EFFECT OF BILATERAL SUBDIAPHRAGMATIC VAGOTOMY ON THE ACTIVITY OF SOME ENZYMES OF ENERGY METABOLISM IN THE LIVER

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Bilateral subdiaphragmatic vagotomy leads to a marked decrease in hexokinase, glucokinase, glucose-6-phosphate dehydrogenase, 6-phosphogluconate dehydrogenase, and lactate dehydrogenase activity in the soluble fraction of rat liver. The blood sugar level was unchanged at all times after the operation. These changes in enzyme activity evidently take place on account of the absence of parasympathetic impulses to the liver cell.

KEY WORDS: vagotomy; liver; enzymes.

After blocking of the parasympathetic innervation degenerative and necrotic changes arise in the organs and the parenchymatous elements are reduced and replaced by connective tissue [3]; in other words, both the structural organization of the cell and its differentiation are under the regulatory influence of the parasympathetic nervous system. The trophic influence of the nervous system is effected through regulation of the activity and synthesis of important metabolic enzymes [1]. Partial desympathization of the liver leads to sharp changes in the activity of its key enzymes of glycolysis and the pentose phosphate pathway. The parasympathomimetic drug carbachol produces different changes in the glucokinase and phosphoenolypyruvate carboxykinase activity in the liver [8].

The object of the present investigation was to study the effect of bilateral subdiaphragmatic vagotomy on hexokinase (HK), glucokinase (GK), glucose-6-phosphate dehydrogenase (G6PD), 6-phosphogluconate dehydrogenase (6-PGD), and lactate dehydrogenase (LD) activity in the soluble fraction of rat liver.

EXPERIMENTAL METHOD

Sexually mature male rats weighing 180-200 g were used. Subdiaphragmatic division of the vagus nerve trunks was carried out under pentobarbital anesthesia (5 mg/100 g body weight). Animals undergoing a mock operation acted as the control. The rats were used in the experiments 43 h and 3, 7, and 21 days after the operation. A liver homogenate was prepared (in four volumes of 0.25 M sucrose) and the activity of the enzymes was determined spectrophotometrically [5, 9] in the supernatant (20,000g, 30 min). Activity of HK, GK, and the dehydrogenases was expressed in μmoles NADP/mg protein reduced during incubation for 1 h. LD activity was expressed in μmoles NAD/mg protein oxidized in 1 min. The protein concentration was determined spectrophotometrically at 310 nm [6]. The blood sugar was estimated by the Hagedorn–Jensen method.

EXPERIMENTAL RESULTS AND DISCUSSION

As Fig. 1 shows, 43 h after bilateral subdiaphragmatic vagotomy the HK, G6PD, and GK activity in the soluble fraction of rat liver was unchanged but the LD activity was reduced by 20%. Activity of all the enzymes tested was reduced after 3 days. The greatest decrease in the activity of the liver enzymes was found after 7 days. Three weeks after the operation the decrease (except LD activity) was no longer so marked. The blood sugar level of the vagotomized rats was unchanged.

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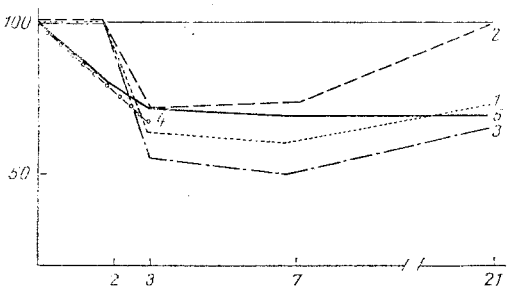

Fig. 1. Changes in enzyme activity of soluble fraction of rat liver after bilateral subdiaphragmatic vagotomy. Abscissa, days after operation; ordinate, deviation of enzyme activity from control, taken as 100%. 1) Hexokinase; 2) glucokinase; 3) glucose-6-phosphate dehydrogenase; 4) 6-phosphogluconate dehydrogenase; 5) lactate dehydrogenase.

The observed decrease in HK, GK, and LD activity in the soluble fraction of the liver after vagotomy is in agreement with the view that glycolysis in the liver is activated by the parasympathetic nervous system [8]. Vagus stimulation leads to an increase in the secretion of insulin, whereas vagotomy causes a transient decrease in the insulin concentration in the peripheral blood [4]. Since insulin induces the synthesis of the key enzymes of glycolysis and the pentose phosphate pathway [2], the observed decrease in enzyme activity could be due to insulin insufficiency. However, the normal level of the blood sugar of the vagotomized animals indicates that any decrease in the secretion of insulin in these experiments was evidently ill-defined and clearly insufficient to produce such a sharp decrease in enzyme activity. There is also immunohistochemical evidence that the insulin content in the β cells is not reduced 7-14 days after subdiaphragmatic vagotomy [7]. A more important role is probably played by the absence of the parasympathetic innervation of the liver cell itself. Activity of the liver enzymes after vagotomy is changed in the opposite way to that observed after partial desympathization of the liver.

These results showing a change in the rate of glycolysis and of the pentose phosphate metabolic pathway in the liver under the influence of bilateral subdiphragmatic vagotomy may help to explain the causes of the disturbance of liver function observed in patients after vagotomy.

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