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UREA SYNTHESIS IS THE MAIN WAY FOR DISPOSAL OF AMMONIA IN THE BODY

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Abstract
The normal concentration of ammonia in the blood is not determined by international standards; it depends on the methodology and reagents used in the laboratory, while the permissible level of ammonia in the blood (normammonemia) usually does not exceed 60 μmol/l. In the cells of the liver and kidneys, ammonia enters the transport forms (glutamine, asparagine, glutamic acid and alanine), which are non-toxic compounds formed during the neutralization (binding) of ammonia. Urea synthesis is the main route for ammonia neutralization. Urea accounts for up to 80–85% of all nitrogen excreted from the body. The amount of urea released depends on the amount of protein supplied with food.

Keywords: hyperammonemia, nitrogen, ammonia, ammonium, L-ornithine L-aspartate, rifaximin alfa, probiotics, prebiotics, lactitol, lactulose, minimal hepatic encephalopathy, liver fibrosis.

Introduction

The human body is an intermediate component of the nitrogen cycle in nature. Consuming nitrogen from the external environment in the form of various compounds (food products), the body processes it into ammonia - one of the end products of the metabolism of nitrogen-containing substances [1], which is excreted from the body in the form of urea. In nervous tissues, liver, intestines, and muscles, the most active conversion of amino acids and biogenic amines into ammonia occurs. In a state of nitrogen equilibrium, the adult human body consumes and excretes about 15 g of nitrogen per day. The amount of nitrogen in the body should be constant, but there is a temporary or permanent imbalance in the nitrogen balance due to diseases and certain pathological conditions of the body. In the tissues of the body, ammonia gas NH_3 is converted into ammonium cation NH_4^+, and the process also occurs in reverse. Ammonia metabolism occurs primarily in liver cells and muscle tissue through the synthesis of urea and glutamine, which are excreted from the body in urine, feces and exhaled air. The following mechanisms of ammonia formation are mainly observed in the human body:

1. Non-oxidative deamination of some amino acids (serine, threonine, histidine) in the liver.
2. Oxidative deamination of glutamic acid in all tissues (except muscle), especially in the liver and kidneys.
3. Deamination of amides of glutamic and aspartic acids in the liver and kidneys.
4. Catabolism of biogenic amines - in all tissues, most notably in nervous tissue.
5. Hydrolytic deamination in intensively working muscles.
6. The breakdown of the amino acid glutamine, the main source of energy for the cells of the intestinal mucosa in the small intestine.
7. Decomposition of purine and pyrimidine bases - in all tissues.
8. The vital activity of urease-producing microorganisms in the stomach, colon and urinary tract.

Significant amounts of ammonia are formed as a result of the metabolism of intestinal bacteria in the colon, from where ammonia enters the blood of the portal venous system. Under normal conditions, the liver quickly removes ammonia from the portal blood and neutralizes it, so the blood leaving the liver contains virtually no ammonia. Ammonia is a toxic gas; in a healthy person it is present in the blood in relatively small concentrations (25–40 μmol/l). The content of free ammonia in the blood is represented by only trace amounts; no more than 1% of the substance in the aqueous environment of the blood circulates in free form. The normal concentration of ammonia in the blood is not determined by international standards, and therefore depends on the methodology and reagents used in the laboratory, while the permissible level of ammonia in the blood (normammonemia) usually does not exceed 60 μmol/l. Symptoms of chronic intoxication are observed when the ammonia content exceeds 2–3 times, but even a slight increase (by 30–50%) has an adverse effect on the body, and, above all, on the central nervous system, which manifests itself in the form of headaches, rapid fatigue, drowsiness.

Almost all ammonia is removed from the body through the kidneys with urine in the form of urea, which is synthesized in the liver, and in the form of ammonium ion salts formed in the epithelium of the kidney tubules. In the cells of the liver and kidneys, ammonia enters the transport forms (glutamine, asparagine, glutamic acid and alanine), which are non-toxic compounds formed during the neutralization (binding) of ammonia. Urea synthesis is the main route for ammonia neutralization. Urea accounts for up to 80–85% of all nitrogen excreted from the body. The amount of urea released depends on the amount of protein supplied with food. If the daily diet includes 80–100 g of protein, then 25–30 g of urea are formed and excreted per day. Urea excreted from the body consists equally of “ammonia” nitrogen and aspartic acid

nitrogen. There are methods for determining ammonia in red blood cells, exhaled air, saliva, sweat and urine. With a decrease in the detoxification function of the liver, the conversion of ammonia into urea is disrupted, as a result of which alternative metabolic pathways for the conversion of ammonia in the muscular system, in astrocytes of the central nervous system and in the kidneys are activated, with skeletal muscle and nervous tissue becoming the main organs for ammonia detoxification.

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