

Testosterone-supplemented SHR as a model of BPH / male LUTS

Model advantages:

The testosterone-supplemented SHR combines erectile dysfunction, prostate enlargement and urodynamic impairment characteristic of LUTS and allows thus the assessment of erectile function in parallel to bladder function and prostate size. This model helps to assess the sexual side-effect profile of new therapeutic strategies for BPH while evaluating their efficacy on LUTS and prostate enlargement.

Pathophysiological features:

Erectile dysfunction:

- Dramatic impairment of erectile responses to electrical stimulation of the cavernous nerve after 3 weeks of testosterone supplementation in anesthetized SHR (figure 1).

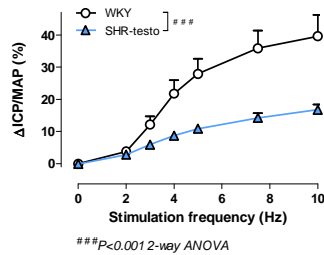


Figure 1: In vivo evidence of erectile dysfunction in testosterone-supplemented SHR. (Pelvipharm, internal data)

Bladder dysfunction:

- Exhibits **abnormal bladder function**: decreased ICI, voided volume and bladder capacity, and increased urinary frequency and amplitude of non voiding contractions characteristic of detrusor overactivity.

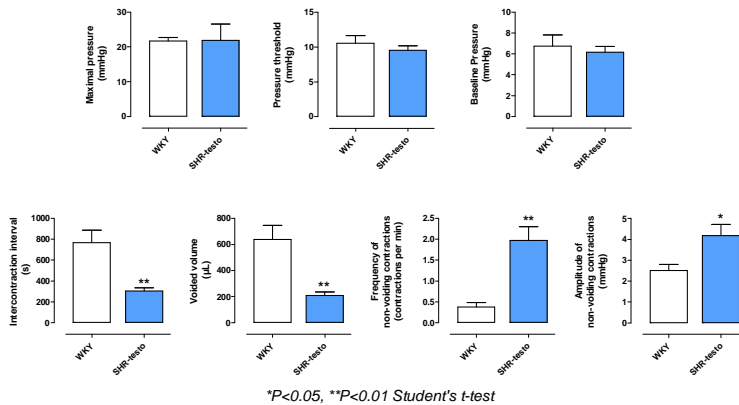


Figure 2: Urodynamic parameters in WKY and SHR supplemented with testosterone (SHR-testo) measured in conscious rats after a 3-week testosterone supplementation period (Pelvipharm internal data).

Prostate enlargement:

The testosterone-supplemented SHR exhibits several common characteristics with the human pathology:

- Prostatic enlargement (figure 3)
- combined increase in both prostate cell size (protein content) and number (DNA content)

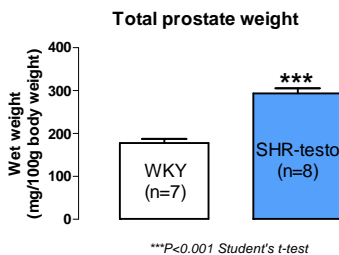


Figure 3: Evaluation of prostate enlargement induced by daily s.c. testosterone injections during 3 weeks in SHR (Pelvipharm, internal data)

Summarized methodology:

Testosterone is administered subcutaneously daily in SHR.

Related Pelvipharm bibliography:
 Oudot A., et al. *J Urol* (2011) : 185, 4, Suppl 1, p.e631
 Oudot A., et al. *J Sex Med* (2010) : 7(s6)

Links to applicable experimental skills:

- Administration routes / regimen**- Plasma / urine / tissue collection****- In vivo experiments – conscious animals**

- * Telemetry
- * Urodynamic evaluation (cystometry experiments)
- * Urine collection - Metabolic cages
- * Ejaculation
- * Tail cuff

- In vivo experiments – anesthetized animals

- * Erection elicited by pharmacological or electrical neural stimulation
- * Ejaculation elicited by pharmacological or electrical neural stimulation
- * Urodynamic evaluation (cystometry)

- Organ bath studies (EFS / Pharmacological studies)

- * Animal tissues

- Biochemistry (Plasma / Urine / Tissue)

- * Spectrophotometric assays
- * Protein expression and activity

- Histology

- * Histomorphology
- * Histomorphometry
- * Oxydative fuorescence

- Immunohistology / Confocal microscopy

- * Protein expression – immunohistochemistry / immunofluorescence
- * Confocal microscopy