A new experimental rat model of erectile dysfunction and lower urinary tract symptoms associated with benign prostate hyperplasia: the testosterone supplemented spontaneously hypertensive rat

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OBJECTIVES

- Lower urinary tract symptoms (LUTS) resulting from benign prostate hyperplasia (BPH) (which comprise storage symptoms related to bladder dysfunction and voiding symptoms due to prostate enlargement) and erectile dysfunction (ED) are common problems in the aging male population. Indeed, several recent studies have shown that ED is closely associated with the presence and severity of LUTS independently of comorbidities. However, the exact pathophysiologic mechanisms linking LUTS / BPH and ED remained largely unexplored.

- The major difficulty of studying such relationships between ED and LUTS/BPH and of exploring the impact of new therapeutic approaches on LUTS/BPH and ED is the lack of experimental model presenting ED, prostate enlargement AND bladder dysfunction. Since the spontaneously hypertensive rat (SHR) is a well-validated model of ED which has been reported to exhibit abnormal bladder function, and since testosterone-supplementation in rats has been repeatedly shown to induce prostate enlargement in rat, there is a strong rationale for the presence of bladder dysfunction, prostate enlargement and the testosterone-supplemented SHR.

Therefore, the aim of this study was to evaluate if Spontaneously Hypertensive Rats (SHR) supplemented with testosterone could represent a new and complete model of LUTS/BPH and ED.

METHODS

Research design

Two groups of animals (12 week-old at the time of cystometry experiments; n=7 per group) were considered: 1/ SHR rats treated with daily subcutaneous testosterone (SHR-testo, 3 mg/kg), and 2/ WKY rats without testosterone treatment (WKY). After 3 weeks of daily treatment, cystometry experiments were performed in conscious rats. After a 4-day recovery-period from cystometry, erectile function was evaluated in urethane-anesthetized animals. Then, prostate and bladder were harvested for the evaluation of prostate enlargement and bladder hyper trophy by weighing.

Bladder function evaluation: Cystometry experiments

- Catheter implantation: Two days before the cystometry experiments, the rats were implanted with an intravesical polyethylene catheter (PE-50) through the apex of bladder dome under isoflurane anaesthesia (1.5-2.0%). The free end of the bladder catheter was tunneled subcutaneously, exteriorized at the back of the neck and sutured.

- Cystometry experiments: At 48 hours after catheter implantation, the free tip of the bladder catheter was connected to a pressure transducer (Elcomatic EM 750) for arterial pressure recording and a syringe-pump KD2-200 (Phymap) allowing continuous bladder perfusion (50 µL/min) with room temperature sterile saline. In addition, voided volume was continuously collected and directly measured by means of a weighing device (Sartorius BP2215). After acclimation period, the bladder was continuously perfused in order to assess the erectile responses. Erectile responses to ES-CN were expressed as a ratio of bladder contraction on a cystometrogram (voided volume).

- Intracavernosal pressure (ICP): ICP was measured using a micro-tip transducer (model 7689; Millar Instruments, Houston, Texas). The time to first voiding contraction and the frequency of non-voiding contractions (NVC) were determined from the cystometric tracings.

RESULTS

- Differences in urodynamic parameters between WKY and SHR rats supplemented with testosterone

Testosterone-supplemented SHR displayed a decrease in the voided volume and in ICI. The filling phase of SHR-testo is also associated with an increase in non-voiding contractions compared to WKY.

CONCLUSIONS

- The testosterone-supplemented SHR is the first described experimental model presenting ED, prostate enlargement and bladder hyperactivity.

- This new model would be of great interest to assess the sexual side effects of LUTS/BPH treatments and to evaluate the efficacy of new therapeutic strategies on both ED and LUTS/BPH.