

EFFICACY OF COMBINATION THERAPY OF α -BLOCKERS, TAMSULOSIN AND NAFTOPIDIL, ON VOIDING DYSFUNCTION AND NEURONAL ACTIVATION IN BENIGN PROSTATIC HYPERPLASIA RATS

Hypothesis / aims of study

Current medical therapies are not always adequate in controlling lower urinary tract symptoms (LUTS) or slowing disease progression. α 1-adrenergic receptor (α 1-AR) blockers improve LUTS such as BPH and overactive bladder. Recently, α 1-AR blockers constitute central nervous system as well as prostate and bladder. And, there have been strong demands for reducing the side effects of medications and enhancing effectiveness. Therefore, we investigated the efficacy and safety of combination therapy of α 1-AR blockers (tamsulosin and naftopidil) mediated by neuronal micutration centers in BPH animal model.

Study design, materials and methods

The animals were randomly divided into the following five groups (n = 10 in each group): sham-operation group, BPH-induced group, BPH induced and tamsulosin-treated group, BPH-induced and naftopidil-treated group, BPH-induced and combination-treated group. The dosage of each drug was administered with reference to recommended daily allowance: tamsulosin (0.2 mg/kg), naftopidil (75 mg/kg), and combination therapy (0.2 mg/kg tamsulosin + 75 mg/kg naftopidil). For the induction of BPH model, the rats were castrated and testosterone (20 mg/kg) was injected subcutaneously once a day for 30 days. The rat in the drug-treated groups orally received each drug once a day for 30 days after orchiectomy. Cystometrography (CMG) for bladder contraction pressure and interval, immunohistochemistry for c-Fos, and nicotinamide adenine dinucleotide phosphate-diaphorase (NADPH-d) histochemistry for nitric oxide synthase (NOS) in the neuronal micturation centers were conducted.

Results

Orchiectomy and testosterone injection enhanced bladder contraction pressure and interval, showing BPH symptoms. Contraction pressure was significantly decreased and contraction interval was significantly increased by combination treatment compared to mono therapy, tamsulosin or naftopidil. Expressions of c-Fos and NOS in the neuronal micturation centers were enhanced by induction of BPH. BPH-induced expressions of c-Fos and NOS were suppressed by combination treatment.

Interpretation of results

Detrusor overactivity (DO) was noted in the BPH animal after orchiectomy and testosterone injection, and therefore; functional change due to BPH was confirmed by CMG. Combination therapy with tamsulosin and naftopidil showed more significant improvement of DO. Significantly decreased expression c-Fos and NOS might be contribute to the improvement of DO after combination therapy with the two type of α 1-AR blockers.

Concluding message

The combination therapy showed more potent alleviating effect on DO induced by BPH. These effects of combination therapy of tamsulosin and naftopidil appeared through inhibition on neuronal activation in the neuronal micturation centers.

References

1. Int Neurourol J 2015;19: 228-236

Disclosures

Funding: None **Clinical Trial:** No **Subjects:** ANIMAL **Species:** Rat **Ethics Committee:** Kyung Hee University College of Medicine