THE EFFECT OF ANALGESICS ON THE REFLEX REACTIONS OF THE CORONARY VESSELS

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One of the most important tasks of research on problems of the therapy of coronary insufficiency is to find pharmacological substances which can be used to influence the reflex reactions which bring about constriction of the cardiac vessels. These reactions are known to play a significant role in the development of angina pectoris attacks. In this connection, the mechanism of the effect of analgesic substances, which have been clinically observed to stop angina pectoris attacks, on the coronary circulation is an interesting question.

Our earlier investigations [2] showed that of the analgesic substances, morphine, thecodine [hydroxy-codeine hydrochloride], promedole [4-phenyl-4-propoxy-1,2,5-trimethyl-piperidine hydrochloride] and phenadone [Methadon], morphine alone has the property of dilating the cardiac vessels; the other analgesics, on the contrary, somewhat increase the tonus of the coronary vessels. One can therefore assume that the clinical efficacy of these agents is not due to their direct effect on the cardiac vessels.

The purpose of this investigation was to study the effect of analgesic substances on the reflex reactions of the coronary vessels in response to stimulation of the carotid sinus receptors and the afferent nerves.

There have been a series of investigations concerned with the question of how analgesic substances affect autonomic reflexes, but the results of these investigations are extremely inconsistent.

For example, Vercauteren [8], who investigated the effect of morphine on the reflex changes of the blood pressure in response to stimulation of the carotid sinus receptors, concluded that morphine, even in small doses, can inhibit these reflexes. According to Z. N. Ivanova's observations [1], promedole inhibits the cardiovascular and respiratory reactions elicited by stimulation of the lower respiratory tract. M. Yu. Ladinskaya [5] also observed analgesics to induce inhibition of the blood pressure reflexes which develop with pressure on a coronary artery.

Other researchers who studied the effect of analgesics on vascular reflexes, however, have concluded the exact opposite. For example, Vandenlinden [7] observed intensification of the blood pressure reflexes in response to stimulation of the carotid sinus receptors to occur under the influence of morphine. R. P. Kruglikova-L'vova [4] concluded that morphine and promedole increase the reflexes on the blood pressure induced by stimulation of the bladder interceptors. G. V. Kovalev [3] reached a similar conclusion after studying the effect of analgesics on vascular reactions induced by stimulation of interceptors.

From the brief review of the literary data given above, it is evident that the research which has been carried out on the effect of analgesic substances on autonomic reflexes is not systematic in nature and has obtained only contradictory results. No specific investigation has been made of the effect of these agents on the reflex reactions of the coronary vessels. This is, however, a question of great clinical, as well as theoretical, importance.
**METHODS**

The experiments were conducted on cats anesthetized with arethan and chloralose. The method of resistography was used to determine the effect of pharmacological substances on the reflex reactions of the heart. This method, proposed by V. M. Khayutin [6], is based on the principle of artificial stabilization of the blood flow in the vessels and uses a special pump to perfuse the vessels with the animals' own blood. A detailed description of this method and a diagram showing the experimental plan can be found in an earlier article of ours [2].

A catheter was introduced into the mouth of the left coronary or circumflex artery; blood from the carotid artery entered this catheter in a volume which was constant per unit of time. Under these conditions, the pressure recorded at the pump outlet reflects changes in vascular resistance, rising with constriction and falling with dilatation of the vessels. The advantage of this method is that it makes it possible to estimate changes in the tonus of the cardiac vessels independently of the changes in systemic arterial pressure which occur in the organism. In connection with the study of the reflex reactions of the coronary vessels, this is of particular value, because the reflex changes in the blood pressure developing in response to stimulation of the afferent system can mask the true condition of the tonus of these vessels when the estimations are based on measurement of the blood flow in the vessels of the heart.

The blood pressure was recorded in the femoral artery with a mercury manometer. Heparin (800-1000 units/kg intravenously) was used to prevent blood coagulation.

Reflexes on the cardiac vessels were induced by stimulating the carotid sinus receptors (pressure on the carotid artery) and the afferent fibers of the tibial and medial nerves. This stimulation was effected by square-wave pulses with a frequency of 50-60 hertz and a voltage of 5-15 volts.

**RESULTS**

The experiments conducted demonstrated that analgetics, in relatively small doses, can inhibit the reflexes of the cardiac vessels. For example, morphine in doses of 1-2 mg/kg decreased the reflexes an average of...