RESEARCH ARTICLE

Comparative evaluation of cost-effectiveness of alpha blockers prescribed in patients with non-neurogenic lower urinary tract symptoms due to benign prostatic hyperplasia

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ABSTRACT

Background: Lower urinary tract symptoms (LUTS) due to Benign Prostatic Hyperplasia (BPH) is a common problem among aging men. Several classes of drugs are efficacious and safe, but the first-line treatment is with alpha-1 adrenergic blockers. They provide symptomatic relief and have to be taken for a longer duration to sustain the effect. The preferred alpha-blockers among the stockpile should be efficacious, tolerable, and also cost-effective. Aim and Objective: This study focuses to compare the cost-effectiveness of various alpha blockers prescribed in patients with LUTS-BPH. Materials and Methods: An observational study of 78 patients who were newly diagnosed with LUTS-BPH from April 2014 to May 2015 was conducted. Patients were followed up at 4 weeks and at 12 weeks after the drugs had been prescribed. Efficacy assessment was done on basis of change in International Prostate Symptom Score (IPSS) score over 12 weeks. Average cost-effectiveness ratio of different alpha-blockers prescribed was evaluated and compared with Mann-Whitney U test in order to find the most cost-effective alpha-blocker in the study. Results: All patients were prescribed alpha-blockers either alone or in combination with other drugs. Tamsulosin was prescribed to \( n = 46 \), Silodosin to \( n = 16 \) and Alfuzosin to \( n = 16 \). The efficacy in terms of Mean change in IPSS after 12 weeks of study was 11.34 ± 5.23 for Tamsulosin, 11.70 ± 5.9 for Silodosin and 10.87 ± 4.77 for Alfuzosin and average cost-effectiveness ratio was 108.74, 183.07 and 127.50 for Tamsulosin, Silodosin, and Alfuzosin, respectively. Conclusion: Tamsulosin was the most cost-effective drug among the prescribed alpha-blockers. Since all the prescribed alpha-blockers had comparable efficacy so we concluded that the most cost-effective drug should be preferred for long-duration treatment.

KEY WORDS: Alpha Blockers; Tamsulosin; Silodosin; Alfuzosin; Cost-effectiveness; Lower urinary tract symptom-Benign Prostatic Hyperplasia

INTRODUCTION

Non-neurogenic Lower urinary tract (LUTS) symptoms arising due to benign prostatic hyperplasia (BPH) are bothersome and exert a significant effect on the quality of life in elderly male population. LUTS has multiple symptoms which are allocated in obstructive (voiding) symptoms and irritative (storage) symptoms. These symptoms can be quantitatively evaluated with help of questionnaires such as the International Prostate Symptom Score (IPSS). Voiding abnormalities are further expressed as slow stream, straining, intermittency, sense of incomplete emptying, hesitancy, and painful voiding, while the storage abnormalities present as increased frequency, nocturia, urgency, and urge incontinence. Nocturia being the important symptom of
LUTS in Bladder outflow obstruction. Recently multiple drugs have been introduced for the treatment of LUTS. These newer and safer drugs brought down surgical indications for the treatment of LUTS significantly. The preferred drug treatment for most men with BPH is with alpha-1 blockers, (i.e Prazosin, Terazosin, Alfuzosin, Doxazosin, Tamsulosin, and Silodosin) which work by relaxing smooth muscle at the bladder neck, and prostate. Symptoms improve within days, but the full effect of the drug comes after few weeks. The efficacy of the oral drugs in the treatment of LUTS is confirmed in the Medical Therapy of Prostatic Symptoms trial, in which only 14% of men with BPH developed symptom progression, 2% developed acute urinary retention, over a follow-up interval of 4 years. Alpha-1-Blockers act symptomatically by reducing both storage and voiding LUTS in most of the cases, however, they have to be taken for a longer duration. Therefore for such a long duration treatment, the cost of medication has a very important role. An ideal drug for the treatment of non-neurogenic LUTS due to BPH must be efficacious, safe, and easily affordable by the patient. Very few studies have been undertaken in the past which have compared the cost-effectiveness of various alpha-blockers used in BPH patients. The present study focuses on a comparative evaluation of cost-effectiveness between commonly prescribed alpha-blockers in non-neurogenic LUTS-BPH patients.

MATERIALS AND METHODS

This observational open-label study was carried out in the Departments of Pharmacology and Urology at Himalayan Institute of Medical Sciences, Dehradun in BPH patients having non-neurogenic LUTS over a period of one year. Necessary approval was obtained from Institutional Ethics Committee before the commencement of the study.

Inclusion Criteria

Male patients above the age of 45 years who were newly diagnosed with nonneurogenic LUTS due to BPH.

Exclusion Criteria

Patients with incomplete demographic or prescription details, patient having neurogenic bladder, patients diagnosed with Prostatic cancer and other malignancies, patients planned for immediate intervention. Patients who had any recent surgery for pelvic trauma or urethral strictures. Patients having history of cognitive and psychiatric disorders were also excluded from the study.

Study Design

From January 2014 to May 2015, total of 84 newly diagnosed male patients with non-neurogenic LUTS-BPH patients was enrolled for the study fulfilling the inclusion and exclusion criteria. Patients were called for follow-up at 4 weeks and at 12 weeks. The total study duration was 12 weeks.

Prescriptions of the patients were analyzed and the average cost of the treatment of prescribed alpha-blockers (either in combination with 5 alpha-reductase inhibitor/antimuscarinic or alone) was evaluated on the basis of the maximum retail price of the particular brand of alpha-blocker which was prescribed in the study. Evaluation of efficacy was done on the basis of change in IPSS after 12 weeks of treatment. The IPSS score is a validated scoring system widely used as a diagnostic tool in urology to assess disease severity and response to therapy. As per the guideline, the score of 7 or less is mildly symptomatic, 8–19 is moderate, and a score of 20–35 is severely symptomatic.

Cost-effectiveness of various alpha-blockers used in the study was analyzed using the average cost-effectiveness ratio (ACER).

ACER was calculated using the formula:

\[ \text{ACER} = \frac{\text{Average cost of alpha blocker}}{\text{Mean change in IPSS with alpha blocker}} \]

A suitable statistical tool (Mann-Whitney U test) was applied to compare the ACER between the prescribed alpha-blockers and the results were analyzed.

Adverse drug reaction monitoring was done throughout the study period according to WHO-UMC guidelines.

RESULTS

A total of 84 BPH patients suffering from non-neurogenic LUTS due to BPH had been enrolled in the study. Out of these, 6 patients lost to follow-up so excluded from the analysis. The remaining patients were assessed by IPSS chart and compliance rate of more than 80% was ensured. Thus 78 patients completed the study.

These patients were prescribed alpha-blockers either alone or in combination with other drugs. Tamsulosin was prescribed to 46 patients, Silodosin was given in 16 patients, and Alfuzosin to 16 patients. Some patients treatment also included antibiotics, analgesics, antacid, pyridium (phenazopyridine), and urinary alkalizer syrup as per the requirement.

Out of 46 patients who were prescribed Tamsulosin, 20 received Tamsulosin alone while 20 were prescribed Tamsulosin + Dutasteride and 6 received Tamsulosin + Tolterodine.

Out of 16 patients who received Silodosin, 11 patients were prescribed Silodosin alone and 5 patients were given Silodosin + Dutasteride.
Out of 16 patients who were put on Alfuzosin, seven patients were given Alfuzosin alone, five patients received Alfuzosin + Dutasteride and four patients were given Alfuzosin + Tolterodine.

Tamsulosin was prescribed by the brand name of Urimax at a dose of 400 mcg and the cost of 1 capsule was INR 14.68. While the brand of Silodosin was used was Silodal (8 mg), whose cost was INR 25.5 per capsule and for Alfuzosin (Flotral 10 mg) it was INR 16.5 per capsule. All Alpha-blockers drugs are prescribed once daily at bed time. Hence, the average cost of the treatment of widely prescribed alpha-blockers during the study was INR 1,233.12 for Tamsulosin, INR 2142 for Silodosin, and INR 1386 for Alfuzosin [Table 1].

The efficacy in terms of Mean change in IPSS after 12 weeks of study was 11.34 ± 5.23 (Mean ± SD) for Tamsulosin, 11.70 ± 5.9 for Silodosin and 10.87 ± 4.77 for Alfuzosin.

The ACER was 108.74, 183.07 and 127.50 for Tamsulosin, Silodosin, and Alfuzosin respectively (Figure 1). Intergroup comparison of ACER showed a significant difference between all the three groups of drugs (Group I- Tamsulosin and Silodosin, Group II- Tamsulosin and Silodosin and Group III- Alfuzosin and Silodosin) on applying Mann Whitney U test (P < 0.05). The significant difference was found between tamsulosin and silodosin, making the tamsulosin the most cost-effective drug among the three [Table 2].

The adverse events recorded during the study period were four in total but none was serious in nature. Two patients complained of Dizziness (1 in Tamsulosin and 1 in the Silodosin group). Dry mouth was seen in 1 patient in the Tamsulosin group. Retrograde ejaculation was reported by 1 patient in the Silodosin group. No adverse drug reaction was reported with Alfuzosin in the present study.

**DISCUSSION**

As far as pharmacotherapy of LUTS is concerned, alpha-blocking agents continue to be the first-line treatment for moderate to severe LUTS in men. Alpha 1 adrenoceptor antagonist are considered as most effective monotherapy for the relief of LUTS, irrespective of prostate size. Different controlled trials have suggested that alpha-1 blockers show early improvement in symptoms and flow rate and are maintained for up to 5 years. Narayan and associates demonstrated that in their study, patients of BPH have sustained relief of symptoms for up to 6 years without the development of any tolerance to Tamsulosin. These trials indicate that oral drugs continue to be efficacious for a longer duration of time. So the cost of the drug plays an important role while selecting among alpha-blockers. Alpha-blockers such as Alfuzosin, Tamsulosin, and Silodosin are the keystone in the treatment of BPH. There is a difference in the efficacy, tolerability, and total costs incurred. This study is in continuation of the study done by Dwivedi et al. where it was found that all three α-blockers Tamsulosin, Silodosin, and Alfuzosin have comparable efficacy. No adverse effect had been reported with alfuzosin as compared to Silodosin and Tamsulosin. According to Parikh A et al., the three alpha blockers Tamsulosin, Silodosin and Alfuzosin improve the IPSS significantly after 2 months of the treatment. However, they found no major difference between the three drugs in terms of IPSS improvement. A randomized study performed on 269 patients concluded that Silodosin is the most efficacious alpha-blocker with the earliest onset of action but with more adverse events than Tamsulosin and Alfuzosin. There is no clear guideline about which alpha-blocker should be started first. On comparison between the ACER in the current study, Tamsulosin is the most cost-effective among the three alpha-blockers prescribed in the study. Whereas Silodosin was the most expensive amongst the three alpha-blockers prescribed and was also significant in terms of IPSS improvement.

**Table 1: Cost analysis with different alpha-blockers**

<table>
<thead>
<tr>
<th>Drug</th>
<th>No. of patients</th>
<th>Cost per capsule (Rs)</th>
<th>Average cost for 12 weeks (Rs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tamsulosin</td>
<td>46</td>
<td>14.68</td>
<td>1233.12</td>
</tr>
<tr>
<td>Silodosin</td>
<td>16</td>
<td>25.5</td>
<td>2142</td>
</tr>
<tr>
<td>Alfuzosin</td>
<td>16</td>
<td>16.5</td>
<td>1386</td>
</tr>
</tbody>
</table>

**Table 2: ACER comparison between different groups**

<table>
<thead>
<tr>
<th>Groups</th>
<th>ACER Comparison</th>
<th>ACER Comparison</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>I-Tamsulosin (A) and Silodosin (S)</td>
<td>T (108.74) &lt; S (183.07)</td>
<td>Silodosin is 1.69 times more than Tamsulosin</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>II-Tamsulosin (T) and Alfuzosin (A)</td>
<td>T (108.74) &lt; A (127.50)</td>
<td>Alfuzosin is 1.17 times more than Tamsulosin</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>III-Alfuzosin (A) and Silodosin (S)</td>
<td>A (127.50) &lt; S (183.07)</td>
<td>Silodosin is 1.43 times more than Alfuzosin</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

ACER: Average cost-effectiveness ratio

Figure 1: Average cost-effectiveness ratio for alpha blockers

![Figure 1](image-url)
associated with two adverse effects. A prospective study done by Manjunatha et al. on cost-effectiveness of alpha-blockers, Alfuzosin was found to be the most economical α-blocker in the management of BPH.[11]

Limitations of the Study

This study was an observational open-label study. Since no blinding was done so chances of bias remained. The sample size of the study was small because the duration of follow-up was kept at 12 weeks. A bigger sample size with a longer duration of follow-up could have yielded different outcomes.

CONCLUSION

The present study showed that the three alpha-blockers (Tamsulosin, Silodosin, and Alfuzosin) have comparable efficacy and the final decision regarding choosing alpha-blockers in patients with LUTS-BPH is dependent upon patient profile. The most cost-effective alpha-blocker is Tamsulosin as per this study and it should be preferred for long-term treatment in LUTS-BPH patients. However, studies with a larger sample size and for a longer duration will be needed to validate the results of our study.

REFERENCES


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