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EFFECT OF PARENTERAL NITROGEN FEEDING ON BLOOD AND LIVER AMINO ACID SPECTRUM IN THYROXINE POISONING

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KEY WORDS: thyroxine poisoning; parenteral nitrogen feeding.

It has been shown in experimental thyrotoxicosis, characterized by marked changes in tissue metabolism, that parenteral feeding lowers the amino nitrogen level in the blood, tissues, and urine, which is raised in this pathology, and restores the normal content of nucleic acids in the tissues, indicating stimulation of anabolic processes [2, 3].

In continuing our investigations of experimental thyrotoxicosis, the aim was to study the effect of parenteral nitrogen feeding on the amino acid spectrum of the blood and liver in this pathology.

EXPERIMENTAL METHOD

Experiments were carried out on 50 albino rats weighing 220-250 g. Thyroxine poisoning was induced in rats kept on the ordinary animal house diet, by injection of thyroxine in a dose of 10 μg/100 g body weight daily for 30 days [4]. After administration of thyroxine for 30 days, all the animals were kept for 3 days on a protein-free diet, consisting of starch, sugar, sunflower oil, yeast, mixed salt, and vitamins. Against the background of this diet, for 7 days the animals of group 1 received subcutaneous injections of physiological saline, those of group 2 received the amino acid mixture polyamine, and those of group 3 improved casein hydrolysate in a dose of 0.3 g conventional protein/100 g body weight. The results of the experiments were compared with data for healthy rats kept on the ordinary animal house diet (normal) and also with data for animals with thyrotoxicosis receiving physiological saline only (protein deprivation). Animals not poisoned with thyroxine, and receiving injections of physiological saline during protein deprivation, formed a separate group.

EXPERIMENTAL RESULTS

Short-term (for 10 days) protein deprivation in rats without thyroxine poisoning led to

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TABLE 1. Effect of Parenteral Nitrogen Feeding on Content of Free Amino Acids in Liver (μmoles/g wet weight of tissue) and in Blood (μmoles/ml) in Albino Rats with Thyrotoxicosis against the Background of Protein Deprivation (M ± m; n = 10)

Amino acid	Liver state		Protein deprivation		Thyrotoxicosis					
					protein deprivation		administration of polyamine		administration of casein	
	liver	blood	liver	blood	liver	blood	liver	blood	liver	blood
Lysine	0,374 ± 0,045	0,224 ± 0,019	0,500 ± 0,107	0,505 ± 0,067*	0,635 ± 0,010*	0,398 ± 0,042*	0,390 ± 0,030‡	0,291 ± 0,082	0,460 ± 0,070‡	0,295 ± 0,040
Histidine	0,291 ± 0,060	0,034 ± 0,004	0,292 ± 0,022	0,075 ± 0,007*	0,430 ± 0,020*†	0,083 ± 0,008*	0,230 ± 0,040‡	0,043 ± 0,010‡	0,293 ± 0,090	0,047 ± 0,007‡
Arginine	Traces	0,109 ± 0,002	Traces	0,153 ± 0,024	Traces	0,150 ± 0,018*	Traces	0,135 ± 0,085	Traces	0,132 ± 0,005*
Threonine	0,227 ± 0,030	0,532 ± 0,029	0,582 ± 0,114*	0,510 ± 0,034	0,150 ± 0,020*†	0,422 ± 0,080	0,840 ± 0,260*†	0,445 ± 0,013*	0,810 ± 0,480	0,322 ± 0,019*
Valine	0,211 ± 0,040	0,099 ± 0,002	0,154 ± 0,038	0,110 ± 0,013	0,199 ± 0,002	0,093 ± 0,006	0,210 ± 0,020	0,066 ± 0,001†	0,165 ± 0,030	0,055 ± 0,001 *‡
Methionine	0,048 ± 0,005	0,029 ± 0,001	0,048 ± 0,007	0,031 ± 0,003	0,025 ± 0,010*	0,030 ± 0,001	0,025 ± 0,008*	0,029 ± 0,006	0,025 ± 0,010*	0,032 ± 0,004
Isoleucine	0,095 ± 0,002	0,035 ± 0,002	0,041 ± 0,013*	0,046 ± 0,003	0,072 ± 0,003*†	0,042 ± 0,002*	0,120 ± 0,020‡	0,033 ± 0,002‡	0,087 ± 0,010	0,027 ± 0,001 *‡
Leucine	0,213 ± 0,019	0,064 ± 0,002	0,132 ± 0,038	0,101 ± 0,003*	0,156 ± 0,004*	0,087 ± 0,003*†	0,200 ± 0,020‡	0,069 ± 0,004‡	1,137 ± 0,030*	0,050 ± 0,006‡
Phenyl-alanine	0,081 ± 0,007	0,035 ± 0,002	0,114 ± 0,012*	0,044 ± 0,005	0,066 ± 0,006†	0,041 ± 0,001*	0,067 ± 0,010	0,040 ± 0,004	0,052 ± 0,004*	0,040 ± 0,001*
Aspartic acid	1,553 ± 0,026	0,050 ± 0,003	1,413 ± 0,280	0,022 ± 0,003*	2,740 ± 0,090*†	0,055 ± 0,005†	1,750 ± 0,320‡	0,039 ± 0,004 *‡	1,339 ± 0,070 *‡	0,041 ± 0,012
Serine	0,801 ± 0,028	0,280 ± 0,041	0,986 ± 0,082*	0,411 ± 0,055	2,130 ± 0,010*†	0,586 ± 0,048*†	1,740 ± 0,170‡	0,348 ± 0,001‡	1,663 ± 0,430*	0,313 ± 0,067‡
Glutamic acid	1,865 ± 0,114	0,140 ± 0,008	1,927 ± 0,309	0,299 ± 0,080	2,600 ± 0,380	0,718 ± 0,095*†	1,590 ± 0,810	0,381 ± 0,003 *‡	2,284 ± 0,780	0,340 ± 0,041*‡
Proline	0,394 ± 0,058	0,237 ± 0,050	0,146 ± 0,008	0,164 ± 0,043	0,190 ± 0,030*	0,371 ± 0,030*†	0,140 ± 0,020*	0,147 ± 0,016 *‡	0,184 ± 0,020*	0,125 ± 0,020 *‡
Glycine	1,715 ± 0,075	0,341 ± 0,049	2,056 ± 0,531	0,510 ± 0,063*	2,520 ± 0,230*	0,749 ± 0,085*†	2,710 ± 0,170*	0,365 ± 0,031‡	2,292 ± 0,450	0,266 ± 0,076‡
Alanine	3,342 ± 0,764	0,453 ± 0,002	1,924 ± 0,332	0,451 ± 0,048	3,240 ± 0,240†	1,048 ± 0,093*†	3,500 ± 0,280	0,607 ± 0,076*‡	2,890 ± 0,100	0,425 ± 0,069‡
Tyrosine	0,072 ± 0,007	0,035 ± 0,003	0,024 ± 0,003*	0,032 ± 0,002	0,056 ± 0,001*†	0,039 ± 0,001†	0,085 ± 0,030†	0,027 ± 0,005‡	0,087 ± 0,010‡	0,028 ± 0,002‡
Total amino acids	11,288 ± 1,271	2,700 ± 0,131	10,339 ± 1,353	3,464 ± 0,162*	15,210 ± 0,460*†	4,912 ± 0,300*†	13,597 ± 0,615‡	3,065 ± 0,005 *‡	12,769 ± 0,700‡	2,538 ± 0,160‡

*P < 0.05 compared with normal.
†P < 0.05 compared with protein deprivation in rats without thyroxine poisoning.
‡P < 0.05 compared with thyrotoxicosis accompanied by protein deprivation.

a very small decrease in the free amino acid level in the liver tissue and an increase in the blood compared with the corresponding data for healthy animals on an ordinary diet (Table 1). In the presence of marked thyroxine poisoning the free amino acid concentration in the liver and blood rose significantly against the background of protein deprivation. The content of free amino acids in the liver increased by 35% and in the blood plasma by 82% compared with observations made on healthy animals receiving an ordinary diet, and by 47 and 42% respectively during protein deprivation. The increase in the amino acid content in the liver occurred on account of an increase in the content of lysine, histidine, asparagine, serine, and glycine. The levels of the other amino acids, especially threonine, methionine, and proline, fell. Concentrations of all free amino acids, especially histidine, serine, glutamic acid, glycine, and alanine, in the blood plasma increased.

The amino acid pool is known to be under constant hormonal control, which is expressed as active transport of amino acids from the extracellular space into the intracellular space and regulation of the rate of their utilization for synthesis of the protein molecule [8].

Thyroxine poisoning leads to an increase in the concentration of both nonessential (by 132%) and essential (by 16%) amino acids in the blood plasma; the level of free amino acids also is increased in the liver — by 38% for essential and by 12% for nonessential.

This imbalance between the free amino acids in the blood is observed in patients with toxic goiter [1, 6, 7]. High concentrations of thyroid hormones in the blood in toxic goiter disturb the coordination between the hydrolysis of tissue proteins and their resynthesis, intensify reactions of amino acid oxidation, and depress the protein-forming function of the liver [5].

In albino rats with thyroxine poisoning the dynamic equilibrium between the anabolic and catabolic phases of protein metabolism is disturbed, as reflected in a deep negative nitrogen balance. The use of protein hydrolysates and amino acid mixtures improves the state of the nitrogen balance and reduces the degree of hypoproteinemia, but does not restore normal protein metabolism in the hypermetabolizing cells of the liver, heart, and skeletal muscle [4]. These data served as the justification for a closer study of the mechanism of action of various nitrogen preparations used in parenteral feeding against the background of this pathology.

Administration of the amino acid mixture polyamine, containing 14 amino acids, in thyrotoxicosis lowered the concentration of all free amino acids in the blood plasma compared with their level in protein deprivation, although the total content of amino acids still remained higher than normally (in healthy animals). The glutamic acid level in the blood remained particularly high.

The level of the essential amino acids except threonine and methionine in the liver was restored to normal. The threonine concentration was considerably increased, whereas the methionine concentration remained low. The concentration of nonessential amino acids in the liver also was lowered compared with their level during protein deprivation, and only the serine and glycine levels remained high, but the proline concentration was lowered. These findings indicate stimulation of anabolic processes, although the amino acid metabolism was not fully restored to normal by administration of polyamine in the presence of thyrotoxicosis.

Administration of improved casein hydrolysate led to a fall in the total concentration of free amino acids in the blood plasma compared with their level during protein deprivation, but the amino acid imbalance remained worse than when polyamine was given.

Consequently, the use of parenteral nitrogen feeding in thyroxine poisoning contributes to normalization of the free amino acid concentration in the blood and liver, although it does not completely abolish their imbalance.

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CORRECTION OF RESPIRATORY DISORDERS BY ELECTRICAL STIMULATION OF STRUCTURES OF THE RESPIRATORY CENTER

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The problem of correction of respiratory disorders is urgent from both theoretical and practical viewpoints. Its successful solution is intimately bound with clear and precise ideas on the site of generation of respiratory rhythmic activity. Disturbances of normal breathing are of many different kinds, as are the principles and conditions producing them. It is not surprising that different methods have been suggested for their correction. Methods of artificial ventilation of the lungs and electrical stimulation of the peripheral part of the nervous system of the respiratory apparatus have been widely used under both experimental and clinical conditions [1-4]. "Inspiratory" and "expiratory" areas, stimulation of which can be used to regulate the rhythm of the respiratory neurons and to restart arrested breathing in cats, have been discovered in the medial and lateral zones of the respiratory center [5, 6].

To study the properties of the central bound rhythm and restoration of respiratory function in cats which have stopped breathing by application of square pulses of current, in the investigation described below the "inspiratory" and "expiratory" areas of the gigantocellular nucleus, tractus solitarius, and nucleus ambiguus and nucleus retroambiguus were stimulatedm as described earlier [5, 6].

EXPERIMENTAL METHOD

Experiments were carried out on 61 cats weighing 2.5-3.8 kg anesthetized with pentobarbital (40 mg/kg, intraperitoneally). Preparation of the animal and the method used to stimulate structures of the respiratory center and to derive activity of the respiratory neurons were described previously [6]. During consecutive stimulation of the "inspiratory" and "expiratory" areas, taking stereotaxic coordinates from the atlas [7], two stimulating electrodes were inserted: One was fixed securely in the occipital bone, and the other, which could be moved, was fixed in the aiming head of the SEZh-3 stereotaxic apparatus and so could be inserted into different structures of the respiratory center. In four experiments electrodes were inserted without preliminary aspiration of the cerebellum. The experiments were divided into two series. In the experiments of series I an arbitrary rhythm was "bound" on respiration by stimulating one of the "inspiratory" areas or by consecutive repetitive stimulation of the "inspiratory" and "expiratory" areas. In the experiments of series II attempts to correct various disturbances of respiration, or to restore respiration if it had ceased, were made by stimulation of the "inspiratory" areas. In 12 experiments respiratory arrest was induced by additional intravenous injection of pentobarbital (20-50 mg/kg) into the animal.

EXPERIMENTAL RESULTS

Responses of unit activity of 113 respiratory neurons to stimulation of the "inspiratory" and "expiratory" areas of the respiratory center were studied. The strongest stimulating effect was obtained by stimulation of the "inspiratory" and "expiratory" areas of the gigantocellular nucleus. About 80% of inspiratory and expiratory neurons of the "ventral and dorsal respiratory nuclei" responded with rhythm binding to stimulation of structures of the gigan-

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