CHANGES IN PRESSOR AND DEPRESSOR RESPONSES AFTER PARTIAL PANCREATECTOMY

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The course of pressor and depressor responses was studied during normal activity of the animal and after partial resection of the body and tail of the pancreas in experiments on 39 sexually mature mongrel dogs. The principal indices characterizing changes in the pressor response to noradrenalin and the depressor response to bradykinin and kallikrein were determined before and 10-12 days after resection of the pancreas. Removal of the body and tail of the pancreas was shown to potentiate pressor responses to noradrenalin and depressor responses to bradykinin and kallikrein; the initial negative chronotropic effect of catecholamines on the heart was strenghtened; the positive chronotropic effects of noradrenalin, bradykinin, and kallikrein on the heart also were strengthened.

KEY WORDS: pancreatectomy; pressor and depressor responses.

Besides its widely known insulin-forming function, the pancreas also possesses a different type of endocrine activity which is interesting in connection with its effect on cardiovascular function [2, 5, 7, 8]. The secretory cells of the pancreas are known to take up highly active biogenic monoamines — serotonin, dopamine and, to a lesser degree, noradrenalin — from the blood and to store them [11, 14]; the pancreas is also known to produce many proteolytic enzymes, including kininogenases: These include kallikrein and trypsin, secreted in the active form. Their biological activity is extremely high, for by interacting with high- and low-molecular-weight kininogens, the pancreatic kallikreins form kallidin whereas trypsin participates in the formation of bradykinin [10, 12, 15].

The production of internal secretions predominantly by β-cells necessitates the study of functional activity mainly of the body and tail of the pancreas, where most of these cells are located.

EXPERIMENTAL METHOD

In experiments on 39 sexually mature mongrel dogs the course of pressor and depressor responses was studied under normal conditions and after partial resection of the body and tail of the pancreas. Certain indices characterizing changes in the pressor response to noradrenalin and the depressor response to bradykinin and kallikrein were determined before and 10-12 days after partial pancreatectomy. Both pressor and depressor substances were injected into the femoral vein in equal volumes and at equal speeds, in the following doses: noradrenalin 0.01 kg/mg, bradykinin 0.05 mg/kg, kallikrein 0.8 kallikrein unit/kg. All experiments were accompanied by controls on dogs undergoing a mock operation.

The course of the vascular response was characterized by the latent period, the degree of maximal changes in the arterial and venous pressure, the maximal rate of change of pressure in the initial phase of the response, the duration of the action, and the presence and character of any after-effect; the cardiac action of the pressor agent was assessed with regard to changes in the cardiac frequency, the state of nutrition of the myocardium, and the presence, type, and duration of arrhythmia.

The numerical results were subjected to statistical analysis by the indirect difference method, using a constant formula [6].

EXPERIMENTAL RESULTS AND DISCUSSION

Control experiments showed that injection of noradrenalin caused a marked increase in the systolic,

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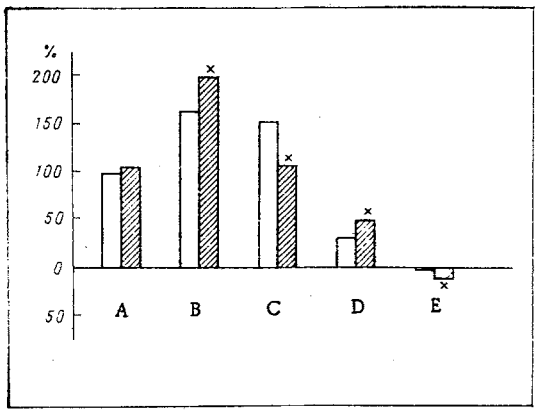

Fig. 1.

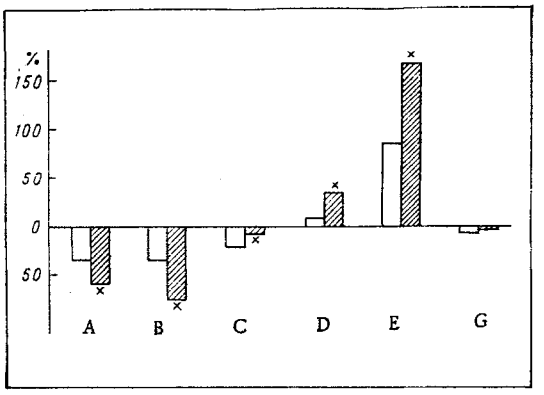

Fig. 2.

Fig. 1. Changes in sensitivity of cardiovascular system to noradrenalin in control and pancreatectomized dogs (in % of initial value). Abscissa: A) maximal rise of systolic pressure, B) maximal rise of diastolic pressure, C) maximal change in venous pressure, D) positive chronotropic response, E) negative chronotropic response. Ordinate: percentages. Unshaded columns represent control animals, shaded columns pancreatectomized dogs. Values differing significantly from corresponding control values marked by cross.

Fig. 2. Changes in sensitivity of cardiovascular system to bradykinin in control and pancreatectomized dogs (in % of initial value). Abscissa: A) Maximal decrease in systolic pressure, B) maximal decrease in diastolic pressure, C) maximal decrease in venous pressure, D) maximal increase in venous pressure, E) positive chronotropic reaction, G) negative chronotropic reaction. Remainder of legend as in Fig. 1.

diastolic, and venous pressure, an initially negative and subsequently positive chronotropic reaction, and in some cases disturbances of pacemaker, the appearance of a varied degree of atrioventricular block, extrasystoles (single ventricular), signs of impairment of myocardial nutrition in the form of a decrease in voltage of the T_{II-III} wave, sometimes a transient biphasic nature of that wave, and lowering of the S—T interval. Injection of bradykinin or kallikrein caused a significant decrease in the systolic and diastolic pressure, biphasic changes in venous pressure (an initial fall and subsequent rise), and an initial brief negative and subsequent prolonged positive chronotropic response.

The results of investigation of the dogs after resection of the body and tail of the pancreas showed that the operation caused no significant changes in the parameters studied; meanwhile, the results of loading tests on these animals were significantly changed: The direction of the changes in many indices was the same, moreover, after injection of pressor and depressor agents. After injection of noradrenalin (Fig. 1), and also of bradykinin (Fig. 2), and kallikrein (Fig. 3) the response of the systolic and diastolic pressure was strengthened, the duration of the vascular effects and the intensity and duration of the positive chronotropic reaction were increased; the latent period of the vascular reaction to these substances also was consistently reduced.

Changes in the other indices were somewhat different: The degree of change of the venous pressure after injection of noradrenalin was less in the pancreatectomized than in the normal control dogs. After injection of depressor substances, just as in the control, the venous pressure gave a biphasic response: an initial decrease in pressure followed by an increase; after pancreatectomy phase I of the change in venous pressure was reduced but phase II was increased. The negative chronotropic action of the depressor agents was weakened whereas that of noradrenalin was strengthened. Cases of disturbance of the cardiac rhythm after injection of noradrenalin into the pancreatectomized dogs were found more frequently and were more marked. Meanwhile, in the pancreatectomized dogs the maximal rate of change of pressure after injection of the depressor polypeptides was virtually unchanged, but after injection of noradrenalin it was considerably reduced. The uniform direction of the changes in most of the parameters studied in pancreatectomized dogs can be explained by functional connections between adrenergic and kininergic structures of the cardiovascular system [3,4,9,13]. Differences found in the direction of the changes in individual indices are perhaps linked with differences in biochemical conversions of catecholamines and peptides in the pancreatectomized animals, the special character of their interaction with structures of the cardiovascular system in these animals, and the degree of participation of other neurohumoral control mechanisms after pancreatectomy, and so on.

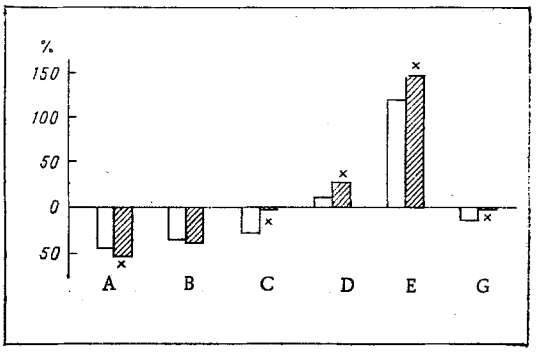

Fig. 3. Changes in sensitivity of cardiovascular system to kallikrein in control and pancreatectomized dogs (in % of initial value). Legend as in Fig. 2.

Removal of the body and tail of the pancreas deprives the animal of its monoamine depot and its depot of trypsin and tissue kallikrein; consequently, the reserves of these biogenic amines and peptides are reduced. It can be postulated that, besides other biochemical and physiological disturbances, resection of the body and tail of the pancreas leads to an adaptive lowering of the threshold of sensitivity of the adrenergic and kininergic structures to exogenous substances [1]. Accordingly, exogenous vasoactive substances injected into pancreatectomized dogs cause a more intensive and more prolonged cardiovascular response than in the control.

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