

A COMPARISON OF TRANSURETHRAL RESECTION OF THE PROSTATE AND MEDICAL TREATMENT FOR THE PATIENT WITH MODERATE SYMPTOMS OF BENIGN PROSTATIC HYPERPLASIA

MASANORI YAMAMOTO, HATSUKI HIBI and KOJI MIYAKE

Department of Urology, Nagoya University School of Medicine

ABSTRACT

Transurethral resection of the prostate is the most common surgical treatment for benign prostatic hyperplasia. We conducted a prospective randomized clinical trial to compare this surgery with medical treatment in men with moderate symptoms of benign prostatic hyperplasia. Of 98 men over the age of 54 years who were screened between June 1993 and June 1995, 53 were studied (25 in the surgery group and 28 in the medication group). Patients' symptoms and the degree to which they were bothered by urinary difficulties were measured with standardized questionnaires and medical evaluations. The men randomly assigned to the surgery group underwent surgery within 2 weeks after the assignment. Surgery was not associated with an impotence or urinary incontinence. The follow-up period was 1 year. Surgery was significantly associated with improvement in residual urinary volume and peak flow rate; and also in the scores for urinary difficulties, sexual performance and interference with activities of daily living ($P < 0.001$ for all comparisons). We concluded that for patients with moderate symptoms of benign prostatic hyperplasia, surgery is more effective than medication in improving genitourinary symptoms and enhancing the quality of life. Thus, medication as treatment should be reserved for patients who are less bothered by urinary difficulty or who wish to delay surgery.

Key Words: Benign prostatic hyperplasia, Transurethral resection, Medical treatment, Moderate obstructive symptom

INTRODUCTION

Obstructive and irritative symptoms in benign prostatic hyperplasia (BPH) patients are extremely common in men over the age of 60;¹⁾ a few BPH patients experience urinary retention or obstruction of the upper urinary tract. For patients with advanced stages of BPH, surgical treatment, usually a transurethral resection of the prostate (TUR-P), is generally required. Patients with a less advanced stage may elect medical therapy (most often an alpha-blocker²⁾ or chlormadinone acetate is chosen³⁾). Furthermore, simple behavioral therapies, such as relaxed voiding, and avoidance of coffee, alcohol and drugs such as alpha-adrenergic agonist may help reduce obstructive symptoms.

Transurethral resection of the prostate (TUR-P) is the most common surgical treatment for BPH. Chlormadinone acetate is safe and clinically effective when given in proper doses in the long-term medical treatment of patients with moderate outflow obstruction.³⁾ However, an

Correspondence: Masanori Yamamoto, M.D., Department of Urology, Nagoya University School of Medicine, 65 Tsurumai-cho, Showa-ku, Nagoya 466, Japan

appropriate therapeutic approach for patients with moderate obstructive symptoms of BPH has not been well established. Therefore, we conducted a prospective randomized clinical trial that compared TUR-P with medical treatment using chlormadinone acetate for handling moderate symptoms of BPH.

MATERIALS AND METHODS

Selection of Patients

Consecutive male patients who visited our urology clinic because of BPH symptoms were asked to participate in this study. All participants gave written informed consent. The initial evaluation included: their medical history, documentation of urinary symptoms, rectal examination, urinalysis, measurement of the serum creatinine concentration, and measurement of residual urinary volume after voiding. Urinary symptoms were graded 0 to 5 according to the American Urological Association's symptom score (AUA score).⁴⁾ A pilot study indicated that the greatest uncertainty about the choice of treatment existed among patients whose scores were between 8 and 19, which was considered moderate. Therefore, such patients were eligible for the study. This scoring system was validated to distinguish BPH patients from non-BPH patients, test/re-test reliability, and internal consistency. It was given to patients who had no symptoms of bladder outlet obstruction, those patients serving as controls, and patients who were seeing urologists because of symptoms of prostatism.⁴⁾

Patients were excluded from the study if they were less than 55 years old, were unable to walk, had an active urinary tract infection not responding to treatment, or had a residual urinary volume over 350 ml after voiding. The criteria that less than 350 ml of residual urinary volume was one of the objective findings in the patients with moderate symptom of BPH was arbitrarily defined. In addition, patients with serious medical conditions that would have made surgery inappropriate or follow-up unlikely were excluded. These conditions included: uncontrolled diabetes, neurogenic bladder, liver cirrhosis, active alcoholism, bleeding diathesis, psychosis, and late-stage cardiac or respiratory disease. Patients were also excluded if their serum creatinine concentration was higher than 2.0 mg per deciliter.

Assignment to Treatment and Follow-up

Eligible patients were randomly assigned to transurethral resection or medical treatment using a random number table. Patients assigned to the surgery group underwent surgery within 2 weeks after randomization; the other patients assigned to drug therapy received 50 mg of chlormadinone acetate twice daily for 1 year. All the participants were examined 6 and 12 months after randomization. Patients who received chlormadinone acetate were asked regarding any side effects at each follow-up visit.

The peak urinary flow and the volume of voided urine were measured during the base-line evaluation and at each semiannual follow-up visit with a uroflowmeter. The measurements were repeated if the volume of voided urine was less than 100 ml. After these measurements had been performed, the residual volume after voiding was determined. At base line and 1 year after, the patients' quality of life was assessed on a 100-point scale. This scale assessed the degree to which urinary difficulties bothered the patients or interfered with their activities of daily living, sexual function, social activities and general well-being.⁵⁾

Statistical Analysis

The Wilcoxon rank sum test was used to evaluate the statistical significance of changes from

SURGERY VERSUS MEDICATION FOR BENIGN PROSTATIC HYPERPLASIA

base line and one year of follow-up in each categorical variables between the two groups. P values less than 0.05 were considered to indicate statistical significance.

RESULTS

Screening

Of the 98 patients over the age of 54 years who were screened and had symptoms consistent with BPH, 21 were excluded because of a high volume of residual urine (> 350 ml) and 3 because of a markedly elevated symptom score (> 20). Of the 74 patients who were eligible for randomization, 17 did not provide informed consent and 4 were randomly assigned to a drug therapy group and later found to be ineligible. The study therefore included 53 patients: 25 in the surgery group and 28 in the drug therapy group.

Characteristics of the Patients

The characteristics of the two groups were similar (Table 1). The mean (\pm SD) age of all randomized patients was 63.7 ± 5 years. The mean volume of residual urine after voiding was 100 ± 74 ml. The serum creatinine concentration, which indicates renal function, was within the normal range (1.1 ± 0.25 mg per deciliter). The mean peak rate of urinary flow was 11 ± 5 ml per second. The most bothersome symptoms were nocturia (76% of all patients), dribbling (24%), urgency (21%), and hesitancy (15%).

Table 1. Base-Line Characteristics of Patients with Benign Prostatic Hyperplasia Randomly Assigned to Surgery or Medical Treatment.*

Characteristic	Surgery (n=25)	Medical Treatment (n=28)
Age (year)	62.1 ± 4.6	65.1 ± 5.2
Concurrent condition		
Hypertension	32.2	38.6
Respiratory disease	12.3	15.6
Diabetes mellitus	21.5	26.1
Congestive heart failure	2.1	1.4
Genitourinary findings		
Symptom score [#]	15.2 ± 2.1	15.8 ± 3.5
Residual urinary volume (mL)	98.5 ± 68	102 ± 79
Peak urinary flow rate (mL/sec)	11.2 ± 7.2	12.1 ± 6.3
Quality-of-life scores ^{##}		
Bother from urinary Difficulties ^{##}	51.2 ± 45.2	49.6 ± 52.1
Sexual performance ^{##}	46.9 ± 39.2	50.1 ± 42.1
Activities of daily living ^{##}	67.2 ± 32.5	69.2 ± 36.8
General well-being ^{##}	75.8 ± 36.9	72.1 ± 29.5
Social activities ^{##}	73.1 ± 27.4	74.3 ± 26.8

*Plus-minus values are means \pm SD; all other values are percentages of patients.

[#]Scored on a scale ranging from 0 (least severe symptoms) to 35 (most severe symptoms).

^{##}Scored on a scale ranging from 0 (greatest impairment) to 100 (least impairment).

Postoperative Events

Eighty-five percent of the patients were hospitalized for 7 days or less after surgery (mean, 7 ± 3 days). Ninety-one percent of the patients had no complications during the first 30 days after surgery. The most frequent complication was a hemorrhage requiring transfusion in 3 patients (12%). Two patients had postoperative urinary tract infections, and one patient had urethral stricture. There were no deaths associated with surgery. Prostate cancer was not found in any specimen removed at surgery.

Adverse Side Effects of Chlormadinone Acetate

Most changes in laboratory parameters remained within the normal limits and none were considered clinically significant. The most frequent side effect of chlormadinone acetate was impotence. Thirty-eight percent of the patients complained of loss of libido. Hypercholesterolemia was noted in 3 patients. Serious side effects of chlormadinone acetate were not observed in any of the patients during the course of the treatment.

Change in Symptoms and Quality of Life

Information on symptomatic and genitourinary outcomes are presented in Table 2. As compared with medical treatment, surgery was associated with improved scores for patients bothered from urinary difficulties, sexual performance and interference with the activities of daily living ($P < 0.001$ for all comparisons). Surgery was also associated with an improved peak flow rate ($P < 0.001$) and a decreased volume of residual urine ($P < 0.001$). However, there was no significant difference in improvement of symptom score between the two groups. Surgery was not associated with changes in general well-being ($P = 0.321$) or social activities ($P = 0.769$). The score for sexual performance at one year's change from base line in the drug therapy group was significantly decreased compared with that in the surgery group ($p < 0.001$). At the end of the study, 2% of the patients in the surgery group and 38% of those in the medical treatment group reported that their sexual performance was worse.

DISCUSSION

BPH, a common cause of bladder outflow obstruction in older men, is often treated by transurethral resection of the obstructing prostatic tissue. There are a number of standard indications for TUR-P which have been accepted by urologists (i.e. acute retention, significant residual urinary volume, recurrent infections and azotemia). However, treatment for the patients with moderate obstructive symptoms of BPH is still controversial. Our present study addresses a long-standing controversy⁶⁾ concerning the indication for TUR-P and management of BPH. It is evident that TUR-P in men with moderate symptoms of BPH is more effective than medical treatment in maintenance of sexual performance, improving genitourinary symptoms, and alleviating the degree of bother from urinary difficulties, and interference with daily activities. Our results also indicate that the onset of short term complications after TUR-P is infrequent and this finding confirms Lu-Yao's recent report.⁷⁾

In contrast, not every patient with prostatic symptoms requires an operation, and not every case of BPH is progressive. There is concrete evidence that in a proportion of patients, there is condition reaches a certain stage and thereafter remains static.⁸⁾ If at that stage an operation is not suitable because of danger to the patient's health, then symptomatic treatment may be all that is required. In the past, no such treatment was truly available, and many patients had to undergo an operation solely to obtain relief. Now, the chlormadinone acetate or alpha blockers

SURGERY VERSUS MEDICATION FOR BENIGN PROSTATIC HYPERPLASIA

Table 2. Genitourinary Findings and Quality of Life after One Year of Follow-up.

Outcome	Surgery (mean \pm SD)	Medical Treatment (mean \pm SD)	P Value
Genitourinary findings			
Symptom score [#]			
At 1 year	6.2 \pm 4.9	7.8 \pm 5.2	
Change from base line	-9.4 \pm 5.2	-8.2 \pm 4.2	0.071
Residual urinary volume (mL)			
At 1 year	52 \pm 58	89 \pm 78	
Change from base line	-58 \pm 84	-15.1 \pm 92	< 0.001
Peak urinary flow rate (mL/sec)			
At 1 year	18.2 \pm 8.2	11.5 \pm 9.20	
Change from base line	7.5 \pm 8.6	0.5 \pm 9.3	< 0.001
Quality of life scores ^{##}			
Bother from urinary difficulties			
At 1 year	78.3 \pm 25.9	56.8 \pm 29.5	
Change from base line	21.2 \pm 28.4	8.2 \pm 32.1	< 0.001
Sexual performance			
At 1 year	39.8 \pm 28.3	23.4 \pm 26.5	
Change from base line	-5.2 \pm 27.5	-19.3 \pm 32.1	< 0.001
Activities of daily living			
At 1 year	89.4 \pm 21.3	78.4 \pm 31.2	
Change from base line	21.4 \pm 37.5	8.5 \pm 25.7	< 0.001
General well-being			
At 1 year	78.5 \pm 27.6	73.4 \pm 28.9	
Change from base line	2.3 \pm 25.9	1.1 \pm 27.2	0.321
Social activities			
At 1 year	75.6 \pm 22.4	73.8 \pm 31.5	
Change from base line	-0.2 \pm 24.1	-1.4 \pm 23.8	0.769

Change denotes change from the base-line value. P values are differences between the two treatment groups with respect to changes in genitourinary findings and quality of life.

[#]Scored on a scale ranging from 0 (least severe symptoms) to 35 (most severe symptoms).

^{##}Scored on a scale ranging from 0 (greatest impairment) to 100 (least impairment).

can provide relief in many of these patients, instead of an operation. As it is not possible to know in advance if the condition will be progressive in a given patient, it is essential to maintain these patients under supervision and reassess them from time to time. Mebust whose research has constituted the largest group of cases studied, found that approximately 40% of patients who do not require an operation when first seen can be maintained indefinitely on medical treatment dealt with.⁹⁾ There is a group of patients with otherwise relatively mild prostatism who have a tendency to develop recurrent transient attacks of acute retention. In many such cases, the attacks of retention can be prevented by continuous therapy with alpha blockers.⁹⁾

However, there seems little doubt that medical treatment can afford a measure of relief to many sufferers of BPH.⁶⁾ The exact role of this treatment in the overall management of these patients has yet to be clearly defined. Furthermore, Wasson et al. recently conducted a multicenter, randomized clinical trial that compared TUR-P with observations for the

management of moderate symptoms of benign prostatic hyperplasia.¹⁰⁾ They concluded that for patients with moderate symptoms of benign prostatic hyperplasia, TUR-P is more effective than observation in reducing the rate of treatment failure and improving genitourinary symptoms.¹⁰⁾

Therefore, transurethral prostatectomy is the gold standard against which other therapeutic modalities must be compared. There is an immediate significant improvement in symptoms and in other objective parameters, such as flow rate or residual urinary volume. There is an associated low mortality and morbidity rate. TUR-P must remain the gold standard against which other forms of therapy are measured.

When selecting a treatment modality, a patient with moderate symptoms of BPH should consider the degree to which urinary difficulties bother him, the cost of medical care, the effect of treatment on the quality of his life, adverse effect of medication and the complication rate of surgery. Comparable and sufficient information about medical treatment and recently developed alternatives to surgical resection, such as transurethral balloon dilation, transurethral microwave thermotherapy, intraurethral stent, visual laser ablation of the prostate, are needed so that patients can decide, in consultation with their physicians, which treatment is best for them.¹¹⁾

We conclude that patients with moderate symptoms of BPH that substantially decrease the quality of their lives have the most benefit to obtain from transurethral resection surgery. For patients who are less bothered by urinary difficulties or who wish to delay surgery, medical treatment is a safe alternative therapeutic modality. For patients in whom an operation is necessary but is not urgent, pharmacologic treatment can be used to ameliorate symptoms during the interim. However, it is important that in such cases the patients should not be lulled into a false sense of security because of symptomatic improvement.

REFERENCES

- 1) Chute, C.G., Panser, L.A. and Girman, C.J.: The prevalence of prostatism: a population-based survey of urinary symptoms. *J. Urol.*, 150, 85–89 (1993).
- 2) Lepor, H.: Medical therapy for benign prostatic hyperplasia. *Urology*, 42, 483–501 (1993).
- 3) Moriyama, M., Kinoshita, Y., Noguchi, K. and Hosaka, M.: Studies on therapeutic effects and adverse effects of chlormadinone acetate for patients with benign prostatic hypertrophy. *Nishinohon J. Urol.*, 53, 563–571 (1991).
- 4) Barry, M.J., Fowler, F.J. and O'Leary, M.P.: The American Urological Association symptom index for benign prostatic hyperplasia. *J. Urol.*, 148, 1549–1557 (1992).
- 5) The Department of Veterans Affairs Cooperative Study of Transurethral Resection for Benign Prostatic Hyperplasia. A comparison of quality of life with patient reported symptoms and objective findings in men with benign prostatic hyperplasia. *J. Urol.*, 150, 1696–1700 (1993).
- 6) Graverson, P.H., Gasser, T.C., Wasson, J.H., Hinman, F. Jr. and Bruskewitz, R.C.: Controversies about indications for transurethral resection of the prostate. *J. Urol.*, 141, 475–481 (1989).
- 7) Lu-Yao, G.L., Barry, M.J., Chang, C-H., Wasson, J.H. and Wennberg, J.E.: Transurethral resection of the prostate among Medicare beneficiaries in the United States: time trends and outcomes. *Urology*, 44, 692–698, (1994).
- 8) Ball, A.J., Feneley, R.C.L. and Abrams, P.H.: The natural history of untreated "prostatism". *Br. J. Urol.*, 53, 613–616 (1981).
- 9) Mebust, W.K.: BPH, patient care policies and guidelines. AUA Update Series, Lesson 29, 12, 226–231 (1993).
- 10) Wasson, J.H., Reda, D.J., Bruskewitz, R.G., Elinson, J., Keller, A.M. and Henderson, W.G.: A comparison of transurethral surgery with watchful waiting for moderate symptoms of benign prostatic hyperplasia. *N. Engl. J. Med.*, 332, 75–79 (1995).
- 11) McConnell, J.D., Barry, M.J. and Bruskewitz, R.C.: Benign prostatic hyperplasia: diagnosis and treatment. Quick reference guide for clinicians. No. 8. Rockville, Md.: Department of Health and Human Services, 1994 (AHCPR publication no. 94-0583).