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The safety and efficacy evaluation of Tamsulosin and Dutasteride and combination therapy in patients with benign prostatic hypertrophy (BPH): a single-blind parallel, randomized, comparative, prospective, phase III trial

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Introduction: BPH is one of the most common medical conditions affecting older men and the most common benign neoplasm in men. Medical management of benign prostatic hyperplasia includes the use of α-adrenergic–blocking agents (Tamsulosin) and 5-ARIs (Dutasteride). Since these two classes of agents have totally different modes of action and both have been shown to be of benefit in well-designed prospective trials, it is logical to hypothesize that giving the two types together would be more effective than giving either type alone.
Objective: To evaluate efficacy of Tamsulosin and Dutasteride combination in patients with BPH having prostate size >30 cm^3 and to evaluate safety of Tamsulosin and Dutasteride combination in patients with BPH.
Methods: *Study design:* A single blinded, parallel, randomized, comparative, prospective phase III trial. *Study population:* Adult patients with BPH meeting inclusion and exclusion criteria from Ram Manohar Lohia hospital were enrolled in this trial. *Study treatment:* Intas Pharmaceutical Ltd. India supplied the investigational products (Tamsulosin 0.4mg, Dutasteride 0.5mg and combination of Tamsulosin 0.4mg and Dutasteride 0.5mg). The investigational drugs were packed in sealed container containing 30 tablets per bottle. The patients were advised to take tablets orally every day preferably at the same time of the day and return to the clinic for follow up visits as described in the protocol. *Study duration:* Three years. *Total number of patients:* 300 in each group (Tamsulosin alone, Dutasteride alone and combination of Tamsulosin and Dutasteride). *Statistical analysis:* Intention to treat (IIT) statistical analysis had been performed on the data. Mean change in urinary symptoms score, bladder outlet obstruction (peak urinary flow rate), prostate volume, residual urine volume, quality of life and prostate specific antigen values from base line was compared using paired two way ANOVA test. All the statistical tests performed were two tailed and p-value less than 0.05 were considered to be statistically significant. All the statistical data represent in the form of mean + standard deviation.
Results and Conclusions: The combination of Tamsulosin and Dutasteride therapy was most effective in the improvement of AUA symptom scores than either treatment alone. No adverse events were observed in entire duration of the study. In summary, combination of Tamsulosin and Dutasteride significantly reduced the growth of prostate and hence prevents the long-term complications of BPH such as acute urinary retention.

UP-03.25

The effects of finasteride on the expression of hypoxia inducible factor (HIF-1a) and vascular endothelial growth factor (VEGF) in benign prostatic hyperplasia

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Objectives: To assess the effects of finasteride on angiogenetic and hypoxia markers in benign prostatic hyperplasia (BPH).
Materials and Methods: One hundred and seventy eight patients aged 51-85 years (mean 68.7), suffering from BPH and awaiting treatment by transurethral prostate resection (TURP), were prospectively randomized into a group of patients receiving finasteride (group A; 88 patients) and into a group of patients where no medication was applied until TURP (group B; 90 patients). Tissue specimens were immunohistochemically stained with monoclonal antibodies against CD34 [for microvessel density (MVD)], vascular endothelial growth factor (VEGF) and hypoxia inducible factor-1alpha (HIF-1α).
Results: Blood loss during TURP was significantly higher at group B, in comparison with group A ($p<0.001$). The distribution of the CD34 immunostaining was mainly at the suburethral prostate. MVD, VEGF and HIF-1a values were statistically significantly lower ($p<0.001$) in group A, in comparison with group B. In the finasteride group, the immunoreactivities of CD34 and HIF-1a, of VEGF and HIF1α, and of VEGF and CD34 were statistically positively correlated ($p<0.001$). In the same group, MVD and the expression of VEGF and HIF-1α were statistically correlated with the duration of treatment.
Conclusion: Finasteride administration in BPH, results in statistically significant suppression of MVD, VEGF and HIF-1α, in a time dependent manner.

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What is effective and safe dose-raising method in patients with concomitant benign prostatic hyperplasia and hypertension after initial doxazosin 4mg: doxazosin 8mg versus combined therapy with doxazosin 4mg and tamsulosin 0.2mg

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Introduction and Objective: To compare the efficacy and safety of doxazosin 8mg with combined therapy with doxazosin 4mg and tamsulosin 0.2mg (permitted maximum dose by Korean medical insurance) in men with concomitant benign prostatic hyperplasia (BPH) and hypertension who have not achieved an adequate therapeutic response to doxazosin 4 mg (Cardura XL®). He (*www.drugs.com*) did not find any drug interactions between the following drugs: tamsulosin, doxazosin. There is no article about combined therapy of different alpha-blockers.
Methods: Between 2000 and 2004, 361 patients with concomitant BPH and hypertension who have not achieved an adequate therapeutic response to doxazosin 4 mg were retrospectively reviewed. Doxazosin was started at 4 mg/day, and then titrated to 8 mg/day or combined with tamsulosin 0.2 mg/day (combined therapy group) after 4 weeks of therapy if the increase in Q_{max} was <3 ml/s or the reduction in total IPSS was <20 %. Of the 361 patients, 263 patients received doxazosin 8 mg (n=96) or combined therapy (n=167). Patients were evaluated with the International Prostate Symptom Score (IPSS), quality of life (QoL), maximum flow rate (Q_{max}), post void residual (PVR), sitting blood pressure (BP) and adverse events (AEs) before and 1 and 3 months or the endpoint following dose-raising.
Results: Both groups were similar with respect to patient age, IPSS, QOL, Q_{max}, PVR, and blood pressure in baseline. Both groups significantly relieved lower urinary symptoms and improved Qmax and PVR from baseline ($P<0.001$). Compared with