ACTION OF PANGAMIC ACID (VITAMIN B_{15}) DURING STARVATION

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Vitamin B_{15} in starving rabbits inhibits the development of ketonemia and hypercholesteremia and also restores depressed hexokinase activity.

Recently pangamic acid has been used on an increasing scale in clinical practice for the treatment of hypoxic states, disturbances of lipid metabolism, atherosclerosis, and coronary insufficiency [1, 3, 8, 14, 15]. The therapeutic effect of pangamic acid is based on the accumulation of high-energy compounds through activation of the aerobic conversion of carbohydrates, and also on stimulation of the oxidation of fatty acids [5, 6, 9, 11, 15-17].

The disturbance of lipid and carbohydrate metabolism in starvation appeared to be a convenient model for the further elucidation of the mechanism of action of pangamic acid.

EXPERIMENTAL METHOD

Experiments were carried out on male rabbits weighing 2500 g. The 20 rabbits of series I were divided into two groups with 10 animals in each group. The animals of both groups were completely starved, receiving only water, for two periods of 7 days each, separated by an interval of 15 days. The animals of group 1 were the control, while those of group 2 received vitamin B_{15} in isotonic NaCl solution (by subcutaneous injections of 20 mg daily throughout the experiment). Before and after starvation, total cholesterol in the rabbits' blood was determined by Bloor's method, β-lipoproteins by the method of Burstein and Samaille [10] in the modification of Klimov et al. [4], lipid phosphorus by the Fiske-Subbarow method [13] in Braunshtein's modification [2], glucose by the anthrone method, and ketone bodies by Behre's method [7].

In the experiments of series II the animals were divided into four groups, with five in each group: group 1 was the control (intact animals), the rabbits of group 2 were starved for 5 days, those of group 3

TABLE 1. Changes in Indices of Lipid and Carbohydrate Metabolism in Starving Rabbits Receiving Pangamic Acid ($M \pm m$)

Group of animals	No. of animals	Total cholesterol (mg %)	Lipoid phosphorus (mg %)	β-lipoproteins (mg %)	NEFA (μeq/ml)	Glucose (mg %)	Ketone bodies (mg %)
Intact	30	44±1,3	3,1±0,16	253±12,6	0,2±0,09	188±3,2	0,32±0,009
Starving	10	148±13,4 $P<0,001$	5,0±0,5 $P<0,001$	656±63 $P<0,001$	0,25±0,01 $P<0,1$	172±6 $P<0,05$	0,8±0,086 $P<0,001$
Starving and receiving vitamin B_{15}	10	55,5±6,1 $P<0,001$	4,3±0,5 $P<0,1$	483,5±14 $P<0,1$	0,33±0,026 $P<0,02$	190±10 $P<0,1$	0,38±0,06 $P<0,001$

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TABLE 2. Changes in Hexokinase Activity in Homogenates of Gastrocnemius Muscle of Starving Rabbits Receiving Vitamin B_{15}

Group of animals	Statistical index	Hexokinase activity (μmoles NADP·H_2)	
		100 mg protein	gram fresh weight
Intact	$M \pm m$ n	0,5±0,06 5	0,31±0,02 5
Starving for 5 days	$M \pm m$ n P	0,34±0,019 5 <0,02	0,18±0,18 5 <0,01
Starving for 10 days	$M \pm m$ n P	0,24±0,03 5 <0,001	0,13±0,017 5 <0,001
Starving for 10 days, administration of vitamin B_{15} on 5 of them	$M \pm m$ n P	0,46±0,07 5 <0,1	0,33±0,08 5 <0,1

Note. P compared with normal.

for 10 days, and those of group 4 also for 10 days, but during the last 5 days of starvation they received injections of vitamin B_{15} in a dose of 20 mg daily.

At the end of the experiment hexokinase activity was investigated in a homogenate of the gastrocnemius muscle [12].

EXPERIMENTAL RESULTS

During repeated starvation for 7 days an increase in the total cholesterol, lipoid phosphorus, and β-lipoproteins and a decrease in the concentration of glucose were observed in the blood serum. Other evidence of disturbance of carbohydrate and lipid metabolism was given by an increase in the blood concentration of ketone bodies (Table 1).

Injection of vitamin B_{15} into the starving rabbits improved the indices of lipid metabolism and restored the normal blood level of ketone bodies. This evidently indicates restoration of the normal carbohydrate metabolism.

The results of the experiments of series II are given in Table 2. They show that starvation for 5 days lowered the hexokinase activity by 1.4 times.

Starvation for 10 days reduced this activity still more. Administration of vitamin B_{15} to the animals starving for 10 days restored normal hexokinase activity.

The decrease in hexokinase activity during starvation may reflect the secondary development of insular insufficiency. The results indicate that activation of the hexokinase reaction by pangamic acid may be one way of eliminating the disturbances of lipid metabolism characteristic of starvation.

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