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# The impact of adding solifenacin to tamsulosin therapy for treatment of storage lower urinary tract symptoms owing to benign prostatic hyperplasia

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## Abstract

**Background:** Benign prostatic hyperplasia (BPH) is a common problem in aging males which has a potential impact on patients' health-related quality of life. In the present prospective study, we evaluated the effect of adding solifenacin to tamsulosin, compared to tamsulosin alone on overactive bladder symptoms scores (OABSS) and patients' quality of life (QoL) in patients with filling lower urinary tract symptoms due to BPH.

**Methods:** Patients included in our study were randomly assigned into 2 groups: group 1 included patients with BPH who received tamsulosin alone and group 2 included patients with BPH who received a combination of tamsulosin and solifenacin. Treatment period was 12 weeks in both groups. Quality of life and overactive bladder symptoms score questionnaires were obtained and compared in both groups before and after treatment.

**Results:** No significant differences were found between both groups before treatment. At the end of treatment period, The QoL score for Group 1 patients was significantly greater than the other group (mean rank was 138.98 in tamsulosin group versus 62.02 in the combination group,  $P$ -value  $< 0.01$ ). Similarly, OABSS for tamsulosin only group was significantly higher than combined treatment patients (mean rank was 145.03 in tamsulosin group versus 55.98 in the combination group,  $P$ -value  $< 0.01$ ).

**Conclusion:** Adding solifenacin to tamsulosin was associated with an improvement of QoL and OABSS in patients with irritative urinary symptoms due to BPH when compared with tamsulosin monotherapy.

**Keywords:** BPH, Tamsulosin, Solifenacin

## 1 Background

Benign prostatic hyperplasia (BPH) is a common benign disease affecting aging males. BPH can affect patients' health-related quality of life. Irritative voiding symptoms secondary to BPH can lead to sleep disruption, depression, anxiety, increased falls, and sexual problems [1, 2].

Patients with BPH may be presented by irritative and/or obstructive symptoms. Irritative symptoms are in the form of urinary frequency, urgency, nocturia, and urinary

incontinence, while obstructive symptoms can be in the form of hesitancy, intermittency, weak stream, or even urinary retention [3, 4].

Different options of treatment are available to treat BPH like, alpha 1 adrenergic blockers ( $\alpha$ 1-blockers), 5- $\alpha$  reductase inhibitors (5ARIs) or a combination of the both, anticholinergic agents,  $\beta$ 3-adrenoceptor agonists, and phosphodiesterase type-5 inhibitors (PDE5i) which have been investigated by new studies for the treatment of BPH.

Recent studies have reported that the add-on effect of anticholinergic to patients already on  $\alpha$ -blockers was associated with significant efficacy and health-related

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quality of life benefits over  $\alpha$ -blockers monotherapy in men with LUTS/BPE [5–7].

The aim of our prospective study is to evaluate the effect of adding Solifenacin to tamsulosin on the overactive bladder symptoms scores (OABSS) and patients' quality of life (QoL) in patients with filling lower urinary tract symptoms due to BPH.

**1.1 Design**

Prospective randomized study.

**2 Methods**

One hundred and seven patients aged 45 years or older, who were being treated for irritative voiding symptoms due to BPH in our urology outpatient clinic, were included in our prospective study. Patients were randomly assigned into 2 groups using opaque envelop technique. The first group ( $n=52$ ) was treated with 0.4 mg tamsulosin capsule once daily, and the other group ( $n=55$ ) was treated with 0.4 mg tamsulosin plus 5 mg

solifenacin tablet once daily for 12 weeks. We obtained the quality of life questionnaire (Table 1) and overactive bladder symptoms score questionnaire (Table 2) and compared them in both groups before and at the end of treatment.

**2.1 Sample size calculation**

The sample size was calculated using  $G^*$  power software version 3.1.9.4 and with test family ( $t$ -tests), type of power analysis (A priori: Compute required sample size—given  $\alpha$ , power and effect size), input parameters, effect size=0.64,  $\alpha$  error=0.05, power( $1 - \beta$ )=0.8, and with assuming allocation ratio  $N_1/N_2=1$  resulting output parameters were sample size for each group 40 patients. This yield a total sample size of 80 patients.

**2.2 Statistical analysis**

Obtained data were presented as mean  $\pm$  SD, numbers and percentages. Results were analyzed using Student  $t$  test and Chi square test ( $\chi^2$  test). Statistical analysis was

**Table 1 Quality of life due to urinary symptoms questionnaire**

Terrible	Unhappy	Mostly dissatisfied	Mixed about equally satisfied and dissatisfied	Mostly satisfied	Pleased	Delighted	Quality of life due to urinary symptoms
6	5	4	3	2	1	0	If you were to spend the rest of your life with your urinary condition the way it is now, how would you feel about that?

**Table 2 Overactive bladder symptom score (OABSS)**

Score	Frequency	Question
0	$\leq 7$	How many times do you typically urinate from waking in the morning until sleeping at night?
1	8–14	
2	$\geq 15$	
0	0	How many times do you typically wake up urinate from sleeping at night until waking in the morning?
1	1	
2	2	
3	$\geq 3$	How often do you have a sudden desire to urinate, which is difficult to defer?
0	Not at all	
1	Less than once a week	
2	Once a week or more	
3	About once a day	
4	2–4 times a day	How often do you leak urine because you cannot defer the sudden desire to urinate?
5	5 times a day or more	
0	Not at all	
1	Less than once a week	
2	Once a week or more	
3	About once a day	
4	2–4 times a day	
5	5 times a day or more	

**Table 3 Effect of tamsulosin only on group A**

P-value	After (mean ± SD)	Before (mean ± SD)	
< 0.001	2.30 ± 0.50	4.36 ± 0.52	(1) Quality of life
< 0.001*	7.87 ± 1.555	11.63 ± 1.475	(2) OABSS

Asterisk represents significant difference between both groups: P value < 0.05 was considered statistically significant

**Table 4 Effect of tamsulosin plus solifenacin on group B**

P-value	After (mean ± SD)	Before (mean ± SD)	
< 0.001	1.29 ± 0.498	4.37 ± 0.485	(1) Quality of life
< 0.001*	5.00 ± 1.064	11.43 ± 1.458	(2) OABSS

Asterisk represents significant difference between both groups: P value < 0.05 was considered statistically significant

**Table 5 Comparison between the change in QOI in group A and group B**

		Mean rank	P-value
Quality of life (before)	Tamsulosin only	100.37	0.970
	Tamsulosin plus solifenacin	100.63	
Quality of life (after)	Tamsulosin only	138.98	< 0.001
	Tamsulosin plus solifenacin	62.02	
P value	Mean rank		
0.970	100.37	Tamsulosin only	Quality of life (before)
	100.63	Tamsulosin plus solifenacin	
< 0.001	138.98	Tamsulosin only	Quality of life (after)
	62.02	Tamsulosin plus solifenacin	

**Table 6 Comparison between the change in OABSS in group A and group B**

		Mean Rank	P value
OABSS (before)	Tamsulosin only	103.78	0.970
	Tamsulosin plus solifenacin	97.22	
OABSS (after)	Tamsulosin only	145.03	< 0.001
	Tamsulosin plus solifenacin	55.98	
P value	Mean rank		
0.970	103.78	Tamsulosin only	OABSS (before)
	97.22	Tamsulosin plus solifenacin	
< 0.001	145.03	Tamsulosin only	OABSS (after)
	55.98	Tamsulosin plus solifenacin	

conducted using the IBM SPSS (Version 23, 2015) for Windows statistical package. P-value < 0.05 was considered statistically significant.

**3 Results**

Out of 52 patients who received 0.4 mg tamsulosin daily, only 48 patients had completed the study period as 3 patients were excluded from the study due to

lost follow-up. The mean age of patients in this group was 63.25 ± 5.1 years old (mean ± SD). The quality of life was significantly improved by the administration of 0.4 mg tamsulosin. Significant improvements were observed in OABSS (Table 3). Out of 55 patients who received tamsulosin 0.4 mg plus solifenacin 5 mg daily, only 49 patients had completed the study period as 5 patients were excluded from the study due to lost follow-up. The mean age of patients in this group was 63.4 ± 5.69 years old (mean ± SD). The quality of life was significantly improved by the administration of 0.4 mg tamsulosin plus 5 mg solifenacin. Significant improvements were observed in OABSS (Table 4).

There was no significant difference between the 2

groups before treatment, but the quality of life score for patients after treatment with tamsulosin only is significantly greater than patients after treatment of tamsulosin plus solifenacin at significant level < 0.01 (Table 5). Also there was no significant difference in OABSS between 2 groups before treatment, but OABSS for group 1 was significantly greater than group 2 patients at significant level < 0.01 (Table 6).

### 4 Discussion

It is well known that the relief of urinary symptoms will improve the patients' QOL. In our study, group (A) showed improvement in the QOL (question 8 of IPSS),  $2.30 \pm 0.50$  after 12 weeks. The mean change in IPSS-QoL score from baseline to endpoint was (2 points). This improvement was statistically significant ( $P$  value  $< 0.001$ ) and also was in agreement with Chapple et al. (2005) observation, (1.3 points;  $P = 0.0005$ ) [8, 9].

In our study, group (B) showed improvement in QOL  $4.37 \pm 0.485$  to  $1.29 \pm 0.498$ . This improvement was statistically significant ( $P$  value  $< 0.001$ ) and in agreement

with Van Kerrebroeck et al.(2013), who reported that the Change from baseline to endpoint in the QOL due to urinary symptoms with a combination of solifenacin 6 mg plus tamsulosin OCAS 0.4 mg was (1.3 points) (Fig. 1).

Significant improvements in IPSS QoL score were also reported ( $P < 0.001$ ). Our study on Egyptian patients showed higher statistically significant differences than that in the NEPTUNE, which is explained by the preference of our patients to the medical treatment rather than other invasive interferences [10, 11].

In present study, combination therapy was associated with significant additional benefits ( $P$  value  $< 0.001$ ) in

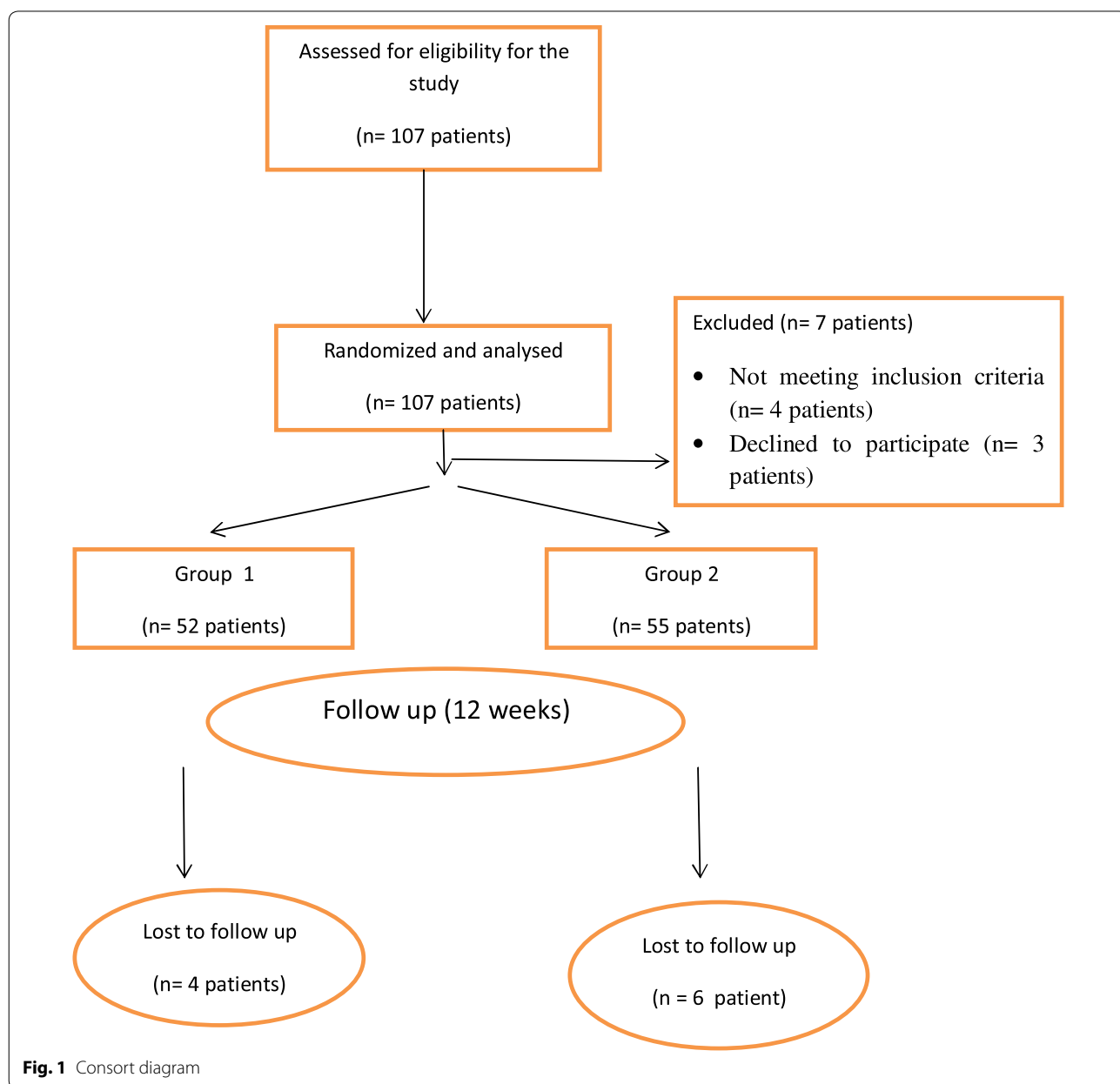


Fig. 1 Consort diagram

QOL when compared with monotherapy with tamsulosin OCAS 0.4 mg; these result in agreement with van Kerrebroeck et al. (2013) who stated significant improvements in IPSS QoL score with combination therapy compared with tamsulosin OCAS ( $P < 0.05$ ) [10].

Regarding overactive bladder symptom score (OABSS), in group (B) the combination therapy proved to be an effective treatment because of a statistically significant difference ( $P$  value  $< 0.001$ ), as OABSS showed significant improvement from a mean  $\pm$  SD of  $11.43 \pm 1.458$  to  $5.00 \pm 1.064$  after 3 months; these results were in agreement with Masumori et al. (2010), and Yamaguchi et al. (2011) who found also a significant improvement by addition of solifenacin to tamsulosin as an improvement from  $8.0 \pm 2.5$  before addition of solifenacin to  $4.8 \pm 2.6$  after 12 weeks of adding solifenacin [12]. In ASSIST study, OABSS also changes from baseline to end of treatment which was statistically significant in cases treated with tamsulosin 0.4 mg plus solifenacin 5 mg ( $P$  value  $< 0.001$ ) [13, 14].

#### 4.1 Study limitations

Our study lacks placebo group, as many patients at the beginning of the study (pilot study) refused to participate as a control group, and also most of patients were suffering from LUTS symptoms, so we found it unethical to deprive them from definitive treatment. So the decision was not to include placebo group at our study.

#### 5 Conclusion

Our study concluded that in a short term of follow-up, the combination of solifenacin plus tamsulosin was associated with a benefit on QOL and OABSS in patients with mainly irritative symptoms due to benign prostatic hyperplasia compared to tamsulosin only.

#### Abbreviations

BPH: benign prostatic hyperplasia; OABSS: overactive bladder symptoms scores; QoL: quality of life;  $\alpha$ 1-blockers: alpha 1 adrenergic blockers; 5ARIs: 5- $\alpha$  reductase inhibitors; PDE5i: phosphodiesterase type-5 inhibitors; LUTS: lower urinary tract symptoms.

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Not applicable.

#### Authors' contribution

All authors have made a significant contribution to the findings and methods in the paper. ME worked on the idea and design. AI shared in the editing. ES helped in data collection and analysis. AK shared in the editing. AG contributed to revision. All authors read and approved the final manuscript.

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No funding was obtained for this study.

#### Availability of data and material

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

#### Ethics approval and consent to participate

All procedures performed were in accordance with the ethical standards of the ethics committee IRB of Faculty of Medicine, Minia University, approved on February 18, 2018. Ethical Approval number: 236/2018. A written consent was taken from all participants after sufficient information about the study.

#### Consent for publication

Not applicable.

#### Competing interest

No competing interest is declared by any of the authors.

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