



IPP AND CHANGES IN IPSS IN BENIGN PROSTATIC HYPERPLASIA (BPH) PATIENTS TREATED WITH α 1-BLOCKER

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ARTICLE INFO	ABSTRACT
Published: Januar 26th, 2023 Keywords: benign prostatic hyperplasia (BPH), IPSS, intravesical prostatic protrusion (IPP), α1-blocker	Benign prostatic hyperplasia (BPH) is a benign enlargement of the prostate gland caused by the proliferation of epithelial cells and stroma, causing Lower Urinary Tract Symptoms (LUTS). One of the ways to treat BPH is through medical therapy with α1-blockers. The success of medical therapy is influenced by many factors, one of which is Intravesical Prostatic Protrusion (IPP). This study was a comparative prospective study that aimed to find the effect of IPP on response to therapy with α1-blockers in BPH patients. IPSS was used as a measuring tool. IPP was examined using transabdominal ultrasound. The study was conducted from July 2020 to December 2020. Data were analyzed using the one way ANOVA average comparison test and Pearson correlation test. A sample of 30 patients was divided into 3 groups based on the IPP degree, namely grade I (<5mm), grade II (5-10mm) and grade III (> 10mm). There were no significant differences in the mean initial IPSS scores in each group, namely 19.6, 18.90, and 21.30 ($p = 0.216$). There was a significant decrease in mean IPSS after 1 month of α1-blocker therapy. In addition, there was also found a significant correlation between the IPP value and the decrease in the final IPSS with a negative correlation. There is a significant correlation between the IPP degree and the decrease in IPSS in BPH patients after receiving α1-blocker therapy as the higher the IPP degree, the lower the final IPSS improvement.

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INTRODUCTION

Benign Prostatic Hyperplasia (BPH) is a benign enlargement of the prostate gland due to the proliferation of epithelial and stromal cells, giving rise to symptoms of lower urinary tract symptoms (LUTS) (Madersbacher et al., 2019). The incidence of BPH increases according to age, generally BPH occurs in men over 50 years old by 50% of cases, but in 20% cases it can occur in men aged 41-50 years, if they are over 80 years old, more than 90% of men get BPH (Basuki, 2015; Dhingra & Bhagwat, 2011; Tanagho, 1995). The structure of the prostate in BPH that undergoes changes includes, volume and histology. Changes in terms of prostate volume it varies with each age. From the reports obtained, prostate volume increased by 25cc in men aged 30 years and 35-45cc in men aged 70 years (Roehrborn & McConnell, 1994).

The estimated number of BPH sufferers in the world is 30 million cases. In the United States, more than 50% of men aged 60-70 years experience symptoms of BPH and 90% of BPH symptoms occur in the age of 70-90 years (Parsons, 2010). In Indonesia, the exact number for the incidence of BPH has never been studied before. An overview of the Hospital Prevalence at Cipto Mangunkusumo Hospital (RSCM) from 1994-2013 found 3,804 cases with an average age of 66.61 years. Based on data from Hasan Sadikin Hospital from 2012-2016 there were 718 cases

with an average age of 67.9 years (Tjahjodjati et al., 2017). The number of BPH patient visits at RSUP. Dr. M. Djamil Padang from 2014 to 2017 was volatile, in 2014 there were 212 inpatient cases and 1116 outpatient cases. In 2017 there were 1379 outpatient cases and 63 inpatient cases (Zul, 2019).

The BPH diagnosis is based on anamnesis, physical examination, and supporting examinations of laboratory and imaging. Complaints of lower urinary tract symptoms (LUTS) were found during anamnesis (Gratzke et al., 2015). LUTS is a collection of symptoms of Bladder Outlet Obstruction (BOO) which consists of obstructive and irritative symptoms. The LUTS complaint was made in the form of a score by a Urologist known as the International Prostate Symptom Score (IPSS) and Quality of Life (QoL) (Dmochowski, 2005; A. Lee et al., 2016; Presti Jr, 2000).

During this time, the magnitude of the prostate volume has been used as a criterion in the diagnosis of BPH. The results of several studies state that prostate volume can be used for therapeutic improvement and surgical management interests such as, determining the type of surgery. Determination of prostate volume can be useful as a surgical therapy plan and monitoring the results of BPH therapy (Terris, 2002). The determination of the prostate volume can be done by rectal plug examination, Ultrasonography (USG), Transabdominal Ultrasonography (TAUS), Transrectal Ultrasonography (TRUS), Computed Tomography (CT), and Magnetic Resonance Imaging (MRI). The object hint for BPH constitutes the volume of the prostate. However, the magnitude of prostate volume is not always related to the weight of LUTS. Some of the tests used in evaluating the risk for the occurrence of BOO include uroflowmetry, Post Void Residual urine (PVR)/residual urine volume, Prostate Specific Antigen (PSA), and also Intravesical Prostatic Protrusion (IPP) (Kent-Hoo et al., 2014; Reis et al., 2008).

BPH treatment can be in the form of watch full waiting, medicamentous, and surgical procedures. Pharmacological or medicamentous treatment includes weighing the type of drug, evaluation during drug administration and long-term use of the drug. Medicamentous treatment aims to reduce the resistance of the smooth muscles of the prostate or reduce the volume of the prostate. Commonly used drugs are the α 1-blocker drug class and 5 α -reductase inhibitors (L. S. Lee et al., 2010).

α 1-blockers were first approved for use as a treatment of lower urinary tract complaints (LUTS)/Benign Prostatic Hyperplasia (BPH) in 1992. The evolutionary use of α 1-blockers for the treatment of LUTS/BPH has improved and improved tolerance after creating a single daily dose preparation with unconditional dose titration. Currently, α 1-blockers are used as a first-line treatment for most men with BPH with the main goal being to free themselves from LUTS disorders. α 1-blockers are used as a first-line treatment in men with LUTS, due to their rapid onset, good efficacy, and low severity of side effects. However, α 1-blockers cannot prevent the occurrence of acute urinary retention (Chapple & Abrams, 2013; Gravas et al., 2022; Tjahjodjati et al., 2017).

The purpose of the mechanism of action of α 1-blockers is to inhibit the effects of noradrenaline which is released endogenously on the smooth muscle cells of the prostate, and thus

will reduce the occurrence of prostate tone from the incidence of BOO (Tjahjodjati et al., 2017). This class of drugs will reduce symptom storage and voiding symptoms and is also able to improve the score of urinary symptoms (L. S. Lee et al., 2010; Tjahjodjati et al., 2017). Variations of α 1-blockers currently available are alfuzosin hydride, doxazosin mesylate, silodosin, tamsulosine hydrochloride, terazosin hydrachloride, and naphthatidyl (L. S. Lee et al., 2010).

Intravesical Prostatic Protrusion (IPP) is one of the factors that influence the success of medicamentous therapy. Intravesical Prostatic Protrusion (IPP) is a prostate lump that starts from the bladder neck into the bladder cavity which will result in a ball valve mechanism on the neck bladder to interfere with the flow of urine that will pass through the bladder neck. From the anatomical configuration of the prostate in the form of this IPP, it has been proven that there is a correlation with BOO. Based on the research of Lee, et al. (2016) conducted on 114 patients aged >50 years in Singapore, it can be concluded that IPP is a good predictor and is also correct in predicting BOO than other variables. Based on the results of the study of Lee et al (2010, 14) in 259 patients aged 63 years in Singapore concluded IPP is a non-invasive predictor of the clinical development of BPH for patients receiving non-surgical care. Incorporation of IPPs for BPH will improve clinical assessment by urologists and improve the effectiveness of the treatment of these common urological diseases in a more holistic and cost-effective way (Tanguay et al., 2009). Shin et al. (2013) in his study on 239 patients aged 70 years obtained an IPP of >5.5 mm significantly related to BOO. This data is useful as one of the variables that determine treatment outcomes in BPH patients (Tjahjodjati et al., 2017).

Intravesical prostatic protrusion is measured by examination by transabdominal ultrasonography (TAUS). Based on the TAUS degrees of the IPP can be divided into several categories. Degree I with a size of <5 mm, degree II with a size of >10 mm (Kent-Hoo et al., 2014).

Evaluation of the relationship of IPP scores to the therapeutic response of BPH patients given medicamentous therapy has never been carried out in the city of Padang. Therefore, researchers are interested in conducting research on the relationship of IPP scores to medicamentous therapy in BPH patients in Padang City. This study aims to determine the relationship between IPP degrees and IPSS scores of BPH patients who received medicamentosa therapy α 1-blockers (Tamsulosin 0.4 mg) in the city of Padang.

METHOD

This study is a comparative prospective study that aims to find a difference in the average therapeutic response of each group of BPH patients who received α 1-blocker therapy (Tamsulosin 0.4mg) in the city of Padang. With the quantitative approach, the research was conducted in several Padang city hospitals, namely Dr. M. Djamil Hospital, Semen Padang Hospital, BMC Padang Hospital, Hermina Padang Hospital. The study was conducted from Juli 2020 to December 2020.

The population of this study was all BPH patients who were conducted IPP scoring with the administration of α 1-blocker (Tamsulosin 0.4mg) therapy in Padang City. The minimum number of samples required in this study was 30 BPH patients who received medicamentous therapy with α 1-blocker (Tamsulosin 0.4mg).

IPP data on BPH in this study was obtained by conducting transabdominal ultrasound on BPH patients who came to the Urological Surgical Outpatient Poly at RSUP Dr. M. Djamil, Semen Padang Hospital, BMC Padang Hospital, Hermina Padang Hospital and conducted interviews to get IPSS scores before and after getting α 1-blocker therapy (Tamsulosin HCL 0.4 mg).

RESULT AND DISCUSSION

Benign Prostate Hyperplasia (BPH) Patients' Characteristics

Characteristics of Benign Prostate Hyperplasia (BPH) Patients are described in table 1.

Table 1. Characteristics of BPH Patients

Variable		n	Mean	%
Age	≤ 60 years	4		13.3%
	>60 years old	26		86.7%
	Lowest age	57 years old		
	Highest age	78 years old		
IPP	Degree I	10	3,72	
	Degree II	10	7,37	
	Degree III	10	12,2	
IPSS-QoL		30	19,93 $\pm$ 3.129	
Beginning	IPP Gr. I	10	19.60-4 $\pm$ 3.502,	
	IPP Gr. II	10	18.90-3.9 $\pm$ 3.107	
	IPP Gr. III	10	23.90-4.2 $\pm$ 5.043	
IPSS-QoL		30	11.47 $\pm$ 4.761	
Ending	IPP Gr. I	10	8.60-1.7 $\pm$ 1.430	
	IPP Gr. II	10	8.90-1.9 $\pm$ 3.725	
	IPP Gr. III	10	16.90-2.9 $\pm$ 2.807	
IPSS Score	IPP Gr. I	10	-11,10 $\pm$ 4,557	
Improvements	IPP Gr. II	10	-10,10 $\pm$ 4,581	
	IPP Gr. III	10	-3,80 $\pm$ 2,530	

Based on table 1, the percentage of BPH patients aged >60 years was 26 people (86.7%) more than the age of ≤ 60 years as many as 4 people (13.3%). The median age was 67.8 years with the lowest age of 57 years and the highest age of 78 years. Patient interviews were conducted before and after being given therapy α 1-blocker (Tamsulosin HCL 0.4 mg) with a distance of 1 month to obtain IPSS values. Each group of IPP degrees has 10 samples (mean 3.72 mm, 7.37 mm and 12.2 mm). Based on table 1 BPH sufferers with the average IPSS-Qol values of each IPP group were 19.6 0-4, 18.90-3.9, and 23.9 0-4.2 while the final IPSS-Qol average values were 8.60-1.7, 8.90-1.9 and 16.90-2.9.

Relationship of IPP Degree with Initial IPSS

The relationship between IPP and the initial IPSS of Benign Prostate Hyperplasia (BPH) patients is described in table 2.

Table 2. Relationship of IPP Degree with Initial IPSS

IPP Grading		P Value
IPP Gr. I	IPP Gr. II	0.918
	IPP Gr. III	0.057
IPP Gr. II	IPP Gr. I	0.918
	IPP Gr. III	0.064
IPP Gr. III	IPP Gr. I	0.057
	IPP Gr. II	0.064

Based on table 2, the average difference in the initial IPSS value of BPH patients did not have a meaningful difference in each group of IPP degrees. The results of the statistical test concluded that there was no significant difference in the initial IPSS value in each group of IPP degrees ($p = 0.918, 0.057$ and 0.064). It shows no tendency of IPP degrees directly proportional to the IPSS value of BPH patients.

Relationship of IPP Degree with Improvement of IPSS Value of BPH Patients Before and After Receiving Medicamentous Therapy α 1-blocker (Tamsulosin HCL 0.4 mg).

Therapeutic response is assessed by evaluating changes in IPSS values before and after getting medicamentous therapy. Correlation of improvement in IPSS values in BPH patients after receiving α 1-blocker therapy (Tamsulosin HCL 0.4 mg) in each IPP group is depicted in figure 1.

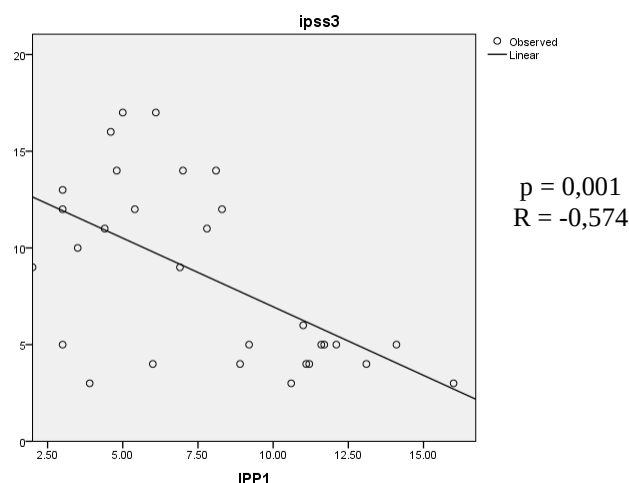


Figure 1. IPSS and IPP Change Correlation Plot Curve

Based on figure 1, the relationship between the degree of IPP and the difference in IPSS values has a strong correlation and is negative ($p=0.001, r = -5.74$). Statistically, with Pearson

correlation test, it was concluded that the degree of IPP and the improvement of IPSS values inversely proportional relationship. It illustrates that the higher the IPP, the smaller the IPSS value's difference.

The relationship of Intravesical Prostatic Protrusion (IPP) degrees with the improvement of IPSS values in BPH patients can be seen in figure table 3:

Table 3. Relationship of IPSS Repair with IPP Grade

IPP Grading		P Value
IPP Gr. I	IPP Gr. II	0.843
	IPP Gr. III	0.001
IPP Gr. II	IPP Gr. I	0.843
	IPP Gr. III	0.004
IPP Gr. III	IPP Gr. I	0.001
	IPP Gr. II	0.004

Based on table 3, the comparison of the therapeutic responses of each group looked the most different if the results of the degree I and II groups were compared with the III degree IPP group (*post hoc* test, $p=0.001$, 0.004). Changes in IPSS values of degrees I and II occur with almost the same difference while in degree III the difference in IPSS values is smaller.

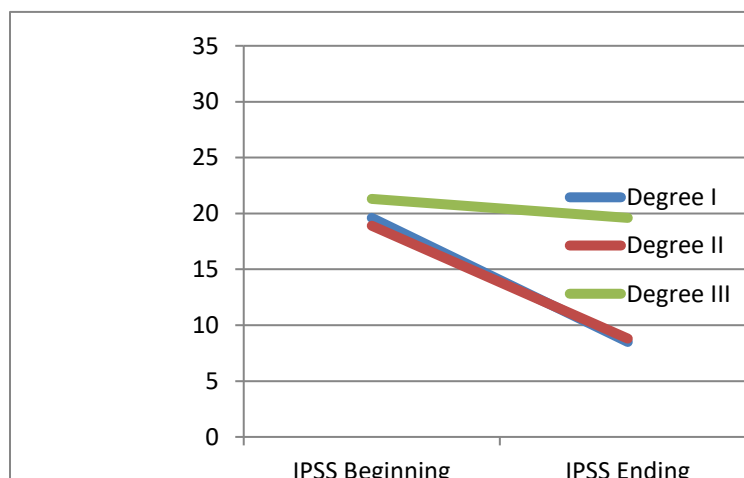


Figure 2. Improvement of IPSS Values of BPH Patients Before and After Receiving Therapy α 1-blocker (Tamsulosin HCL 0.4 mg)

Figure 2 shows that the therapeutic response of α 1-blocker (Tamsulosin HCL 0.4 mg) was more visible in groups I and II where there was a greater change in IPSS values than in degree III ($p=0.001$).

This study was conducted on 30 BPH patients who came to the outpatient polyclinic of urological surgery at RSUP Dr. M. Djamil, Semen Padang Hospital, BMC Hospital and Hermina Padang Hospital in July 2020-December 2020. This study found 13.3% (4 people) at age ≤ 60 years

and 86.7% (26 people) at age >60 years with an average age of 67.8 years. This is in accordance with the incidence of BPH increasing according to age increase, generally BPH occurs in men over 50 years old by 50% of cases, but in 20% cases it can occur in men aged 41-50 years, if they are over 80 years old then more than 90% of men get BPH (Basuki, 2015; Dhingra & Bhagwat, 2011; Tanagho, 1995).

In this study, an assessment of the IPSS value was carried out in each sample, the initial IPSS (Before therapy) was obtained on average 19.93 with the lowest score of 12 and the highest value of 26. While the final IPSS (After therapy) averaged 11.47 with the lowest score of 4 and the highest score of 19.

Of these 30 patients, the researchers grouped based on the degree of IPP of 10 patients each, IPP assessment was carried out by transabdominal ultrasound examination. IPP is a non-invasive method used to describe BOO that occurs in patients with LUTS/BPH. The use of ultrasound to measure IPP was first proposed by Chia et al. (2003) for the evaluation of BOO which is an important factor in describing the severity of the disorder and can be used in assessing therapeutic outcomes. Lee et al's research in 2010 and 2015 concluded that IPP is a non-invasive predictor of the clinical development of BPH for patients receiving non-surgical treatment and can predict the occurrence of BOO compared to other variables (A. Lee et al., 2016).

In this study, the average IPP in each group was 3.72 mm (IPP degree I), 7.37 mm (IPP degree II) and 12.2mm (IPP degree III). It is not much different from the Topazio study (in 2018) where an average of 2.7 mm (IPP degree I), 6.5 mm (IPP degree II) and 11.4 mm (IPP degree III) was obtained in 142 BPH patients (Topazio et al., 2018).

All samples were given applied treatment α 1-blocker (Tamsulosin HCL 0.4 mg) for one month. Group α 1-blocker drugs can improve voiding and storage symptoms in LUTS/BPH patients as well as can improve urinary symptoms scores by 30-45% or can reduce 4-6 IPSS values (Abrams et al., 2006; Gravas et al., 2022; Greco & McVary, 2008). Therapeutic responses were assessed by knowing changes in IPSS-QoL values before and after therapy. The results of the Oelke (2012) study concluded that the existence of IPP illustrates the reduced effect of α 1-blocker treatment in LUTS/BPH cases. The use of IPP as a therapeutic basis is expected to improve treatment success in LUTS patients and studies evaluating all factors that could be used for boo evaluation can be considered to improve treatment effectiveness.

In this study, it was found that there was no significant difference between the IPP degree and the initial IPSS value before patients received α 1-blocker therapy, namely $19.60 \pm 3,502$, $18.90 \pm 3,107$ and $23.80 \pm 5,043$ ($p=0.111$). Park's (2012) study also found no meaningful association of IPP degrees with total IPSS and QoL in 134 BPH patients before being given α 1-blocker for 3 months. Topazio et al. (2018) obtained the average initial IPSS score in 142 BPH patients based on the IPP group of 17.7, 18 and 22.2. This is different from the As'ari study (2009) in 85 BPH patients found a tendency, if the IPP degree increases, then the IPSS also increases. The homogeneous distribution of data and the small number of samples were shortcomings in this study.

Therapeutic response was assessed by assessing IPSS improvement after receiving α 1-blocker therapy (Tamsulosin HCL 0.4 mg) by looking at the difference in initial and final IPSS values. In this study, the difference in the average IPSS value in each IPP degree group was $11.10 \pm 4,557$, 10.10 ± 4581 and $3.80 \pm 2,530$ ($p=0.001$). The correlation test conducted in this study obtained a negative correlation, the higher the degree of IPP change in the IPSS value after the lowest α 1-blocker. It is in accordance with the analysis of multivariate multiregression conducted by Topazio et al. (2018) in BPH patients who received tamsulosin therapy for 12 weeks concluded that IPP had an inversely proportional relationship with the success of α 1-blocker therapy in LUTS/BPH patients. The odd ratio of the improvement rate of IPSS values in the low IPP degree group is 8 times higher than the medium IPP degree group, 69 times higher than the heavy degree IPP (Topazio et al., 2018). Lim's (2006) study states that the degree of IPP affects the emergence of BOO and the effectiveness of α 1-blocker treatment in BPH cases. Prostate protrusion will inhibit the flow of urine to the bladder neck causing obstruction which will affect the effectiveness of α 1-blocker therapy in managing LUTS (Seo & Kim, 2012).

Limited number of samples and short research time were shortcomings in this study. The IPSS score data obtained from patients who fill out the IPSS score sheet is subjective data so a deep interview is needed to get more predictive final IPSS results.

CONCLUSION

Of the 30 BPH patients who were treated with α 1-blockers (Tamsulosin HCL 0.4 mg) at RSUP Dr. M. Djamil, Semen Padang Hospital, RSU Bunda BMC and Hermina Padang Hospital in July 2020-December 2020, the most were > 60 years old with an average age of 67.8 years. Data were taken by 30 BPH patients who received α 1-blocker therapy (Tamsulosin HCL 0.4 mg)

The average IPSS-Qol value of BPH patients before receiving α 1-blocker therapy (Tamsulosin HCL 0.4 mg) was $19.93-4.03 \pm 3.129$. The average IPSS-Qol value of BPH patients after receiving α 1-blocker therapy (Tamsulosin HCL 0.4 mg) for 1 month was $11.47-2.2 \pm 4.761$. The average IPP values of BPH patients who received α 1-blocker therapy (Tamsulosin HCL 0.4 mg) were 3.72mm (IPP degree I), 7.37mm (IPP degree II) and 12.2mm (IPP degree III).

There is a strong correlation between IPP and changes in IPSS values. The higher the IPP degree of BPH patients the smaller the change in the final IPSS value after receiving therapy α 1-blocker (Tamsulosin HCL 0.4 mg).

It is hoped that the IPP assessment can be used as a routine examination in BPH patients and can be used as a guide in choosing the management of BPH patients. It is hoped that the IPP assessment can be used as a reference for the prognosis of BPH patients, thereby reducing the cost of hospitals in providing medicamentous therapy. Furthermore, the researchers expected discussions regarding this topic can be brought up, especially ones surfacing more significant variables affecting BPH, whether during the infection or the healing process.

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