Effects of ketamine on the peripheral sympathetic nervous system of the rat

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Ketamine (2-(*o*-chlorophenyl) 2-methylamino cyclohexanone) is unique among the intravenous anaesthetics in elevating arterial pressure in man and animals (Virtue, Alanis, Mori, Lafargue, Vogel & Metcalf, 1967). One mechanism suggested to account for this pressor effect is blockade of neuronal uptake of noradrenaline (NA) leading to potentiation of the effects of sympathetic nerve activity. Studies indicating this action, however, involved high concentrations of ketamine *in vitro* or continuous infusion *in vivo* (Nedergaard, 1973; Montel, Starke, Gorlitz & Schumann, 1973). We have, therefore, compared the effects of a wide range of doses of ketamine both *in vitro* on the rat anococcygeus muscle and *in vivo* on the pithed rat arterial pressure and anococcygeus. The *in vivo* experiments were on rats pithed by the method of Gillespie, MacLaren & Pollock (1970). Carotid arterial pressure and anococcygeus tension were recorded. Preganglionic sympathetic nerves to blood vessels and to the anococcygeus were stimulated via the pithing rod electrode at L1-2; postganglionic sympathetic nerves to the anococcygeus at S1-S2 (Gillespie & McGrath, 1973). The *in vitro* preparation of the anococcygeus was set up according to Gillespie (1972).

In the pithed rat, ketamine (2-50 mg/kg) initially lowered, then raised arterial pressure. Pressor responses to stimulation at L1-2 (10 Hz, 10 s) were inhibited at doses above 2 mg/kg whereas those to NA (400 ng/kg) were not significantly affected. Ketamine did not change anococcygeus resting tension, but potentiated its motor response to NA at doses above 10 mg/kg and inhibited its responses to pre- and post-ganglionic stimulation; inhibition of responses to pre-ganglionic stimulation was greater.

In the anococcygeus *in vitro*, ketamine (3.7×10^{-7}-3.7×10^{-3} M) produced a dose-related inhibition of responses to carbachol, NA and field stimulation. The inhibition of NA responses was significantly less than that of carbachol responses in the range 3.7×10^{-5}-3.7×10^{-4} M. Cocaine (10^{-7}-10^{-5} M) potentiated responses to NA and field stimulation without affecting responses to carbachol; cocaine 10^{-4} M depressed responses to carbachol and field stimulation.

The results in the anococcygeus confirm that the sensitivity of smooth muscle to NA can be potentiated by high doses of ketamine (Nedergaard, 1973; Montel, Starke, Gorlitz & Schumann, 1973) although to a much lesser extent than by cocaine. At such doses, however, ketamine also possesses a non-specific depressant action which can produce ganglionic blockade and post-synaptic depression and would contribute only to a depressor effect.

This suggests that in the doses used clinically or in intact animals, ketamine owes its effect on arterial pressure to no single effect such as block of neuronal NA uptake and that the vasopressor response is not peripherally mediated.

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