EFFECT OF IPRAZID ON EXPERIMENTAL MYOCARDIAL INFARCTION

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Iprazid (iproniazid), in a dose of 2 mg/kg, improves the course and outcome of myocardial infarction produced in dogs by ligation of the anterior branch of the left coronary artery, and also stimulates oxidative phosphorylation in the mitochondria of the intact and, in particular, the ischemic myocardium of rabbits.

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The effect of iprazid (iproniazid), a monoamide oxidase inhibitor, on the functional state of the heart and the course of experimental myocardial infarction, produced in dogs and rabbits by ligation of the descending branch of the left coronary artery, was studied.

EXPERIMENTAL METHOD

The dynamics of the ECG and histological changes were investigated. Sections of the heart were stained with hematoxylin-eosin, by Van Gieson's method alone and with fuchselin, and with Heidenhain's iron-hematoxylin. The region and character of the lesion were determined in histotopography sections prepared by Kristeller's method and stained by Van Gieson's method. The intensity of oxidative phosphorylation in the mitochondria of the myocardium isolated from ischemic and intact regions was studied in rabbits.

EXPERIMENTAL RESULTS

Immediately after ligation of the coronary artery in control dogs a monophasic curve appeared in the epicardial ECG, and a sharp rise of the S-T segment took place in lead I and, in particular, in leads V_2-V_6. During repeated observations for 1-2 days, a QRS complex of the QS type appeared in these leads in 5 of the 7 control dogs. Subsequently the ECG usually showed no significant change, but in some cases a slight depression of the S-T segment took place, and the T wave became negative and symmetrical. In the dogs receiving iprazid (2 mg/kg daily for one week), a picture of acute coronary failure developed in most experiments after ligation of the coronary artery—a sharp rise of the S-T segment in most leads. However, the subsequent course of the ECG changes in this group of dogs differed significantly from the dynamics of the ECG in the control animals. As a rule the signs of acute coronary failure gradually subsided and the normal ECG was restored within about one week.

In the control dogs, the myocardial lesion became obvious by the end of the first day, was diffuse in character or consisted of a number of large foci, and was accompanied by marked edema, hemorrhages, and leukocytic infiltration of the greater part of the anterolateral wall of the left ventricle and part of the septum, by the development of a leukocytic barrier around the zone of necrosis, and by aneurysm formation. It terminated by scar formation 3-4 weeks after the operation. Against the background of administration of iprazid, significant changes in the myocardium were not observed until 2-3 days after ligation of the coronary artery. The region of the spread was somewhat smaller, and the lesions were not complicated by hemorrhages into the myocardium and were not diffuse in character, but took the form of focal degeneration of muscle fibers with moderate leukocytic infiltration. After 2-3 weeks healing of the infarct was practically complete, in most cases without aneurysm formation.

Daily administration of iprazid to the rabbits stimulated oxygen consumption and fixation of inorganic phosphorus by mitochondria from nonischemic and, in particular, ischemic areas. Ability to esterify in-

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organic phosphorus showed particularly marked changes: the oxygen consumption by the tissue mitochondria from the ischemic part of the myocardium increased by 66% ($P < 0.01$), fixation of inorganic phosphorus by 261%, ($P < 0.001$), and the P/O ratio was doubled ($P < 0.02$).

Hence, although iprazid does not prevent the formation of an infarct, it increases the functional capacity of the heart and considerably reduces the severity of morphological changes in the myocardium and facilitates the more rapid healing of the infarct.