Prostate hypertrophy induced by testosterone: effect of oxybutynin in an experimental model of overactive bladder in conscious rats

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Abstract

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OBJECTIVES

- Benign prostatic hyperplasia (BPH) is characterized by a nodular enlargement of prostatic tissue resulting in proximal urethra obstruction. Experimental models of BPH have been developed for both the study of the pathogenesis of BPH and the evaluation of new therapeutic strategies.
- To date, animal models of spontaneous prostate hypertrophy are limited to the chimpanzee and the dog. Ethical and financial factors restrict the applicability of these models. In dogs, microscopic or macroscopic BPH is observed after age of 6 years.
- Testosterone-induced prostate hypertrophy in rats is an interesting alternative model for BPH. Indeed, a recent publication has reported that testosterone treatment in rats induces a 2-fold increase in prostatic weight in adult Sprague-Dawley rats. Moreover, this prostate enlargement is associated with bladder overactivity (Maggi, et al., Gen Pharmacol. 1989;20(3):345-9, Pandita et al., Prostate 1998;35(2):102-8).

CONCLUSIONS

- We aimed to investigate the effect of oxybutynin, a reference antimuscarinic compound, on bladder overactivity due to testosterone-induced prostatic hypertrophy in conscious rats.

MATERIALS & METHODS

Testosterone treatment

Sprague-Dawley rats (weighing 170-250 g) were treated for 2 weeks by daily subcutaneous sesame oil or 3 mg/kg testosterone injections.

Cystometry

Under isoflurane (3%) anesthesia, a trumpet tip polyethylene catheter (PE56), filled with saline, was inserted through the dome into the bladder, secured with a suture, and subcutaneously tunnelled to the back of the neck. Cystometry was performed in conscious rats placed in a diuresis cage as detailed in the figure 2. Bladder was continuously infused at the infusion rate of 50 µl/min. The intravesical pressure was recorded continuously. The volume of voided urine was collected and measured during the experiment. After a 30 min stabilization period, bladder was emptied before a 30 min control period. Then, oxybutynin was intravenously delivered at the dose of 1 mg/kg. Intravesical pressure was recorded during 60 min after oxybutynin administration.

Assessment of prostate weight

At the end of the cystometry, animals were reanesthetized with pentobarbital (10 mg/kg i.p.) the prostate and urethra were harvested. Prostate lobes were identified, dissected and weighed.

RESULTS

Prostate hypertrophy

We evaluated the effect of oxybutynin, a reference antimuscarinic compound, on bladder overactivity due to testosterone-induced prostatic hypertrophy in conscious rats.

Testosterone-induced prostate hypertrophy in rats is an interesting alternative animal model for BPH. Indeed, a recent publication has reported that testosterone treatment in rats induces a 2-fold increase in prostatic weight in adult Sprague-Dawley rats. Moreover, this prostate enlargement is associated with bladder overactivity (Maggi, et al., Gen Pharmacol. 1989;20(3):345-9, Pandita et al., Prostate 1998;35(2):102-8).

CONCLUSIONS

In conclusion, chronic testosterone treatment elicited micrulation patterns changes i.e. an increase in bladder capacity, residual volume and number of non voiding contractions. These alterations have been observed in rats with partial ligature of the proximal of the urethra suggesting that enlargement of prostate induced by chronic treatment of testosterone elicits bladder outlet obstruction.

Antimuscarinic agents such as oxybutynin, act by blocking detrusor muscarinic receptors stimulated by acetylcholine released from cholinergic (parasympathetic) nerves, thereby decreasing the ability of the bladder to contract. In chronic testosterone-treated rats with prostate hypertrophy, oxybutynin only reversed the increase in the maximal intravesical pressure during voiding and non voiding contractions without affecting other urodynamic parameters.

In testosterone-treated rats, oxybutynin significantly reduced the basal intravesical pressure, the maximal intravesical pressure, the area under the curve and the duration of non voiding contractions. No changes in the frequency of voiding and non voiding contractions were observed (Table 2).

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