ABSTRACT

Objective: This study aims to determine the effect of tamsulosin administration on alteration in PSA levels in BPH patients in Padang. Material & Methods: This study employed an analytical method with a prospective cohort design. The research was conducted at M. Djamil General Hospital, BMC Hospital, Hermina Hospital, and Semen Padang Hospital in August - December 2022. Sampling was carried out by consecutive sampling. Results: At the end of the study, there were 23 patients with BPH. The mean age was 67.5 ± 7.7, which most of them having good education. Patients were mostly self-employed. The highest IPSS score is the severe stage. The PSA levels before and after tamsulosin administration were 1.7 ± 0.9 ng/ml and 1.6 ± 0.8 ng/ml, respectively. Bivariate analysis showed that tamsulosin administration affects PSA levels in benign prostatic hyperplasia patients in Padang. Conclusion: There is an effect of tamsulosin administration on PSA levels.

Keywords: Benign prostatic hyperplasia, tamsulosin, prostate-specific antigen.

INTRODUCTION

Benign prostatic hyperplasia (BPH) is a nonmalignant growth or hyperplasia of prostate tissue and is a common cause of lower urinary tract symptoms (LUTS) in men. The development of BPH is characterized by the proliferation of stromal and epithelial cells in the prostatic transition zone (around the urethra). It leads to compression of the urethra and development of bladder outflow obstruction, which may result in the clinical manifestations of LUTS, urinary retention or infection due to incomplete bladder emptying. The prevalence of BPH worldwide varies from 20 – 62% in men age>50 years, including in the United States, United Kingdom, Japan and Ghana.

Patients with BPH usually come with complaints of the lower urinary tract, known as LUTS. LUTS symptoms and rectal touch examination were performed to assess prostate enlargement. LUTS is best measured with a validated questionnaire, such as the International Prostate Symptom Score (IPSS). Blood tests, urinalysis, ultrasound, cystoscopy, uroflowmetry examination, and Prostate-specific antigen (PSA) examination.

Tamsulosin is an alpha-1 adrenoreceptor antagonist designated as BPH therapy because it is...
selective for the urinary tract. Tamsulosin has been the most commonly prescribed Alpha1 blocker since the mid-2000s and continues to be used today. Several studies have stated that PSA is related to symptoms in patients where the higher the PSA, the more severe the symptoms found in patients. PSA is produced by prostate stromal cells. Prostate volume and serum PSA predict certain aspects of the natural history of LUTS and BPH, and men with higher PSA and larger prostate size generally have higher rates of progression as measured by various parameters.1,3,4

In prostate cancer patients, PSA increased significantly after treatment. However, PSA decreased in the BPH/LUTS patients. Alpha-blockers can cause a decrease in PSA. This event can occur due to the process of apoptosis caused by alpha-blockers.

The BPH group of drugs, both 5-ARI and alpha-blockers such as tamsulosin, increase TGFβ-modulated apoptosis, stimulating cell death and involving several transcription factors. Studies have suggested that apoptosis is a good target for the long-term therapeutic effects of doxazosin and terazosin in BPH. PSA is an examination to assess the degree of prostate growth resulting from prostate stromal cells. It is known so far alpha-blockers can reduce symptoms in patients because of their properties that can relax smooth muscles.

Theories regarding the apoptotic effect of alpha-blockers which can reduce prostate volume may also be related to a decrease in these symptoms and will indirectly affect reducing PSA due to reduced volume. Therefore, this study aims to determine the effect of tamsulosin administration on alteration in PSA levels in BPH patients in Padang.

**OBJECTIVE**

This study aims to determine the characteristics of BPH patients and the effect of tamsulosin administration on changes in prostate-specific antigen (PSA) levels in BPH patients in Padang City.

**MATERIALS & METHODS**

This study employed an analytical method with a prospective cohort design. The research was conducted at M. Djamil General Hospital, BMC Hospital, Hermina Hospital, and Semen Padang Hospital in August - December 2022. In consecutive sampling, medical records of the 23 patients in the same laboratory before and after administration of tamsulosin 0.4 mg were collected. Patient medical records after administration of tamsulosin were collected after 4-8 weeks. The patient's demographic data, such as age, education, occupation, and IPSS score, were also collected.

\[
\begin{align*}
    n &= \left( \frac{Z_\alpha \times S}{d} \right)^2 \\
    n &= \left( \frac{(1.59) \times 2.8}{1} \right)^2 \\
    n &= 19.02 - 20 \text{ samples}
\end{align*}
\]

Caption:

\(Z_\alpha\) : alpha standard derivative = 1.59

\(S\) : Standard Deviation = 2.8

\(d\) : set as 1

\[\text{Figure 1. Sample size formula to test the hypothesis of the mean difference before and after treatment.}\]

**RESULTS**

As shown in , we obtained the mean age of BPH patients was 67.5 ± 7.7 years. Most of the patients had good educational status (high school [60.9%] and college [17.4%]). Most patients' occupations were entrepreneurs (39.1%) and farmers (21.7%). In assessing the IPSS score, 17 patients (73.9%) had a severe score, while the rest (6 patients, 17%) had an average score.

In this study, we obtained the initial PSA level of 1.78 and the final PSA level of 1.68, which means the average PSA level decreased by 0.10 after the administration of tamsulosin.

The bivariate analysis used to determine the effect of tamsulosin administration on changes in PSA levels in BPH patients was the T-dependent test. However, before this analysis, the PSA level data must be tested for normality first. The normality test used was the Shapiro-Wilk test since the number of samples was less than 50. shows that the data were normally distributed as indicated by the significance value of the normality test > 0.05, namely 0.212 and 0.102. Hence, the T-dependent test analysis was appropriate to use. In T-dependent analysis, it was also seen that there was a significant effect of administering tamsulosin on changes in PSA level in BPH patients, with a p-value <0.05.
Table 1. The characteristics of BPH patients in Padang City.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Mean ± SD</th>
<th>f</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>67.5 ± 7.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elementary school</td>
<td>3</td>
<td>13.0</td>
<td></td>
</tr>
<tr>
<td>Middle school</td>
<td>2</td>
<td>8.7</td>
<td></td>
</tr>
<tr>
<td>High school</td>
<td>14</td>
<td>60.9</td>
<td></td>
</tr>
<tr>
<td>College/University</td>
<td>4</td>
<td>17.4</td>
<td></td>
</tr>
<tr>
<td>Occupation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Farmer</td>
<td>5</td>
<td>21.7</td>
<td></td>
</tr>
<tr>
<td>Labourer</td>
<td>1</td>
<td>4.3</td>
<td></td>
</tr>
<tr>
<td>Seller</td>
<td>2</td>
<td>8.7</td>
<td></td>
</tr>
<tr>
<td>Entrepreneur</td>
<td>9</td>
<td>39.1</td>
<td></td>
</tr>
<tr>
<td>Civil servant</td>
<td>2</td>
<td>8.7</td>
<td></td>
</tr>
<tr>
<td>Retired</td>
<td>4</td>
<td>17.4</td>
<td></td>
</tr>
<tr>
<td>IPSS Score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>6</td>
<td>26.1</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>17</td>
<td>73.9</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>23</td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Descriptive test of PSA levels before and after administering tamsulosin to BPH patients in Padang City.

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Median</th>
<th>Min-max</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial PSA level</td>
<td>1.78</td>
<td>1.56</td>
<td>0.52-3.77</td>
<td>0.95</td>
</tr>
<tr>
<td>Final PSA level</td>
<td>1.68</td>
<td>1.66</td>
<td>0.48-3.42</td>
<td>0.86</td>
</tr>
</tbody>
</table>

Table 3. Bivariate analysis of PSA levels before and after administering tamsulosin to BPH patients in Padang City.

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>Shapiro-Wilk (p-value)</th>
<th>T dependent (p-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial PSA level</td>
<td>1.78</td>
<td>0.95</td>
<td>0.212</td>
<td>0.01</td>
</tr>
<tr>
<td>Final PSA level</td>
<td>1.68</td>
<td>0.86</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

DISCUSSION

In this study, the average age of BPH patients was 67.5 ± 7.7 years old. Several studies also stated that most BPH patients are aged 61-70. The histological prevalence of BPH at autopsy is approximately 50-60% in men 60 years of age and increases to 80-90% in patients 70 years and over. The Prostate is a male accessory reproductive gland with a high incidence of benign and malignant diseases that occur with aging. Studies in mouse models found prostate mass increased significantly between young and old mice due to increased cell proliferation. In addition, there was a significant increase in fibrosis and collagen deposition within the prostatic urethra in mice with voiding disorders, suggesting that collagen changes may alter normal urination. Finally, hormonal changes that occur with age also contribute to the discovery of more older adults with BPH.

Most of the patients had good educational status (high school [60.9%] and college [17.4%]). Research by Sarauw et al. states that education's influence on BPH is related to the level of awareness of treatment. Patients with low educational status usually come to the hospital after the condition of BPH gets worse, which causes higher patient management and insufficient medical treatment. However, in this study, the majority of patients came with a high IPSS score which indicated a fairly good educational status does not determine a person's attention to their disease.

Most patients' occupations were entrepreneurs (39.1%) and farmers (21.7%). Patients with heavy work produce more testosterone, so the risk of BPH events increases. Most people with
BPH have heavy work (90% of respondents). In this study, the distribution of jobs varies with the proportion of heavy work (laborers, traders, and farmers) having a smaller proportion. In assessing the IPSS score, 17 patients (73.9%) had a severe score, while the rest (6 patients, 17%) had an average score. This condition may be influenced by factors where Dr. M. Djamil General Hospital is a tertiary referral hospital, so the patients treated are advanced patients who cannot be managed at previous health facilities.

In this study, the initial PSA level was 1.78 ng/mL and the final PSA level was 1.68 ng/mL, so it can be seen that the average PSA level decreased by 0.10 ng/mL after administration of tamsulosin. The study by Tubaro suggested that reduced PSA levels in patients with negative prostate biopsy findings may result from improvements in voiding dynamics with reduced reflux of urine into the prostatic ducts because PSA is related to the degree of inflammation. Reducing urinary reflux and improving micturition dynamics will reduce inflammation around the Prostate. There is currently no reason for a direct pharmacological effect of tamsulosin on prostate epithelial cells.

Nonetheless, the apoptotic effects of doxazosin and terazosin on prostate cells are mediated by quinazo line-based alpha-blockers. Apart from causing pure relaxation of smooth muscle, certain alpha1-blockers can also influence prostate growth dynamics by altering the balance between prostate cell proliferation and apoptosis without affecting the proliferative process. It occurs through a mechanism of sympathetic/ catecholamine activity on target cell growth and differentiation. Doxazosin inhibits vascular smooth muscle cell proliferation despite its antagonistic effect on α1-adrenoceptors. Doxazosin and terazosin can affect prostate growth through differential signal transduction pathways that potentially involve TGF-β signaling or disturbances in cell cycle development. Besides that, through their alpha receptor antagonist effects, these drugs interfere with gland vascularization which causes tissue ischemia.

This study showed a significant effect of tamsulosin administration on changes in PSA levels in BPH patients. Alpha-blockers reduced the stromal/epithelial ratio predicted by PSA. Another study also found a decrease in PSA after tamsulosin therapy, where this change was found to be statistically significant. Tamsulosin with TGF-β on glomerular endothelial cells was found to have a relationship where tamsulosin inhibits the expression of high glucose-induced fibrosis factors such as Col-1 and TGF-β1, thereby preventing fibrosis from occurring.

BPH also occurs due to increased tissue fibrosis. With the effect of tamsulosin on TGF-β1, prostate volume can be reduced, leading to a decrease in PSA. Another mechanism for decreasing PSA due to tamsulosin is a decrease in inflammation due to decreased urinary reflux when using alpha-blockers. As previously known, the increase in PSA occurs due to damage to the integrity of the epithelial layer due to the inflammatory response.

CONCLUSION

We conclude that there was a decrease in PSA level after tamsulosin administration, and there was a relationship between tamsulosin administration and a statistically significant decrease in PSA level.

REFERENCES


