A STUDY OF THE CENTRAL VASOMOTOR EFFECTS
OF 2-DIMETHYL AMINOETHANOL (DEANOL)

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There are a number of observations which suggest that acetylcholine exerts an excitatory influence over the medullary vasomotor center. Dhawan et al. (1) reported that both acetylcholine and carbachol produce a pressor response on intracerebroventricular (i.c.v.) administration in dogs and this pressor response is blocked by atropine. Sinha et al. (2) observed that hemicholinium, which blocks the synthesis of acetylcholine depresses the responsiveness of vasomotor center on i.c.v. administration as well as after topical application to the floor of the fourth ventricle. Release of acetylcholine by tyramine has been suggested to be involved in the pressor response produced by i.c.v. administration of tyramine (1).

Pfeiffer et al. (3) studied several compounds to find out longer acting parasympathomimetic agents or precursors of acetylcholine which might affect the central nervous system. They reported parasympathomimetic and central effects of 2-dimethyl aminoethanol (deanol) and suggested that it owes the actions to its conversion to acetylcholine. We, therefore, thought it worthwhile to study the central vasomotor effects of deanol and to investigate if these effects are due to its conversion into acetylcholine.

METHODS

The present study was carried out on twenty adult mongrel dogs of either sex. The animals were anesthetized with pentobarbitone (30 mg/kg i.v.). Both the vagi were cut and the animals were maintained on positive pressure artificial respiration. The blood pressure was recorded on a kymograph, from a common carotid artery, using mercury manometer. Pressor responses were elicited by reflex as well as direct stimulation of the vasomotor center. Vasomotor center was reflexly stimulated by the occlusion of the common carotid arteries for 30 seconds. The direct stimulation of the medullary vasomotor center was carried out by stereotaxically oriented, bipolar, concentric electrodes. Horseley Clarks instrument was employed for electrode placement using the parameters described by Wang and Ranson (4).

The drugs used in the study were deanol acetamidobenzoate (Deaner) and atropine sulphate and were administered either intracerebroventricularly or applied directly to
the floor of the fourth ventricle. The technic for the implantation of the cannula in the lateral cerebral ventricle has been described by Bhargava and Tangri (5). The drugs were dissolved in 0.2 ml of normal saline and injected intracerebroventricularly followed by 0.1 ml of normal saline.

RESULTS

The effect of intracerebroventricular administration of deanol (0.1 to 2.0 mg) was studied on the blood pressure and carotid occlusion response in ten dogs. There was slight rise of blood pressure after higher doses of deanol while all the doses produced a potentiation of the carotid occlusion response. The effect appeared within 15 minutes and persisted for 3 hours. Central atropinization (8.0 mg i.c.v.) did not abolish the effect of centrally administered deanol on the carotid occlusion pressor response (Fig. 1).

In five dogs the effect of topical application of deanol (5.0 mg dissolved in 0.5 ml of normal saline) to the floor of the fourth ventricle was studied on the reflex excitability of the medullary vasomotor center. It potentiated the carotid occlusion response without affecting the systemic blood pressure significantly. In five experiments the medullary vasomotor center was directly stimulated by means of square wave pulses to elicit pressor responses. Topical application of deanol (5.0 mg dissolved in 0.5 ml of normal saline) to the site of electrode penetration did not produce any significant change in the systemic blood pressure, but potentiated the pressor responses elicited by the threshold and optimal stimuli (Fig. 2).
Fig. 2. Effect of topical application of deanol at the electrode site on the blood pressure and the pressor responses obtained by the direct electrical stimulation of the vasomotor center. Parameters for threshold stimulus (T) were: 0.5 V, 60 shocks/sec for 10 seconds and for optimal stimulus (O): 3.0 V, 60 shocks/sec for 10 seconds. Note that the responses elicited by threshold and optimal stimuli have been potentiated after topical application of deanol.

DISCUSSION

Deanol produces many actions similar to acetylcholine to which it is structurally related. It produces a vasodepressor response in anaesthetized dogs and has a muscarinic effect on guinea pig uterus and rabbit ileum. It has been suggested that deanol exerts its effects by getting converted into acetylcholine. However, in contrast to acetylcholine, deanol produces distinct central effects in animals and human beings on systemic administration. Acetylcholine is devoid of central effects on systemic administration, probably because of its slow transit across the blood brain barrier (3). Acetylcholine, which produces a fall in blood pressure peripherally causes a rise in blood pressure when administered i.c.v. (1, 2). Deanol also produces a fall in blood pressure peripherally, but nothing is known about its effect on the vasomotor center. Therefore, in the present study the drug was given by i.c.v. route and it was observed that like acetylcholine deanol exerts a central vasomotor stimulant effect. Deanol, on topical application was also found to potentiate the pressor response obtained by direct electrical stimulation of the medullary vasomotor center.

There can be three possibilities regarding the mode of action of deanol. Firstly, deanol may be getting converted into acetylcholine as suggested by Pfeiffer et al. (3) and this acetylcholine may be responsible for the stimulant effect observed in the present study. Secondly, because of its structural similarity with acetylcholine deanol may be acting on the cholinoreceptive receptor sites. Thirdly, it may be acting not on the cholinoreceptive
receptors but on some other receptors to produce the stimulant effect. The first possibility does not seem likely as Pepeu et al. (5) have shown that deanol does not increase the total acetylcholine content of the rat brain. The second possibility is not supported by the fact that atropine fails to block the central vasomotor stimulant action of deanol whereas the action of acetylcholine and carbachol is blocked by atropine. Thus, it seems that deanol does not act through acetylcholine but has a direct stimulant action on the vasomotor center.

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REFERENCES