ACTION OF OCTADINE, ORNIDE, AND DIHYDROERGOTOXIN ON THE CIRCULATION IN THE HEART

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The dynamics of the coronary blood flow after administration of octadine (1 mg/kg), ornide (5 mg/kg), and dihydroergotoxin (0.2 and 1 mg/kg) repeated the character of changes in the systemic arterial pressure. In experiments with stabilization of the arterial pressure and perfusion of the isolated cat's heart, octadine had no unfavorable action on the tone of the coronary vessels, ornide had a coronary dilator action, while dihydroergotoxin produced slight constriction of the coronary vessels.

The effect of octadine (1 mg/kg), ornide (5 mg/kg), and dihydroergotoxin (0.2 and 1 mg/kg) on the coronary ciculation was investigated in acute experiments on 50 cats, in which the blood flowing from the coronary sinus [4] was recorded by means of pump-flowmeter [2]. To determine the role of hemodynamic changes in the changes of the coronary blood flow and the role of the myotropic component in the action of these compounds on the coronary vessels, experiments were carried out with stabilization of the systemic arterial pressure and perfusion of the isolated heart of 28 cats (61 perfusions). In this case octadine and ornide were given in dilutions of 10^{-5} and $2.5 \cdot 10^{-5}$, and dihydroergotoxin in dilutions of 10^{-6} and $2.5 \cdot 10^{-6}$.

The dependence of the coronary blood flow on changes in arterial pressure was assessed by means of the coefficient K: the ratio between these values expressed as percentages of the initial level.

All drugs were injected intravenously and observations were continued for 60 min.

EXPERIMENTAL RESULTS

The compounds tested produced changes in the coronary blood flow which took place synchronously and were parallel with changes in the arterial pressure. In the initial sympathomimetic phase of action of octadine [12], ornide [9, 10], and dihydroergotoxin [1], lasting for 15-25 min, the outflow of blood from the sinus venosus increased to a maximum: by 92.1 ± 11.5 ($P < 0.001$), 146.4 ± 11.5 ($P < 0.001$), and $42.1 \pm 13.8\%$ ($P < 0.05$) respectively. With the development of the hypotensive effect, the coronary blood flow decreased. After injection of octadine the greatest decrease in the coronary blood flow was $30.3 \pm 3.3\%$ ($P < 0.01$), of ornide $29.9 \pm 4.2\%$ ($P < 0.001$), and of dihydroergotoxin $49.8 \pm 4.0\%$ ($P < 0.001$) respectively.

After injection of octadine and ornide, the outflow of blood from the sinus venosus in the phase of hypertension was increased to a greater degree than the arterial pressure was raised (this is shown by the high values of the coefficient K: 1.2 and 1.5 respectively), whereas after injection of dihydroergotoxin the volume velocity of the coronary blood flow was increased by a lesser degree than the systemic arterial pressure rose (coefficient $K = 0.6$).

The dynamics of the coronary blood flow in the phase of hypotension was similar in all experiments and was characterized by more marked negative changes in the velocity of the blood flow compared with the level of the arterial pressure, as is clearly illustrated by the values of the coefficients K during maximal changes in venous outflow: in the experiments with octadine 0.84, with ornide 0.85, and with dihydroergotoxin 0.89.

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In experiments with stabilization of the arterial pressure, octadine lowered the velocity of the coronary venous outflow from 16.2 ± 3.3% ($P < 0.01$) after 5 min to 23.7 ± 5.1% ($P < 0.01$) after 60 min. Injection of ornide after stabilization of the systemic arterial pressure led to an increase in the outflow of blood from the coronary sinus during all 60 min of observation (maximum after 50 min, by 61.4 ± 9.2%; $P < 0.01$). Dihydroergotoxin (0.2 mg/kg), under the same experimental conditions, reduced the volume velocity of the coronary blood flow from 8.3 ± 2.8% ($P < 0.05$) after 2 min to 18.8 ± 3% ($P < 0.01$) after 60 min.

The decrease in the velocity of the coronary blood flow after injection of octadine, when the arterial pressure was stabilized, is probably associated with the abolition of metabolic [3, 4, 6, 11, 13] dilator effects and dilator effects of the sympathetic nervous system mediated through β-adrenergic receptors of the coronary vessels [5], on the coronary circulation. In fact, this effect cannot be associated with any direct vasoconstrictor action of octadine on the coronary vessels, for in experiments on the isolated heart no negative changes in the dynamics of the general coronary flow were observed.

The increase in volume velocity of the coronary circulation detected in experiments with a stabilized arterial pressure after injection of ornide and the increase in outflow of perfusion fluid in experiments on the isolated heart (maximum by 18.5 ± 12.1%; $P < 0.05$) suggest that ornide has a vasodilator action on the coronary vessels.

The decrease in the velocity of the venous outflow after injection of dihydroergotoxin, the arterial pressure being stabilized, indicates a vasoconstrictor action of this compound on the coronary circulation. However, the possibility is not ruled out that this effect of dihydroergotoxin is produced through a decrease in the intensity of metabolism in the myocardium [7] and by blocking of the β-adrenergic receptors of the coronary vessels [14]. This conclusion is supported by the results of experiments on the isolated heart. Changes in the total outflow of perfusion fluid in these experiments were only just outside the limits of spontaneous variations in outflow associated with the duration of perfusion.

It can be concluded from the facts described above that the decrease in volume velocity of the coronary blood flow observed in the period of hypotensive action of octadine and ornide is due primarily to the level of the arterial pressure. Remembering that drugs of the octadine type reduce the energy metabolism of the ventricles and the oxygen demand of the heart [8], it may be supposed that octadine and ornide have no negative effect on the blood supply to the myocardium in the absence of severe arterial hypotension; this is particularly true of ornide, which has a direct vasodilator action on the coronary vessels. The results of electrocardiographic investigations indirectly confirm this conclusion.

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