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THE EFFECTIVE AND SAFE DOSE-ESCALATING METHOD IN PATIENTS WITH CONCOMITANT BENIGN PROSTATIC HYPERPLASIA AND ANTIHYPERTENSIVE MEDICATIONS AFTER INITIAL DOXAZOSIN GITS 4 MG: DOXAZOSIN GITS 8 MG VERSUS COMBINED THERAPY WITH DOXAZOSIN GITS 4 MG AND TAMSULOSIN 0.2 MG

Hypothesis / aims of study
To compare the efficacy and safety of doxazosin 8 mg with combinded therapy with doxazosin 4 mg and tamsulosin 0.2 mg in men with concomitant BPH and hypertension who have not achieved an adequate therapeutic response to doxazosin 4 mg.

Study design, materials and methods
Between January 2000 and December 2004, 361 patients with concomitant BPH and antihypertensive medications who have not achieved an adequate therapeutic response to doxazosin 4 mg were enrolled. Doxazosin was started at 4mg/day, and then titrated to 8mg/day or combined with tamsulosin 0.2mg/day after 4weeks of therapy if the increase in Qmax was ≤2ml/s or the reduction in total IPSS was ≤20%. Patients were evaluated with the International Prostate Symptom Score (IPSS), quality of life (QOL), maximum flow rate (Qmax), post void residual (PVR), blood pressure (BP) and adverse events(AEs) at baseline, before and 3months after dose escalating. Efficacy assessments included IPSS, QOL, Qmax, and PVR and safety assessments included changes in blood pressure (BP) and adverse events (AEs). Adverse events (AEs) were divided into 3 groups : vasodilatory AEs, sexual AEs, and other relevant AEs.

Results
Of the 361 patients, 263 patients completed the study :doxazosin GITS 8 mg (n=96) and combined therapy with doxazosin GITS 4 mg and tamsulosin 0.2 mg (n=167). Both groups were similar with respect to patients age, total IPSS, QOL, Qmax, PVR, and systolic blood pressure in baseline data. The mean changes in the IPSS, QOL, Qmax (ml/s) and PVR (ml) from doxazosin 4mg were -4.9 ± 4.5, -0.5 ± 0.8, 3.1 ± 3.0 and -8.5 ± 19.4 in the doxazosin GITS 8 mg and -6.4 ± 4.9, -0.6 ± 0.9, 3.9 ± 2.6 and -6.1 ± 26.3 in combined therapy group. Both groups significantly relieved lower urinary symptoms and significantly improved Qmax and PVR after dose-escalation(P<0.001). Compared with both groups, combined therapy produced significantly greater improvements than doxazosin GITS 8mg in changes of total IPSS (p=0.018) and Qmax (p=0.030). The mean change after dose-escalation in sitting systolic and diastolic blood pressure in patients treated with doxazosin GITS 8 mg was -4.1 ± 13.5 mmHg, -4.9 ± 9.7 mmHg. But there was no apparent changes in sitting systolic and diastolic blood pressure (-0.5 ± 9.2 mmHg, 0.2 ± 7.5 mmHg) in combined therapy group after dose-escalation. At least one adverse event was reported by 35.9% and 25.1 % of patients in doxazosin GITS 8mg and combined therapy group respectively(p=0.033). Of the patients 8 (5.6 %) and 9(4.1%) in doxazosin GITS 8 mg and combined therapy group dropped out of the study due to adverse events. The incidence of vasodilatory AEs was higher with doxazosin 8 mg than combined therapy group(27.5% and 15.1% respectively, p=0.012). The respective incidence rates of sexual function AEs were 2.1 % and 5.5 % of patients in doxazosin GITS 8 mg and combined therapy groups (p=0.176).

Interpretation of results
After dose escalation or adding tamsulosin, lower urinary tract symptoms was significantly improved in both groups. But, the efficacy was more prominent in combinded therapy group than doxazosin GITS 8 mg group in terms of total IPSS and Qmax. Adverse events regarding blood pressure or other vasodilatory symptoms were much lower in combined therapy group.

Concluding message
The combined therapy was more effective and safe than doxazosin GITS 8mg in men with concomitant BPH and antihypertensive medications.

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HUMAN SUBJECTS: This study did not need ethical approval because It was retrospective study and was not different from everyday prescribing. but followed the Declaration of Helsinki Informed consent was not obtained from the patients.