Efficacy and Safety of Tamsulosin in the Treatment of Benign Prostatic Hyperplasia

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Introduction/Objective: The α-adrenergic receptor antagonists represent the most frequently prescribed first line treatment for benign prostatic hyperplasia. Tamsulosin is a uroselective α1A/α1D adrenergic receptor antagonist. The objective of this study is to establish the efficacy and safety of a daily dose of tamsulosin 0.4 mg in patients with functional symptoms of benign prostatic hyperplasia through an evaluation of reduction of subjective symptoms, quantified through the International Prostate Symptom Score.

Materials and methods: 45 patients with lower urinary tract symptoms caused by benign prostatic hyperplasia used tamsulosin 0.4 mg over the course of 12 weeks; their International Prostate Symptom Score (IPSS) value was ≥ 8 points, while their Quality of Life Index (QLI) value was ≥ 3 points. Checkups were scheduled 4 and 12 weeks following the initiation of treatment, during which the values for IPSS and disease-specific quality of life (QLI) were obtained.

Results: At the beginning of tamsulosin treatment, the total IPSS was 24.95 points. After the 4- and 12-week checkups, the total IPSS fell to 16.09 and 11.20 points, respectively. The reduction in symptoms, quantified through IPSS, was 35.51% after 4 weeks of treatment, and 55.11% after 12 weeks. The Quality of Life Index was initially 4.49 points, it decreased to 2.49 points after 4 weeks, and to 1.40 points after 12 weeks, marking an improvement of 44.54% after 4 weeks and 68.82% after 12 weeks. There was a statistically significant difference between the initial values for IPSS and QLI and their values after both checkups (p<0.05). Side effects were observed in three patients (6.66%), with one (2.22%) experiencing problems with ejaculation and the other two (4.44%) having vasodilatatory effects such as vertigo and headache.

Conclusion: Clinical response to a 12-week tamsulosin treatment improved during the course of treatment, reflected in a reduction in all of the lower urinary tract symptoms, with rare and insignificant side effects.

Key words: benign prostatic hyperplasia, lower urinary tract symptoms, International Prostate Symptom Score, Quality of Life Index, voiding symptoms, storage symptoms.

1. INTRODUCTION

Benign prostatic hyperplasia (BPH) is a chronic disease, with incidence and prevalence growing with age. Its clinical description includes lower urinary tract symptoms (LUTS) present in approximately 3 out of 4 men after age 70. It is estimated that in 2006, approximately 115 million men over age 50 displayed symptoms of BPH (1).

BPH has negative effects on the quality of life in men (2). LUTS has a negative effect on normal daily activities. It cause slow quality sleep, anxiety, increased fear of medical, especially surgical treatment, affects sexual activity etc. (3, 4, 5). The medical objective of BPH treatment is a reduction in severity of lower urinary tract symptoms, thus lowering the risk of acute urinary retention (AUR), reducing the need for surgical intervention, and achieving an improvement in an overall quality of life (6, 7). Patients with mild-to-moderate LUTS are recommended medical treatment involving two types of medications- α-adrenergic receptor antagonists (α-blockers) and 5α-reductase inhibitors (5ARIs). However, α-blockers are more frequently utilized as first line treatment in cases of men with mild-to-moderate LUTS (8). The adrenoceptors in the smooth muscle of the bladder neck and prostate are target tissues in α-blockers treatment. Therefore, blocking these adrenoceptors induces the relaxation of smooth muscles, resulting in aswift reduction of LUTS and an improvement in the disease-specific quality of life (9, 10). There are three types of α-1 adrenoceptors (α-1-A, α-1-B, α-1-D) and different types of α-1 adrenoceptor antagonists. However, comparative characteristics in clinical efficacy and side effects of these -1 adrenoceptor antagonists are still controversial (11, 12, 13, 14). Tamsulosin is a uro-selective α1-A/α1-D adrenoceptor antagonist.

2. STUDY OBJECTIVES

The objective of this study was to determine the efficacy and safety of tamsulosin 0.4 mg in patients with functional symptoms of benign prostatic hyperplasia (BPH), after a once-daily
usage, through an evaluation of the re-
duction of subjective symptoms, quant-
ified through the International Pro-
state Symptom Score (IPSS).

3. MATERIALS AND METHODS

The clinical study included 45 pa-
tients with functional symptoms of be-
nign prostatic hyperplasia. The mean
age was 66.3 with a standard deviation
of 5.8 (Table 1). The oldest patient was
age 78 and the youngest age 53, with the
variation interval of 25 years.

The inclusion criterion was a diag-
nosis of benign prostatic hyperplasia.
BPH was diagnosed according to med-
ical history, clinical image and physi-
ocal exam, IPSS, QLI, PSA, urine anali-
sys and urinary tract ultrasound to de-
termine post-void/residual urine. In ad-
dition, hepatic, renal and cardiac func-
tion tests showed no need for surgical
treatment (prostatectomy).

Exclusion criteria included prosta-
tectomy, acute urinary retention and
other lower urinary tract conditions
such as prostate cancer, neurogenic
bladder, bladder stones, relapse of ur-
inary tract infection, as well as cardiac,
hepatic, renal insufficiency, and de-
mentia. No study-compromising med-
icines were administered to patients,
including α/β-adrenoceptor agonists
and antagonists, anticholinergics, anti-
androgens, and 5α-reductase inhibitors.

All patients were prescribed a daily
dose of 0.4 mg of tamsulosin, over the
study course of 12 weeks, with check-
ups after the 4th week and at the end of
the study.

The following parameters were used
to evaluate the clinical efficacy of tam-
sulosin:
- Irritation symptoms (IPSS-I) –
  storage symptoms,
- Obstructive symptoms (IPSS-O)
  – voiding symptoms,
- Complex symptomatology-total
  IPSS (IPSS-T),
- Quality of life as a consequence of
  urinary symptoms (QoL),
- Side effects.

IPSS (IPSS-T) questionnaire con-
sisted of the following questions:
- Over the past month, how often
did you feel an incomplete dis-
charge upon urination?
- Over the past month, how often
did you have the need to urinate in
under than two hours after
previous urination?
- Over the past month, how of-
ten have you had intermittent
urination, where the stream is
interrupted?
- Over the past month, how often
did you have difficulties holding
off urination?
- Over the past month, how of-
ten did you have a weak urin-
ary stream?
- Over the past month, how of-
ten did you have to strain and push
to get the stream going?
- Over the past month, how of-
ten did you have the need to get
up during the night to urinate?

Answers to previous questions were
divided into six categories:
- None.
- One to five times.
- Less than half the times.
- Around half the times.
- More than half the times.
- Almost always.

Questions 2, 4, and 7, were getting
at irritation symptoms (IPSS-I), while
questions 1, 3, 5 and 6 identified ob-
structive symptoms (IPSS-O). The max-
imum score was 35 points.

This research utilized IPSS-QoL in
the eighth question, which was getting
at disease-spe-
cific quality of life. It referred
to quality of life as a con-
sequence of urinary symp-
toms:
1. If you had to spend the rest of your life with the
voiding situation as it is now, how would you describe it?

The answer utilized the following scale:
- fascinated
- 1-satisfied
- 2-somewhat satisfied
- 3-semi-satisfied (equally satisfied and dissatisfied)
- 4- mainly dissatisfied
- 5- dissatisfied

The efficacy of tamsulosin at the
beginning of the study and during the
checkups was evaluated through IPSS-
T in time intervals of 4 and 12 weeks,
as shown in Table 2 and Table 3. At the
beginning of tamsulosin treatment, the
total IPSS was 24.95 points. During the
checkups at 4 and 12 weeks, the total
IPSS was 16.09 and 11.20 points, re-
spectively. A reduction in pain intensity,
quantified through IPSS, was 35.51% af-
ter 4 weeks of treatment and 55.11% af-
ter 12 weeks. Tables below show statisti-
cally significant differences between
the initial value of IPSS and the values
after all checkups (p<0.05).

Questions related to irritation
symptoms (storage symptoms) were 2,
4 and 7, while obstructive symptoms
(voiding symptoms) were identified by
questions 1, 3, 5 and 6. As shown in Ta-
ble 4, there is a statistically significant
difference between the initial values
for irritative and obstructive symptoms
and the values for these symptoms af-
ter the two checkups (p<0.05). The ini-
tial value of mean for irritative symp-
toms was 3.25 points and 3.82 points
for obstructive symptoms. During

<table>
<thead>
<tr>
<th>Variables</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>45</td>
</tr>
<tr>
<td>Patient age (± SD)</td>
<td>66.3 ± 5.8</td>
</tr>
<tr>
<td><strong>Table 1. Patient Age</strong></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Variable (AM, SD)</th>
<th>First checkup</th>
<th>Second checkup (after 4 weeks)</th>
<th>Third checkup (after 12 weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Question no. 1</td>
<td>3.88 ± 1.10</td>
<td>2.58 ± 1.23</td>
<td>1.64 ± 0.96</td>
</tr>
<tr>
<td>Question no. 2</td>
<td>3.38 ± 1.26</td>
<td>2.02 ± 0.99</td>
<td>1.33 ± 0.88</td>
</tr>
<tr>
<td>Question no. 3</td>
<td>3.60 ± 1.01</td>
<td>2.37 ± 1.07</td>
<td>1.64 ± 1.07</td>
</tr>
<tr>
<td>Question no. 4</td>
<td>2.80 ± 1.32</td>
<td>1.77 ± 1.14</td>
<td>1.31 ± 0.92</td>
</tr>
<tr>
<td>Question no. 5</td>
<td>4.16 ± 0.93</td>
<td>2.42 ± 1.17</td>
<td>1.95 ± 1.11</td>
</tr>
<tr>
<td>Question no. 6</td>
<td>3.66 ± 1.15</td>
<td>2.27 ± 1.25</td>
<td>1.40 ± 0.92</td>
</tr>
<tr>
<td>Question no. 7</td>
<td>3.57 ± 1.19</td>
<td>2.67 ± 1.15</td>
<td>1.93 ± 1.03</td>
</tr>
<tr>
<td><strong>Table 2. The efficacy of tamsulosin on total IPSS (IPSS-T).</strong></td>
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<td></td>
</tr>
</tbody>
</table>

Legend: AM – arithmetic mean, SD – standard deviation

<table>
<thead>
<tr>
<th>Variable</th>
<th>IPSS – T</th>
<th>Difference</th>
<th>Difference (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>First checkup</td>
<td>24.95 ± 6.04</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Second checkup (after 4 weeks)</td>
<td>16.09 ± 6.18</td>
<td>-8.86</td>
<td>-35.51%</td>
</tr>
<tr>
<td>Third checkup (after 12 weeks)</td>
<td>11.20 ± 4.16</td>
<td>-13.75</td>
<td>-55.11%</td>
</tr>
</tbody>
</table>
| **Table 3. The efficacy of tamsulosin – total IPSS**
checkups, in time intervals of 4 and 12 weeks, the means for irritative symptoms were 2.16 and 1.53 points, respectively, while these values were 2.41 and 1.66 points for obstructive symptoms, respectively.

The sum of means for irritative and obstructive symptoms was calculated as well. This sum for obstructive symptoms was 15.20 points at the beginning of treatment, 9.64 points after 4 weeks and 6.63 points after 12 weeks. Moreover, the sum of means for irritative symptoms was 9.75 points in the beginning, 6.45 points after 4 weeks and 4.57 points after 12 weeks of the tamsulosin treatment.

5. DISCUSSION

Quality of life as a consequence of urinary symptoms was quantified using the Quality of Life Index (QLI), i.e. question No. 8 in IPSS. Quality of Life Index was initially 4.49 points, while it decreased to 2.49 points after 4 weeks and to 1.40 points after 12 weeks, marking an improvement of 44.54% after 4 weeks and 68.82% after 12 weeks. There is a statistically significant difference between the initial value of QLI and its values during checkups (p<0.05).

Side effects, as shown in Table 6, were observed in three patients (6.66%), with one (2.22%) experiencing problems with ejaculation and the other two (4.44%) vasodilator side effects such as vertigo and headache. These side effects were mild and required no treatment interruption or exclusion from the study.

### Table 6. Side effects

<table>
<thead>
<tr>
<th>Types of side effects</th>
<th>Number of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retrograde ejaculation</td>
<td>1 (2.22%)</td>
</tr>
<tr>
<td>Vertigo</td>
<td>1 (2.22%)</td>
</tr>
<tr>
<td>Headache</td>
<td>1 (2.22%)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>3 (6.66%)</td>
</tr>
</tbody>
</table>

The efficacy of tamsulosin – obstructive and irritative symptoms IPSS Legend: AM-arithmetic mean, SD – standard deviation

### Table 5. The efficacy of tamsulosin on quality of life

<table>
<thead>
<tr>
<th>Variables (AM, SD)</th>
<th>First checkup</th>
<th>Second checkup (after 4 weeks)</th>
<th>Third checkup (after 12 weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IPSS – O</td>
<td>3.82 ± 1.06</td>
<td>2.41 ± 1.18</td>
<td>1.66 ± 1.02</td>
</tr>
<tr>
<td>IPSS – I</td>
<td>3.25 ± 1.30</td>
<td>2.16 ± 1.15</td>
<td>1.53 ± 0.98</td>
</tr>
</tbody>
</table>

The efficacy of tamsulosin – obstructive and irritative symptoms IPSS Legend: AM-arithmetic mean, SD – standard deviation

### Table 4. The efficacy of tamsulosin – obstructive and irritative symptoms IPSS Legend: AM-arithmetic mean, SD – standard deviation

<table>
<thead>
<tr>
<th>Variables (AM, SD)</th>
<th>First checkup</th>
<th>Second checkup (after 4 weeks)</th>
<th>Third checkup (after 12 weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IPSS – O</td>
<td>15.20 ± 4.19</td>
<td>9.64 ± 4.72</td>
<td>6.65 ± 4.06</td>
</tr>
<tr>
<td>IPSS – I</td>
<td>9.75 ± 3.77</td>
<td>6.45 ± 3.28</td>
<td>4.57 ± 2.83</td>
</tr>
</tbody>
</table>

5. DISCUSSION

For many decades, the use of α1-adrenoceptor antagonists in the relaxation of the bladder neck and prostate smooth muscle, with consequential re-
duction of subvesical obstruction and increased urinary flow, represented the most frequent method of BPH treatment (15). A high incidence of side effects, primarily orthostatic hypotension, was typically associated with the first generation of α1/α2 antagonists, such as phenoxybenzamine, which often led to treatment interruption (16). The subsequent period saw the introduction of short-term selective α1-adrenoceptor antagonists, such as tamsulosin and alfuzosin, followed by long-term and additionally uroselective α1-adrenoceptor antagonists (17). A side effect of serious hypotension is typically associated with the use of prazosin, terazosin, doxazosin and alfuzosin (18, 19, 20). Although this side effect can be reduced by dose titration, approximately 10% of patients decide to abandon treatment (21). The latest pharmacological studies identified three subtypes of α1-adrenoceptors: α1-A, α1-B and α1-D (22). The α1-A subtype is the most highly concentrated in the prostate and is a primary regulator of smooth muscle tone (23). Conversely, α1-B is predominant in larger arteries, while α1-D is in the detrusor. Given this, the medications with a relatively high affinity for α1-A adrenoceptors are uroselective α1AR antagonists, with tamsulosin being a newer uroselective α1-A/α1DAR antagonist, along with naftopidil and silodosin. Research shows a 38 times higher affinity of tamsulosin for α1-A, as opposed to α1-B adrenoceptors (12), which is exactly why tamsulosin has significantly lower number of vasodilatory side effects.

Most clinical studies to date showed a high level of tamsulosin efficacy on storage and voiding symptoms. Osamu U. et al found that total initial value for IPSS was 18.9 points, while after two weeks of tamsulosin treatment total IPSS was 11.5 points and 9.2 points after 6-8 weeks – both statistically significant differences (p<0.0001). Like IPSS, the Quality of Life Index also improved (26). Our study found that the beginning of the tamsulosin treatment, the total IPSS was 24.95 points. During checkups at 4 and 12 weeks, total IPSS was 16.09 and 11.20 points, respectively. A reduction in subjective symptoms, quantified by IPSS, amounted to 35.51% following 4 weeks of treatment, and 55.11% following 12 weeks. Also, the quality of life improved by 44.54% after 4 weeks and 68.82% after 12 weeks. There is a statistically significant difference between the initial value of IPSS and QLI and their values following all checkups (p<0.05).

Analyzing the efficacy of tamsulosin against voiding and storage symptoms, Osamu U. et al found a statistically significantly increased daily frequency of voiding and nocturia from initial 3.5 to 2.0 points in case of voiding (p=0.025) and 3.4 to 1.7 points in case of nocturia (p<0.0001) (26). In terms of voiding symptoms, they found a significant improvement of urinary flow from 3.2 to 1.4 points (p=0.003) (26). The present study found a statistically significant difference between the initial voiding and storage symptoms values and the values after checkups (p<0.05). The values for voiding symptoms decreased from 3.82 to 2.41 points after 4 weeks, and to 1.66 points after 12 weeks. The values for storage symptoms were initially 3.25 points, decreasing to 2.16 points after 4 weeks, and 1.53 points after 12 weeks.

Discussing the side effects of α1-AR antagonists, a study by B. Davan found that vertigo is much more frequent during the treatment with alfuzosin and terazosin than tamsulosin. In addition, the incidence of syncope and hypotension was similar for both tamsulosin and alfuzosin. Treatment interruption due to vasodilatory effects was similar for tamsulosin and alfuzosin, while...
Efficacy and Safety of Tamsulosin in the Treatment of Benign Prostatic Hyperplasia

higher for terazosin. Interruption due to vertigo was 0.6% for tamsulosin and 2.0% for alfuzosin. The same study found increased incidence of ejaculatory abnormalities caused by tamsulosin (5-11%), also identified in European and US studies.

Within the present study study, side effects were observed in three patients (6.66%), with one (2.22%) displaying problems with ejaculation and the other two (4.44%) having vasodilatatory side effects such as vertigo and headache. These side effects were mild and required no treatment interruption or exclusion from the study.

6. CONCLUSION

During a 12-week tamsulosin treatment, all lower urinary tract symptoms were significantly reduced. The clinical response significantly improved after a longer treatment (4-12 weeks). The side effects were rare and mild, and did not require treatment interruption.

Conflict of interest: none declared.

REFERENCES