Response of the cardiovascular system to lower body negative pressure (LBNP) in rabbits treated with 6-hydroxydopamine

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Application of negative pressure to the hindquarters of an anaesthetised rabbit pools blood therein, reducing cardiac output and mean systemic arterial blood pressure (MAP) and thus activating compensatory cardiovascular reflexes (Yates & Fentem, 1975). The compensation includes a tachycardia and an increase in peripheral resistance (TPR) and is mediated by peripheral noradrenergic nerves (Bennett, Fentem, Tomlinson & Yates, 1976). This technique has therefore been employed to study cardiovascular adaptations to chronic sympathectomy with 6-hydroxydopamine (6-OHDA).

New Zealand white male rabbits (weight range 2.0–2.6 kg) were anaesthetised and prepared as described by Yates & Fentem (1975). LBNP at −50 mm Hg for 75 sec was employed throughout. All values cited below are means ± s.e. mean for 5 rabbits.

Untreated rabbits (resting MAP = 97.2 ± 2.9 mm Hg) exhibited a transient hypotension at the onset of LBNP followed by brisk compensation (MAP = 96.9 ± 4.2 mm Hg at 45 s into LBNP) on the basis of an increase in TPR from a resting value of 0.67 ± 0.02 to 1.05 ± 0.13 (arbitrary units) 45 s into LBNP and a slight increase in heart rate (15 beats min^{-1}).

Two groups of rabbits were studied 2 and 10 days after administration of 6-OHDA (100 mg/kg i.v.). The 2 day group were hypotensive at rest (MAP = 63.9 ± 5.8 mm Hg), but the MAP 45 sec into LBNP (76.3 ± 8.9 mm Hg) actually exceeded the resting level. TPR increased from 0.37 ± 0.04 at rest, to 0.53 ± 0.03 45 s after onset of LBNP though negligible tachycardia occurred. The MAP compensatory response and the increase in TPR elicited by LBNP in these animals were not markedly altered by intravenous administration of bretylium tosylate (10 mg/kg) and propranolol HCl (2 mg/kg). In normal rabbits such acute sympathetic blockade completely obliterated the compensatory response.

Ten days after 6-OHDA rabbits ($n = 4$) were almost normotensive (MAP = 81.3 ± 6.5 mm Hg), but TPR was still below normal (0.44 ± 0.06). Again these animals showed a marked compensatory response to LBNP; 45 s into the manoeuvre MAP was 85.8 ± 5.7 mm Hg and TPR was 0.67 ± 0.10. The effect of bretylium and propranolol (treatment as above) on this compensation was insignificant.

Microscopic examination for noradrenaline histofluorescence indicated that the sympathectomy was extensive in rabbits 2 days after 6-OHDA. Signs of re-innervation of the cardiovascular system were present in the 10 day animals.

Two days after 6-OHDA the haematocrit was reduced suggesting that the 6-OHDA-treated rabbit became hypervolaemic. These animals did not experience as great a fall in cardiac output on application of LBNP (approximately 17% reduction after 45 s, compared with approximately 41% for normal rabbits). It is therefore suggested that the blood pressure of the hypervolaemic sympathectomised rabbit is very sensitive to modest change in TPR. The mechanism responsible for this modest TPR change in 6-OHDA-treated rabbits exposed to LBNP is as yet unexplained.

E.C. was an MRC Student.

References

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