THE DEVELOPMENT OF THE RAT MODEL WITH PROSTATE HYPERPLASIA AND DETRUSOR UNDERACTIVITY INDUCED SEX HORMONES IN MALE CASTRATED WISTER RAT

Hypothesis / aims of study
With the aim of developing a new model of lower urinary tract dysfunction (LUTD) presenting with lower urinary tract symptoms (LUTS) seen in patients with benign prostatic hyperplasia (BPH) or chronic prostatitis (CP), we created rat models of BPH by using 0.25 mg/kg 17β-estradiol (E) with 25 mg/kg testosterone (T) or dihydrotestosterone (DHT) in castrated rats and investigated the bladder function in this model.

Study design, materials and methods
We divided 13-month-old male Wistar rats into the following six groups: Sham (Group 1); Castration (Group 2); Castration + E (Group 3); Castration + E + T (Group 4); Castration + E + 12.5 mg/kg DHT (Group 5); and Castration + E + 25 mg/kg DHT (Group 6). Castration was performed under anesthesia, and beginning on the day after castration, E/T or E/DHT was administered subcutaneously daily for one month. We investigated several parameters; (1) voiding behavior in metabolic cages overnight for 12 hours, (2) bladder and prostate blood flow, (3) measurements of the bladder and prostate weight, (4) Bladder contractile responses to electrical field stimulation (EFS: 2, 8, 32 Hz), carbachol (100 µM), and KCl (100 mM).

Results
(1) No significant changes in voiding behavior (average micturition volume, total urine volume and number of micturitions) were noted in any of the groups. (2) Compared to Group 1, there were no changes in bladder blood flow in any of the other groups, though a significant decrease was noted in prostate blood flow in Groups 4, 5 and 6. (3) The weight of the bladder was significantly increased in Groups 5 and 6. On the other hand, the weight of the prostate was significantly decreased in Groups 2 and 3 and significantly increased in Groups 4, 5 and 6. (4) Bladder contractile forces in response to EFS caused a significant decrease in Groups 4 and 5, but not in Group 6. In response to carbachol, the contractile forces decreased significantly in Group 3, and also decreased further in Groups 4, 5 and 6. In response to KCl, the contractile forces decreased in Groups 4, 5 and 6.

Interpretation of results
This result suggested that we developed a new rat model with prostate hyperplasia and detrusor underactivity induced sex hormones in male castrated Wister rat.

Concluding message
Tatemichi et al. reported that sex hormone treatment (only one dose with 0.125 mg/kg E and 12.5T) of young SD rats induced BPH and caused detrusor overactivity [1]. We previously reported that prostate weight decreased and bladder function was not affected in the E induced model in castrated Wistar rats [2]. These models were created by injecting sex hormones into rats that had been castrated. Through combined use of E/T or E/DHT in castrated rats, we developed a new rat model of "prostatic hyperplasia and detrusor underactivity", features observed in human LUTS/LUTD. Further detailed studies are needed to examine the sensitivities to the sex hormones and impacts on the micturition reflex.

References

Disclosures
Funding: None Clinical Trial: No Subjects: ANIMAL Species: Rat Ethics Committee: Asahikawa Medical University Institutional Animal Care and Use Committee and conducted in compliance with the Internal Regulations on Animal Experiments at Nippon Shinyaku Co., Ltd.