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Effect of a selective β 3-adrenergic agonist (CL-316,243) on cystometric parameters in conscious normal and spinal cord injured female rats

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INTRODUCTION AND OBJECTIVES: In rats with detrusor overactivity secondary to bladder outlet obstruction, β 3-adrenergic agonists were shown to increase bladder capacity and decrease non-voiding contractions (NVC). The aim of this study was to determine the effect of CL-316,243 (CL) a selective β 3-adrenergic agonist on cystometric parameters in conscious normal rats and to evaluate its effects in a model of bladder overactivity in conscious female rats after spinal cord injury (SCI)

METHODS: Adult female Wistar rats were used. Cystometry was performed in two different sets of experiments, one in conscious normal animals and the other in conscious rats after SCI at the T8 level for 5 weeks (or sham).

Briefly, under anesthesia the jugular vein and urinary bladder were catheterized. 2 days later the bladder was continuously infused with saline. After stabilization (basal cystometric values), vehicle or CL were administered intravenously. Then, intravesical pressure was recorded for 1 hour. Micturition frequency (MF), intercontraction interval (ICI) and amplitude of micturition (AM) were analyzed and averaged for the 60 min period post-administration. For each parameter, results were compared to baseline. CL was tested at 0.01, 0.03 and 0.1 mg/kg in normal rats and at 0.01 mg/kg in rats with SCI.

RESULTS: *Normal rats.* CL significantly increased ICI and decreased MF in a dose dependent manner (-39±4, -46±5, -50±6% at 0.01, 0.03 and 0.1 mg/kg, respectively). No effect on AM was observed with low doses of CL (0.01 and 0.03 mg/kg), while at the highest dose (0.1 mg/kg) AM was significantly decreased (-19±6%).

SCI rats. In comparison to sham, SCI rats presented with increased ICI (475±38 vs. 318±53 sec, p=0.025), decreased MF (4±0.3 vs. 8±1.4 pics/30min, p=0.024), increased AM (p=0.0004) and increased bladder weight (435±39 vs. 147±6 g, p<0.0001). During the filling phase NVCs were also observed.

CL (0.01 mg/kg) significantly increased ICI in sham and SCI rats (42±17% and 49±17%, respectively). MF was significantly reduced by 38±10% in SCI rats (p=0.007) while no effect on AM was observed in either group. At this dose, CL specifically reduced the frequency (-53±14%) but not the amplitude of NVCs.

CONCLUSIONS: This is the first demonstration that stimulation of β 3-adrenoceptors produces a decrease in MF and NVCs in SCI rats. These effects are observed at low doses without deleterious effects on AM. Our results suggest that β 3-adrenergic agonists could be useful for the treatment of neurogenic bladder overactivity.

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