EFFECT OF PENTOBARBITAL AND SODIUM HYDROXYBUTYRATE ON CENTRAL MECHANISMS REGULATING VASCULAR TONE

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The effect of pentobarbital and sodium hydroxybutyrate on the responses of the systematic arterial and perfusion pressures in the limb vessels and on electrical responses recorded in the renal nerve to stimulation of afferent nerves and activation of receptors of the carotid sinus zone was studied in experiments on cats with an intact brain. Observations showed considerable differences between the effects of the two anesthetics, with their different chemical structures, on the central regulation of vascular tone.

The effect of anesthetics disturbing electrogenesis in postsynaptic membranes [10] on the changes in systemic arterial pressure and on its pressor responses to direct stimulation of central structures or to afferent stimulation has been studied in detail [2, 3, 8, 13, 14]. However, the effects of anesthetics similar in structure to γ-aminobutyric acid, but with a different mechanism of action [4] on the integration of vasomotor reflexes, have so far received little investigation [1]. The effect of anesthetics on inhibitory mechanisms participating in the regulation of vascular tone has also been inadequately studied.

The object of this investigation was to compare the effects of pentobarbital and sodium hydroxybutyrate on central structures responsible for maintaining the initial neurogenic vascular tone and for the closure of vasomotor reflexes.

EXPERIMENTAL METHOD

Experiments were carried out on 55 unanesthetized (the experiments began 2-2.5 h after the preparatory operation performed under ether anesthesia) and anesthetized (chloralose 40 mg/kg, urethane 400-600 mg/kg, intravenously) cats. The systemic arterial pressure, the perfusion pressure in the vessels of the fore- and hindlimbs [6], and the electrical activity in the renal nerve were recorded. The cutaneous branch of the peroneal nerve and the central end of the divided splanchnic and vagus nerves were stimulated electrically (0.5-6 V, 0.1-20/sec, 0.2-1 msec, 10-15 sec) while the carotid sinus baroreceptors were stimulated by injecting physiological saline into the region of the sinus under a pressure of 200 mm Hg for 10-15 sec after ligation of all the arterial branches. During the experiment the animals (after injection of muscle relaxants) were artificially ventilated and heated. Pentobarbital (1-40 mg/kg) and sodium hydroxybutyrate (50-200 mg/kg) were injected intravenously.

EXPERIMENTAL RESULTS

In response to stimulation of low-threshold cutaneous afferent fibers depressor effects on the arterial pressure and inhibition of electrical activity in the sympathetic nerves are observed only in anesthetized or decerebrate animals [7, 9]. For this reason the study of the effect of pentobarbital and sodium hydroxybutyrate on the inhibitory effects due to activation of low-threshold afferent fibers of the cutaneous branch of the peroneal nerve were studied in previously anesthetized animals. In these experiments sodium hy-

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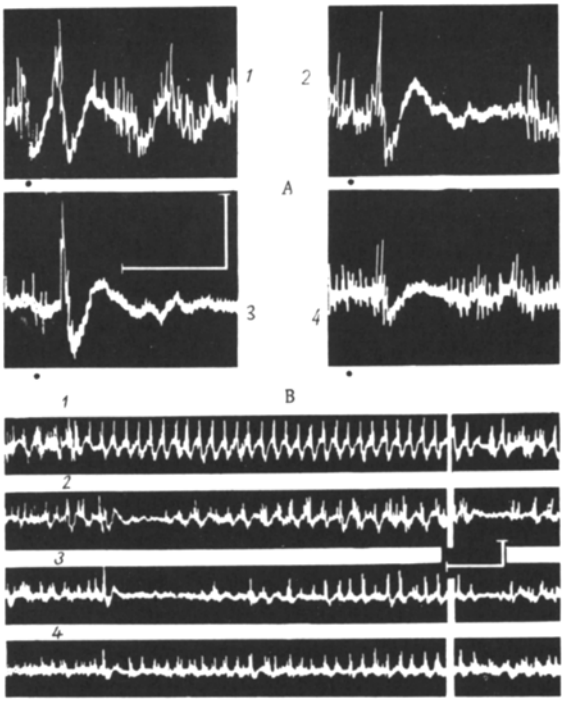

Fig. 1

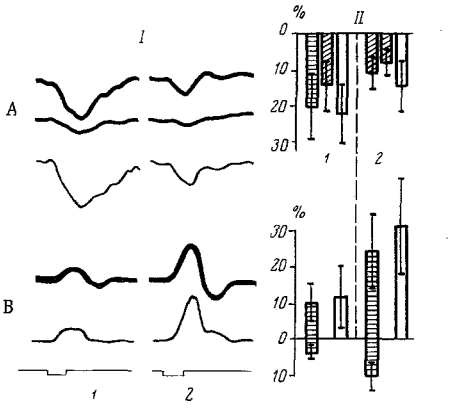

Fig. 2

Fig. 1. Effect of pentobarbital on reflex responses to single (A) and repetitive (B) stimulation of afferent fibers of the greater splanchnic nerve: 1) before injection of pentobarbital; 2) after injection of pentobarbital in a dose of 10 mg/kg; 3) in a dose of 15 mg/kg; 4) in a dose of 25 mg/kg. Black dots and line under records denote moment of stimulation. Frequency of stimulation 5/sec, duration 15 sec. Calibration: A) 500 msec, 20 μV; B) 1 sec, 20 μV.

Fig. 2. Effect of sodium hydroxybutyrate (200 mg/kg) on responses of systemic arterial and perfusion pressures to stimulation of central end of divided vagus nerve (A) and cutaneous branch of peroneal nerve (B). I: A (From top to bottom) – perfusion pressure in vessels of hindlimb, of forelimb, systemic arterial pressure; B – perfusion pressure in vessels of hindlimb, systemic arterial pressure, marker of stimulation (15 sec). II (Aggregated data): ordinate, magnitude of pressor (above abscissa) and depressor (below abscissa) responses (in % of initial level of systemic arterial or perfusion pressure). Columns with horizontal shading denote responses of hind-limb vessels; columns with oblique shading – responses of forelimb vessels; unshaded columns – responses of systemic arterial pressure. Pressor–depressor responses of perfusion pressure in vessels of hindlimb to stimulation of cutaneous branch of peroneal nerve shown by columns above and below zero line, reflecting value of each component of the response. 1) Before injection of sodium hydroxybutyrate; 2) after its injection.

droxybutyrate did not affect the depressor response of the systemic arterial and perfusion pressures in the limb vessels or the duration of depression of electrical activity in the renal nerve. Pentobarbital reduced the degree of lowering of the pressure in proportion to the dose administered. After administration of 10 mg/kg pentobarbital no depressor responses occurred. Under the influence of pentobarbital the period of depression of spontaneous electrical activity in the renal nerve also was shortened.

The effect of increasing doses of pentobarbital on reflex responses in the renal nerve to stimulation of afferent fibers composing the splanchnic nerve was studied in unanesthetized animals (Fig. 1). Pentobarbital in a dose of 10-15 mg/kg definitely prolonged the period of postactivation depression of spontaneous electrical activity after single stimulation and also after repetitive stimulation of the nerve. The pressor response of the arterial pressure was converted into depressor. In a large dose (25-40 mg/kg) pentobarbi-

tal shortened both the period of postactivation inhibition of spontaneous electrical activity after a single stimulus and also the inhibition of electrical activity after repetitive stimulation. Meanwhile the depressor responses of the systemic arterial pressure were reduced in magnitude.

Sodium hydroxybutyrate increased the pressor responses of the systemic arterial pressure and the pressor component of the biphasic (pressor–depressor) responses of the perfusion pressure in the limb vessels to stimulation of high-threshold afferent fibers of the cutaneous nerve (Fig. 2), whereas pentobarbital in a dose of 10 mg/kg completely inhibited these responses.

Sodium hydroxybutyrate and pentobarbital also had different effects on the changes in electrical activity recorded in the renal nerve in response to repetitive stimulation of high-threshold afferent fibers. After injection of sodium hydroxybutyrate (50-100 mg/kg) no change was observed in the amplitude of the reflex responses, and in some experiments an improvement in the synchronization of the reflex responses with the frequency of stimulation was observed. Pentobarbital always disturbed synchronization between the frequency of the stimuli and the appearance of reflex responses, and it simultaneously reduced their amplitude.

Stimulation of afferent fibers composing the cutaneous nerve at 5-20/sec in unanesthetized animals always leads to increased electrical activity in the renal nerve with a latent period of 200-400 msec [9]. Sodium hydroxybutyrate (100-200 mg/kg) shortened by 30-40% the latent period of the reflex response. Administration of pentobarbital (10-25 mg/kg) under those conditions had the same action as during stimulation of the afferent fibers in the splanchnic nerve.

Depressor responses of the systemic arterial and perfusion pressure in the limb vessels evoked by stimulation of the central end of the vagus nerve (Fig. 2) and by activation of the carotid sinus baroreceptors were reduced after administration of sodium hydroxybutyrate. The decrease in magnitude of the depressor responses was accompanied by shortening of the period of depression of the spontaneous electrical activity recorded in the renal nerve during activation of the afferent systems of the carotid sinus–aortic zone.

Responses of the systemic and perfusion pressures in the limb vessels evoked by activation of the afferent systems of the carotid sinus–aortic zone were more resistant to the action of pentobarbital than responses to stimulation of the cutaneous nerve. In a dose of 3-5 mg/kg, pentobarbital reduced the depressor responses by only 40-50%. After administration of pentobarbital in a dose of 10 mg/kg the amplitude of the depressor responses was significantly ($P < 0.05$) reduced by 80-85%.

Definite differences thus exist in the effects of the two anesthetics, with their different chemical structures, on the central regulation of vascular tone. Sodium hydroxybutyrate, which can potentiate presynaptic segmental inhibition [4], increases the amplitude of the pressor responses of the systemic and perfusion pressures to activation of cutaneous afferent fibers. A similar action is shown by diazepam [5], which also belongs to the group of compounds potentiating presynaptic inhibition [11, 12], another important factor in its action is the inhibition of electrogenesis in postsynaptic membranes [10]. This mechanism evidently also lies at the basis of the depriming action of nembutal on vascular responses and changes in electrical activity of the renal nerve, since urethane [3, 9], an anesthetic which inhibits presynaptic inhibition [11], has a similar action.

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