

VARDENAFIL DECREASES BLADDER AFFERENT NERVE ACTIVITY IN UNANESTHETIZED DECEREBRATE SPINAL CORD-INJURED RATS

Hypothesis / aims of study

PDE5 inhibitors improve IPSS scores in BPH patients, despite a lack of effect on Qmax. Moreover, a single dose of vardenafil improves urodynamic parameters in spinal cord-injured (SCI) patients with neurogenic detrusor overactivity (NDO). SCI rats also display NDO characterized by non-voiding contractions (NVC) during bladder filling due to functional and morphological plasticity of bladder afferent pathways resulting in an increased bladder afferent nerve firing (BANF). We postulated that vardenafil could improve urodynamic parameters by reducing BANF. We thus investigated concomitantly the effect of vardenafil on intravesical pressure (IVP) by cystometry experiments while recording single BANF in response to bladder filling.

Study design, materials and methods

Complete T7-T8 spinalization was performed in 15 female adult Sprague-Dawley rats (250-275 g). To avoid confounding effect of anesthesia, SCI rats were decerebrated at day 21-29 post-spinalization. Fine filaments were dissected from the L6 dorsal roots and placed across a bipolar electrode. Afferent nerve fibers originating from the bladder were identified by electrical stimulation of the pelvic nerve and by bladder distension. First, bladder filling was performed to determine the maximal bladder filling volume (BFV). Then, bladders were stabilized at 75% of maximal BFV (non-noxious BFV). Saline (n=7) or vardenafil 1 mg/kg (n=8) was delivered iv. NVC were characterized by the force generated (AUC, in mmHg.s) while the frequency of BANF (spikes/s) was determined during 45 minutes. All results were expressed as % of baseline and compared using two-way ANOVA.

Results

In all SCI rats, BANF was already present and regular at resting conditions (26.2±4.1spikes/s). During bladder filling, IVP slowly increased with transient NVC superimposed. Concomitantly, BANF progressively increased to reach a 2.4-fold increase at maximal BFV (2.65±0.28ml). After stabilization, the increase in BANF elicited by submaximal BFV was 186±37%. Vardenafil injection induced an immediate decrease in NVC compared to saline (p<0.001). Likewise, BANF also decreased very rapidly after vardenafil injection (52% decrease versus 28% in saline after 45 minutes, p<0.001).

Interpretation of results

Systemic administration of vardenafil strongly reduced both NVC and BANF elicited by submaximal bladder filling in unanesthetized decerebrate SCI rats.

Concluding message

These findings may give us a new insight into the mechanism of action of PDE5 inhibitors at reducing storage symptoms i.e. in men with LUTS /BPH.

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<i>Is this a clinical trial?</i>	No
<i>What were the subjects in the study?</i>	ANIMAL
<i>Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?</i>	Yes
<i>Name of ethics committee</i>	All procedures were performed in accordance with the legislation on the use of laboratory animals (NIH publication N°85-23, revised 1996) and Animal Care Regulations in force in France as of 1988 (authorization from competent French Ministry of Agriculture – Agreement No. A91-471-109, May 2009).