS) using appropriate statistical methods.

RESULTS

- The three groups were comparable (Table 1).
- The mean age was 61.82 ± 8.794 years with mean duration of LUTS were 2.51 ± 1.576 years.
- A statistically significant change in IPSS $score[7.93 \pm 6.90 (p = .001) in Group A,$ 7.00 ± 5.59 (p = .000) in Group B and 5.80 ± 5.51 (p = .001) in Group C] was observed.
- However, there was no significant difference on intergroup comparison (p=0.628).
- Current study had documented that LUTS symptoms do improve with tadalafil. However, maximum benefit is obtained from tamsulosin and combination therapy does not have added benefit.
- Significant improvement in the QOL Index in Group A (p = .000) and B (p = .003) was noted.

- IPSS score.
- (Group B and C).
- failed to improve Qmax.

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Conclusions

Tamsulosin and tadalafil significantly improved LUTS secondary to BPH. However, combination therapy did not give added benefit. The improvement in erectile function with tamsulosin was insignificant. Therefore, for patients with symptomatic BPH with bothersome ED, monotherapy with tadalafil may be considered rather than as a combination with tamsulosin. Interesting to note that the subjective improvement in LUTS was not reflected objectively in urodynamic parameters.

- - The mean change in Qmax, Pdet Qmax and PVR were insignificant and similar in all the three groups.
 - The bladder outlet obstruction index (BOOI) and bladder contractility index (BCI) failed to show any significant change following therapy (Table 2).
 - Combination therapy had documented greater reduction in post void residual urine.
 - Adverse events (headache and body aches) were noted more frequently in Group C although none discontinued treatment.

	Group A	Group B	Group C	n		Group	Baseline [X]	3 months [Y]	Mean Change [X-Y]	р		Group	Baseline [X]	3 months [Y]	Mean Change [X-Y]	р
	(n=15)	(n=15)	(n=15)	Ч		А	15.27 ± 6.8	7.33 ± 3.71	7.93 ± 6.90	0.001	Omey	A	7.93 ± 4.06	7.00 ± 2.95	0.93 ± 3.32	0.296
Age (years)	65.133 ± 8.096	60.07 ± 10.053	60.27 ± 7.667	.205	IPSS	В	14.40 ± 6.506	7.40 ± 4.53	7.00 ± 5.59	<0.0 01	Qmax (mL/sec)	В	6.93 ± 2.94	7.67 ± 4.03	-0.73 ± -2.25	0.228
												С	9.27 ± 4.37	8.12 ± 3.44	1.13 ± 3.29	0.204
Duration Of LUTS (years)	2.67 ± 1.988	2.53 ± 1.506	2.33 ± 1.234	.850		С	13.13 ± 6.12	7.33 ± 3.87	5.80 ± 5.51	0.001		А	62.20 ± 19.57	58.20 ± 16.0	4.00 ± 12.63	0.240
DM	13.3%	20.0%	13.2%	.844		А	3.87 ± 1.30	1.67 ± 0.90	2.20 ± 1.61	<0.0 01	PdetQmax (cmH20)	В	75.13 ± 43.71	72.93 ± 43.42	2.20 ± 12.64	0.511
					QOL	В	3.07 ± 1.16	2.00 ± 0.66	1.07 ± 1.16	0.003		С	56.33 ± 21.2	54.27 ± 21.01	1.07 ± 10.95	0.712
HTN	40.0%	20.0%	13.3%	.209		С	2.67 ± 1.29	2.20 ± 1.08	0.47 ± 1.25	0.169		A	73.00 ± 72.11	82.20 ± 97.76	-9.20 ± 99.8	0.726
Mean IPSS	15.27 ± 6.798	14.40 ± 6.566	13.13 ± 6.116	.667		A	10.87 ± 10.41	11.07 ± 10.55	-0.20 ± 0.77	0.334	PVR (mL)	В	96.93 ± 100.91	86.67 ± 54.17	10.24 ± 112.43	0.729
	0.07 + 1.000	0.07 + 1.100	0.07 . 1.001	007	IIEF-5	В	17.40 ± 6.62	20.20 ± 7.27	-2.80 ± 4.75	0.039		С	71.47 ± 71.98	36.53 ± 46.93	34.93 ± 57.88	0.035
Mean QOL	3.87±1.302	3.07 ± 1.163	2.67±1.291	.037		C	19.52 ± 6.27	22.53 ± 3.69	-3.00 ± 3.33	0.004		А	46.63 ± 22.474	44.20 ± 17.473	-2.1333 ± 11.59351	0.488
Mean IIEF	10.87 ± 1.405	17.40 ± 6.620	19.53 ± 6.266	.013		Ū					BOOI	В	61.27 ± 45.998	57.60 ± 46.355	-3.6667 ± 15.64182	0.379
												C	3680 + 26047	38.00 + 22.216	1.2000 ± 11.99524	0 704

Table 1. Demographic profile of the study population.

- documented by urodynamic parameters).
- Hence, we can not recommend combination of alpha blocker with PDE5 inhibitors in all patients with BPH.
- The improvement in erectile function with tamsulosin was insignificant.
- tamsulosin.
- Interesting to note that the subjective improvement in LUTS was not reflected objectively in urodynamic parameters.

• The similar findings of no added benefit of combination therpy was also reflected in the field of QOL as the percentage improvement in QOL Index was 56.84%, 34.76% and 17.49% in Group A, B and C respectively. Off course the baseline QOL index was lower in the combination group.

• 61.54% (n=24) of the symptomatic BPH patients had associated ED . However, majority of them had either mild(n=10) or mild to moderate (n=9) sexual dysfunction as measured by IIEF5 scale.

 Our study also confirmed that there was a trend to have higher ED score amongst patients with higher

• Statistically significant improvement of ED was noted only in patients who received Tadalafil

• The maximum benefit of combination therapy was noted for IIEF improvement. The percent improvement in IIEF was 1.84%, 16.09% and 15.38% in Group A, B and C respectively.

Uroflow Qmax was improved by 2.2 points amongst patients who were on tamsulosin. Tadalafil did improve Qmax but to a lesser extent (<1 point). Surprisingly combination therapy had

 Despite the improvement in Qmax, improvement in Pdet Qmax, the most important urodynamic parameter of bladder outlet obstruction did not achieve statistical significance with either of the regime. However, there was a trend towards decreasing Pdet Qmax in all three regimes.

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Table 2. Change in clinical and urodynamic parameters with treatment in the study groups.

CONCLUSION

• Current study documented subjective improvement of LUTS parameters and sexual dysfunction with either tamsulosin, tadalafil or combination of both. • However, combination of both the drugs with different mechanism of action failed to achieve additive benefit either subjectively or objectively (as

• Therefore, for patients with symptomatic BPH with bothersome ED, monotherapy with tadalafil may be considered rather than as a combination with