BIOCHEMISTRY AND BIOPHYSICS

AMMONIA AND GLUTAMINE CONTENT OF THE BLOOD OF ATROPHIC HEPATIC CIRRHOSIS PATIENTS, BEFORE AND AFTER ESTABLISHMENT OF A PORTOCAVAL ANASTOMOSIS

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Dangerous hemorrhages occur in many patients suffering from atrophic hepatic cirrhosis as a result of increased pressure in the portal system. In order to save the lives of such patients, and to prevent development of ascites, F. G. Uglov has performed the operation of establishing an anastomosis between the portal and caval systems, and this operation has fulfilled its object. All the patients admitted to the hospital for this condition were subjected to a through clinical and biochemical examination. We determined the ammonia and glutamine content of the blood of these patients.

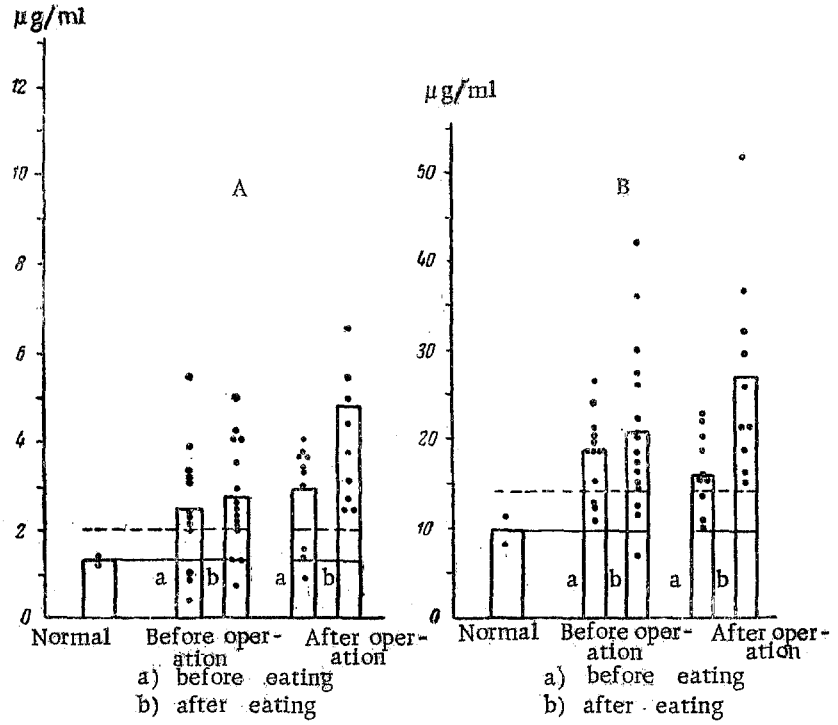
Although the normal range for blood ammonia is considered to be 0.025-0.04 mg-% [4, 5], values of 0.2% are accepted as being within the upper limits of normal. M. L. Evtukhova [3] found 0.83-1.06 mg-% ammonia in the blood of patients with liver disease. She ascribed these high values to disturbed urea synthesis in the liver and to disturbances in the portal circulation due to formation of anastomoses permitting the blood to by-pass the liver. According to this author, the level of blood ammonia varies parallel with the extent of liver damage, although she notes that this parallelism does not always hold, either for the extent of liver damage or for the way in which the disease progresses. The same was also noted by American workers [5], who, however, emphasized that blood ammonia affords a better indication of the condition of a patient than does any other blood constituent [5, 7].

Inasmuch as rise in blood ammonia is one of the symptoms of liver insufficiency (impaired synthesis of urea), some authors have suggested that blood ammonia determinations could serve as diagnostic tests [5]. Since it is now thought that glutamine plays an important part in ammonia metabolism we determined both ammonia and glutamine in the blood of our patients.

Ammonia was determined in the centrifugate obtained after deproteinization of blood with trichloroacetic acid, by a vacuum distillation method [6], and amide nitrogen of glutamine in a second portion of centrifugate by determining the increase in ammonia content after hydrolyzing for 10 minutes with 2 N sulfuric acid.

Altogether we studied 17 subjects, including 2 healthy controls and 15 patients with chronic hepatitis; of these, 7 were again examined after establishment of a portocaval anastomosis. The normal fasting values for blood ammonia were found to be 0.12 and 0.14 mg-%, and the corresponding figures for glutamine amido-group nitrogen were 1.16 and 0.84 mg-%. The mean fasting value for unoperated patients was 0.26 mg-% (2.6 μg-per ml) of ammonia, rising to 0.28 mg-% after a meal; the corresponding values for operated patients were 0.3 and 0.5 mg-%. The content of amido-group nitrogen before operation was 1.91 mg-% fasting, and 2.24 mg-% after

a meal, as compared with 1.74 and 2.84 mg-%, respectively, after operation. It thus appears that the ammonia and glutamine contents of the blood of hepatic cirrhosis patients are elevated, both before and after the operation.



(A) Ammonia content, (B) Glutamine amido-group nitrogen content, of the blood of patients before and after establishment of a portocaval anastomosis. • individual points, —— normal value, ----- upper limit of normal for ammonia, and mean value for glutamine (from published data).

A particularly large rise in blood ammonia and glutamine (by 66% on the average) was observed regularly after meals in operated patients (see figure).

Similar results were obtained in experiments on dogs with an Eck-Pavlov fistula [1]. Soon after the operation, and before there was any possibility of any derangement of hepatic function, considerable elevations in blood ammonia and glutamine were observed, particularly during digestion.

It follows that the raised ammonia content of the blood of operated patients found by us should be ascribed in the first place to circulatory changes, and not to deterioration in the urea-synthesizing capacity of the liver, the more so as the glutamine content rose parallel with the ammonia content; this appears to us to be a favorable sign of compensation.

It is of interest to consider what effect the rise in blood ammonia might have on the patient. According to the literature, a blood ammonia content of 5 mg-% represents a dangerous level in the rabbit, as convulsions are seen when it reaches 2 mg-% or more. A. L. Mikhnev [4] found 0.92 mg-% of ammonia, and M. L. Evtukhova [3] 0.83-1.06 mg-%, in patients suffering from cirrhosis of the liver. We found a value of 1.26 mg-% ammonia nitrogen in the blood of an operated patient in good condition, 3 hours after a meal. A. S. Borzunova gave intravenous injections of ammonium salts to epileptics and schizophrenics, as a therapeutic measure, and found no ill effects from high blood ammonia (over 1 mg-%). American workers [7] gave intravenous injections of 2% ammonium chloride to alcoholic hepatic cirrhosis patients, only one of four of whom developed rigors and loss of consciousness, characteristic of impending coma, after receiving 750 ml of the solution. The highest blood ammonia content of this patient was 1.4 mg-%, whereas another patient receiving the same dose, but not showing signs of coma, had a blood ammonia of 1.8 mg-%.

It can be concluded that the blood ammonia levels found by us in our patients should not be regarded as being dangerous. Appropriate dietetic and therapeutic measures should, of course, be taken to ensure that large amounts of ammonia do not enter the blood stream, and that it is effectively detoxified and eliminated. Proper functioning of the intestines should be assured.

Researches conducted by N. V. Veselkin and B. G. Gordon on the feeding of dogs with an Eck-Pavlov fistula showed that casein is a suitable source of dietary protein in such animals. They can be fed with casein over prolonged periods without showing any toxic symptoms whatsoever[2].

It is known that feeding cheese curds to patients with liver disease has been widely applied with good results.

The diet prescribed to such patients hence consists of carbohydrates, cheese curd, vitamins, and anything which restricts ammonia formation, or promotes its elimination. . It might be supposed, from published data [8] and from our experimental results [2], that it might be of benefit to administer glutamic acid to such patients.

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