

TRAMADOL INHIBITS RAT DETRUSOR OVERACTIVITY INDUCED BY APOMORPHINE AND EXPERIMENTAL CEREBRAL INFARCTION

Aims of Study

Cerebrovascular disease, such as Parkinson's disease and stroke, may result in detrusor overactivity and urinary incontinence. In patients suffering from Parkinson's disease, an imbalance between stimulatory D₂-like receptors and inhibitory D₁-like receptors have been suggested to contribute to detrusor overactivity. Apomorphine, which stimulates D₁-like and D₂-like dopamine receptors, induces detrusor overactivity in rats, and may be used as a model for the urinary tract dysfunction found in Parkinson patients.

Intraluminal occlusion of the middle cerebral artery (MCA) in rats, which produces detrusor overactivity, has been introduced as a useful model of stroke-induced lower urinary tract symptoms.

Tramadol, an analgesic drug, which stimulates opioid receptors and inhibits reuptake of serotonin and noradrenaline, was recently found to possess inhibitory actions on normal rat micturition. In order to evaluate a potentially inhibitory effect of tramadol on detrusor overactivity associated with cerebrovascular disorders, the drug was given to rats with apomorphine- and cerebral infarction-induced detrusor overactivity.

Methods

Female Sprague-Dawley rats were used. In animals given apomorphine, catheters were introduced in the bladder dome, femoral vein and subcutaneously (s.c). Three days later, the rats were placed in a metabolism cage and voiding was stimulated by infusing saline into the bladder. Micturition parameters were recorded and compared after administration of apomorphine and tramadol or vehicle. Desmopressin was given as a pre-treatment to suppress the diuresis produced by tramadol.

Cerebral ischemia was induced by occlusion of the MCA and the urinary bladder was catheterised. Three days later, continuous cystometry was performed in awake animals and the effects of tramadol given intravenously (i.v.) were studied.

Results

Apomorphine 30 µg.kg⁻¹ s.c. produced no effects. However, apomorphine 60 and 100 µg.kg⁻¹ s.c. induced a transient detrusor overactivity. Tramadol 1 mg.kg⁻¹ was without effect, but tramadol 5 and 10 mg.kg⁻¹ i.v. attenuated the effects of apomorphine while inducing a prominent diuresis. Pre-treatment with desmopressin, which did not alter the cystometry or the effects of apomorphine, abolished the diuresis. In these rats, tramadol 5 and 10 mg.kg⁻¹ i.v., abolished the overactivity caused by s.c. apomorphine.

In MCA-occluded rats, bladder capacity was lower (48±9%) and micturition pressure higher (76±21%) than in control rats. Tramadol 5 mg.kg⁻¹ given i.v., increased bladder capacity (59±29%) and threshold pressure (47±32%) to values similar to those in control rats (figure). However, micturition pressure was not significantly altered. Tramadol induced diuresis in some, but not all, MCA-occluded rats.

Conclusion

Tramadol effectively suppressed apomorphine-induced detrusor overactivity in doses shown to have analgesic activity. The drug also normalised detrusor overactivity in MCA-occluded rats. Tramadol may have a treatment potential in patients with lower urinary tract disorders involving dopamine receptor activation, and in patients with detrusor overactivity after stroke.

Figure

