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Title: ACTIONS OF TRAMADOL ON THE MICTURITION REFLEX IN AWAKE, FREELY MOVING RATS.

Introductions and Objectives:

Few drugs with a defined target within the central nervous system have been used clinically to treat detrusor overactivity. Among these are imipramine and other antidepressants, which inhibit the reuptake of noradrenaline and 5-HT. Furthermore, an effective way of blocking micturition reflexes at the spinal level is intrathecal administration of morphine and its derivatives. Tramadol, which is widely used as an analgesic, combines weak effects on opioid receptors with inhibition of the uptake of noradrenaline and 5-HT. To analyse the combination of these mechanisms we have studied the effects of tramadol and its enantiomers on micturition in unanesthetized rats.

Methods:

Continuous cystometry was performed in conscious, freely moving normal Sprague-Dawley rats. Cystometric parameters were evaluated before and after iv drug administration.

Results:

The most conspicuous effect of iv (±) tramadol (0.1-10 mg/kg) was a dose-dependent increase in threshold pressure (at 1 mg/kg from 14.0±2.0 to 21.0 ±3.1 cm H_2O, n= 6, $p<0.01$), and an increase in the intercontraction interval, eventually resulting in dribbling incontinence. The effect of (+) tramadol (0.1-5 mg/kg iv), was similar to that of the parent compound (at 0.5 mg/kg threshold pressure increased from 7.9±1.0 to 15.0±2.6 cm H_2O, n= 5, $p<0.05$); (-) tramadol (up to 5 mg/kg, iv) was almost ineffective.

Conclusions:

(±) Tramadol effectively inhibits the micturition reflex in awake rats. The activity seems to be produced mainly by the opioid component which is carried together with the 5-HT uptake inhibition by the (+) enantiomer, whereas the (-) enantiomer comprises the noradrenaline inhibitory activity.

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