EFFECT OF HYDROCORTISONE AND ACUTE HYPOXIA ON GLUCONEOGENESIS IN THE RAT LIVER

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Acute hypoxic hypoxia leads to increased glucose formation by rat liver slices from pyruvate, α-glycerophosphate, α-ketoglutarate, and fructose. During exposure to hypoxia after prolonged administration of hydrocortisone acetate, increasing gluconeogenesis from the above-mentioned substances and also from alanine, lactate, and glycerol, the rate of glucose synthesis in liver slices was higher than in the control but lower than after the action of hydrocortisone alone.

KEY WORDS: hypoxia; hydrocortisone; rat liver; glucose formation; glycogen.

The effect of hydrocortisone on the rate of gluconeogenesis by liver slices from rats was studied under normal conditions and during acute hypoxia.

EXPERIMENTAL

Albino rats weighing 160-200 g, previously deprived of food for 18 h in order to reduce the quantity of preformed glycogen in the liver, were used. Hypoxic conditions were created in a pressure chamber ("altitude" 10,000 m above sea level) for 3 h. Hydrocortisone acetate (Richter, Hungary) was injected twice a day in a dose of 2.5 mg/100 g for 4 days. The rate of gluconeogenesis was determined by Krebs' method [4].

Four groups of animals (8-10 rats in each group) were investigated: 1) control rats, 2) rats kept in a pressure chamber, 3) rats receiving hydrocortisone, 4) rats exposed to hypoxia after preliminary administration of the hormone.

RESULTS

The investigation showed (Table 1) that during incubation of liver slices from "hypoxic" rats, glucose formation was increased from α-ketoglutarate, α-glycerophosphate, pyruvate, and fructose, in agreement with the increased glucose formation observed by the writers previously in the renal cortex of rats in acute hypoxia [3]. With a low initial glycogen content in the liver of the fasting rats the accumulation of glucose in the incubated slices was due to an increase in the intensity of gluconeogenesis rather than to the more rapid glucose formation from glycogen [1, 5].

Prolonged administration of hydrocortisone to the rats, inducing the synthesis of the key enzymes of gluconeogenesis [2, 6], led to a marked increase (by more than 20 times) in the carbohydrate reserve of the rats' livers, despite the short period of starvation, both on account of free glucose and as a result of increased deposition of glycogen (809.6 ± 121.7 and 2626.2 ± 312.2 mg%, respectively). Under the influence of the hormone the rate of gluconeogenesis both from endogenous precursors of carbohydrates and from all the substrates used, rose sharply in the liver slices. Not only glucose but also glycogen accumulated in the incubated slices.

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TABLE 1. Glucose Formation by Rat Liver Slices after Injection of Hydrocortisone under Normal and Hypoxic Conditions (M ± m)

Substrate	Glucose content (in μmoles/10 mg protein/h)			
	Control	hipoxia	hydrocortisone	hydrocortisone+ hypoxia
—	0,36±0,03	0,40±0,02	1,22±0,13 (2,66±0,37)	0,63±0,06
P			<0,001	<0,01
Alanine	0,69±0,04	0,74±0,03	2,46±0,37 (4,45±0,59)	1,07±0,04
P			<0,001	<0,001
Lactate	0,65±0,07	0,77±0,04	2,69±0,36 (4,75±0,64)	1,00±0,06
P			<0,001	<0,01
Pyruvate	0,70±0,05	0,86±0,04	2,42±0,32 (4,58±0,51)	1,09±0,05
P		<0,05	<0,001	<0,001
α-Glycerophosphate	0,58±0,04	0,73±0,04	2,36±0,40 (4,43±0,61)	1,09±0,06
P		<0,05	<0,001	<0,001
Glycerol	0,77±0,07	0,94±0,07	2,84±0,31 (5,24±0,46)	1,30±0,05
			<0,001	<0,001
α-Ketoglutarate	0,56±0,05	0,70±0,03	3,19±0,37 (5,13±0,41)	1,16±0,11
P		<0,05	<0,001	<0,001
Fructose	1,28±0,12	1,67±0,10	3,74±0,40 (6,17±0,38)	2,23±0,06
P		<0,05	<0,001	<0,001

Legend: P calculated relative to the control; only values less than 0.05 are given. Total glucose + glycogen given in parentheses.

It will be clear from Table 1 that the rate of glucose formation by the liver slices of animals exposed to the action of both factors – hydrocortisone and hypoxia – exceeded the intensity of gluconeogenesis from all the substrates studied in the liver slices from the control and "hypoxic" rats, although it was lower than that observed after injection of the hormone under normal conditions. When oxygen is deficient and the initial glycogen content low, processes of glucose formation from glycogen evidently predominate in the liver.

The intensity of glucose formation by liver slices of "hypoxic" rats thus depends on the initial state of the carbohydrate reserves and is probably determined by changes in the ratio between the rates of gluconeogenesis and glycolysis.

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