The effect of acute adrenergic neurone blockade on the response of the cardiovascular system of the rabbit to lower body negative pressure (LBNP)

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Application of negative pressure to the hindquarters of a rabbit causes pooling of blood therein, thus reducing venous return and hence cardiac output (CO). Systemic arterial blood pressure therefore falls at the onset of LBNP and compensatory mechanisms are activated including an increase in total peripheral resistance (TPR) and heart rate (Yates & Fentem, 1975). Both of these responses are dependent on functional noradrenergic sympathetic nerves (Bennett, Fentem, Tomlinson & Yates, 1976). The cardiovascular compensation for LBNP therefore provides a useful physiological event for examination of the pharmacology of drugs which act on noradrenergic nerves.

Rabbits (male New Zealand White, 2.0–2.6 Kg) were anaesthetised and prepared as described by Yates & Fentem (1975). LBNP at −50 mm Hg for 75 s was employed in all experiments. CO was measured 45 s into the manoeuvre. All rabbits responded as described above before drug treatment (see Table 1).

Intravenous administration of either bretylium (10 mg/kg) or debrisoquine (10 mg/kg) lowered resting mean arterial blood pressure (MAP), heart rate, cardiac output and TPR. The compensatory response (MAP) to LBNP was abolished (Table 1).

In bretylium-treated rabbits the blood pressure was elevated either by a parenteral vasoconstrictor or by inducing acute hypervolaemia. St 91, a peripherally-acting α-adrenoceptor stimulant (Hoefke, Kobinger & Walland, 1975), was infused until the blood pressure was within normal limits. Subsequent application of LBNP caused a fall in MAP and there was no compensation—hence the response itself resembled that evoked before administration of the vasoconstrictor (Table 1). Infusion of dextran 110 (20–25 ml) after acute sympathectomy also raised the MAP but not to original level. However, these hypervolaemic rabbits did show a compensatory rise in MAP during LBNP (Table 1). Table 1 shows that the hypervolaemia limited the fall in cardiac output induced by LBNP. Thus very modest reflex elevation of TPR caused a much greater rise in MAP than was seen in the normovolaemic sympathectomised rabbit.

EC was an MRC student.

References

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Table 1 Resting cardiovascular status and the response to LBNP in anaesthetised rabbits. Values are means ± s.e. mean. Significance of difference between means was tested by Student's *t*-test for paired samples; * denotes $P < 0.05$.

	MAP (mm Hg)		*CO (ml kg⁻¹ min⁻¹)*		*TPR (arbitrary units)*	
	Rest	*LBNP 45 s*	*Rest*	*LBNP 45 s*	*Rest*	*LBNP 45 s*
Untreated rabbits	104.9 ± 6.5	103.6 ± 3.8	169.1 ± 21.5*	107.4 ± 14.7	0.62 ± 0.08*	1.00 ± 0.10
Debrisoquine	46.4 ± 4.4*	35.3 ± 1.8	149.5 ± 15.7*	102.5 ± 23.8	0.33 ± 0.04	0.39 ± 0.08
Bretylium	51.3 ± 3.4*	39.2 ± 2.8	120.0 ± 7.5*	80.5 ± 6.0	0.43 ± 0.10	0.50 ± 0.04
Bretylium + Dextran 110	61.9 ± 3.3	64.4 ± 4.7	176.6 ± 18.6*	126.5 ± 16.6	0.32 ± 0.03*	0.44 ± 0.01
Bretylium + St 91	105.8 ± 3.2*	91.6 ± 6.2	136.5 ± 21.2*	87.0 ± 13.6	0.82 ± 0.13	1.01 ± 0.11