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THE EFFICACY AND SAFETY OF DOSE-ESCALATING METHODS IN PATIENTS WITH BENIGN PROSTATE HYPERPLASIA AFTER INITIAL DOXAZOSIN 4MG: DOXAOSIN 8MG, COMBINED THERAPY WITH DOXAZOSIN 4MG AND TAMSULOSIN 0.2MG OR FINASTERIDE 5MG

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Introduction & Objectives: To compare the efficacy and safety of the doxazosin 8mg with combined therapy with doxazosin 4mg and tamsulosin 0.2 mg or finasteride 5mg in men with benign prostate hyperplasia (BPH) who have not achieved an adequate therapeutic response to initial doxazosin 4mg.

Material & Methods: Between 2000 and 2005, 374 patients with BPH who have not achieved an adequate therapeutic response to initial doxazosin 4mg were evaluated in this study. Doxazosin was started at 4mg/day, and then titrated to 8mg/day or combined with tamsulosin 0.2mg or finasteride 5mg if the increase in Qmax was <3 ml/s or the reduction in total IPSS was <20% after 4 weeks of therapy. Patients were evaluated with the International Prostate Symptom Score (IPSS), quality of life (QOL), maximum flow rate (Qmax) and adverse events (AEs) at the baseline, 3 and 12 months after combination.

Results:

Table 1. Changes in IPSS, Qol, Qmax and PVR in each group from baseline after treatments.

	I (n=84)	II (n=115)	III (n=70)
Δ IPSS			
3 mons	-7.0 ± 6.0	-7.1 ± 5.9	-4.3 ± 7.0 †
12 mons	-6.8 ± 6.2	-7.0 ± 6.1	-5.9 ± 7.7
Δ QoL			
3 mons	-0.8 ± 1.0	-0.8 ± 0.9	-0.6 ± 0.9
12 mons	-0.6 ± 1.0	-0.8 ± 0.9	-0.7 ± 0.9
Δ Qmax (ml/s)			
3 mons	4.3 ± 4.0	5.2 ± 3.4	1.7 ± 4.2 †
12 mons	4.4 ± 5.4	4.9 ± 3.5	2.1 ± 4.4 †

†: p < 0.05 compared with group I and II The study comprised of 269 patients who were followed up after 12months later: doxazosin 8mg (group I, n=84), doxazosin 4mg plus tamsulosin 0.2mg (group II, n=115) and doxazosin 4mg plus finasteride 5mg (group III, n=70). Three groups were similar with respect to IPSS, QOL and Qmax at baseline. All groups significantly improved in their lower urinary symptoms and Qmax after combined therapy. Among three groups, there were statistically significant improvement in the mean changes of IPSS from baseline at 3 months and Qmax from the baseline at 3months and 12 months in group I and group II compared with group III (Table 1). At least one AEs was reported by 29.3%, 19.4% and 17.3% of patients in group I, group II and group III respectively. Especially, the incidence of vasodilatory AEs (27.9%, 14.5% and 10.9% in group I, group II and group III respectively) were higher with group I than group II and group III, and sexual function AEs were higher with group III than group I (p<0.05).

Conclusions: Doxazosin 4mg plus tamsulosin 0.2mg is more effective than the combined therapy with doxazosin 4mg and finasteride 5mg and has less vasodilatory adverse events than doxazosin 8mg in men with BPH.

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CHANGES IN PATIENTS PROFILE FOR SURGERY OF BENIGN PROSTATIC HYPERPLASIA IN ERA OF MEDICAL TREATMENT: DECADE (1996-2005)

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Introduction & Objectives: To investigate the changes in patients profile (age, comorbidity, prostate volume, International Prostata Symptom Score (IPSS), the type and duration of medical treatment, and indication for surgery for benign prostatic hyperplasia (BPH) in 1996 and 2005 in our urologic department.

Material & Methods: Retrospective analysis of medical history of patients who had surgery for BPH in 1996(98) and 2005(88) was done. Preoperatively, age, comorbidity, prostate volume and IPSS were evaluated. The type and duration of medical BPH treatment was determinated from medical history. Indication and type of surgery, (open and transurethral resection), volume of operative tissue, duration of stay in hospital were analyzed and compared.

Results: At our department, surgery for BPH decreased for 9.8% comparing 1996 with 2005. Patients in 2005 were older than patients in 1996: 71.2+/-11.1 vs. 67.1+/-10.5 year i.e.3.9 years older (P=0.028). Cardiomyopathy, diabetes mellitus, arterial hypertension were main comorbidities. Indication for surgery in 1996/2005 were AUR in 46/34 patients, failure of medical treatment in 37/41, hematuria 8/5 in and bladder stones7/4. The medical therapy was used in 35% of patients in 1996 (phytotherapy-83%) vs. 91% in 2005(p<0.01) (alpha-adrenergic antagonist-71%, 5- alpha reductasa inhibitors-22% and 7% phytotearpy therapy). Open surgery was performed in 37% in 1996 vs. 21% in 2005. Mean weight of operative material was 57.7+/-31.4g vs. 37.3+/-23.4g (p=0.017). The mean hospital stay was 15.7+/- 5.7 days in 1996 vs. 9.9+/-4.5 in 2005 (p<0.01) for open surgery and 4.7+/- 3.7 vs. 2.1+/- 1.9 days(p<0.01) for transurethral resection. Preoperatively IPSS was reduced from 23.5+/- 7.1 in 1996 to 19.1+/- 4.4 in 2005, and postoperatively from 16.3+/2.1 to 9.1+/- 1.9 in 30 days.

Conclusions: In 2005 patients with BPH surgery were older, with failure of medical therapy, with reduced IPSS pre- et postoperatively. The majority of patients used medical treatment, predominantly, alpha-adrenergic antagonist. Prostate volume was smaller and hospital stay was shorter.

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THE EFFECT OF FINASTERIDE TREATMENT ON SUBURETHRAL MICROVESSEL DENSITY (MVD) IN BENIGN PROSTATE HYPERPLASIA (BPH) PATIENTS

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Introduction & Objectives: Finasteride is a 5 alpha reductase inhibitor that blocks the convertion of testosterone to dihydrotestosterone. It has been confirmed in clinical trials to limit hematuria that results from BPH. However the exact mechanism has not been adequately explained. Previous data suggest that gross hematuria in patients with BPH associated with increased MVD in the suburethral portion of the prostate. In the present study we evaluated the effect of finasteride treatment on MVD which is an indicator of prostatic angiogenesis.

Material & Methods: Thirty patients who were candidates for BPH surgery were prospectively included in the study. All patients had macroscopic hematuria and evaluated by ultrasonogram and cystoscopy. The patients were randomized into two groups. The first group comprised of 13 patients who received 5 mg finasteride for a month prior to surgery and the second group comprised of 17 patients who remained as controls. During the surgery resected suburethral and hyperplastic prostate specimens were sent for histopathologic MVD determination separately. Both groups were compared regarding age, prostate volume, PSA, MVD in suburethral and hyperplastic prostate tissues.

Results: The two groups were similar regarding mean age, prostate volume, PSA and hyperplastic prostate MVD. Mean MVD counts in suburethral prostate tissue in the first group were significantly lower when compared to the second group (table 1). Table 1. Mean MVD values of prostate.

	1st group	2nd group	p value
Suburethral MVD value	9.07 ± 5.5	13.9 ± 5.8	0.03
Hyperplastic MVD value	14.2 ± 7.1	19.7 ± 9.7	0.09

Conclusions: The potential role of finasteride on prostate related hematuria may be the suppressive effect on MVD in the suburethral tissue.

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MANAGEMENT OF ACUTE URINARY RETENTION BY A TRIAL OF SINGLE EMPTYING CATHETERIZATION AND α-BLOCKER ADMINISTRATION

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Introduction & Objectives: To determine whether a trial of single emptying catheterization (TSEC) combined with concurrent a-blocker administration is a feasible option for treating acute urinary retention (AUR) in the setting of benign prostatic hyperplasia (BPH).

Material & Methods: From January 2004 to November 2006, we studied 34 consecutive males presenting at the emergency room (ER) with AUR. The bladder was emptied using a 16Fr Foley catheter under antibiotic coverage along with the administration of a tablet of alfuzosine 10mg, which was then prescribed once daily. Upon release the patients were instructed to return to the ER in case of persistent inability to void or pay a visit to the Outpatient Clinic (OC) in a week, if voiding resumed. Afterwards they were followed as outpatients at 3-monthly intervals in an open label manner.

Results: Voiding resumed in 13 out of 34 patients (38.2%) after their first ER visit. On weekly follow-up visit it was documented that these patients had established satisfactory micturition with Qmax of 10.3 ml/sec and PVR of 63.2ml on average. Of the 21 patients who returned to the ER within 24hrs because of recurrent AUR, 5 (14.7%) were able to resume voiding after a second emptying catheterization. Follow-up visit of these patients a week later revealed Qmax of 6.5 ml/sec and PVR of 98.1ml on average. Late AUR in resolved cases occurred in 3/18 patients (16.7%) at 6,3 months on average. The patients that didn't manage to void after two unsuccessful TSECs were left with indwelling catheters that were removed 7 days later. Patients that responded to TSEC and a-blocker administration had a markedly lower incidence of factors predisposing to AUR, such as large adenoma volume (>60 ml), prominent median lobe and high IPSS score. Of these 16 patients, 6 (17.6%) managed to void, leaving 10 (29.4%) with permanent bladder catheters. Complications of TSECs were seen in 3/18 (16.6%) patients treated with TSEC, namely transient hematuria (2/3 pts) and urinary tract infection (1/3 pts). To present time, prostatectomy has been performed in 5/18 (27.7%) patients with AUR treated with intermittent catheterizations and alfuzosin and in 13/16 (81.2%) patients with permanent bladder catheter. Median times to prostatectomy were 11.8 months for patients with AUR treated with TSEC and 4.2 months for those with permanent catheters.

Conclusions: A trial of a single emptying catheterization (TSEC) combined with administration of alfuzosin 10mg once daily seems an efficient way to treat AUR. In our study, more than half of the patients (52.9%) were able to resume voiding. 27.7% of the responsive patients underwent prostatectomy because of deteriorating IPSS scores or late AUR at almost 1 year. A comparison between this treatment modality and the standard trial without catheter (TWOC) after 48 hrs is already under investigation by a randomized prospective trial.