HYPERTENSION INDUCED BY SALT LOADING IS RELATED TO STORAGE DYSFUNCTION IN RATS

Hypothesis / aims of study
Clinical observations indicate that many non-urological diseases seem to be associated with lower urinary tract symptoms (LUTS). According to a population-based study LUTS is an important part of the symptomatology of hypertension (HT), DM, and neurological disease. HT is one of the risk factors for worsening LUTS and decreasing the improvement of storage symptoms by α1-blocker (Int J Urol 2003, 10:569). Sympathetic nerve activity also influences HT and LUTS (J Urol 2005, 174:1327). The spontaneous hypertensive rat is considered a valuable tool for exploring the pathogenesis of detrusor overactivity, but, pathological changes in the bladder are thought to be irreversible. In salt-sensitive HT, increased oxidative stress elevates arterial pressure through central sympathoexcitation (Hypertension 2007, 50:360). However, it has not yet been determined whether salt-sensitive HT contributes to LUTS and influences urine production rhythm. Thus, we examined whether salt-sensitive HT influences LUTS and urine production.

Study design, materials and methods
The sympathetic nerve activity is augmented with salt loading in Dahl salt-sensitive rats (DSs), but not in Dahl salt-resistant rats (DRs). Six-week-old male DSs and DRs were fed with a normal (0.252%) or high-salt (8%) diet and 40 ml water/day for 12 weeks. Blood pressure was measured through the tail artery in a non-anesthetized state. Urine volume and frequency were recorded all day long in a metabolic cage. We calculated the inactive period (sleeping) urine volume index (IUi), which was defined as urine volume during inactive period divided by 24-h urine output. Whole bladders were excised from 18 week rats and made to distend with Krebs solution. We measured adenosine triphosphate (ATP) and prostaglandin E2 (PGE2) from the collected solution.

Results
Twenty A 20-to 30-mmHg increase in systolic and diastolic blood pressure was noted in DSs after 2-week salt loading. Salt loading increased urine production during the active (awake) period of the day both in DSs and DRs. In the inactive period, the mean voided volume gradually increased in DRs fed with a normal or high-salt diet, while it did not change in DSs fed with a high-salt diet. There were significant differences in mean voided volume after 10-week salt loading between DRs and DSs fed with a high-salt diet. In DSs fed with a high-salt diet, IUi increased 2 weeks after salt loading, and remained returned to within the normal range within at 4 weeks. Bladder distension significantly increased ATP and PGE2 release from the urothelium in DSs rats fed a high-salt diet when compared to DSs fed a normal diet, DRs high-salt diet, and DRs normal diet.

Concluding message
These results indicate that that salt loading induces HT and decreases the voided volume, also changing the rhythm of urine production of throughout the day. This model will be useful in defining the mechanisms governing the induction of storage dysfunction in patients with HT.

We measured expression level of α1a, α1b, α1d, AT1 and AT2 receptor from the bladder tissue.
Disclosures
Funding: none Clinical Trial: No Subjects: ANIMAL Species: Rat Ethics Committee: Animal ethical commission of university of Fukui