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ANABOLIC EFFECTIVENESS OF NITROGEN PREPARATIONS FOR PARENTERAL FEEDING IN TOXIC HEPATITIS

R. M. Glants, E. V. Skovronskaya, G. P. Vovk, and L. I. Mikolishin

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Assimilation of the nitrogen preparations moriamine S-2 and improved casein hydrolysate when given parenterally to 100 albino rats was studied. Both healthy animals and animals with toxic hepatitis induced by CCl_4 were used. Administration of the nitrogen preparations to healthy animals converted the negative nitrogen balance to positive and restored the normal content of amino nitrogen in the blood and tissues when disturbed as a result of protein deprivation. In toxic hepatitis the rate of assimilation of the preparations was considerably reduced. Parenteral feeding for eight days did not convert the negative nitrogen balance into positive and did not abolish the hypoproteinemia, although it restored the normal amino-nitrogen concentration in the blood and tissues. KEY WORDS: parenteral feeding; protein hydrolysates; amino acid mixtures; assimilability of administered nitrogen; toxic hepatitis.

Parenteral feeding in clinical practice is used in the treatment of patients with considerable disturbances of tissue metabolism due to disturbances of the functions of the nervous and endocrine systems, pancreas, liver, and so on [1, 5, 6]. The writers have shown both experimentally and clinically that disturbances of function of the endocrine part of the pancreas and of the thyroid gland considerably limit the assimilability of parenterally administered nitrogen preparations [3, 4].

The object of this investigation was to study the role of the initial state of liver function in the assimilability of parenterally administered nitrogen preparations.

EXPERIMENTAL METHOD

Experiments were carried out on 100 albino rats of both sexes weighing 180-250 g, some of which were healthy, whereas the rest had parenchymatous hepatitis. Toxic hepatitis was induced by three subcutaneous injections of a 50% oily solution of CCl_4 in a dose of 0.5 ml/100 g body weight in the course of one week. The presence of hepatitis was confirmed histologically. The animals as a whole were divided into eight groups; the rats of six groups were kept throughout the experimental period on a synthetic protein-free diet [2], and those of the other two groups on the ordinary animal house diet. Daily for 8 days the protein-deprived rats received subcutaneous injections of physiological saline and of nitrogen preparations: moriamine S-2 (Japan) and improved casein hydrolysate (USSR) [7] in a dose of 0.3 g conventional protein/100 g body weight. Glucose solution (0.5 ml of a 40% solution/100 g body weight) was injected at the same time. The volume of fluid injected was equivalent to 7 ml/100 g body weight. Periodically the nitrogen balance of the animals and the excretion of amino nitrogen in their urine were determined. At the end of the experimental period (8 days) animals of all groups were decapitated and the concentrations of amino nitrogen and total protein were determined in their blood and the concentration of amino nitrogen in the tissues (muscle, heart, liver). Total nitrogen in the urine and feces was determined by the micro-Kjeldahl method and amino nitrogen by the ninhydrin method [8]. The nitrogen balance was judged from the difference between the nitrogen administered and excreted in the urine and feces.

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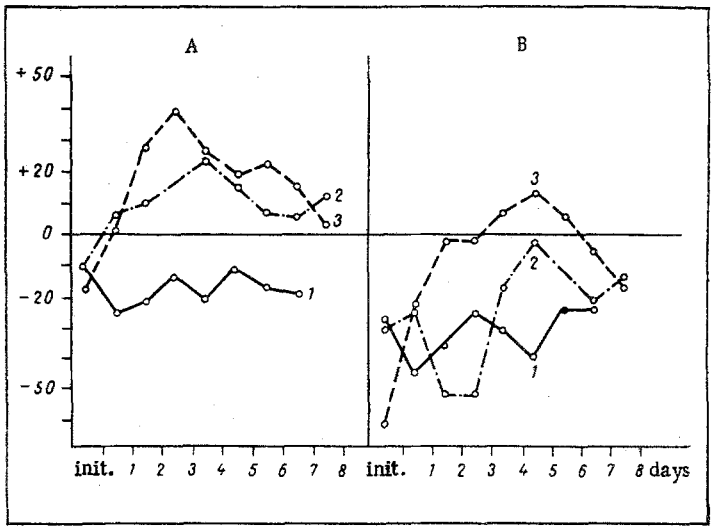

Fig. 1. Dynamics of nitrogen balance in healthy albino rats and in rats with toxic hepatitis during protein deprivation treated by parenteral feeding. A) Healthy, B) hepatitis. 1) Physiological saline; 2) moriamine S-2; 3) improved casein hydrolysate. Init.) Initial state before parenteral feeding. Abscissa, duration of parenteral feeding (in days); ordinate, nitrogen balance (in mg/100 g body weight).

EXPERIMENTAL RESULTS

In healthy rats protein deprivation was accompanied by a negative nitrogen balance, the depth of which was almost identical throughout the experimental period (Fig. 1A). Administration of moriamine S-2 and improved casein hydrolysate to the healthy rats receiving a protein-free diet led to conversion of the negative nitrogen balance to positive after the first day. In protein-deprived rats with toxic hepatitis the negative nitrogen balance was more marked than in the healthy animals (Fig. 1B).

During administration of moriamine S-2 to rats with toxic hepatitis the nitrogen balance remained negative, although it improved a little on the fifth day. Improved casein hydrolysate converted the negative nitrogen balance to positive for a short time between the fourth and sixth days.

Protein deprivation of healthy rats for eight days did not cause the level of their total blood protein to fall below its value in animals on an ordinary diet (7.20 ± 0.28 and 7.38 ± 0.07% respectively). Administration of the nitrogen preparations to healthy protein-deprived rats had no significant effect on the total protein concentration (7.30 ± 0.08% for moriamine S-2, 7.00 ± 0.10% for improved casein hydrolysate). Toxic hepatitis in rats on an ordinary diet was accompanied by a significant decrease in the blood protein concentration (6.73 ± 0.15%), which was greater in the case of protein deprivation (6.14 ± 0.23%).

Administration of nitrogen preparations did not raise the total blood protein level in rats with toxic hepatitis (5.90 ± 0.33 for moriamine S-2, 6.33 ± 0.28% for casein hydrolysate).

In healthy animals receiving an ordinary diet, the quantity of amino nitrogen excreted daily with the urine (2.30 ± 0.35 mg) was a little less than that excreted by the rats with toxic hepatitis (2.95 ± 0.20 mg), although this difference is not statistically significant. During protein deprivation the quantity of amino nitrogen excreted by the healthy rats (3.10 ± 0.96) and by the rats with toxic hepatitis (3.45 ± 0.44 mg) was almost the same and somewhat higher than the amount excreted on an ordinary diet.

After administration of moriamine S-2 and casein hydrolysate for eight days the excretion of amino nitrogen with the urine was increased in all groups of animals. A difference was found in the excretion of amino nitrogen depending on the state of the liver function and the quality of the nitrogen preparations used for parenteral feeding. The healthy rats excreted 3% of the amino acids administered with moriamine S-2 and 5.3% of those administered with casein hydrolysate, whereas the rats with toxic hepatitis excreted 5.2% and 10.0% respectively.

TABLE 1. Effect of Parenteral Feeding on Amino-Nitrogen Concentration (in mg%) in Tissues of Healthy Rats and Rats with Toxic Hepatitis (M ± m)

Group of animals	No. of rats	Blood	Muscle	Heart	Liver
Healthy, ordinary diet	29	3,62±0,12	16,20±0,94	16,18±0,52	19,51±0,79
Rats with hepatitis, ordinary diet	10	6,82±0,65*	16,93±1,24	25,00±1,06*	21,92±1,62
Healthy, receiving physiological saline	9	9,08±1,08*	35,52±3,62*	34,16±3,86*	24,59±2,18*
Rats with hepatitis receiving physiological saline	9	8,97±0,82*	31,63±4,53*	32,97±3,63*	33,28±3,37*
Healthy, receiving moriamine S-2	5	2,56±0,39†	15,33±1,83†	19,18±0,97†	24,40±2,59
Healthy receiving casein hydrolysate	5	2,21±0,26†	18,10±3,80†	23,14±4,77	23,46±3,12
Rats with hepatitis receiving moriamine S-2	19	2,76±0,69†	11,29±0,76†	17,13±1,23†	18,91±1,00†
Rats with hepatitis receiving casein hydrolysate	14	3,58±0,55†	14,98±1,43†	21,86±2,43†	27,18±3,54*

Legend. *) $P < 0.05$ for comparison of all groups with group 1; †) $P < 0.05$ for comparison of group 3 with groups 5 and 6 and of group 4 with groups 7 and 8. Animals of groups 3-8 received a protein-free diet throughout the experimental period.

The blood amino nitrogen in the rats with toxic hepatitis receiving an ordinary diet was almost twice as high as that in healthy animals (Table 1). The blood amino-nitrogen concentration was significantly increased in both healthy animals and rats with toxic hepatitis on a protein-free diet.

Both in the healthy rats and in the rats with toxic hepatitis administration of nitrogen preparations restored the normal blood amino-nitrogen level when increased as a result of protein deprivation.

In rats with toxic hepatitis on an ordinary diet the amino-nitrogen concentration was increased only in the heart muscle. Protein deprivation was accompanied by an increase in the amino nitrogen concentration in all the tissues studied both in healthy rats and in rats with toxic hepatitis. Administration of moriamine S-2 and casein hydrolysate both to healthy rats and to rats with toxic hepatitis lowered the amino-nitrogen concentration in the skeletal and heart muscles if raised through protein deprivation. The amino-nitrogen level in the liver was significantly lowered in rats with toxic hepatitis only by administration of moriamine S-2.

Parenteral feeding in healthy animals is thus accompanied by a positive nitrogen balance and by normalization of the amino-nitrogen concentrations in the blood and tissues. In rats with toxic hepatitis protein deprivation led to a severe negative nitrogen balance and marked hypoproteinemia.

Parenteral nitrogen feeding improved the state of the nitrogen balance only a little, but did not convert it to positive; it restored the normal amino-nitrogen concentration in the blood and tissues but did not raise the blood protein concentration if lowered by toxic hepatitis.

Consequently, the assimilability of nitrogen preparations administered parenterally largely depends on the initial state of the liver function.

These findings served as the basis for clinical trials of parenteral feeding together with physiological metabolic regulators (insulin, neurabolile, vitamins of the B group, vitamin C) with the aim of increasing the anabolic efficacy of nitrogen preparations in disturbances of liver function.

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