Objectives

Litoxetine (LTX) is a highly selective serotonin (5-HT) reuptake inhibitor and a Multifunctional Serotonin Agonist Antagonist (1,2). The aim of this study was to characterize the effects of LTX, in comparison to duloxetine (DLX), a non-selective norepinephrine (NE)/5-HT reuptake inhibitor, on both detrusor and striated anal sphincter functions in a rabbit model of detrusor overactivity (3). The external anal sphincter model was used as a proxy of urethral sphincter activity (4).

Methods

Animals: Female New Zealand white rabbits (~3 kg).

Surgery: Under halothane-anesthesia, a catheter was inserted in the bladder through the dome and secured with a purse-string suture. Two electrodes were inserted into the striated anal sphincter (SAS).

Cystometry was performed in halothane-anesthetized animals with continuous intravesical infusion of 0.5% acetic acid (AA).

Treatments: In each animal, two successive intravenous administrations of vehicle or two doses of LTX or DLX (1 and 3 mg/kg) were performed in a time-matched manner and their effects on bladder capacity (BC), micturition volume (MV), residual volume (RV), baseline pressure (BP), contraction duration (CD), intercontraction interval (ICI) and contraction amplitude (CA) were measured.

Bladder Pressure and Striated anal sphincter electromyographic (SAS-EMG) activity were recorded simultaneously.

Vehicle, LTX and DLX effects were analyzed and compared with stabilization period (basal values) using Wilcoxon rank test.

Conclusions

LTX significantly reduced bladder hyperactivity, resulting in increased bladder capacity, while simultaneously increasing splinter activity. At the dose of 3 mg/kg, the effects of LTX and DLX were similar.

The current results support that LTX could be useful for treating lower urinary tract dysfunctions such as mixed urinary incontinence.

References


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