THE INFLUENCE OF SOME DERIVATIVES OF THE PHENOTHIAZINE GROUP ON REFLEXES FROM THE HEART

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A number of investigators have established that certain derivatives of the phenothiazine group possess the ability to dilate coronary blood vessels [1,5]. Moreover, it is known that neuroplegic compounds have found application in cardiac surgery. In connection with this it appeared interesting to investigate the influence of phenothiazine derivatives on reflex reactions arising on constriction of coronary vessels. Two preparations were selected for this investigation, viz. aminazine* and mepazine **.

EXPERIMENTAL METHODS

Experiments were performed on cats under urethane anesthesia and on decerebrate cats. The effect of mepazine and aminazine on reflex changes in blood pressure and respiration upon clamping of the descending branch of the left coronary artery was studied. When the vessel was completely compressed for 10 seconds acute ischemia of the corresponding area of the myocardium occurred and was accompanied by reflex changes in blood pressure and respiration. In a series of short-term experiments and one of prolonged experiments the electrocardiographic changes associated with these phenomena were recorded; these changes were characteristic of impaired coronary circulation. The preparations being tested were given intravenously in the short-term experiments and intraperitoneally in the prolonged ones. A more detailed description of the experimental methods has already been published in an earlier communication [4].

EXPERIMENTAL RESULTS

The experiments showed that compression of the coronary artery is associated with the appearance of reflexes affecting blood pressure and respiration. In the majority of the experiments the reflexes from the heart were depressor in character (95-97%) and only in some cases were these reflexes pressor (3-5%). Reflexes affecting respiration led to increased depth and frequency of respiratory movements.

The investigation showed that aminazine in doses of 0.1-0.5 mg/kg depressed the reflexes from the heart on blood pressure by 50-67% over 7-25 minutes. When the doses are increased to 1-2 mg/kg the vascular reflexes are depressed by 70-80% for 30-40 minutes (Fig. 1, I). The maximum effect following intravenous

* Transliteration of Russian – Publisher’s note.

** Mepazine (N-methyl-piperidyl-3-methylphenothiazine) corresponds in its chemical structure to pacatal**; it was synthesized at the Chemistry Department of the Institute of Pharmacology and Chemotherapy, AMN SSSR, by S. V. Zhuravlev, A. N. Gritsenko and M. L. Dorokhova. Yu.L Vikhlyaev has carried out a detailed pharmacologic investigation of mepazine [2].
administration of aminazine occurs after 4-7 minutes. These data were obtained in experiments on anesthetized and decerebrate animals.

In a number of experiments aminazine altered the character of the reflexes, transforming them from depressor into pressor ones.

Injection of aminazine also diminishes the reflexes affecting respiration. The experiments also showed that aminazine diminished slightly the electrocardiogram changes arising upon impairment of coronary circulation. The electrocardiogram changes associated with impaired blood supply to the heart usually consist of the following features: a sharp increase in the T-wave, inversion of the ventricular QRS complex, deviation of the ST interval from the isoelectric line, disturbance of rhythm (Fig. 1, II). Such electrocardiographic changes, arising on compression of the coronary artery, are not abolished but only somewhat diminished by intraperitoneal injection of 1 mg/kg aminazine. The effect lasts for 25-30 minutes.

It must be noted that aminazine possesses, in addition to its depressing effect on reflexes from the heart, marked hypotensive properties. In connection with this it seemed essential to find out the relationship between changes in reflexes from the heart and the level of blood pressure. Artificial lowering of blood pressure was achieved in 2 ways: 1) acute blood-letting and 2) intravenous injection of 1-2 mg/kg papaverine*.

![Fig. 1. Effect of aminazine on reflexes from the heart. Cat weighing 2.5 kg. Decerebrate.](image)

I) Change in reflexes affecting blood pressure under the influence of aminazine: a) background; b) 10 minutes after intravenous injection of 2 mg/kg aminazine; c) 31 and 34 minutes after injection of aminazine. Records (from above down): blood pressure, stimulus mark, time marker (5 seconds).

II) Changes in the electrocardiogram on clamping the descending branch of the left coronary artery: a) normal cat electrocardiogram; b) electrocardiogram with the coronary artery clamped; c) electrocardiogram 10 minutes after intravenous injection of aminazine 1 mg/kg; d) electrocardiogram 30 minutes after injection of aminazine.

It was established on the basis of these experiments that as the blood pressure decreased, the reflexes from the heart showed some diminution. When the blood pressure is lowered by 10 mm Hg the reflexes from the heart decrease by 10-20% (the variability of the changes is connected with the initial absolute magnitude of the reflex). Following injection of aminazine under conditions of lowered blood pressure to a similar level, the vascular reflexes diminish by 50-60%. These data permit the conclusion that aminazine possesses a marked ability to inhibit reflexes from the heart.

* Control experiments showed that papaverine did not depress the reflexes from the heart.