## Preliminary Report

# The Resolution of Detrusor Over Activity after Medical and Surgical Treatment in Patients with Bladder Outlet Obstruction

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***Objective:*** *This study was design to evaluate the efficacy of transurethral resection of prostate (TURP) compared to alpha-adrenoceptor antagonists (Alfuzosin SR) for the treatment of patients with benign prostatic hyperplasia BPH concomitant with detrusor overactivity (DO).*

***Material and Method:*** *The patients presenting with lower urinary tract symptoms (LUTS), due to benign prostatic enlargement were invited into the present study. These patients completed the International Prostatic Symptom Score (IPSS), the Quality of Life score (QoL), and underwent urodynamic investigation. Twenty-five patients with urodynamics proving bladder outlet obstruction and concomitant detrusor overactivity were allocated into two groups. Group 1 was treated by TURP (surgical treatment group) and group 2 was treated with Alfuzosin SR (medical treatment group). Twelve patients were allocated to group 1 and the remainder 13 to group 2. Reassessment was performed after three months when the patients completed the International Prostatic Symptom Score (IPSS), Quality of Life score (QoL), and urodynamics study.*

***Results:*** *Mean patient age was compared for both groups (70 $\pm$ 2.5 years in group 1 and 70.7 $\pm$ 1.8 in group 2, p = 0.84). There were no statistically significant differences between baseline clinical and urodynamic characteristics of patients in the different treatment groups. IPSS and QoL scores improved significantly after treatment in each group. A statistically significant difference after treatment was noted in group 1 for the obstruction urodynamic parameters (Qmax, PdetQmax, Bladder outlet obstruction index). In group 2, a significant improvement was found in PdetQmax and Bladder outlet obstruction index, but not in Qmax. Detrusor overactivity persisted in three patients of group 1 (75% resolution), while two patients in group 2 were free from detrusor overactivity (15% resolution) (Chi-square = 0.001).*

***Conclusion:*** *Surgical treatment of benign prostatic hyperplasia, particularly TURP, significantly reduces the incidence of detrusor overactivity concurrent with bladder outlet obstruction, when compared with the use of alpha-adrenoceptor antagonists alone.*

***Keywords:*** *Detrusor overactivity, Benign prostatic hyperplasia*

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Benign prostatic hyperplasia (BPH) is a common condition among elderly men, occurring in up to 70% of men older than 60 years[1]. Symptomatic BPH is thought to be due to bladder outlet obstruction and is often referred to as lower urinary tract symptoms (LUTS). Although obstructive urinary symptoms such as slow urinary stream, straining to urinate and sense of incomplete urination are the important symptoms of bladder outlet obstruction, storage urinary symptoms including frequency of urination, urgency and nocturia are also bothersome to the patient, interference with daily life activities and have a negative impact on the quality of life[2,3]. Storage symptoms are mainly attributable to detrusor over activity, which is thought to occur in approximately 50-75% of patients with benign prostatic obstruction[4-6]. There are a variety of methods

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for the management of BPH depending on severity of the symptoms and the patients' preference. Two main therapeutic options are medical and surgical therapy. Medical treatment is usually the initial choice and alpha-adrenoceptor antagonists remain the most widely used pharmacological agents aimed at the dynamic component of benign prostatic obstruction. Surgical treatment is usually preserved for patients with severe symptoms or complication of BPH that indicates more invasive treatment such as recurrent urinary retention, massive hematuria, recurrent urinary tract infection, stone formation or renal deterioration. However, the patient's decision for the type of treatment is another important factor that has to be considered before initiating a course. Detrusor over activity is detected in concurrence with BPH, and some authors have found it could be resolved after treatment of BPH[7-9]. The authors prospectively analyzed the clinical and urodynamic resolution of detrusor over activity in a group of patients with bladder outlet obstruction, who were treated with alpha-adrenoceptor antagonists and transurethral resection of prostate (TURP).

## Material and Method

During 2004-2005, the patients presenting with lower urinary tract symptoms (LUTS), due to benign prostatic enlargement, were invited into the present study. These patients completed the International Prostatic Symptom Score (IPSS) and Quality of Life score (QoL), and underwent digital rectal and urine examination, a serum test for creatinine, and a prostatic specific antigen (PSA) level and urodynamic study. Twenty-five patients with urodynamics proving bladder outlet obstruction and concomitant detrusor over activity were enrolled in the final analysis. The bladder outlet obstruction index was determined by the formula PdetQmax-2Qmax [where Qmax was the peak urinary flow rate, measured in milliliters per second (ml/sec) and PdetQmax was the detrusor pressure at Qmax, measured in cm $H_2O$]. The bladder outlet obstruction was defined when its index is more than 40[10]. According to the International Continence Society[11], detrusor over activity is defined as any phasic detrusor contraction during the filling phase, or terminal detrusor contraction occurring at the cystometric capacity. The exclusion criteria were neurogenic bladder dysfunction, disease with bladder outlet obstruction other than BPH, suspected prostate cancer, known bladder cancer or stones, chronic cystitis or other inflammation. All patients completed the informed consent form that was approved by the ethics committee of the authors' institute. Eligible patients were informed about their diseases and the treatment options, medication and surgery. Twelve patients decided to be treated by TURP. This surgical treatment group accepted the details of surgical technique and complications then signed the inform consent form. The other 13 patients preferred to be treated with Alfuzosin SR at 10 mg once daily (medical treatment group). Reassessment was performed after three months when the patients completed the International Prostatic Symptom Score (IPSS), Quality of Life score (QoL), and urodynamics study. Statistical analysis was performed using the mean, standard error of mean (SEM), range, and the chi square test to compare the evolution of detrusor over activity before and after treatment in each group. The unpaired F test was used to compare mean between groups and paired F test was used to compare mean before and after treatment. A $p<0.05$ was considered to indicate significance.

## Results

### *Baseline characteristics*

Mean patient age $\pm$ SEM was comparable for both groups ($70 \pm 2.5$ years in group 1 and $70.7 \pm 1.8$ in group 2, $p = 0.84$). There were no statistically significant differences between baseline clinical and urodynamic characteristics of patients in the different treatment groups (Table 1).

### *Resolution of symptoms and bladder outlet obstruction at follow-up*

IPSS and QoL scores improved significantly after treatment in each group. A statistically significant difference after treatment was noted in the surgical treatment group for the obstruction urodynamic parameters (Qmax, PdetQmax, Residual urine, Bladder outlet obstruction index). In the Alfuzosin SR treatment group, a significant improvement was found in PdetQmax and Bladder outlet obstruction index, but not in Qmax (Table 2).

Comparisons of clinical and urodynamic parameters between both groups after treatment revealed a statistically significant difference only for Qmax ($p = 0.03$) and bladder outlet obstruction index ($p = 0.04$) (Table 3).

### *Resolution of detrusor over activity at follow-up*

Detrusor over activity persisted in three patients in the surgical treatment group (75% resolution), while two patients in the medical treatment group were free from detrusor over activity (15% resolution) at three months follow up (Chi-square = 0.001) (Fig. 1).

**Table 1.** Baseline clinical and urodynamic characteristics of patients in group 1 (surgical treatment group) and group 2 (medical treatment group)

| | Group 1 mean ± SEM (Min-Max) | Group 2 mean ± SEM (Min-Max) | p-value |
|---|---|---|---|
| Age (year) | 70.1 ± 2.5 (56-82) | 70.7 ± 1.8 (56-82) | 0.84 |
| IPSS | 19.4 ± 2.0 (14-35) | 21.1 ± 2.0 (11-31) | 0.55 |
| QoL score | 5.2 ± 0.2 (4-6) | 5.2 ± 0.3 (4-6) | 0.95 |
| Qmax (mL/sec) | 5.1 ± 1.0 (1-13) | 6.7 ± 1.3 (2-15) | 0.10 |
| PdetQmax ($cmH_2O$) | 82.1 ± 5.9 (42-116) | 77.7 ± 8.0 (38-110) | 0.66 |
| Voided volume (mL) | 174.3 ± 28.5 (76-300) | 178.6 ± 26.6 (50-250) | 0.92 |
| Residual urine (mL) | 83.3 ± 30.4 (5-240) | 72.1 ± 16.3 (5-127) | 0.76 |
| Bladder outlet obstruction index | 71.9 ± 5.1 (40-99) | 61.9 ± 9.5 (22-106) | 0.35 |

**Table 2.** Baseline and follow up characteristics of patients in each group

| | Mean ± SEM (Min-Max) | | | | | |
|---|---|---|---|---|---|---|
| | Surgical treatment group | | | Medical treatment group | | |
| | Baseline | Follow up | p-value | Baseline | Follow up | p-value |
| IPSS | 19.4 ± 2.0 (14-35) | 8.1 ± 1.3 (3-14) | 0.00 | 21.1 ± 2.0 (11-31) | 12.3 ± 2.0 (10-18) | 0.01 |
| QoL score | 5.2 ± 0.2 (4-6) | 2.0 ± 0.6 (1-6) | 0.00 | 5.2 ± 0.3 (4-6) | 3.1 ± 0.6 (1-6) | 0.01 |
| Qmax (mL/sec.) | 5.1 ± 1.0 (1-13) | 10.7 ± 1.3 (7-17) | 0.00 | 6.7 ± 1.3 (2-15) | 8.0 ± 1.1 (7-15) | 0.22 |
| PdetQmax ($cmH_2O$) | 82.1 ± 5.9 (42-116) | 49.9 ± 6.4 (30-103) | 0.00 | 77.7 ± 8.0 (38-110) | 56.0 ± 6.8 (22-85) | 0.04 |
| Voided volume (mL) | 174.3 ± 28.5 (76-300) | 296.7 ± 42.3 (200-470) | 0.60 | 178.6 ± 26.6 (50-250) | 204.2 ± 37.5 (80-580) | 0.85 |
| Residual urine (mL) | 83.3 ± 30.4 (5-240) | 33.0 ± 23.8 (0-240) | 0.16 | 72.1 ± 16.3 (5-127) | 43.5 ± 12.3 (2-150) | 0.19 |
| Bladder outlet obstruction index | 71.9 ± 5.1 (40-99) | 23.8 ± 7.5 (2-97) | 0.00 | 61.9 ± 9.5 (22-106) | 45.3 ± 7.0 (16-98) | 0.00 |

**Table 3.** Comparison of treatment outcome in each group

| | Surgical treatment group | Medical treatment group | p-value |
|---|---|---|---|
| IPSS | 8.1 ± 1.3 (3-14) | 12.3 ± 2.0 (10-18) | 0.10 |
| QoL score | 2.0 ± 0.6 (1-6) | 3.1 ± 0.6 (1-6) | 0.20 |
| Qmax (mL/sec) | 10.7 ± 1.3 (7-17) | 8.0 ± 1.1 (7-15) | 0.03 |
| PdetQmax (cmH2O) | 49.9 ± 6.4 (30-103) | 56.0 ± 6.8 (22-85) | 0.55 |
| Voided volume (mL) | 296.7 ± 42.3 (200-470) | 204.2 ± 37.5 (80-580) | 0.13 |
| Residual urine (mL) | 33.0 ± 23.8 (0-240) | 43.5 ± 12.3 (2-150) | 0.67 |
| Bladder outlet obstruction index | 23.8 ± 7.5 (2-97) | 45.3 ± 7.0 (16-98) | 0.04 |

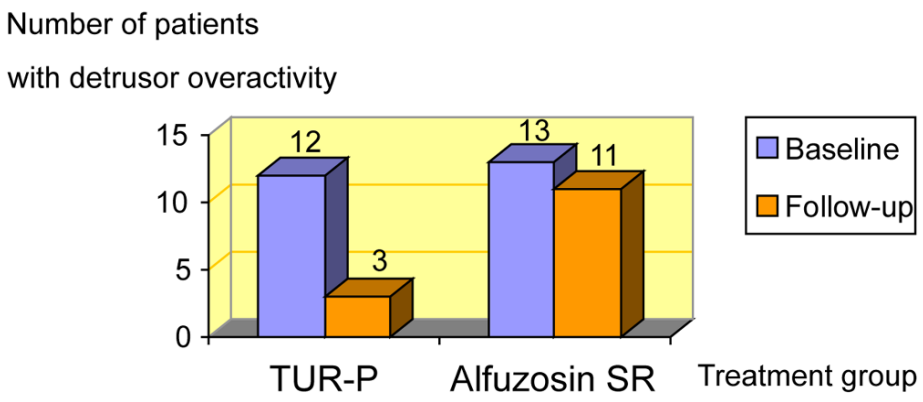


**Fig. 1** The resolution of detrusor overactivity at 3 months follow up in each group of treatment

**Discussion**

Detrusor over activity is one of the common causes of lower urinary tract symptoms and is often associated with bladder outlet obstruction from benign prostatic enlargement. Several hypotheses have been proposed to explain the etiology of detrusor overactivity, which happens concurrently with bladder outlet obstruction. Different studies have shown that increased bladder pressure such as that observed with bladder outlet obstruction can lead to partial denervation of the detrusor muscle resulting in detrusor over activity caused by post-junctional cholinergic super sensitivity[12,13]. Other studies have suggested that abnormal sensory stimuli from an anatomically altered prostatic urethra, as in patients with BPH, can induce detrusor over activity[6,8,14]. Other mechanisms proposed include altered adrenoceptor function, neurotransmitter imbalance and a myogenic change[5]. However, some authors believe that detrusor over activity and bladder outlet obstruction are unrelated events occurring in elderly men because the incidence of detrusor over activity increases with age in more than 50% of men older than 70 years. Nevertheless, for those not suffering from obstruction, the changes in detrusor nerve density and fibrosis observed in bladder outlet obstruction are not distinguishable from those of aging[15].

The authors evaluated patients who presented with obstruction, due to BPH combined with urodynamically proven detrusor over activity. Patients' age, IPSS, QoL score and degree of obstruction were comparable in both groups. In the surgery group, a statistically significant improvement in all obstruction parameters as well as significant relief of detrusor over activity was observed. A total of 75% of patients with detrusor over activity in this group presented with normal behavior at three months after surgery. This finding corresponded with other studies[4,6,9]. These findings might be explained by a sensory denervation effect on the bladder neck and the prostatic urethra obtained by surgical ablation of sensory stimuli, as proposed by Abrams[6]. Chalfin and Bradley also demonstrated that the selective blocking of sensory stimuli from the prostatic urethra with lidocaine injection, without relief of obstruction, could eliminate detrusor over activity[14]. Other studies demonstrated the reinnervation of detrusor muscle and the recovery of bladder stability after the relief of obstruction[8,13,16]. In the alfuzosin SR treatment group, a statistically significant improvement in obstruction parameters was observed, except for the peak urinary flow rate and detrusor over activity, which were still presented in 11 patients at three months follow up. These results indicated that alpha-adrenoceptor antagonists alone had not shown a significant reduction of detrusor overactivity. Some studies proposed that alpha-adrenoceptor antagonists exert a positive role in the over active bladder by the direct effect on the alpha-adrenergic receptor at the detrusor muscle of patients who have bladder outlet obstruction[17,18]. However, many authors have recommended using the combination of alpha-adrenoceptor antagonists and anticholinergic drugs to eliminate both storage and voiding symptoms, due to detrusor over activity and bladder outlet obstruction[19-21]. To date, no studies have confirmed the exact duration of treatment by medication, so patients have to use both alpha-adrenoceptor antagonists and anticholinergic drugs regularly in the

long-term to maintain satisfactory results of the treatment. With respect to cost-effectiveness, in comparison to long-term combined medication, TURP has the potential to be an inexpensive treatment that provides satisfactory results in a majority of this group of patients. Only one fourth of the patients still have overactive bladder symptoms after surgery and need anticholinergic drugs to control thereafter.

**Conclusion**

Surgical treatment of benign prostatic hyperplasia, particularly TURP, significantly reduces the incidence of detrusor over activity concurrent with bladder outlet obstruction, when compared with the use of alpha-adrenoceptor antagonists alone.

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## *การลดลงของภาวะกระเพาะปัสสาวะบีบตัวไวเกินปกติเปรียบเทียบการใช้ยาและการผ่าตัดรักษาในผู้ป่วยต่อมลูกหมากโต*

***ศุภณ ศรีพลากิจ, กฤษณะ พรหมวัชรานนท์***

***วัตถุประสงค์****: เพื่อเปรียบเทียบผลการรักษาผู้ป่วยที่มีโรคต่อมลูกหมากโต ร่วมกับภาวะกระเพาะปัสสาวะ บีบตัวไวเกินปกติ (DO) ด้วยวิธีการผ่าตัด TURP และการให้ยารับประทาน alpha-adrenergic blocker (alfuzosin SR)*
***วัสดุและวิธีการ****: ผู้ป่วยใหม่ที่มีอาการของโรคต่อมลูกหมากโตร่วมกับภาวะกระเพาะปัสสาวะบีบตัวไวเกินปกติ ได้รับการซักประวัติเพื่อบันทึกระดับความรุนแรงของอาการโดยใช้ IPSS และ QoL score การตรวจร่างกาย ตรวจพื้นฐานทางห้องปฏิบัติการ รวมถึงการตรวจยูโรพลศาสตร์เพื่อสนับสนุนการวินิจฉัย โดยแบ่งผู้ป่วยออกเป็นสองกลุ่มตามความสมัครใจ กลุ่มที่หนึ่งเลือกการรักษาด้วยการผ่าตัด TUR-P กลุ่มที่สองต้องการรักษาด้วยยาหลังจากนั้นติดตามผลการรักษาของทั้งสองกลุ่มเมื่อครบ 3 เดือน โดยประเมินจาก IPSS, QoL และ ผลการตรวจยูโรพลศาสตร์*
***ผลการศึกษา****: ผู้ป่วยจำนวน 25 คน ได้รับการรักษาด้วยการผ่าตัด 12 คน และเลือกรับยา 13 คน โดยข้อมูลพื้นฐาน (อายุ, IPSS, QoL score, bladder outlet obstruction index) ของทั้งสองกลุ่มไม่แตกต่างกันอย่างมีนัยสำคัญ 3 เดือนหลังจากได้รับการรักษาพบว่าผู้ป่วยกลุ่มที่ได้รับการผ่าตัด มี detrusor over activity หายไป 9 ใน 12 คน (75%) ส่วนผู้ป่วยที่ได้รับยา มีเพียง 2 ใน 13 คน (15%) ซึ่งแตกต่างกันอย่างมีนัยสำคัญ ($p = 0.01$), เมื่อเปรียบเทียบก่อนและหลังการรักษา พบว่าผู้ป่วยทั้งในกลุ่มที่ได้รับการผ่าตัดและกลุ่มที่ได้รับยา มีระดับความรุนแรงของอาการ (IPSS, QoL score) และ bladder outlet obstruction index ลดลงอย่างมีนัยสำคัญ ($p < 0.05$)*
***สรุป****: การผ่าตัด TUR-P หรือการใช้ยารับประทานในการรักษาผู้ป่วยที่มีทั้งโรคต่อมลูกหมากโตร่วมกับภาวะกระเพาะปัสสาวะบีบตัวไวเกินปกติ มีผลทำให้ผู้ป่วยมีอาการดีขึ้นจากการลดการอุดกั้น แต่การผ่าตัด TURP ยังสามารถลดภาวะกระเพาะปัสสาวะบีบตัวไวเกินปกติได้อย่างมีนัยสำคัญเมื่อเปรียบเทียบกับการรักษาโดยการใช้ยารับประทาน*