

Cystometric Effects of TRPV1 Oral Antagonist, GRC6211, in the Rat Model of Neurogenic Bladder

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Introduction and objective

The rat neurogenic bladder has increased frequency, intensity and duration of detrusor contractions; urinary bladder C fibers afferent neurons are increased in neurogenic rats and mediate, at least partially, the detrusor overactivity. TRPV1 receptor is expressed in those C fibres. We used the TRPV1 oral antagonist, GRC 6211 (Glenmark®), to see if there is any effect in the frequency, intensity and duration of detrusor contractions.

Material and methods

10 female Sprague-Dawley female rats, mean weight of 320 ± 11.6 g, were spinalized by spinal cord transection at T13 level. After recovery of spinal shock, cystometry was performed under urethane anesthesia (0.02 mL/Kg, SC). Each rat was submitted to one baseline cystometry, and three consecutive cystometrys, each performed 02:30 hours latter after administration of increasing doses of GRC 6211 (first 0.01 mg/Kg, second 0.1 mg/Kg third 1 mg/Kg) in the first portion of the duodenum. Tracigs were recorded during 20 minutes. The frequency of contractions is reported in a time frame of 20 minutes. Results are presented as mean \pm SD. Statistical significance was considered when p was inferior to 0.05.

Results

The mean frequency, intensity and duration of detrusor contractions in the baseline cystometry were 14.2 ± 4.5 contractions, 48.4 ± 4.4 cm H₂O and 85.8 ± 24.7 sec, respectively; after administration of 0.01 mg/Kg of GRC 6211, the results were 10.6 ± 4.5 contractions ($p < 0.05$), 47.1 ± 4.3 cm H₂O ($p = 0.17$) and 78.8 ± 13.3 sec ($p = 0.36$), respectively, (p values when compared to baseline data); after administration of 0.1 mg/Kg of GRC 6211, the results were 7.9 ± 3.9 contractions ($p < 0.05$), 45.6 ± 5.6 cm H₂O ($p < 0.05$), and 73.6 ± 5.5 sec ($p = 0.73$), respectively, (p values when compared to the baseline data); after administration of 1 mg/Kg of GRC 6211, the results were 3.8 ± 2.5 contractions ($p < 0.05$), 40.2 ± 4.1 cmH₂O ($p < 0.05$) and 73.9 ± 3.3 sec ($p = 0.72$), respectively (p values when compared to the baseline data).

Discussion and Conclusion

TRPV1 oral antagonist, GRC 6211, was effective in decreasing the frequency of detrusor contractions; even the lowest dose was effective; GRC 6211 also decreased the intensity of detrusor contractions, but this effect was not noticed in the lower dosage (0.01 mg/kg). There was not any change in the duration of detrusor contractions. More studies with this new type of drugs are needed.