Cardiovascular responses to amantadine hydrochloride in the rat and rabbit

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Amantadine, an antiviral agent, has been reported to be effective in the treatment of Parkinson's disease (Schwab, England, Poskanzer & Young, 1969). It has been suggested that amantadine releases catecholamines from nerve storage sites on the basis of a pressor response in the anaesthetized dog which was increased by prior injection of dopamine (DA) (Grelak, Clark, Stump & Vernier, 1970). We have investigated the cardiovascular actions of amantadine and attempted to confirm an interaction with dopamine.

In the urethane anaesthetized rat and rabbit amantadine (20 μg to 2 mg) produced a pressor response with no change in heart rate. DA had qualitatively different effects and was ten times more potent. In the rat the DA pressor effect was accompanied by an increase in heart rate and in the rabbit it gave a depressor response. No potentiation of amantadine was observed in the rat, after injection of DA.

Reserpine pretreatment (5 mg/kg, I.P., 18 h) and guanethidine, in a dose which blocked the pressor response to tyramine (2 μg), did not significantly affect the amantadine pressor response in the rat. Repeated injections af amantadine showed no evidence of tachyphylaxis and there was no cross tachyphylaxis with tyramine. In the pithed rat the mean blood pressure responses to low doses of amantadine (20 to 200 μg) were reduced but the response to 2 mg was increased.

Phentolamine in a dose which antagonized the pressor response to noradrenaline (100 ng) also blocked the pressor response to amantadine. However, when amantadine was tested on the rat isolated aortic strip it produced a maximum contraction at 62·5 μg/ml, which was only 15% of a noradrenaline maximum. Addition of amantadine relaxed an aortic strip fully contracted with noradrenaline.

In conclusion, amantadine is a weak pressor agent in the rat and rabbit and is neither DA-like nor tyramine-like in its actions. There is some evidence that an intact central nervous system is required for the pressor response to low doses, and work on the isolated aorta suggests it may be a partial agonist at α-adrenoceptors.

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Receptors for dopamine in some isolated vascular tissues of the dog

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In many peripheral tissues dopamine (DA) has been shown to have agonist activity at both α- and β-adrenoceptors (Rossum, 1965 and Tsai, Langer & Trendelenburg,