MECHANISM OF ACTION OF INSULIN

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UDC 615.361.37-015

Many workers consider that the effect of insulin on carbohydrate metabolism takes place by the humoral route directly in the organs and tissues [5, 18, 20], while others [4, 19] consider that insulin acts by a central reflex mechanism. This last view is maintained by workers who have obtained conditioned-reflex hypoglycemia to an "empty needle" [2, 14-17].

However, in some cases a conditioned-reflex hypoglycemia could not be obtained [11, 13]. In S. V. Zakharov's opinion [11], the level of the blood sugar may be regulated by the passage of impulses to subcortical centers in which the reflex arc is closed.

S. G. Genes [6, 7] considers that in ordinary conditions insulin influences carbohydrate metabolism through the participation of the central nervous system, but its action is completely preserved even after severe inhibition of the central nervous system and of the vascular interoceptors.

Data are presented in this paper showing that after resection of the stomach under local anesthesia, combined with moderate neuroplegia, the hypoglycemic effect of insulin disappears.

EXPERIMENTAL METHOD

A state of moderate neuroplegia was induced by intramuscular injection of a lytic mixture of the following composition: 2.5% chlorpromazine 1.5-2 ml, 2% trimeperidine 2 ml, 0.5% phenethazine 3 ml, and 0.05% scopolamine 1 ml.

The blood sugar concentration was investigated on the morning of the day of operation, and again 1 h after administration of the mixture. Subsequently, investigations were carried out every hour during the operation and on the second day after its end. At the end of the operation, after the last blood sample had been taken for investigation, all the patients received an intravenous injection of 20-40 ml of 40% glucose solution.

In consideration of the sharp rise of the blood sugar level in the first 2 h of the operation, insulin was injected during induction of local anesthesia or during the first hour of the operation, i.e., at the height of increase of the operation hyperglycemia. Usually the time from injection of the lytic mixture to injection of insulin was 1.0-1.5 h. By this time all patients showed marked signs of moderate neuroplegia. Initially insulin was injected in a dose of 10-12 units. Later, because this dose did not give the desired effect, it was increased to 16-20 units.

The effect of insulin on the blood sugar concentration after development of neuroplegia was studied in 24 patients (18 men and 6 women) aged from 21 to 70 years. The operation was performed on 15 patients for gastric and duodenal ulcer, on 4 for carcinoma of the stomach, on 1 for polyposis, and on 4 for post-operative conditions of the stomach. Two-thirds of the stomach was resected by the Finsterer technique, or resection of this proportion of the stomach combined with gastrojejunostomy was performed on 15 patients, total and subtotal gastrectomy on 5 patients, and repeated operation on the stomach on 4 patients.

EXPERIMENTAL RESULTS

The blood sugar concentration before the operation was 81 ± 20.2 mg%. Despite injection of insulin against the background of neuroplegia, 1 h after injection of the lytic mixture the blood sugar rose to 105 ± 16.8 mg%, and 1 h after the operation began its level was 126 ± 19.4 mg%, rising after 2 h to 128 ± 20.2 mg% and after 3 h to 132 ± 26.9 mg% ($P < 0.01$). On the second day after operation the blood sugar

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Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 64, No. 12, pp. 36-37, December, 1967. Original article submitted December 30, 1965.

level fell to 104 ± 18.7 mg%. Consequently, when administered against the background of neuroplegia, insulin neither lowered the blood sugar concentration nor prevented hyperglycemia associated with operative trauma.

It was subsequently decided to inject insulin before the development of neuroplegia, i.e., 3-5 min before injection of the lytic mixture. These investigations were carried out on 26 patients aged from 27 to 72 years. In relation to number of patients, type of disease, extent of operative procedures, and dose of insulin injected, this group was essentially indistinguishable from the preceding group. Whereas the mean blood sugar before the operation was 89 ± 19.9 mg%, after injection of the lytic mixture it was 90 ± 16.5 mg%, 1 h after the beginning of the operation it was 96 ± 16.5 mg%, 2 h after operation 102 ± 14.4 mg%, and 3 h after—100 ± 18.5 mg% ($P > 0.05$). On the second day after operation the blood sugar level exceeded its initial value by 13 mg%.

Hence, despite injection of insulin (before the development of neuroplegia), the blood sugar level did not fall. However, the hyperglycemia usually developing as a result of operative trauma did not appear. Administration of ganglion-blocking agents without neuroplegics has been found [8, 9] to potentiate the hypoglycemic action of insulin.

It may be assumed that administration of insulin against the background of marked neuroplegia does not have a hypoglycemic effect because of the development of inhibition of the reticular formation of the brain under the influence of chlorpromazine [1, 10]. If, however, insulin is given before premedication, i.e., before the functional integrity of the reflex arc has been disturbed, it prevents the development of hyperglycemia in the subsequent stages of the operation.

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