Vasodilating and alpha-receptor blocking activity of a new ergoline derivative

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Several ergoline derivatives are highly potent and selective pharmacological agents (Beretta, Ferrini & Glässer, 1965; Fregnan & Glässer, 1968). Nicotinic acid esters of 1,6-dimethyl-8β-hydroxymethyl-10α-metoxyergoline possess α-receptor blocking properties. The presence of a properly placed halogen substituent in the pyridine ring of nicotinic acid increases this activity.

The vasodilating and alpha-receptor blocking activities of 1,6-dimethyl-8β-5-bromonicotinoxy methyl)-10α-metoxyergoline (MNE) were investigated in several tests and in different animal species. On the isolated guinea-pig seminal vesicles MNE reduced the responses to adrenaline at concentrations (EC50 = 0.007 μg/ml.) not yet active on histamine (EC50 = 0.05 μg/ml.) or eledoisin (EC50 = 7.5 μg/ml.). The catecholamine antagonism is fairly specific, easily washed out and surmountable.

In vivo MNE inhibited α-receptor responses to adrenaline, to sympathetic nervous stimulation (Gillespie & Muir, 1967) and to the nicotinic agent leptodactyline (Erspamer & Glässer, 1960). In the pithed adrenalectomized rat, MNE in doses as low as 0.01–0.1 mg/kg intravenously produced a 50% inhibition of the rise in blood pressure, caused by adrenaline or by leptodactyline or by stimulation of the sympathetic outflow from the spinal cord. MNE decreased systemic blood pressure in conscious rats, and in anaesthetized rabbits and dogs, and did not cause hypertensive responses in spinal cats and pithed rats.

Blood flow changes through intact vessels were studied by a Nycotron electromagnetic flowmeter. MNE (0.01 to 0.45 mg/kg intravenously) increased the blood flow to the hind limb of the dog without affecting the splanchnic and aortic blood flow. The vasodilating activity of MNE was also present after the intra-arterial injection of doses as low as 0.1–1 μg/kg.

The α-receptor block produced by MNE, although quantitatively similar to that of hydrogenated ergot alkaloids, differs qualitatively in the absence of vascular smooth muscle stimulation and of vomiting. Therefore MNE does not act as a "partial agonist" (Nickerson & Hollenberg, 1967). Vasoconstriction and vomiting are not expected to be important side-effects in human trials.

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