

Improvement of quality in clinical care for patients with benign prostatic hyperplasia: Cost effectiveness analysis

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ABSTRACT

Introduction: Currently, St. Carolus Hospital (SCH), Jakarta, Indonesia is using a combination therapy for patients with benign prostatic hyperplasia (BPH) based on the clinical practice guidelines (CPG). In this study, we used two methods of administering combination therapy, namely, the standard method and the modified method. To date, no research has been conducted to reduce the cost burden of BPH medication without reducing the quality of service. Thus, this study aimed to compare the clinical outcomes and quality of life (QoL) of the modified therapeutic method with those of the standard therapeutic method and perform cost-effective analysis of the two therapeutic methods available at SCH.

Materials and Methods: The study design used was a retrospective cohort. Data were obtained from medical records at SCH and interviews. Decision tree analysis was used for this study based on clinical outcomes and costs. Clinical outcomes and costs were compared between the standard and modified therapy models. Interviews were conducted to obtain cost data from a societal perspective. Then, the data were analyzed using SPSS statistics program and MS Excel.

Results: A total of 100 BPH patients met the inclusion criteria. The mean age in the standard therapy and modified therapeutic method groups was 66.92 (SD±6.67) and 67.10 (SD 8.49) years, respectively. At the start of therapy, the mean international prostate symptom score (IPSS) in the standard method group was lower than that in the modified group (15 vs 17), but the mean Qmax in both groups was the same (9 ml/s). In addition, the mean QoL score in both groups was 4 (not satisfied). At the end of therapy, there was an improvement in the IPSS, Qmax and QoL was observed in both groups. In the Mann Whitney statistical test, there was no significant difference in IPSS and QoL was found between the standard therapeutic method group and the modified therapeutic method group ($P = 0.07$ and $P = 0.498$). In the unpaired T test, there was a significant difference in Qmax was found between the standard method group and the modified method group ($p = 0.039$, 95%CI, -3.20529 to -0.8769). The effectiveness of standard therapeutic methods and modified therapy methods is 82% and 90%, respectively. The average cost of standard therapeutic methods is greater than that of modified therapeutic methods per visit. Furthermore, the average cost-effectiveness ratio of the

modified therapeutic method is lower than that of the standard therapeutic method.

Conclusion: The Modified therapeutic method has better results regarding the maximum urinary flow rate compared with the standard therapeutic method. The modified therapeutic method is also more cost-effective than the standard therapeutic method. This study can be used as the basis for service standards in hospitals and national health technology assessments as a policy direction for the national health insurance benefit package.

KEYWORDS:

Benign prostate hyperplasia, combine therapy, cost, cost-effective analysis

INTRODUCTION

The prevalence rate of lower urinary tract symptoms (LUTS) worldwide varies widely, and it is significantly increasing with age. The number of patients with LUTS worldwide is approximately 2.3 billion people or 45.8% of the world population in 2018, which shows an 18.4% since 2008.¹ The incidence of benign prostatic hyperplasia (BPH) in Indonesia remains unknown, but based on the data obtained from Cipto Mangunkusumo Hospital (RSCM) from 1994 until 2013; a total 3,804 cases of BPH with a mean age of the patients 66.61 years have been reported. In addition, Hasan Sadikin Hospital reported 718 cases of BPH, from 2012 to 2016, with a mean age of patients 67.9 years old.²

The treatment of choice is a major factor contributing to the cost of treatment from medical therapy (a combination of alpha blockers and 5-alpha reductase inhibitor (5-ARI)) to invasive action, such as transurethral resection of prostate.

The combination of alpha blocker and 5-ARI has been proven to be more effective than monotherapy based on studies from several countries.^{3,4}

The high prevalence rate of BPH can cause a huge economic burden and medical costs to the authorities. The cost of BPH treatment in the UK is estimated around £ 180 million annually, of which 60% are due to complications from BPH. Long-term treatment will also increase costs, thereby causing a heavy burden to the government and society.⁵

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In addition, cost-effectiveness analysis (CEA) has been conducted to evaluate the BPH medical therapy in several American and European countries, which shows that combination of pharmacological therapy is more cost-effective than monotherapy.^{3,4,6-9}

At present, St. Carolus Hospital (SCH), Jakarta, Indonesia is using combination therapy for patients with BPH, based on the clinical practice guidelines (CPG). Thus, in this study, we used two methods of administering combination therapy. Based on the CPG, in the standard method, the combination drug is given for 6 months every day and routine follow-up is conducted every month. On the contrary, in the modified method, the drug is given every day for 3 months, and then the administration of drug is continued intermittently for 3 months, and follow-up is conducted once a month in the first 3 months and then once at the end of 6 months.

In this study, we compare the objective clinical outcome and quality of life (QoL) of the modified therapeutic method with those of the standard therapeutic method and perform cost-effective analysis of the two therapeutic methods available at SCH.

MATERIALS AND METHODS

The study design used was a retrospective cohort. Data were obtained from the medical and financial record of SCH. Interviews were also conducted with BPH patients in regard to their international prostate symptoms score (IPSS) and QoL. Decision tree analysis was performed in this study with financing and clinical outcomes as parameters. The inclusion criteria were as follows men above 50 years who were diagnosed with BPH from urologist, and currently taking Tamsulosin (0.4 mg) and Dutasteride (0.5 mg). We excluded patients with prostate cancer or other diseases that can cause LUTS except BPH. All patients who refused and didn't complete the routine follow up were also excluded. Then we divided the patients into standard therapy method group (Group 1), and modified therapy method (Group 2). Clinical outcomes and costs were then analyzed between the two groups.

RESULTS AND DISCUSSION

1. Respondent Characteristics

BPH is a benign enlargement of the prostate in elderly men. Patients aged 60-69 and 70-79 were the largest age group included in this study at SCH. All respondents in Group 1 showed moderate symptoms, whereas in Group 2, 49 patients showed moderate symptoms, and one people had severe symptoms (IPSS > 20). Group 1 had fewer patients with IPSS (16-19) compared with Group 2 (44% vs 68%, Table I). The quality of life (QoL) of patients in both groups at the beginning of therapy showed dissatisfaction and unhappiness toward their condition. In all 86% of the patients in Group 1 were "mostly dissatisfied" with their condition, whereas only 60% of the patients in Group 2 were "mostly dissatisfied" with their condition. However, a total of 20 patients (40%) in Group 2 reported "unhappiness", whereas only six patients (12%) in Group 1 reported "unhappiness". The majority of patients in both groups had

an initial maximum urinary flow rate (Q_{max}) of < 10 mL/s (86% in Group 1, 66% in Group 2) (Table I).

2. Clinical Outcomes and Effectiveness

Group 1 was given standard combination therapy for BPH (Tamsulosin 0.4 mg q.d. and Dutasteride 0.5 mg q.d.) continuous for 6 months, and routine follow-up was conducted every month. On the contrary Group 2 was given modified combination therapy using the same drugs, but the administration of the drug was continued for the first 3 months and then every 2 days for the last 3 months. Follow-up was also conducted monthly for the first 3 months, and at the end of 6 months. The data during each follow-up was collected and analyzed the basis of clinical improvement and costs.

Post Therapy IPSS, QoL and Q_{max}

Improvement on IPSS was observed in both groups. A total of 37 people in Group 1 (74%) had an IPSS of 4-7, and only 13 (26%) patients had an IPSS ≥ 8. Meanwhile, 41 patients (82%) in Group 2 had an IPSS of 4-7, and 9 patients (18%) had an IPSS ≥ 8. Forty-seven patients in Group 2 showed improvement in IPSS compared with Group 1 (50 patients, 94% vs 100%) with different mean improvements (7.22 vs 8.20). Based on the statistical analysis, using Shapiro-Wilk test to evaluate the normality of post therapy IPSS, we found that the data were nonparametric in both groups. We then analyzed the data using Mann Whitney test to compare both groups ($p = 0.077$). $p > 0.05$ indicates no significant difference between IPSS of groups 1 and 2. (Table II)

At the end of therapy, Group 1 and Group 2 showed a "mostly satisfied" QoL (52% vs 50%). Mixed feeling and dissatisfied QoL were also observed in both groups, but most of the patients showed improvement. Forty-seven patients (94%) in Group 1 showed improvement in QoL, whereas 46 patients (92%) in Group 2 showed improved same mean improvement. Normality test using the Shapiro-Wilk test on post-therapy QoL showed that the data were nonparametric ($p < 0.001$). Therefore, statistical analysis was conducted using the Mann Whitney test with a significance value of 0.498. p value > 0.05, indicates no significant difference in QoL between two groups. (Table II)

The Maximum urinary flow rate (Q_{max}) at the end of therapy in both groups mostly showed Q_{max} > 10 mL/s. The number of patients that had Q_{max} > 10 mL/s was greater in group 2 than in group 1 (90% vs 82%). The number of patients that had improved Q_{max} during 6 months of therapy was 41 (82%) in Group 1, and 45 (90%) in group 2 with different mean improvement (4.19 vs 5.20; Table III). Normality test on post-therapy Q_{max} showed normal distribution of data. We used unpaired T-test with $P = 0.039$. $P < 0.05$, indicates significant difference in Q_{max} after therapy between the two therapy groups. (Table II).

Effectiveness of Therapy

Effectiveness of therapy can be seen from the improvement of IPSS, QoL score, and Q_{max}. Effectiveness of each parameter in both groups can be seen in Table III.

Table I: Age group of distribution, initial IPSS, QoL, Qmax of BPH patients in the standard therapeutic method and modified therapeutic method at St. Carolus Hospital

Characteristics	Standard Method		Modified Method	
	Total	%	Total	%
Age				
50-59	4	8	12	24
60-69	30	60	17	34
70-79	14	28	20	40
≥ 80	2	4	1	2
Initial IPSS				
8-11	0	0	1	2
12-15	28	56	14	28
16-19	22	44	34	68
≥ 20	0	0	1	2
Initial QoL				
Mixed about equally satisfied and dissatisfied	1	2	0	0
Mostly dissatisfied	43	86	30	60
Unhappy	6	12	20	40
Initial Qmax				
< 10 mL/s	43	86	33	66
≥ 10 mL/s	7	14	17	34

Table II: IPSS, QoL, Qmax at the end of the therapy in the standard therapeutic method and modified therapeutic method at St. Carolus Hospital

Post Therapy	Standard Method		Modified Method	
	Total	%	Total	%
IPSS				
0-3	0	0	0	0
4-7	37	74	41	82
≥ 8	13	26	9	18
Changes in IPSS				
Improved	50	100	47	94
Not Improved	0	0	3	6
QoL				
Pleased	9	18	7	14
Mostly satisfied	26	52	27	50
Mixed about equally satisfied and dissatisfied	10	20	9	22
Mostly dissatisfied	5	10	7	14
Changes in QoL				
Improved	47	94	46	92
Not Improved	3	6	4	8
Qmax				
< 10 mL/s	9	18	5	10
≥ 10 mL/s	41	82	45	90

Table III: Effectiveness of standard therapy and modified therapy method

Effectiveness	Standard Method	Modified Method
IPSS	7.22	8.20
QoL	1.88	2.06
Qmax	4.19	5.20

Table IV: Direct cost, indirect cost, and the average cost between the standard and modified therapy groups

Cost	Standard Method	Modified Method
Direct Cost	Rp 278,866,476	Rp 219,814,417
Indirect Cost	Rp 18,000,000	Rp 12,000,000
Total	Rp 296,866,476	Rp 231,814,417
Average Cost in 6 Months	Rp 5,937,330	Rp 4,636,288
Average Cost / Visit	Rp 989,555	Rp 927,258

Table V: ACER and ICER based on IPSS, QoL and Qmax

Method	ACER			ICER		
	IPSS	QoL	Qmax	IPSS	QoL	Qmax
Standard	822,345	3,158,154	1,415,672			
Modified	565,401	2,250,625	891,251	-1,327,593	-7,228,007	-1,290,715

Group 2 has shown to be more effective with regard to of IPSS, QoL and Qmax improvement compared with group 1.

3. BPH Clinical Service Cost

The Cost of BPH clinical services at SCH includes direct cost and indirect cost. Direct cost includes medical and non-medical cost, whereas indirect cost includes consumption cost, transportation and cost incurred by caretakers of patients. Cost difference was found between the two groups. The cost in Group 2 was cheaper than that in Group 1, both direct cost and indirect cost. In Group 1, the total cost of illness reached was Rp 296,866,746 in 6 months and the average cost per visit was Rp. 989,555. By contrast, in Group 2, the total cost of illness reached was Rp, 231,814,417 in 6 months and the average cost per visit was Rp. 927,258 (Table IV).

Based on the higher level of effectiveness in QoL, and the lower cost of medical services in Groups 2 compared with Group 1, we performed CEA which was expressed in the form of average cost-effectiveness ratio (ACER) and incremental cost-effectiveness ratio (ICER). The ACER of Group 2 was smaller than that of Group 1. Therefore, group 2 can be considered as more cost-effective compared with Group 1. Based on the indicators of clinical quality, including IPSS, QoL and Qmax, the ICER Group 2 was -1,327,593, -7,228,007, and -1,290,715 respectively. This result indicates the improvements in the effectiveness and cost savings of modified therapeutic methods (Table V).

DISCUSSION

BPH is a benign enlargement of the prostate in elderly men. Patients aged 60-69 years and 70-79 years were the largest age group included in this study at SCH. LUTS caused by BPH are progressive complaints, which occur at the age of 70 years or more.⁴ Some researchers reported that BPH began at the age of 50. Patients with BPH will then be assessed on the basis of the degree of complaint and QoL using the IPSS, and the maximum urinary flow rate using uroflowmetry. At present, medical therapy is given for patients with moderate or severe complaints. The Indonesian Association of Urologists recommends daily combination therapy for 6 months among patients with moderate to severe symptoms.² However, long-term treatment will cause a large increase in costs which can cause a heavy burden to the government and society.⁵ Therefore, finding a cost-effective therapy without losing the quality of the clinical outcome is necessary.

The initial severity of complaints by the patients determines the treatment option, cure rate, and complications that will occur in the future. In Europe, 63% patients with BPH come with moderate to severe complaints.⁴ In several other studies,

improvement in complaints was observed after combination therapy.^{8,10} This finding is consistent with the result of this study, where patients in combination therapy showed improvement in complaints. However, modified therapeutic methods provide greater improvement when compared with standard therapeutic methods.

In this study with regard to the QoL, patients in both groups at the beginning of therapy showed dissatisfaction and unhappiness toward their condition. This situation caused the patients to come for treatment. This result is also in accordance with several other studies, that is people with BPH come for treatment if it interferes with daily life and activities.⁸ QoL has improved after receiving either standard therapy or modified therapy. The improvement in QoL showed almost the same percentage in both groups. Early combination therapy reduces prostate growth progression and reduces the incidence of acute urinary retention; thus, giving early combination therapy will improve the QoL patients with BPH.

The maximum urinary flow rate (Qmax) examined by uroflowmetry in both groups showed an inadequate flow of urine (obstruction). Obstruction was found in 86% of patients in the standard method group and 66% of patients in the modified method group. Qmax in both groups improved after combination therapy. The modified therapeutic method group showed a higher Qmax improvement than the standard therapeutic method group within 6 months of clinical observation.

The high prevalence rate of BPH causes a huge economic burden and medical costs. The cost of BPH treatment in the United Kingdom is approximately £ 180 million annually, of which 60% are due to complications from BPH. Medical costs were also found to be 1.1 billion USD in the US per year.¹⁰ Evaluation of BPH medical therapy in several American and European countries shows that combination medical therapy is more cost effective than monotherapy.^{3,4,6-9}

The medical costs of the modified therapeutic method are less than that of the standard method. The cost per visit of the modified therapeutic method is also less than that of the standard therapeutic method. CEA is the conversion of cost and effectiveness in the form of a ratio. CEA is expressed as the ACER and ICER. The effectiveness of this study based on the clinical quality indicators shows different values. The maximum urinary flow rate is an objective indicator of clinical quality compared with other indicators, and it showed a significant difference in statistical tests in favor to the modified therapeutic method. Given its better effectiveness and lower clinical service costs, the ACER in the modified method group is smaller. ACER does not show real

economic value compared with ICER.¹² The ICER is more important than ACER, because it shows the degree of cost effectiveness of an intervention. In addition, the ICER of the modified therapeutic method is more cost-effective, where one clinical quality effectiveness value can reduce costs by Rp. 890,225.

Research on clinical quality and cost provides an understanding of the importance of coordination and collaboration with clinicians. Management encourages peer groups or medical staff to perform therapy in accordance with CPG; conduct clinical evaluations or audits of high-volume, high-risk, and high-cost cases; and monitor and evaluate the applicable CPG in hospitals. Therefore, collaborative care will be created in hospitals. Our study shows the importance of the role of head management in the hospital for clinical values in Continuous Quality Improvement. Hospital leaders can encourage cross-functional team performance among health professionals by setting budgets on clinical services. Data on the successful cost-effective health services can be used as an adequate promotional value.

Moreover, a comprehensive understanding of the application of pharmacoeconomic studies is necessary. Cost-effectiveness analysis is widely used to compare two or more health interventions that have different degree of effectiveness.¹³⁻¹⁵ The existence of the HTA (Health Technology Assessment) team and the committee for quality improvement in hospitals are necessary because it can ensure that the dimensions of quality run well in the hospital. Understanding the quality of services related to clinical quality is a common need for clinicians and management in accordance with the dimensions of health service quality. The Institute of medicine defines six dimensions of health service quality: patient safety, effectiveness, efficiency, patient-centered, punctuality and equity. The modified BPH therapy method that is conducted in this study also pays attention to other quality dimensions such as patient safety, where patients are monitored in the same way as standard therapeutic methods. Another dimension of quality that can be observed is patient centeredness, where this study can also answer patients desire not to take medication every day for life. Therefore, the modified therapeutic method conducted in this study for patients will be low-cost service to be implemented in the future. This modified therapeutic method will be great help to the National Health Insurance (JKN) of Indonesia with regard to of balancing cost-effectiveness while maintaining service quality.

Ensuring the quality of hospital health services based on the dimensions of health service quality, requires directors of hospital with meta-leadership quality. Quality of service must be the indispensable part of the hospitals. This way, a hospital with services that are affordable, feasible and of good quality will be achieved.

CONCLUSION

Clinical quality indicators, including IPSS, maximum urinary flow rate, and QoL have improved in both combinations therapeutic methods. The modified therapeutic method was more effective in improving clinical IPSS and maximum urinary flow rate than the standard therapeutic method.

A significant relationship was found between the maximum urinary flow rate in the standard therapeutic and the modified therapeutic groups.

The total and average cost of therapy for clinical services of patients with BPH in the modified therapeutic methods was less than that of the standard therapeutic methods. Furthermore, the cost-effectiveness ratio of the modified therapeutic method group was less than that of the standard therapeutic method group.

REFERENCES

1. Zhang AY and Xu X. Prevalence, burden, and treatment of lower urinary tract symptoms in men aged 50 and older: A systematic review of the literature. SAGE; 2018:4.
2. IAU. Panduan Penatalaksanaan Klinis Pembesaran Prostat Jinak. Ikatan Ahli Urologi Indonesia; 2017: 1-38.
3. Walker A, Doyle S, Posnett J, Hunjan M. Cost-effectiveness of single-dose tamsulosin and dutasteride combination therapy compared with tamsulosin monotherapy in patients with benign prostatic hyperplasia in the UK. *BJU Int* 2013; 112:638-46.
4. Geitona M, Karabela P, Katsoulis IA, Kousoulakou H, Lyberopoulou E, Bitros E, et al. Dutasteride plus tamsulosin fixed dose combination first line therapy versus tamsulosin monotherapy in the treatment of benign prostatic hyperplasia: a budget impact analysis in the Greek healthcare setting. *BMC Urol* 2014; 14:78.
5. McAninch JM, Lue TF. Smith & Tanaho's General Urology 18th edition. Lange. 2013
6. Udeh EI, Ofoha CG, Adewole DA, and Nnabugwu II. A cost-effective analysis of fixed-dose combination of dutasteride and tamsulosin compared with dutasteride monotherapy for benign prostatic hyperplasia in Nigeria: a middleincome perspective; using an interactive markov model. *BMC Cancer* 2016; 16:405.
7. DerSarkissian M, Xiao Y, Sheng MD, Lefebvre P, Swensen AR, and Bell CF. Comparing clinical and economic outcomes associated with early initiation of combination therapy of an alpha blocker and dutasteride or finasteride in men with benign prostatic hyperplasia in the United States. *J Manag Care Spec Pharm* 2016.
8. Erman A, Masucci L, Krahn MD, and Elterman DS. Pharmacotherapy vs surgery as initial therapy for patients with moderate to severe benign prostate hyperplasia: a cost effectiveness analysis. *BJU Int* 2018; 879-88.
9. Bahia RL, Araujo DV, Pepe C, Javaroni V, Trindade M, Camargo CM. Cost-effectiveness analysis of medical treatment of benign prostatic hyperplasia in the Brazilian public health system. *Int Braz JUrol* 2012; 38(5).
10. Kim HW, Moon DG, Kim HM, Hwang JH, Kim SC, Nam SG, et al. Effect of shifting from combination therapy to monotherapy of alpha blocker or 5 ARI on prostate volume and symptoms in patients with benign prostatic hyperplasia. *Korea JUrol* 2011; 681-6
11. Speakman M, Kirby R, Doyle S, Ioannou C. Burden of male lower urinary tract symptoms (LUTS) suggestive of benign prostatic hyperplasia (BPH) – focus on the UK. *BJU Int* 2015; 115:508–19.
12. Haslinda NI, Juni MH, Rosliza AM, Faisal I. Designing and conducting cost effectiveness analysis studies in healthcare. *IJPHCS* 2017; 4: 62-76.

13. Eisenberg JM, Schulman KA, Glick H, and Koffer H. Pharmacoeconomics: Economic evaluation of pharmaceuticals. In: Strom BL, Editor. Pharmacoeconomics, John Wiley & Sons Ltd.; 1994: 469-493.
14. Sanchez LA. Applied pharmacoeconomics: Evaluation and use of pharmacoeconomic data from literature. Am J Health Syst Pharm1999; 56:1630-40.
15. Sanchez LA, Lee JT. Applied pharmacoeconomics: Modeling data from internal and external resources. Am J Health Syst Pharm2000; 57:146-158.