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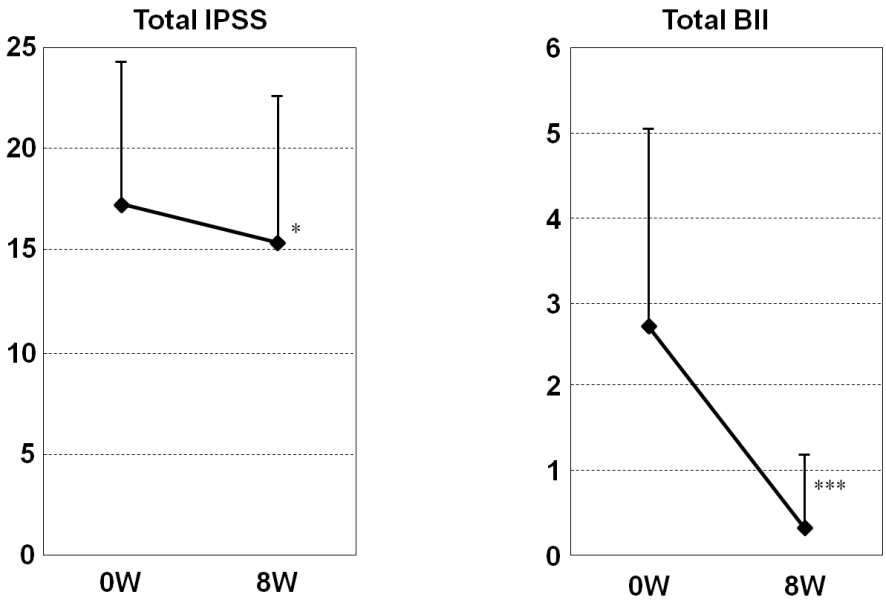
EVALUATION OF CLINICAL EFFICACY OF NAFTOPIDIL IN BENIGN PROSTATIC HYPERPLASIA: SWITCHING FROM ALPHA1A RECEPTOR BLOCKER IN POOR RESPONDERS

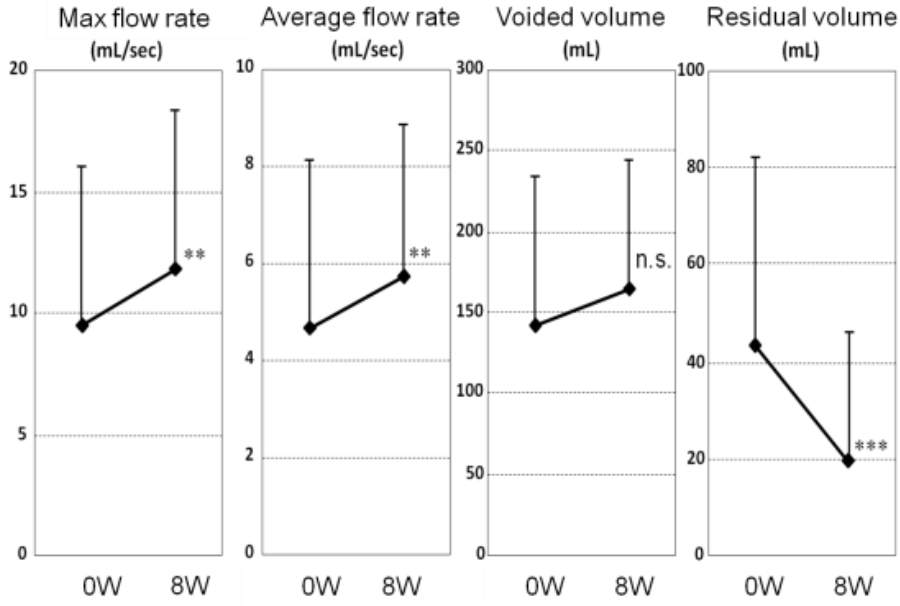
Hypothesis/aims of study
Major adrenalin receptor subtypes associated with benign prostatic hyperplasia (BPH) are $alpha_{1A}$ and $alpha_{1D}$ receptors. The percentage of $alpha_{1A}$-predominant human prostates has been reported to be approximately equal to that of $alpha_{1D}$-predominant human prostates [1]. Therefore, in the BPH patients who are poor responders to ongoing $alpha_1$ receptor blocker therapy, better responses are expected if the current blocker is switched to another $alpha_1$ receptor blocker with a different receptor subtype affinity. The present study was undertaken to evaluate the clinical efficacy of naftopidil (an $alpha_{1D}$ receptor blocker) switched from tamsulosin hydrochloride or silodosin ($alpha_1$ receptor blockers with high affinity for $alpha_{1A}$ receptor) because of poor responses to these drugs.
Study design, materials and methods
The study involved patients with BPH who had a quality of life score (QOL-S) rated with the international prostate symptom score (IPSS) of 3 or higher despite 8-week or longer treatment with 0.2 mg/day tamsulosin hydrochloride or 8 mg/day silodosin. Thirty-nine patients were enrolled to the study (mean age: 70.5 years). The previous oral drug therapy was switched to oral naftopidil therapy (75 mg/day, once daily after breakfast), and the responses were evaluated 8 weeks later. In one case, naftopidil therapy was discontinued because of mild orthostatic hypotension. Subjective symptoms were investigated before and 8 weeks after the start of naftopidil therapy using IPSS and BPH impact index (BII). As objective symptoms, urinary flow was tested before and 8 weeks after the start of naftopidil therapy, and voided volume, residual volume, maximum flow rate, and mean flow rate were calculated. Values with $p < 0.05$ were regarded statistically significant.
Results
Of the patients studied, 29 had received tamsulosin hydrochloride and 10 had received silodosin before the start of this study. Both the total IPSS score and the total BII score decreased significantly 8 weeks after the start of naftopidil therapy (Fig.1.; IPSS: 0W, 17.2 ± 7.1; 8W, 15.3 ± 7.2; $P < 0.0334$. BII: 0W, 2.7 ± 2.4; 8W, 0.3 ± 0.8; $P < 0.0001$). Of the IPSS subscores, urinary flow strength improved significantly (0W, 3.3 ± 1.5; 8W, 2.4 ± 1.5; $p = 0.0034$). The scores for all IPSS parameters other than urinary flow strength showed decrease, although none of these changes was statistically significant. All BII subscores improved significantly. In the urinary flow test, the maximum flow rate, mean flow rate, and residual volume improved significantly after 8 weeks of treatment with naftopidil (Fig.2; Qmax, $p < 0.01$; Qave, $p < 0.01$; residual volume, $p < 0.005$).
Interpretation of results
It is noteworthy that all the subjective and objective parameters related to urinary flow strength (IPSS, Qmax, and Qave) improved following treatment with naftopidil. Furthermore, in poor responders to tamsulosin hydrochloride or silodosin, improvement in QOL following naftopidil therapy (75 mg/day) was accompanied by alleviation of symptoms of urine pooling, suggesting that 75 mg/day naftopidil is effective both against symptoms related to voiding and symptoms related to urine pooling.

Fig.1 Changes in subjective symptoms after the start of naftopidil treatment from the pre-treatment period



*: p<0.05, ***: p<0.005 ; Wilcoxon signed-rank test

Fig.2 Changes in the objective parameters after the start of naftopidil treatment from the pre-treatment period



**: p<0.01 ***: p<0.005 ; Wilcoxon signed-rank test

Concluding message

In poor responders to tamsulosin hydrochloride or silodosin, treatment with naftopidil (75 mg/day) alleviated the discomfort, anxiety, distress, and trouble related to urination, accompanied by improvement in objective parameters. These results suggest that naftopidil is useful in poor responders to tamsulosin hydrochloride or silodosin.

References

1. Prostate 2006:66: 761-767

Specify source of funding or grant	**None**
Is this a clinical trial?	**Yes**
Is this study registered in a public clinical trials registry?	**No**
Is this a Randomised Controlled Trial (RCT)?	**No**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**Nagasaki university hospital**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**