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Efficacy of Tamsulosin and Tadalafil Combination Therapy for Lower Urinary Tract Symptoms due to Benign Prostatic Hyperplasia (BPH) without Erectile Dysfunction (ED)

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ABSTRACT

Introduction and Objective: Lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia (BPH) is quite complex to manage . Many drugs with various mechanisms of action are available Since erectile dysfunction commonly accompanies LUTS, drugs covering both these disorders shall be advantageous. We evaluated the efficacy of combination of tamsulosin and tadalafil in patients with LUTS without ED

Methodology: prospective randomized study in which patients with LUTS without any erectile dysfunction within the age group of 45 – 65 yrs and prostate gland size up to 50 cc were enrolled for three months and patients were assessed for International Prostatic Symptom Score (IPSS), quality of life (IPSS QoL), maximum urinary flow rate (Qmax) and post-void residual urine (PVR) volume before and at 3 months of treatment and this data was analysed

Results: Mean IPSS score in groups 1, 2, 3 & 4 were 22.81, 23.06, 23.30, 24.32 respectively which after three month drug treatment were noted to be 16.91, 11.31, 12.07 & 8.11. The difference in the maximum flow rate were statistically significant. Mean QoL scores before and after the study were 5.25, 4.81, 5.17 & 4.76 and 2.88, 2.15, 2.20 & 1.55 respectively , the change being statiscally significant ($p < 0.001$).The improvement in mean peak flow rate were also very remarkable. The mean Qmax rates initially in groups 1, 2, 3 & 4 were 10.81, 10.80, 10.77 & 10.82 ml/sec respectively which after three months became 11.62, 17.43, 12.75 & 18.86 ml/sec respectively. PVR reduced significantly in group 2 and 4.

Conclusion: From the results and analysis of our study we can conclude that combination Tadalafil and α-Blocker therapy is superior to tamsulosin or tadalafil alone for Benign Prostatic Hyperplasia in patients with LUTS even in patients not having erectile dysfunction for improving IPSS, QoL and Qmax significantly but not significant change in post-voidal residue.

Keywords: Combination, Tamsulosin, Tadalafil

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INTRODUCTION

BPH is a chronic, complex disease that is progressive in many men. The term 'BPH disease progression' encompasses a range of clinical outcomes, including not only symptom deterioration but also potentially serious complications such as acute urinary retention (AUR) and a need for BPH-related surgery.[1] Medical therapies extensively i nvestigated for LUTS and BPH include α-adrenergic blockers, 5α-reductase inhibitors, aromatase inhibitors, and numerous plant extracts. Newer therapies include antimuscarinic drugs, β3-agonists, phosphodiesterase inhibitors (PDEIs), and several combinations of these agents.[2] the occurrence of both ED and LUTS in men as they age raises the possibility of a common underlying mechanism atleast contributing to both processes, which in turn raised the possibility of new treatment options that might affect both processes.[3] Since erectile dysfunction commonly accompanies LUTS drugs covering both these disorders shall be advantageous.[3] However, whether patients without erectile dysfunction benefit from these drugs is yet to be fully eleucidated. Here we evaluate the efficacy of combination of tamsulosin and tadalafil in patients with LUTS without ED.

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AIM & OBJECTIVE

To evaluate the efficacy of tamsulosin and tadalafil combination therapy for Benign Prostatic Hyperplasia in terms of IPSS, QoL, Qmax and Post-voidal residual urine

MATERIALS AND METHODS

It was a prospective randomized study in which male patients with LUTS without any erectile dysfunction within the age group of 45 – 65 yrs and prostate gland size up to 50 cc were enrolled for three months duration starting from July 2016 to September 2016. Patients with median lobe involvement, upper tract abnormalities on USG (Abd) and de-ranged renal function were excluded from this study. Patients were randomised to four groups: First group of control patients received placebo treatment, second received tamsulosin 0.4 mg/day alone, third received tadalafil 5mg/day, and fourth group received combination therapy with tamsulosin and tadalafil. After a 2-week medication free run-in period, patients were assessed for International Prostatic Symptom Score (IPSS), quality of life (IPSS QoL), maximum urinary flow rate (Qmax) and post-void residual urine (PVR) volume before and at 3 months of treatment **(table 1).** Post voidal residue was recorded as significant or non-insignificant with respect to the pre-voidal volume as assessed sonographically with PVR more than 10% of prevoid-void volume taken as significant **(table 2).** The measurements were made, then tabulated and anthologised.The data was analysed using SPSS software 20 using ANOVA test, post-hoc test and chi-square test.

RESULTS

Total of 165 patients were enrolled in the study out of which 11 patients were lost to follow-up. So at the time final assessment the number of patients in groups 1, 2, 3 and 4 were 32, 54, 30 and 38 respectively. We can easily infer from the above charts the mean IPSS score in group 1, 2, 3 & 4 were 22.81, 23.06, 23.30, 24.32 ml/sec respectively which after three month drug treatment were noted to be 16.91, 11.31, 12.07 & 8.11 ml/sec. The difference in the maximum flow rate were statistically significant (p <0.001).

Mean QoL scores before and after the study were 5.25 ,4.81, 5.17 & 4.76 and 2.88, 2.15, 2.20 & 1.55 respectively , the change being statiscally significant (p < 0.001).

The improvement in mean peak flow rate were also very remarkable. The mean Qmax rates initially in groups 1,2,3 & 4 were 10.81, 10.80, 10.77 & 10.82

Table 1. Comparison analysis of all groups

Variables	Group 1 (n=32)	Group 2 (n=54)	Group 3 (n=30)	Group 4 (n=38)	P value *	P value#
IPSS (mean and SD)						
At 2wks	22.81 (2.57)	23.06 (2.23)	23.30 (2.30)	24.32 (2.68)	0.043	
End of 3mon	16.91 (3.83)	11.31 (3.82)	12.07 (3.20)	8.11 (2.10)	<0.001	<0.001a
						<0.001b
						<0.001c
QoL (mean and SD)						
At 2wks	5.25 (0.76)	4.81 (0.99)	5.17 (0.74)	4.76 (0.78)	0.03	
End of 3mon	2.88 (0.79)	2.15 (0.40)	2.20 (0.88)	1.55 (0.72)	<0.001	<0.001a
						<0.001b
						0.001c
Qmax (mean and SD)						
At 2wks	10.81 (1.17)	10.80 (1.25)	10.77 (1.19)	10.82 (0.76)	0.998	
End of 3mon	11.62 (2.80)	17.43 (1.73)	12.75 (2.47)	18.86 (1.53)	<0.001	<0.001a
						0.008b
						<0.001c

*P value based on one way ANOVA #p value based on post hoc analysis using Tuckey's test

a- comparison between group 1 and 4; b- comparison between group 2 and 4; c- comparison between group 3 and 4

Table 2. Significance of Post Void Residual Urine

Variable	Group 1 (n=32)	Group 2 (n=54)	Group 3 (n=30)	Group 4 (n=38)	P value^
PVRU					<0.001
Significant	27 (84.4)	6 (11.1)	9 (30.0)	1 (2.6)	
Non-significant	5 (15.6)	48 (88.9)	21 (70.0)	37 (97.4)	

Table 3. Analysis of post voidal residual urine among all groups

Groups	Significant	Non-significant	Group 3 (n=30)
Control * tamsulosin	27 (84.4)	5 (15.6)	<0.001
	6 (11.1)	48 (88.9)	
Control * tadalafil	27 (84.4)	5 (15.6)	<0.001
	9 (30.0)	21 (70.0)	
Control * both	27 (84.4)	5 (15.6)	<0.001
	1 (2.6)	37 (97.4)	
Tamsulosin* tadalafil	6 (11.1)	48 (88.9)	0.03
	9 (30.0)	21 (70.0)	
Tamsulosin * both	6 (11.1)	48 (88.9)	0.131
	1 (2.6)	37 (97.4)	
Tadalafil * both	9 (30.0)	21 (70.0)	0.002
	1 (2.6)	37 (97.4)	

^p value based on Chi square test

respectively which after three months became 11.62, 17.43, 12.75 & 18.86 respectively (p<0.001). This was significant in group 2 and 4 but not in group 3. The difference among pre and post therapy though significant, is not significant in between the groups 2, 3 & 4. Post voidal residue improved in all groups but the efficacy of reducing PVR was similar for group 2 and 4, both significantly better than in group 3 (p<0.001) **(table 3).**

DISCUSSION

Oelke et al[4] had found an Overall treatment satisfaction was greater for tadalafil vs placebo (P = 0.005), based on greater satisfaction with efficacy (P = 0.003); neither overall treatment satisfaction nor satisfaction with efficacy was greater for tamsulosin vs placebo (P ≥ 0.409). IN our study the treatment satisfaction was more for the tamsulosin group, which may be because of the inherent design of the study. However combination therapy was not in the study so no comparative argument can be advanced in this regard.

Brock et al[5] found in their study that Tadalafil 5 mg once daily improved BPH-LUTS in men without ED by a magnitude similar to that observed in men with ED. IPSS score and QoL scores were assessed in the study. In our study also the patient population was without the history of erectile dysfunction

Study done by Carson CC et al[6] tadalafil significantly improved total International Prostate Symptom Score (IPSS) following 12 weeks of treatment with once daily tadalafil 5 mg. Statistically significant improvements in Benign Prostatic Hyperplasia Impact Index (BII), IPSS subscores, IPSS QOL and International Index of Erectile Function (IIEF) were also observed. Improvement in urinary symptoms occurred regardless of age, previous treatment with an α1 -adrenergic blocker, BPH-LUTS severity at baseline or ED status. Similarly our study also showed improvements in IPSS, Qmax, QoL scores with combination therapy being superior in the improvements, however, our study was based on a population where erectile dysfunction had already been excluded

Meta-analysis by Gacci et al[7] found that, the use of PDE5-Is alone was associated with a significant improvement of the International Index of Erectile Function (IIEF) score (+5.5; p<0.0001) and International Prostate Symptom Score (IPSS) (-2.8; p<0.0001) but not the maximum flow rate (Q(max)) (-0.00; p=not significant) at the end of the study as compared with placebo. The association of PDE5-Is and α1-adrenergic blockers improved the IIEF score (+3.6; p<0.0001), IPSS score (-1.8; p = 0.05), and Q(max) (+1.5; p<0.0001) at the end of the study as compared with α-blockers alone. Here in our study, we evaluated efficacy of tadalafil alone as well as in combination with tamsulosin and found statistically significant improvements in IPSS and QoL. Though post void residue and Qmax did not have significant reduction with tadalafil alone group.

Martinez[8] et al in their critical analysis found that consistent evidence of improvements in LUTS has been shown with PDE5-Is, either alone or in combination with α-blockers but they also warranted that effects on urodynamics or objective measures of urinary flow are lacking. Having improvements in Qmax, our study portends to have an objective evidence to this aspect as well.

In our study we were able to reproduce the improvements seen in the above studies but at the same time our study might have had some deficiencies. A selection bias might have occured while selecting the patient for medical management. Three patients in tadalafil group developed acute urinary retention following which catherisation along with combination therapy was started and TWOC done two weeks later which was successful.

CONCLUSION

From the results and analysis of our study we can conclude that combination Tadalafil and α-Blocker therapy is superior to tamsulosin or tadalafil alone for Benign Prostatic Hyperplasia in patients with LUTS even in patients not having erectile dysfunction for improving IPSS, QoL and Qmax significantly but not significant change in post-voidal residue.

END NOTE

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Conflict of Interest: None declared

Editor's Remarks: This original study was designed to compare the efficacy of Tamsulosin and Tadalafil alone or in combination in the medical management of patients with Benign Hyperplasia of Prostate without Erectile Dysfunction. It explores the actions and usefulness of newer medicines for the treatment of Benign Hyperplasia of Prostate.

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