The effect of tamsulosin and dutasteride combination drug therapy on prostate volume in patients with benign prostatic hyperplasia

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Abstract. Benign prostatic hyperplasia (BPH) is a benign enlargement of the prostatic gland. This study was conducted to measure the improvement of prostate volume after treatment with Tamsulosin and Dutasteride as a combination drug in BPH patient at RSUD Kota Mataram from February 2020 to April 2020. The data were obtained by documenting the medical records of 20 new BPH patients ultrasound before and after 2 months therapy. This study was conducted using a comparative numerical analytical research model. The analysis was carried out by paired T-test in SPSS. A total of 20 medical records observed, the mean age of the study sample was 67.4 years, with the lowest age at 56 years and the oldest were 79 years, and 85% (17) of samples are more than 60 years old. The average prostate volume pre-therapy was 51.71 cc with the lowest volume was 25 cc and the highest volume 118 cc. Average prostate volume post-therapy was 42.38 cc, with the lowest volume was 22 cc and the highest 92 cc. The ratio of prostate volume more than 40 cc at pre-therapy was 50% (10 samples), and after therapy was decreased to 40% (8 samples). There are significant difference in comparison of pre and post-therapy prostate volume.

1. Introduction

Benign prostatic hyperplasia (BPH) is a condition when the stromal and epithelial cells that form the prostate experiencing a benign enlargement or hyperplasia[1]. The prevalence of the disease tends to increase with age. Research to determine the exact number of BPH in Indonesia does not accomplish yet, but based on data from the Cipto Mangunkusumo Hospital (RSCM) from 1994 to 2013, it shows that the incidence of BPH reached 3,804 cases with the mean age of the patiens are 66.61 years old[2].

Benign prostatic hyperplasia can cause many complaints such as nocturia, straining, incomplete voiding, intermittent or frequency, these symptoms known as Lower Urinary Tract Symptoms (LUTS)[3][4]. The diagnosis of BPH is based on anamnesis or history taking, physical examination, and supporting examination. Measurement of the size of the prostate volume can be done with a supporting examination such as ultrasonography (USG) and it is very helpful in the management of BPH[5][6].

Pharmacological therapy that can be given to BPH patients are groups of alpha-adrenergic antagonist drugs and 5-alpha-reductase inhibitors[7][8]. Alpha-adrenergic antagonist inhibit the contraction of smooth muscle of the prostate which will reduce resistance to bladder neck contraction and urethra. One drug that have widely used was Tamsulosin[8][9]. While the 5-alpha-reductase inhibitors work by inhibiting the conversion of testosterone to its active form, dihydrotestosterone (DHT), and prevent the hyperplasia process, slowing disease progression and reducing the size of the prostate. Dutasteride was one member of that drug group[2]. The time takes for each drug groups to reach peak drug effectiveness is varies, whereas the Alpha-adrenergic antagonists take only several days, while the 5-alpha-reductase inhibitors take several months to show significant clinical effects[7][8]. The administration of combination therapy of these two groups of drugs has better therapeutic effectiveness than administration of either one alone, because these two groups of drugs have different benefits of therapy[7][8].
2. Material and Methods

2.1. Data collected
This study was conducted using a comparative numerical analytical research model with the cross sectional method. The data were obtained by documenting the medical records of 20 new BPH patients who were undergo combination therapy of Tamsulosin and Dutasteride at the RSUD Kota Mataram from 14 February to 14 April 2020. The study sample was chosen using consecutive sampling technique, which is including all patients diagnosed with BPH with a prostate volume using transabdominal urology ultrasound and had never taken any BPH therapy before. There were 20 samples that met the inclusion criteria. The inclusion criteria in this study were patients who were diagnosed with BPH for the first time or had never received Dutasteride and Finasteride therapy and were willing to participate in the study. The exclusion criteria in this study were a history of prostate cancer. This study has received approval from the Health Research Ethics Commission of the University of Mataram.

2.2. Variables
The variables in this study were age, prostate volume before therapy and prostate volume after combination therapy of Tamsulosin and Dutasteride. The prostate volume is then analyzed for statistical differences between before and after combination therapy of Tamsulosin and Dutasteride.

2.3. Statistical Analysis
Statistical data analysis in this study using SPSS software. The statistical analysis performed is paired T-test comparative hypothesis test if the data is normal and the Wilcoxon test if the data distribution is not normal.

3. Result and Discussion

3.1. Patient Characteristics
This study used 20 new BPH samples patients, and received Tamsulosin and Dutasteride therapy at the RSUD Kota Mataram from 14 February to 14 April 2020. The data taken were obtained through medical record data. Patient characteristics in this study were distributed according to age, pre-therapy prostate volume, and post-therapy prostate volume.

| Table 1. Sample distribution according to age |
|-----------------------------------------------|
| Age              | Frequency (n) | Percentage (%) |
|------------------|---------------|----------------|
| <60 years old    | 3             | 15%            |
| >60 years old    | 17            | 85%            |
| Total            | 20            | 100%           |

Table 1 shows the sample distribution according to age. From the 20 research subjects studied, there were 3 BPH patients less than 60 years old (15%) and 17 people more than or equal to 60 years old (85%) with a mean age of 67.4 years.

| Table 2. Sample distribution according to prostate volume pre-therapy |
|---------------------------------------------------------------|
| Volume Prostate (cc) | Frequency (n) | Percentage (%) |
|----------------------|---------------|----------------|
| <40cc                | 10            | 50%            |
| >40cc                | 10            | 50%            |
| Total                | 20            | 100%           |

Characteristics of prostate volume obtained by transabdominal ultrasound showed that the mean pre-therapy prostate volume was 51.71 cc with the lowest volume 25 cc and the highest volume 118 cc.
Meanwhile, 10 patients (50%) with prostate volume less than 40 cc and 10 patients (50%) had prostate volume more than 40 cc at the time they had not received therapy (Table 2).

| Volume Prostate (cc) | Frequency (n) | Percentage (%) |
|---------------------|---------------|----------------|
| <40 cc              | 12            | 60%            |
| >40 cc              | 8             | 40%            |
| Total               | 20            | 100%           |

Table 3. Sample distribution according to prostate volume post-therapy

Post-therapy prostate volume mean are 42.38 cc with the lowest volume 22 cc and the highest volume 92 cc. Meanwhile, 12 patients (60%) with prostate volume less than 40 cc and 8 patients (40%) had prostate volume more than 40 cc after receiving Tamsulosin and Dutasteride combination therapy (Table 3).

3.2. Comparative Hypothesis Test

After doing a comparative hypothesis test, the comparison between the age variable and the decrease in prostate volume post-therapy through unpaired T-test, shows no significant difference (p = 0.497). The comparison between the pre-therapy prostate volume variable and the post-therapy prostate volume using the paired T-test, shows significant difference (p <0.001). The age variable was not further analyzed by the correlative test because there was no significant difference in the comparative test, while the pre-therapy and post-therapy prostate volume variables had a further assessment by correlation test using the linear regression method and obtained strong correlation results (r = 0.799).

Benign prostatic hyperplasia (BPH) is a condition which is stromal and epithelial cells that forming the prostate had a benign enlargement or hyperplasia[1]. Based on the existing theory, it is known that the size of the prostate volume that is said to be normal is 25 cc[2][6]. From the age distribution, most of the samples diagnosed with BPH at the age >60 years. This is consistent with several studies which state that the incidence of BPH increases with age. One of the studies conducted by Loeb et al. (2009) to 278 male patients with an average age of 58 years showed that prostate volume increased by 0.6 cc per year[10]. Research from Zhang et al (2013) strengthen the findings of the characteristics of the respondents in this study, which from their research found a significant relationship between prostate volume and the age of BPH patients especially after 60 years of age[11]. Meanwhile, in our research there was no significant difference between age and prostate volume variables.

Dutasteride therapy is given to reduce the size or volume of the prostate in BPH patients, while Tamsulosin is given to relieve symptoms such as LUTS or Lower Urinary Tract Symptoms that often occur in people with BPH. Administration of Tamsulosin can be done as a single therapy or as a combination therapy, however, combination therapy is more preferable nowadays. Our result in this study is consistent with several studies such as Roehrborn et al. (2008) test on 4.844 men with BPH, and 3.822 (79%) of them completed the combination therapy for 2 years, resulting in decreased prostate volume and LUTS symptoms disappeared, and shows significant difference with the patients who did not complete the drug combination course for 2 years[8]. Nickel et al. (2011) confirm that Dutasteride for BPH patients has a good results on prostate volume reduction[11]. While Manohar et al (2017) showed that monotherapy with alpha-blocker gives significant symptoms improvement[12]. Another study by Zhou Z et al (2019) stated that Dutasteride has a significant effect when compared to other drugs in the same class like finasteride. In addition, the dose used in Dutasteride is smaller than that of other drugs in the same group. The therapeutic dose for Dutasteride is 0.5 mg while Finasteride 5 mg. Combination with tamsulosin is also required to reduce LUTS symptoms, so that this combination therapy is better than Tamsulosin alone therapy or Dutasteride alone[13].

4. Conclusion
Based on the results of this study, it can be concluded that there are significant differences in prostate volume in BPH patients treated using a combination drugs Tamsulosin and Dutasteride at the RSUD Kota Mataram. Although not directly correlated, this combination therapy will make an improvement in the prostate symptoms and size more rapidly, and will reduce the time for the patients to consume the drugs, hopefully will reduce the drugs chemical waste and faster improvement for the quality of life and patients productivity.

5. References

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