

The effect of 5HT-2c receptor agonist on urethral closure mechanism in female rats after vaginal distension



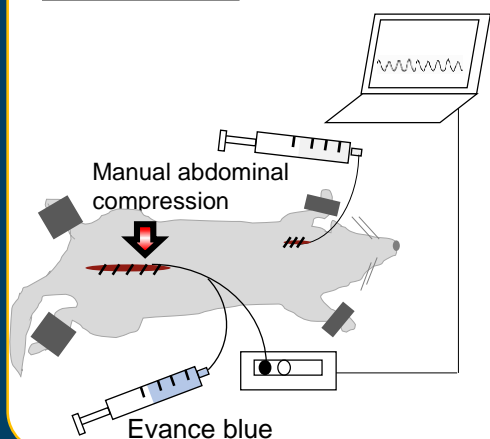
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Hypothesis / aims of study

- Noradrenergic and serotonergic pathways is considered to play an important role in maintaining urethral resistance (ref 1). Urethral closure was enhanced activated motoneurons through alpha1-adrenergic and 5-(hydroxytryptamine: HT) 2C receptors which directly innervate external urethral sphincter and pelvic floor muscles in Onuf's nucleus.
- Pharmacological treatment the lorcaserin (Belviq®) received Food and drug Administration approval for the treatment of obesity in the United States in 2012.
- The aims of this study is to investigate whether lorcaserin enhances urethral closure mechanism in female rats with vaginal distention (VD).

Methods



Sprague-Dawley female rats (12 weeks old) weighing 258-291g were used. Rats randomly assigned to vaginal distention (n=4-5). Four days after VD, we evaluated urethral function with leak point pressure induced by manual abdominal compression (crede-LPP) (ref 3).

A polyethylene catheter (PE-50) was inserted for the intravenous injection of saline, lorcaserin 0.03, 0.3 and 0.9 mg/kg.

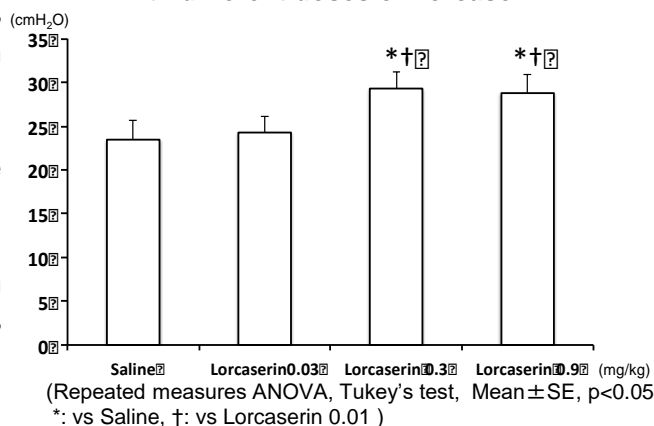
Statistical analysis were carried out by using the repeated measures ANOVA and Tukey's test with $p < 0.05$ considered significant.

Results

The changes of crede-LPP with different doses of lorcaserin were shown in Figure 1. The mean bladder pressure with saline, lorcaserin 0.03, 0.3, 0.9 mg/kg were 23.5 ± 2.2 , 24.3 ± 1.9 , 29.3 ± 1.8 and 28.8 ± 2.1 cmH₂O in female rats, respectively.

However, there were no differences between Saline and the lowest lorcaserin 0.03mg/kg as well as lorcaserin 0.3 and 0.9 mg/kg.

Fig.1 Changes of Crede-Leak point pressure with different doses of Lorcaserin



Interpretation of results

- Our results show that treatment with lorcaserin, a selective 5-HT_{2c} agonist, significantly increased LPP in female rats after VD. Since the lorcaserin increased in LPP dose-dependently, it might suggest that 5-HT_{2c} enhances the urethral closure mechanism in these rats.
- 5HT receptors subtypes that contribute to the modulation of the sneeze-induced continence reflex. Figure 2 demonstrates that descending bulbospinal serotonergic pathways enhance activity of spinal excitatory interneurons in Onuf's nucleus (ref1).
- 5-HT_{2c} may have double mechanisms for SUI patients. 5-HT_{2c} can contribute to not only losing body weight, but also enhancing active urethral closure mechanism in these patients.

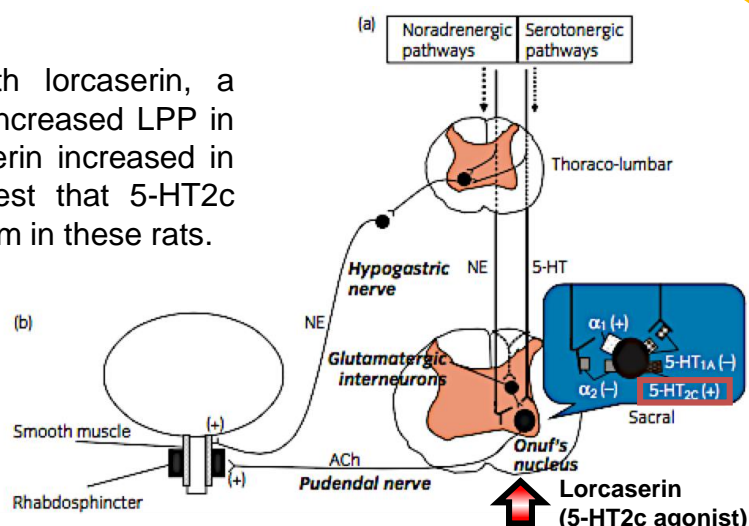


Fig2 The urethral closure mechanism of noradrenergic & serotonergic pathway at the Onuf's nucleus