

Title: PENTAZOCINE-INDUCED CATECHOLAMINE EFFLUX FROM THE PERFUSED DOG ADRENALS

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Introduction. It has been reported that pentazocine would cause an elevation of the arterial pressure associated with an increase in the plasma catecholamine level.¹ Although a central mechanism was suggested to be involved in the increase in circulating catecholamines,¹ conclusive evidences have not been obtained on the mechanism of the sympathetic stimulation by this compound. The present study was carried out to determine whether pentazocine had a direct effect on the adrenal medulla to induce catecholamine efflux, and if so, to ascertain the site of action of this compound.

Methods. Mongrel dogs of either sex weighing 7-11kg were anesthetized with sodium pentobarbital. The adrenal glands were isolated outside the body, and perfused retrogradely via the adrenolumbar vein at a pressure ranging from 45-80cm H₂O with a warmed (37°C) modified Locke's solution, aerated with 95% O₂ and 5% CO₂. The solution was composed as follows; NaCl 154mM, KCl 5.6 mM, CaCl₂ 2.2mM, glucose 10mM and 40mM Tris-HCl buffer (pH 7.4). Perfusion was carried out at a constant rate, ranging from 0.9 to 1.3ml/min, in each experiment. About 80min were allowed to elapse before any treatment to achieve equilibrium. Pentazocine dissolved in Locke's solution was administered by continuous infusion by switching a valve on the tubing leading to the gland. The stimulation by pentazocine was carried out for 10min in the presence and absence of naloxone. In addition to racemic (dl-) pentazocine, the effects of optic isomers of dextro (d-) and levo (l-) form of pentazocine were examined. The effect of pentazocine on acetylcholine (ACh)-induced catecholamine release was examined by stimulating the adrenals by ACh in the presence and absence of pentazocine. The effluent from the adrenals was collected into ice-cooled glass tubes at 2-min intervals, and catecholamine content was measured by trihydroxyindol method.² Dopamine-β-hydroxylase (DBH) and lactate dehydrogenase (LDH) activities in the effluent were also measured.³ Data were analyzed by one-way analysis of variance followed by the Student's t-test. P < 0.05 was considered significant.

Results. Spontaneous efflux of catecholamines during the 2-min period prior to drug administration amounted to 0.15 ± 0.14 μg/min (mean ± SE, n=11). Pentazocine increased catecholamine efflux in a dose-dependent manner at doses between 50-200 μM (0.51 ± 0.11 μg/min catecholamine efflux at 100 μM). Naloxone had no effect on the pentazocine-induced catecholamine efflux. Although d-pentazocine tended to induce catecholamine efflux more potently than dl- and l-pentazocine, there was no significant difference among these. ACh-induced release of catecholamines was accompanied with the release of DBH and without LDH, whereas pentazocine-induced

catecholamine release was not accompanied with either DBH or LDH. ACh-induced catecholamine release was not enhanced but inhibited by pentazocine in a dose-dependent manner.

Discussion. The results demonstrate that pentazocine has a direct effect on the adrenal medulla to induce catecholamine efflux, whereas it inhibits the catecholamine release induced by ACh, the physiological neurotransmitter for the adrenal medulla. The pentazocine-induced catecholamine efflux was not either stereospecific or inhibited by naloxone, indicating that the action of pentazocine on the adrenals would not be mediated by the opiate receptors. It is likely that pentazocine would induce catecholamine efflux by a non-exocytotic mechanism, because DBH, a marker of exocytosis, was not accompanied with the catecholamine efflux.

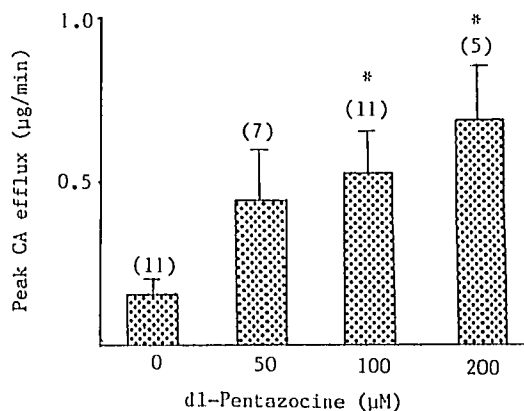


Figure. Effect of pentazocine on catecholamine (CA) efflux from the perfused dog adrenals (mean ± SE, number is indicated in the parenthesis). *P < 0.05 compared with control.

References.

1. Takki S, Nikki P, Tammisto T, et al: Effect of epidural blockade on the pentazocine-induced increase in plasma catecholamines and blood pressure. *Br J Anaesth* 45: 376-380, 1973
2. Sumikawa K, Hirano H, Amakata Y, et al: Mechanism of the effect of droperidol to induce catecholamine efflux from the adrenal medulla. *Anesthesiology* 62: 17-22, 1985
3. Nagatsu T, Udenfriend S: Photometric assay of dopamine-β-hydroxylase activity in human blood. *Clin Chem* 18: 980-983, 1972