EFFECT OF HEXAMETHONIUM ON PULOMONARY CIRCULATION AND BRONCHIAL TONE

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Administration of small doses of hexamethonium to animals with pulmonary hypertension lowers the pressure in the pulmonary artery and tone of the pulmonary vessels. Administration of large doses of hexamethonium to animals with a normal or reduced pressure in the pulmonary artery raises arterial pressure in the lungs and the tone of the pulmonary vessels. Hexamethonium causes no changes in bronchial tone.

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Many experimental and clinical investigations of the effect of hexamethonium on the pulmonary circulation have been made, but they have yielded conflicting results. Some authors [8], found no changes in the normal arterial pressure following administration of hexamethonium. Others [11] found a decrease in pressure in the pulmonary artery after administration of hexamethonium to persons with normal pulmonary arterial pressure.

According to Yu and co-workers [13], hexamethonium reduces the pressure in the pulmonary artery if administered against a background of pulmonary hypertension without actively influencing tone of the pulmonary vessels or significantly changing the stroke volume of the heart. Other workers [8, 9, 12] have stressed the primary and dominant role of a decrease in tone of the pulmonary vessels in the reduction of pressure in the pulmonary artery produced by hexamethonium.

Because of the conflicting nature of data in the literature concerning the effect of hexamethonium on tone of the pulmonary vessels, and also because of disagreement on whether the pulmonary arterial pressure is regularly lowered in response to administration of hexamethonium, we decided to study the action of this substance on pulmonary arterial pressure and tone of the pulmonary vessels. Another object of the investigation was to determine whether the reactions of these indices of the pulmonary hemodynamics are dependent on their initial level, the method of administration and the dose of hexamethonium, and possible changes in tone of the bronchial muscles.

EXPERIMENTAL METHOD

Experiments were performed on 26 cats anesthetized with Nembutal and maintained on artificial respiration. The pressure in the pulmonary artery was recorded through a catheter by means of a water manometer. The pressure in the carotid artery was recorded by a mercury manometer. The pulmonary vascular resistance was investigated by V. M. Khayutin's method of resistography [5-7]. Tone of the bronchial muscles was recorded by the method of Konzett and Rössler [10] as modified by T. M. Turpaev [4]. The experimental method was described more fully elsewhere [1-3].

EXPERIMENTAL RESULTS

The investigations revealed considerable variability of the responses of the pulmonary arterial pressure and tone of the pulmonary vessels to hexamethonium. This variability led to considerable scatter of the results obtained and made the assessment of statistical significance difficult. However, comparison of changes in the pulmonary arterial pressure from its initial value reveals a distinctly regular pattern. Depressor responses were observed mainly in experiments in which hexamethonium was injected against the background of a considerably increased pulmonary arterial pressure. After intravenous injection of hexamethonium in a dose of 5 mg/kg against the background of pulmonary hypertension, the pressure in the pulmonary artery fell on the average by $15 \pm 6\%$ ($P = 0.05$).

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In another series of experiments in which hexamethonium was injected in the same dose into animals with a normal or lowered pulmonary arterial pressure, its level distinctly rose, on the average by 19 ± 6% ($P = 0.05$). As a rule the pressure in the carotid artery fell considerably, on the average by 74 ± 7% ($P < 0.01$).

No statistical correlation could be found between the decrease in systemic arterial pressure and the change in level of the pulmonary arterial pressure. This could indicate relative independence of the responses of systemic and pulmonary vessels to hexamethonium.

A series of experiments to study the effect of hexamethonium (2 mg/kg) on the pulmonary vascular resistance showed that the drug lowers the tone of the pulmonary vessels by 20 ± 9% ($P = 0.05$). Frequently the response of pulmonary vascular tone to administration of hexamethonium occured in two phases: a first phase of decrease and second phase of increase in tone of the lung vessels. After administration of hexamethonium in large doses (5 mg/kg) directly into the pulmonary artery of a perfused lobe of the lung a marked increase in pulmonary vascular resistance was observed (by 31.2 ± 8.52%; $P = 0.02$).

No significant change took place in the tone of the bronchial muscles under the influence of hexamethonium.

The results of these investigations thus show that the vasodilator effect of hexamethonium on the pulmonary vessels is inconstant. The hypothesis put forward by a number of investigators, according to which the direction of the responses of pulmonary pressure to injection of hexamethonium is dependent on the initial conditions of the pulmonary circulation, is confirmed.

The results obtained agree with those reported by Werkö and co-workers [12] and Gilmore and co-workers [9], indicating that the lowering of tone of the pulmonary vessels plays a primary and dominant role in the decrease of pressure in the pulmonary artery caused by hexamethonium. However, we cannot agree with Yu and co-workers [13], who deny that the action of hexamethonium on pulmonary vascular tone plays any part in the lowering of pulmonary arterial pressure.

Our experiments further showed that the effects of hexamethonium depend on the dose of the drug administered. If injected in relatively small doses, hexamethonium most commonly produces a vasodilator effect on the pulmonary vessels. Conversely, when given in large doses, hexamethonium more regularly has a vasoconstrictor effect on the pulmonary vessels. Hexamethonium does not cause changes in the bronchial tone. This suggests that bronchomotor reactions play no part in the dynamics of pulmonary arterial pressure caused by hexamethonium.

LITERATURE CITED

1. R. M. Zaslavskaya, Farmakol. i Toksikol., No. 1, 22 (1964).
2. R. M. Zaslavskaya, Farmakol. i Toksikol., No. 2, 194 (1965).
3. R. M. Zaslavskaya, Pat. Fiziol., No. 4, 69 (1965).
4. T. M. Turpaev, Fiziol. Zh. SSSR, No. 6, 732 (1953).
5. V. M. Khayutin, Fiziol. Zh. SSSR, No. 7, 643 (1958).
6. V. M. Khayutin, Fiziol. Zh. SSSR, No. 4, 440 (1959).
7. V. M. Khayutin, in: Physiology and Pathology of the Circulation and Respiration [in Russian], Moscow (1960), p. 55.
8. M. H. Ellestad and W. H. Olson, J. Am. Med. Assn., 161, 49 (1956).
9. H. K. Gilmore, et al., Lancet, 2, 898 (1952).
10. H. Konzett and R. Rössler, Arch. Exp. Path. Pharmak., 195, 71 (1940).
11. B. Malamos, S. Moulopoulos, D. Dimakis, et al., Z. Kreisl.-Forsch., 46, 681 (1957).
12. L. Werkö et al., Lancet, 2, 470 (1951).
13. P. N. Yu et al., J. Clin. Invest., 37, 194 (1958).