SUCCESS RATES OF TAMSULOSIN AND DUTASTERIDE AS MEDICAL THERAPY BASED ON IPSS IN SYMPTOMATIC BPH PATIENTS IN ARIFIN ACHMAD HOSPITAL PEKANBARU RIAU

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ABSTRACT

Objective: *To evaluate the success rates of tamsulosin and dutasteride as medical therapy based on international prostate symptom score (IPSS) in symptomatic benign prostatic hyperplasia (BPH) patients.* ***Materials & Methods:*** *We reviewed medical records of the symptomatic BPH patients in Arifin Achmad Regional General Hospital, Pekanbaru, Riau Province, Indonesia in 2011-2016. The previous and after IPSS of administering tamsulosin 0.2 mg or 0.4 mg or dutasteride 0.5 mg as a single therapy and tamsulosin 0.4 mg with dutasteride 0.5 mg as a combination therapy were assessed. Wilcoxon test was used for statistical analysis. Approval on the study was obtained from the Ethical Review Board for Medicine and Health Research, Medical Faculty, University of Riau.* ***Results:*** *100 patients fulfilled the inclusion criteria. The results showed 50% patients with mild IPSS and 50% patients with severe IPSS before the medication. 70% patients administered tamsulosin 0.2 mg as first-line therapy, 35% patients administered medication for 6 months-1 year, and 3% patients with mild IPSS, 44% with moderate IPSS and 53% with severe IPSS after the medication. The Wilcoxon test showed there was a significant different ($p<0.005$) between IPSS levels before and after the medication with success rate 18%.* ***Conclusion:*** *There were good success rate of tamsulosin 0.2 mg, tamsulosin 0.4 mg, dutasteride 0.5 mg as single therapy and tamsulosin 0.4 mg with dutasteride 0.5 mg as combination therapy in symptomatic BPH patients based on IPSS, and the medical therapy are still recommended.*

Keywords: *Benign prostatic hyperplasia, international prostate symptom score, medical therapy.*

ABSTRAK

Tujuan: *Untuk mengevaluasi angka keberhasilan tamsulosin dan dutasteride sebagai terapi medikamentosa berdasarkan international prostate symptom score (IPSS) pada pasien bergejala benign prostatic hyperplasia (BPH).* ***Bahan & Cara:*** *Kami menilai kembali catatan medis pasien dengan gejala BPH di Rumah Sakit Daerah Arifin Achmad, Pekanbaru, Provinsi Riau, Indonesia, pada tahun 2011-2016. IPSS sebelum dan sesudah memakai tamsulosin 0.2 mg atau 0.4 mg atau dutasteride 0.5 mg sebagai terapi tunggal, dan tamsulosin 0.4 mg dengan dutasteride 0.5 mg sebagai terapi kombinasi dinilai. Uji Wilcoxon digunakan untuk analisis statistik. Persetujuan untuk penelitian ini diberikan oleh Ethical Review Board for Medicine and Health Research, Fakultas Kedokteran, Universitas Riau.* ***Hasil:*** *100 pasien memenuhi kriteria inklusi. Hasil penelitian menunjukkan 50% pasien dengan IPSS sedang, dan 50% pasien dengan IPSS berat sebelum pemakaian obat. 70% pasien yang mengkonsumsi tamsulosin 0.2 mg sebagai terapi pertama, 35% pasien mengkonsumsi obat selama 6 bulan - 1 tahun, dan 3% pasien dengan IPSS ringan, 44% dengan IPSS sedang dan 53% pasien dengan IPSS berat setelah mengkonsumsi obat. Uji Wilcoxon menunjukkan terdapat perbedaan yang bermakna ($p<0.005$) antara IPSS sebelum dan sesudah pemberian obat dengan angka keberhasilan 18%.* ***Simpulan:*** *Terdapat angka keberhasilan yang baik pada pemberian tamsulosin 0.2 mg, tamsulosin 0.4 mg, dutasteride 0.5 mg sebagai terapi tunggal dan tamsulosin 0.4 mg dengan dutasteride 0.5 mg sebagai terapi kombinasi pada pasien dengan gejala BPH berdasarkan IPSS, dan terapi medikamentosa masih disarankan untuk digunakan.*

Keywords: *Benign prostatic hyperplasia, international prostate symptom score, terapi medikamentosa.*

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INTRODUCTION

Prostate gland is one of male genital organ in inferior part of bladder, in front of rectum wrapping prostatic urethra.[1] Prostate volume increases as age is increasing. Several cross sectional studies on prostate volume according to ages showed prostate volume becoming 25 ml in 30 year old man and 35-45 ml in 70 year old man.[2] The prostate enlargement can be benign prostatic hyperplasia (BPH) or prostate cancer.[3]

Benign prostate hyperplasia is a histopatologic term, namely hyperplasia of stromal cells and prostate gland epithelial cells.[4,5] Several factors are considered playing roles in the proliferation or growth of BPH. BPH grows in aging man and has active testicles producing testosterone. Other hormone (estrogen and prolaktin) influences, diet pattern, microtrauma, inflamation, obesity and physical activity were supposed to be correlating to prostate gland cell proliferation indirectly. The factors can influence the prostate cells synthesizing growth factor in turn inducing prostate gland cell proliferation.[6]

Benign prostate hyperplasia is the second most disease in urology and the incidence becomes improving. BPH incidence was 20% in 40 year old man and increased around 70% in man over 60 years old and 90% in man over 80 years old. It is not all BPH becomes symptomatic BPH.[7] In 2010, 14 millions of men in the United States of America suffered from lower urinary tract symptoms (LUTS) related to BPH. The exact BPH incidence in Indonesia has not been published directly but hospital prevalence in Cipto Mangunkusumo Hospital Jakarta in 1994-2013 there was 3.804 cases.[8]

Although it seldom suffers from the soul, BPH results in clinical symptoms disturbance every day activities. The prostate enlargement process occurs slowly and the changing effect on the urinary tract also slowly. Pathophysiologic changes resulted in prostate enlargement actually due to the combination of prostate urethral resistance, trigonal and bladder neck tones, and detrusor contraction power and finally result in total urinary retention and result in patient symptoms. Guidelines for directing and assessing the obstruction due to prostate enlargement is symptom scoring system. One of the widely used is International Prostate Symptom Score (IPSS) developed from American Urological Association (AUA) and standardized by World Health Organization (WHO). The score is used for assessing and monitoring the BPH patient quality of life.[9,10]

Medical therapy is given to a patient with IPSS >7. The drugs used are α-blocker, 5α-reductase inhibitor, muscarinic receptor antagonist, phospodiesterase 5 inhibitor groups and combination therapy with several drugs. The therapy administration should consider drug kinds used and evaluation during drug administration. The medical therapy outcome besides improving the patient quality of life also in order to lessen prostate muscle resistance as the dynamic component, and to lessen the prostate volume as the static component.[11]

Study on medical therapy have not ever been done and published in Riau Province. A study on the profile of BPH patients in our hospital had been done by Dwindra (2007) but it did not explain medical therapy of symptomatic BPH patients. The study showed that the highest BPH incident underwent transurethral resection of the prostate (TURP) in our hospital was in 60-69 year old group.[12] Another study by Sabri in similar hospital (2011) only showed the prevalence of TURP in BPH patients in which the highest prevalence was in 70-79 age group.[13]

OBJECTIVE

Based on there is not yet available data on success rate in medical therapy managements on symptomatic BPH patients in our hospital, we conducted a study on the success rate of medical therapy managements on symptomatic BPH patients using tamsulosin and dutasteride based on IPSS.

MATERIAL & METHODS

We reviewed medical records of the symptomatic BPH patients in Urology Clinic of Arifin Achmad Regional General Hospital, Pekanbaru, Riau Province Indonesia in 2011 - 2016. Inclusion criteria of patients were (1) 45-80 years old, (2) IPSS score > 7, (3) normal digital rectal examination, (4) prostate specific antigen (PSA) ≤ 4 ng/ml, (4) transrectal ultrasound (TRUS): enlargement of prostate volume > 25 ml, no signs of malignancy. Exclusion criteria were BPH patients with recurrent urinary retention and BPH with complication, prostate cancer, history of prostate surgery, BPH with diabetes mellitus, neurologic disease and disorder related to voiding physiology. The statistical amount of patients were minimal 96. Previous and after IPSS of administering tamsulosin

0.2 mg or 0.4 mg or dutasteride 0.5 mg as single therapy or combination of tamsulosin 0.4 mg with dutasteride 0.5 mg were assessed. Wilcoxon test was used for statistical analysis. Approval on the study was obtained from the Ethical Review Board for Medicine and Health Research, Medical Faculty, University of Riau.

RESULTS

There were 100 symptomatic BPH patients included in the study. Most (38%) patients were in 60–69 year age group (Table 1). Most (70%) patients with single therapy of tamsulosin 0.2 mg, 27% patients with single therapy of tamsulosin 0.4 mg, 1% patients with single therapy of dutasteride 0.5 mg and 2% patients with combination of tamsulosin 0.4 mg and dutasteride 0.5 mg (Table 2). Most (35%) patients administered the medical therapy for 6 months – 1 year, 34% patients administered the medical therapy for 1–2 years, 21% patients administered the medical therapy for 2–3 years and 10% patients administered the medical therapy for < 6 months (Table 3). IPSS before medical therapy were 50% moderate and also 50% were severe. IPSS after medical therapy were 3% mild, 44% moderate and 53% severe (Table 4). There were 3% patients had improvement of IPSS became mild, 44% had improvement of IPSS became moderate after medical treatment but 53% patients had IPSS became severe after medical treatment. Wilcoxon test showed there were significant different ($p<0.0001$) between the previous IPSS and IPSS after medical treatment (Table 5).

Tabel 1. Patient characteristic.

Age (year)	n	f (%)
45 – 49	5	5
50 – 59	26	26
60 – 69	38	38
70 – 80	31	31
Total	100	100

Table 2. Medical therapy.

Medical Therapy	n	f (%)
Tamsulosin 0.2 mg	70	70
Tamsulosin 0.4 mg	27	27
Dutasteride 0.5 mg	1	1
Tamsulosin 0.4mg + Dutasteride 0.5 mg	2	2
Total	100	100

Table 3. Medical therapy duration.

Medical therapy duration	n	f (%)
< 6 months	10	10
6 months -1 year	35	35
1 year - 2 years	34	34
2 years - 3 years	21	21
Total	100	100

DISCUSSION

This study showed there were 100 symptomatic BPH patients included. Most (38%) patients were in 60 – 69 year age group (Table 1). Males > 50 years old have 6.24 risks bigger than males < 50 years old due to aging process decreases bladder ability to maintain the urinary flow in adaptation process of obstruction due to prostate enlargement resulting in symptoms. BPH incidence is 20% in 40 year old males and increases around 70% in > 60 year old and 90% in > 80 year old males.7 70 – 80 year old age male incidence of BPH is relatively lower due to life maintaining factor. This suited a study by Nadya (2014) in our hospital showed that most (38.9%) BPH patients were in 60 – 69 year old age group and 28.3% BPH patients in 70 – 79 year old age group.[14] A study by Kamaleswaran

Table 4. Previous IPSS and IPSS after medical therapy.

IPSS grade	Previous			After			p
	n	f (%)	Mean	n	f (%)	Mean	
IPSS (0-7) Mild	-	-	-	3	3	8 ± 1.3	
IPSS (8-19) Moderate	50	50	19 ± 4.1	44	44	17 ± 4.2	0.0001
IPSS (20-35) Severe	50	50	21 ± 5.8	53	53	22 ± 5.5	
Total	100	100		100	100%		

$p<0.05$

et al (2015) showed most (6.2%) BPH patients were in 70–79 year old age group.[12] A study by Sabri (2011) showed that BPH patients mostly (37.4%) were 70 – 79 year old age group but they were BPH patients underwent TURP.[10]

This study showed that most (70%) patients with single therapy of tamsulosin 0.2 mg, 27% patients with single therapy of tamsulosin 0.4 mg, 1% patients with single therapy of dutasteride 0.5 mg and 2% patients with combination of tamsulosin 0.4 mg and dutasteride 0.5 mg (Table 2). Tamsulosin 0.2 mg was more administered due to as the first line therapy should begin with lower dose depending on LUTS in IPSS. The medical therapy dose was influenced by the previous IPSS before medical therapy, the assessment of Urologists on patients voiding symptoms and the duration of medical therapy. Dutasteride 0.5 mg were least used and were used more in combination with tamsulosin 0.4 mg to gain maximal IPSS changing results. A report and a meta analysis by Shim et al (2016) showed that tamsulosin 0.2 mg was the first line treatment for symptomatic BPH due to lower side effects, inhibits α1-receptor in prostat smooth muscle resulting in reducing prostate smooth muscle tones (dynamic component), tamsulosin effect is significantly higher in decreasing IPSS ($p<0.01$) and indicated as LUTS therapy and BPH sign.[14]

A study by Perinchery et al (1994) showed selective medical therapy was effective compared to nonselective α-blocker in BPH medical therapy.[15] Tamsulosin is a selective α-blocker in symptomatic BPH therapy. A study by Djavas et al (2010) showed that combination therapy of tamsulosin and dutasteride was effective in medical therapy > 4 years in BPH patients with mild – severe IPSS.[16] Final Report by Portland (2007) showed that combination therapy administered by high PSA and large prostate volume patients in initial therapy prevented from urinary retention and increasing IPSS > 4 points but result in erectile dysfunction compared to single therapy of alfa bloker.[17] In this study the combination therapy was low used due to the PSA < 4 ng/ml and the therapy duration mostly were 7 month – 1 year in our hospital.

In this study most (35%) patients administered the medical therapy for 6 months – 1 year, 34% patients administered the medical therapy for 1–2 years, 21% patients administered the medical therapy for 2 – 3 years and 10% patients administered the medical therapy for < 6 months (Table 3). A study by Stephan et al (2007) showed therapy duration in symptomatic BPH patients resulting in IPSS improvement after 12 month in 21.4% patients, after 2 years in 10.9% patients and after 4.5 years in 15.9% patients.[4] A study by Perinchery (1994) showed minimal treatment evaluation was > 6 months for gaining maximal therapeutic effects resulted in the researcher made a classification of duration > 6 months.[15] The study was similar to our study in which the α-blocker was evaluated after 6 months of administering but the symptoms could be varied becoming better, worst or constant. Therapy duration of 2–3 years was lower due to the least amount of BPH patients in 70 – 80 year age group having medical therapy in our hospital.

In this study IPSS before medical therapy were 50% moderate and also 50% were severe. IPSS after medical therapy were 3% mild, 44% mild and 53% severe (Table 4). This was due to our BPH patients came when they had symptoms with IPSS moderate –severe. It was not different from a study by Kamaleswaran (2015) showing BPH patients mostly (71.4%) with moderate IPSS, 25% with severe IPSS and 3.6% with mild IPSS.[12] Previous study by Nadya (2014) in our hospital showed IPSS of BPH patients was mostly (53.4%) with severe IPSS, 38.3% was with moderate IPSS and 8,3% with mild IPSS.[11] The study was similar to a study by Cristie et al (2015) showed BPH patients were mostly (54.1%) with severe IPSS, 32.4% with moderate IPSS and 13.5% with mild IPSS.[13]

In this study 3% patients had improvement of IPSS became mild, 44% had improvement of IPSS became moderate after medical treatment but 53% patients had IPSS became severe after medical treatment. Wilcoxon test showed there were significant different ($p<0.0001$) between the previous IPSS and IPSS after medical treatment (Table 5). In this study severe IPSS were mostly in our hospital due to the longest therapy duration was in 6 moths – 1 year duration group. Drug effect influenced this due to α1-blocker dominantly used in our hospital was the lowest dose 0.2 mg of tamsulosin. Actually the higher the drug dose used the better effects could be gained but the side effects of each α1-blocker had tolerability and different effects on cardiovascular system resulting in the patients stopped the therapy by himself. The BPH patients in our hospital sometimes were with other diseases such as heart disease, diabetes mellitus and other degenerative disease resulting in the urologists considered the kinds, dose and side effects of the

drugs. There were various therapy results in this study such as worst, better or constant in which could influencing the patient commitment in administering the drugs. Several patients stopped the medical therapy without permission of the Urologist when the symptoms became better while BPH medical therapy needed long duration and tappering off to stop the therapy. The body response on the therapy administration and therapy duration mostly in 6 months – 1 year resulting in various changes of IPSS on BPH patients. A study by Claus (2008) showed 25% decreasing of IPSS was significant in administering of tamsulosin 0.4 mg dan dutasteride 0.5 mg compared to monotherapy after 2 years.[18]

CONCLUSION

There were good success rate of tamsulosin 0.2 mg, tamsulosin 0.4 mg, dutasteride 0.5 mg as single therapy and tamsulosin 0.4 mg with dutasteride 0.5 mg as combination therapy in symptomatic benign prostate hyperplasia patients based on IPSS, and the medical therapy are still recommended.

REFERENCES

1. National Institute of Diabetes and Digestive and Kidney Diseases. Prostate enlargement: Benign prostatic hyperplasia. Emedicine website. http://www.urologic.niddk.nih.gov. NIH publication No.14-3012 August 2014. Accessed 9 September 2015.
2. Soetapa H, Djatisoesanto W, Soebadi DM. Prostate volume measurement using digital rectal examination and transrectal ultrasound by the same operator compared to the one using transabdominal ultrasound by different operator. Indonesian Journal of Urology. 2006; 14: 34-9.
3. Aprilia RD. Correlation between leukosituria incidence and prostate volume in BPH patients by abdominal ultrasound. Website. http://digilib.uns.ac.id. Accessed 29 September 2015.
4. Roehrborn CG. Benign Prostatic Hyperplasia: Etiology, phatophysiology, epidemiology, and natural history. In: Campbell's Urology, 10th Edition. Editor: Walsh PC, Retik AB, Vaughan ED, dan Wein AJ. Philadelphia: WB Saunders Co.; 2012. p. 2570-91.
5. Indonesian Urological Association. Guidelines on benign prostate hyperplasia; 2015.
6. McVary KT, Roehrborn CG, Avins AL, Barry MJ, Bruskewitz RC, Donell RF, et al. Update on AUA guideline on the management of benign prostatic hyperplasia. J Urol. 2011; 185: 1793-803.
7. Gerber GS, Brendler CB. Evaluation of the Urologic Patient: History, Physical Examination, and Urinalysis. In: Campbell-Walsh Urology. 10th edition. Philadelphia: Elsevier Saunders; 2012. p. 71-80.
8. Indonesian Urological Association. Temporary consensus guidelines on benign prostate hyperplasia in Indonesia; 2000. p. 5-14.
9. Dwindra M. Profile of Benign Prostate Hyperplasia in Arifin Achmad Pekanbaru 2005-2006 [Scription]. Pekanbaru: Medical Faculty, University Riau; 2007.
10. Sabri M. Profile Benign Prostate Hyperplasia underwent in Arifin Achmad Regional General Hospital Pekanbaru 2009-2010 [Scription]. Pekanbaru: Medical Faculty, University Riau; 2011.
11. Fitriana N, Zuhirman, Suyanto. Correlation between benign prostate hypertrophy and erectile dysfunction in Arifin Achmad General Hospital Pekanbaru, Riau Province. [Sription]. Medical Faculty, Riau University; January 2014.
12. Chandrasegaran K. Profile of Prostate Symptome Score in Benign Prostate Hyperplasia patients in Adam Malik Hospital Medan. Accessed from: http://www.repository.usu.ac.id. 26 Desember 2016.
13. Mondang, Monoarfa, Salem. Correlation between IPSS and Quality of Life in BPH with LUTS patients in Kandou Hospital. eCI [serial on the internet]. 2015; 3(1). Accessed from: http://ejournal.unsrat.ac.id. 26th December 2015.
14. Shim SR, Kim JH, Chang JH, Shin IS, Hwang SD, Kim KH, et al. Is Tamsulosin 0,2 mg Effective and Safe a First Line Treatment Compared with Other Alpha Blocker?: A Meta-Analysis and a Moderator Focused Study. Yonsei Med J. 2016; 57(2): 407-18. Diakses dari: http://10.3349/ymj.2016.57.2.407. [Pubmed: 26847294]
15. Naraya P, Indudhara R. Conferences and Review: Pharmacotherapy for Benign Prostatic Hyperplasia. West J Med. 1994; 161: 495-506.
16. Djavas B, Handl MJ, Dianat S. Combined Medical Treatment Using Dutasteride and Tamsulosin for Lower Urinary Tract Symptoms Suggestive of Benign Prostatic Hyperplasia. Expert Opin Pharmacother. 2010; 11(15): 2535-47. Dikutip dari: http://10.1517/14656566.2010.516901. [Pubmed: 20854184]
17. Madersbacher S, Marszalek M, Lackner J, Berger P, Schatzl. The Long-Term Outcome of Medical Therapy for BPH. European Urology; 2007. p. 1522-33. Diakses dari: http://www.eu-acme.org/europeanurology
18. Roehrborn GC, Siami P, Barkin J, Damiao R, et al. The Effect of Dutasteride, Tamsulosin and Combination Therapy on Lower Urinary Symptoms in Men with Benign Prostatic Hyperplasia and Prostatic Enlargement: 2 Year Results From the CombAT Study. J Urol. 2008; 179: 616-21. Diakses dari: http://www.richardhaddadurology.com.au/Uploads/News/900%20BPH/(2).pdf