

LETTER TO THE EDITOR

EFFECTS OF NITROXAZEPINE ON GUINEA-PIG ISOLATED  
DETRUSSOR AND TRIGONE MUSCLES

Sir,

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Like other tricyclic antidepressants, nitroxazepine also is effective in controlling nocturnal enuresis (1). In an open clinical trial, nitroxazepine (25 mg PO at bedtime for 2-6 weeks) was found to be effective in 80% of the subjects. In a double blind trial, nitroxazepine was significantly superior to the placebo (2). Nitroxazepine is 5-10 times weaker than imipramine as anticholinergic on salivary secretion (3). Imipramine itself is 157 times weaker than atropine on guinea-pig ileum (4). Further, enuresis cannot always be controlled by anticholinergic drugs. Thus the beneficial effect of tricyclic drugs in nocturnal enuresis appears to be based on some other mechanism.

The present work was undertaken to study actions of nitroxazepine on isolated detrussor and trigone muscle of guinea-pig to find out whether there is any peripheral useful action component for nocturnal enuresis.

Urinary bladder was obtained from freshly sacrificed male or female guinea-pigs (600-800 g). The detrussor and trigone muscle preparations were made on lines described by Burnstock *et al* (5). The preparations were suspended in mammalian ringer (composition : Sodiumchloride 9 g, potassium chloride 0.42 g, calciumchloride 0.24 g, glucose 1 g, sodium-bi-carbonate 0.5 g, dissolved in 1000 ml of distilled water), maintained at 37°C, and gassed with 5% CO<sub>2</sub> in O<sub>2</sub>. The records were isotonic (magnification × 5) with tissue under resting tension of 1 g. Tissues were equilibrated for 45 min before the

experiments. Acetylcholine-Cl (for detrussor) and (-) adrenaline-HCl (for trigone) were used as standard agents to induce contractions.

Isolated detrussor muscles showed dose related contractile responses to acetylcholine and to nitroxazepine-HCl (n=6, Fig. 1A), those with nitroxazepine were not blocked by atropine (n=6). Nitroxazepine was much weaker than acetylcholine (potency 35 times less) where comparisons were at 0.1 μg of Ach and 1 μg of nitroxazepine giving 21 mm and 6 mm contractile response.

Isolated trigone muscle showed contractile dose related responses to adrenaline. Nitroxazepine showed a very weak, insignificant contractile responses even in very high doses, the maxima being very low as compared to adrenaline responses (Fig. 1B).

To be use ful in nocturnal enuresis, a drug should peripherally cause a relaxation of detrussor muscle and a contraction of trigone muscle of urinary bladder. We observed that nitroxazepine caused atropine resistant contractions of detrussor muscle, and weak contractions of trigone muscle. It is hard to imagine that these actions can contribute to its usefulness in nocturnal enuresis, since there is significant contraction of detrussor muscle. In enuresis, nitroxazepine may have a central action such as one affecting NREM sleep reported in rhesus monkeys (6).