Original paper

Tamsulosin plus a new complementary and alternative medicine in patients with lower urinary tract symptoms suggestive of benign prostatic hyperplasia: Results from a retrospective comparative study

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Summary
Background: We aimed to compare the efficacy of tamsulosin 0.4 mg once a day alone and the combination therapy involving tamsulosin 0.4 mg once a day plus the complementary and alternative medicine consisting of vitamins (C and D), herbal products (Cucurbita maxima, Capsicum annum, Polygonum capsicatum) and amino acid L-Glutamine bid in patients with lower urinary tract symptoms related to benign prostatic hyperplasia (LUTS/BPH).

Methods: We performed a retrospective matched paired comparison. The clinical records of LUTS/BPH patients who underwent medical therapy with tamsulosin 0.4 mg/day plus the complementary and alternative medicine consisting of vitamins (C and D), herbal products (Cucurbita maxima, Capsicum annum, Polygonum capsicatum) and amino acid L-Glutamine bid between January 2019 to September 2019 were reviewed (Group 1). These patients were compared in a 1:1 fashion with LUTS/BPH patients who underwent therapy with tamsulosin 0.4 mg/day alone (Group 2). Total, storage, voiding and Quality of Life (QoL) international prostate symptom (IPSS) score, as well as overactive bladder (OAB)-v8 score and treatment-related adverse events recorded at 40 days follow-up in both groups were compared.

Results: At 40 days follow-up mean total, storage, voiding and QoL IPSS sub-scores as well as OAB-v8 score significantly improved in both groups. Intergroup comparison showed statistically significant lower mean total IPSS score (11.6 vs 12.4, p = 0.04) mean storage IPSS sub-score (6.5 vs 7.5, p = 0.01), and mean OAB v8 score (16.7 vs 18.8, p = 0.03) in patients in the Group 1.

Conclusions: The combination of tamsulosin 0.4 mg/die plus the complementary and alternative medicine consisting of vitamins (C and D), herbal products (Cucurbita maxima, Capsicum annum, Polygonum capsicatum) and amino acid L-Glutamine bid provides statistically significant advantages in terms of storage LUTS improvements in patients with LUTS/BPH compared to tamsulosin 0.4 mg/day alone. These findings are preliminary and further prospective studies on a greater number of patients are needed to confirm it.

Key words: Benign prostatic hyperplasia; Combination therapy; Lower urinary tract symptoms; Phytotherapy.

Submitted 20 February 2020; Accepted 13 March 2020

Introduction
Lower urinary tract symptoms related to benign prostatic hyperplasia (LUTS/BPH) represent a common complaint in everyday urological practice and their prevalence increases with ageing (1-3). In the EPIC study, Riboli et al. reported an incidence of storage and voiding LUTS of about 51% and 26% of men evaluated, respectively (3). Interestingly, approximately 18% of men reported the coexistence of storage and voiding symptoms (4, 5). The European Association of Urology (EAU) guidelines strongly recommend α1-adrenoceptor antagonists as first-line therapeutic option in patients with moderate to severe symptoms as they significantly improve urinary symptoms and maxim urinary flow (Qmax) (6). In men with moderate-to-severe LUTS who mainly have bladder storage symptoms EAU Guidelines strongly recommend muscarinic receptor antagonists (strong recommendation) or beta-3 agonists (weak recommendation) (7). However, a number of concerns have been reported with the prescription of these drugs. Antimuscarinics might theoretically decrease bladder strength, thus increasing post-void residual volume (PVR) urine and causing urinary retention. Moreover, not all antimuscarinics have been evaluated in elderly men, and long-term studies on their efficacy in men of any age with LUTS are not yet available. Furthermore, antimuscarinics are contraindicated in patients with angle-closure glaucoma, gastrointestinal obstruction, paralytic ileus, myasthenia gravis, severe heart disease (8, 9). On the other hand, mirabegron has been evaluated mainly in female patients (8, 9). In recent years the prescription of phytotherapeutic compounds in patients with LUTS/BPH has gained growing interest (10). These agents represent a heterogeneous group and may contain differing concentrations of active ingredients. The complementary and alternative medicine Kubiher (Naturmed, Italy), consisting of vitamins (C and D), herbal products (Cucurbita maxima, Capsicum annum, Polygonum capsicatum) and amino acid L-Glutamine, has been proposed in the treatment of overactive bladder syndrome (OAB) (11). We aimed to compare the efficacy of the combination therapy involving tamsulosin 0.4 mg once a day plus Kubiher bid and therapy with tamsulosin 0.4 mg alone in patients with LUTS/BPH.

Materials and methods
We performed a retrospective comparative study. The clinical records of LUTS/BPH patients who underwent
medical therapy with tamsulosin 0.4 mg/day plus *Kubiker*
bid between January 2019 to September 2019 were
reviewed (Group 1). These patients were compared in a
1:1 fashion with LUTS/BPH patients who underwent
therapy with tamsulosin 0.4 mg/day alone (Group 2). The
followings were considered exclusion criteria: post-void
residual volume (PVR) > 150 ml, prostate specific antigen
(PSA) > 10 ng/ml, concomitant therapy with 5-alpha
reductase inhibitors and/or phosphodiesterase type 5
inhibitors and/or muscarinic receptor antagonists or beta-
3 agonists, presence of neurological disorders, previous
cervical surgery, diabetes, urticaria, infections, history of
acute urinary retention. The matched-pair comparison
was based on the following criteria: PSA, prostate volume
(PV), Q<sub>max</sub>, PVR, total international prostate symptom
score (IPSS), and 8-item overactive bladder questionnaire -
8 (OAB-v8) score. Total, voiding, voiding and Quality of
Life (QoL) IPSS scores, as well as OAB-v8 score and treat-
ment-related adverse events recorded at 40 days follow-
up in both groups were compared. Descriptive data of
continuous variables were expressed as mean ± standard
deviation (SD) and compared using the Student's t tests.
The analyses were considered significant for a p-value
< 0.05. All statistical analyses were performed with SPSS
version 16.0 software.

The study was performed in accordance with the ethical
standards laid down in the Declaration of Helsinki. Verbal
informed consent was obtained from subjects.

**Results**

Overall, 36 eligible patients who underwent medical
therapy with tamsulosin 0.4 mg/day plus *Kubiker* were
identified and compared to 36 patients who underwent
therapy with tamsulosin 0.4 mg/day alone. Baseline
patients' characteristics in both groups are reported in
Table 1. At 40 days follow-up mean total, storage, void-
ing and QoL IPSS sub-scores significantly improved in
both groups (Table 2). Similarly, a statistically signifi-

cant improvement in terms of OAB v8 score and Q<sub>max</sub>
was observed in both groups (Table 2).

Intergroup comparison showed statistically significant
lower mean total IPSS score, mean storage IPSS sub-score,
and mean OAB v8 scores in patients in the Group 1.
Not statistically significant differences in terms of voiding
IPSS sub-score, Q<sub>max</sub> and PVR emerged from intergroup
analysis. Not clinically significant treatment-related
adverse events were recorded in both groups.

**Discussion**

Benign prostatic obstruction has been reported to cause
morpho-functional alterations involving the detrusor
muscle. Clinically, these alterations can impair bladder
contractility and cause detrusor overactivity, decreasing
bladder compliance, and onset of storage LUTS charac-
terized by an altered bladder sensation, increased day-
time frequency, nocturia, urgency and urgency inconti-

ence (121). Experimental models have shown that
bladder outlet obstruction causes detrusor smooth muscle
cells hypertrophy and hyperplasia as well as extracellular
matrix alterations that may lead, over time, to
detrusor overactivity and, later, to reduced bladder con-
tractility (13-15). As reported in the EpiLUTS study,
45.7% of the 14.139 men evaluated had storage LUTS
(16). α1-blockers act by inhibiting the effect of endoge-
nously released noradrenaline on smooth muscle cells in
the prostate thus reducing prostate tone and bladder out-
let obstruction (17). These drugs can reduce both storage
and voiding LUTS and are considered the first-line drug
treatment for male LUTS due to their good efficacy, and
low rate and severity of adverse events. LUTS/BPH
patients with mainly bladder storage symptoms repres-
ent a difficult subset of patients. Indeed, thera-

py with α1-blockers may be suboptimal. On the other
hand, both muscarinic receptor antagonists and beta-3
 agonists should be prescribed with cautions and adher-
ence to treatments with these drugs is often inadequate.
Herbal treatments are an increasingly popular possibility
for treating storage LUTS (18). To the best of our knowl-
dge, we compared, for the first time, the clinical efficacy
of the combination of tamsulosin 0.4 mg/day plus
*Kubiker* and tamsulosin 0.4 mg/day alone in patients
with LUTS/BPH. We found that the combination therapy
provided statistically significant advantages in terms of
storage LUTS as demonstrated by lower IPSS storage
sub-scores as well as lower OAB-v8 score. A number of
experiments exist about the potential beneficial effects pro-
vided by the compounds contained in the food supple-

**Table 1.**

Baseline patients’ characteristics in both groups.

| Group 1 (n = 36) | Group 2 (n = 36) | p  |
|-----------------|-----------------|---|
| Age, mean (SD)  | 65.3 (8.6)      | 63.4 (8.5)      | 0.32 |
| Prostate volume, mL, mean (SD) | 44.1 (24.4) | 46.1 (22.7) | 0.73 |
| PSA, ng/ml, mean (SD) | 2.9 (0.8)   | 3.2 (0.4)   | 0.91 |
| PVR, mL, mean (SD) | 37.0 (11.2) | 39.0 (10.8) | 0.26 |
| Q<sub>max</sub>, mL/sec, mean (SD) | 11.2 (1.7)  | 12.5 (3.8)  | 0.18 |
| IPSS total, mean (SD) | 17.9 (8.9)  | 18.0 (8.4)  | 0.59 |
| IPSS voiding, mean (SD) | 8.5 (2.5)  | 9.1 (3.5)  | 0.15 |
| IPSS storage, mean (SD) | 9.3 (2.0)   | 8.8 (2.1)   | 0.18 |
| OAB-v8, mean (SD) | 19.6 (9.9)   | 20.1 (9.9)  | 0.29 |

IPSS: International Prostate Symptom Score; Q<sub>max</sub>: maximum urinary flow; SD: Standard Deviation.

**Table 2.**

IPSS and OAB v8 scores in both groups at 40-day follow-up.

| Group 1 (n = 36) | Group 2 (n = 36) | p  |
|-----------------|-----------------|---|
| IPSS total, mean (SD) | 11.6 (1.7)  | 12.4 (1.5)  | 0.04 |
| IPSS voiding, mean (SD) | 5.1 (2.3)   | 4.8 (1.1)   | 0.58 |
| IPSS storage, mean (SD) | 6.5 (1.9)   | 7.5 (1.6)   | 0.01 |
| IPSS QL, mean (SD) | 2.1 (0.9)   | 2.4 (0.9)   | 0.20 |
| Q<sub>max</sub>, mL/sec, mean (SD) | 13.8 (8.8)  | 14.1 (7.1)  | 0.20 |
| PVR, mL, mean (SD) | 26.0 (10.2) | 32.0 (8.8) | 0.42 |

IPSS: International Prostate Symptom Score; OAB-v8: 8-item overactive bladder questionnaire; PVR: Post-void residual volume; Q<sub>max</sub>: maximum urinary flow; SD: Standard Deviation. * p < 0.05 with respect to baseline.
The role of Kubiker in women with storage LUTS represents a further area of interest (11, 30).

CONCLUSIONS

The combination of tamsulosin 0.4 mg/die plus Kubiker bid provides statistically significant advantages in terms of storage LUTS improvements in patients with LUTS/BPH compared to tamsulosin 0.4 mg/day alone. These findings are preliminary and further prospective studies on a greater number of patients are needed to confirm it.

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