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Research Article

HEPATIC ENCEPHALOPATHY CAUSED BY ENDOGENOUS INTOXICATION IN PATIENTS WITH DIABETES MELLITUS COMPLICATED BY PURULENT-SEPTIC LESIONS OF SOFT TISSUES, WAYS OF THEIR CORRECTION

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ABSTRACT

Objective: to study hepatic encephalopathy caused by endogenous intoxication in patients with diabetes mellitus (DM) complicated by necrotic soft tissue lesion (PNSTL) and ways of their correction.

Materials and methods: 58 patients with diabetes mellitus complicated by purulent-necrotic soft tissue lesion and the effect of endotoxicosis on the functional state of the liver were examined in the intensive care unit, with optimization of correction of hepatic encephalopathy. In addition to traditional therapy, hepatoprotections and drugs that stop transaminase activity are included in patients.

Conclusions: Early detection of hepatic encephalopathy before clinical manifestations and timely correction is pathogenetically justified and optimizes the outcomes of such a formidable complication as hepatic encephalopathy and coma.

KEYWORDS

Liver, liver failure, hepatic encephalopathy, endotoxicosis, endotoxemia, intoxication, diabetes mellitus.

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INTRODUCTION

Severe endocrine disorders underlying the pathogenesis of DM lead to almost multiple organ disorders, significantly aggravating the course of DM itself and its complications

According to recent estimates, liver damage is one of the most common pathologies in DM [1, 20]. The fact of liver damage in DM is beyond doubt.

Depending on the diagnostic methods used, diabetic hepatopathy (DH) was detected in a different percentage of cases. The authors [9, 13] indicate the frequency of liver damage in 33% a, lesions from the hepatobiliary system in 38.8% of patients with DM.

During magnetic resonance imaging of the liver in patients with diabetes, a violation of the hepatobiliary system was detected in a significantly higher percentage of cases than with traditional clinical and laboratory methods of examination.

It should be assumed that the violation of the functional state of the liver in DM is closely related to the violation of hepatic blood flow caused by hepatic microangiopathies. A number of authors have clearly demonstrated a decrease in volumetric blood flow in the portal vein and hepatic artery basin in patients with DM, especially at the stage of decompensation and its late complications, and the diagnosis of liver pathology in patients with DM is difficult because clinical manifestations of this complication are often asymptomatic, erased, an absolute majority of authors adhere to this opinion [3, 6,]

Pathomorphologically, fat infiltration is more often detected, the frequency and severity of which researchers directly associate with the duration and severity of the course of DM [14]. It is considered the most correct term – fat infiltration, because excess fat enters the hepatocyte from the outside, and is not formed in it itself [15]. However, the most common term is "fatty liver dystrophy", although there are still such names for this process as: fatty hepatosis, liver steatosis. Many authors consider fat infiltration not only as the most typical liver lesion in DM [10], but also as specific [2].

Fat infiltration in DM affects the clinical course of the disease, because it leads to various disorders of liver function, including absorption and antitoxic [17, 21].

Violations of the enzymatic function of the liver were found in many patients with DM. Almost all researchers emphasize the ambiguity and difficulty of their laboratory diagnostics [5]. Therefore, it is not always possible to detect functional liver disorders using conventional clinical and laboratory methods, even with decompensated diabetes.

When analyzing the literature, we identified a number of works devoted to the study of individual liver functions in patients with DM. They are contradictory, for the most part without a comprehensive study of liver functions, without specifying the type of diabetes, assessing the severity, compensating for its purulent - necrotic complications [4, 7, 22]. There is little data on the main clinical and biochemical syndromes of liver lesions in type 2 diabetes, the prevalence of which is currently being compared with the epidemic. In this regard, further studies are needed to clarify the biotransformation function and the role of the identified changes in the development of diabetic hepatopathy. It is necessary to expand the methods of early diagnosis of diabetic hepatopathy and hepatic encephalopathy in clinical settings. In DM, changes in the spectrum of serum proteins were revealed,

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characterized by the development of hypoalbuminemia and hyperglobulinemia. [12, 24].

Generalized lesions of the vascular system, pronounced endotoxemia in patients with diabetes with diabetic foot syndrome, PNSTL certainly involve the liver - organ in the pathological process, one of the main functions of which is detoxification and excretion of toxic products. It should be assumed that early diagnosis of liver damage in patients with DM and its complicated forms and targeted correction of the detected disorders will contribute to improving the results of treatment of this category of patients [18, 19, 25].

In general, summing up all of the above, it can be noted that DM is associated with a wide range of liver diseases, including an increase in the level of liver enzymes, the formation of fatty liver disease, cirrhosis and even acute liver failure. Ideal treatment regimens for various complications of DM with liver pathology have not yet been developed [23,]. In this regard, in daily practice, the doctor, first of all, should focus on the underlying cause of the disease.

A significant frequency of complications as in DS, high mortality in these conditions, numerous unresolved problems of endotoxemia and endotoxicosis, the frequency of generalization of the process with the development of sepsis with multiorgan insufficiency, cannot satisfy clinicians and urgently require further research [16].

Materials and methods of research.

58 patients with diabetes mellitus complicated by purulent-necrotic soft tissue lesion were examined.

Purulent-necrotic lesion of the foot was more often noted in men. Age of patients (Table.1) ranged from 19 to 75 years, and the absolute majority of them were aged from 20 to 60 years.

Table 1.

Distribution of PNSTL patients by age and gender

№	Age (years)	Number of patients
1.	Below 19	7 (13%)
2.	20 – 44 old	17 (31,5%)
3.	45 – 60 old	25 (46,2%)
4.	61 – 75 and older	5 (9,3%)
	Total	58 (100%)
	Men	**41 (70,7%)**
	Women	**17 (29,3%)**
5.	Overall	58 (100%)

The patients who underwent surgical and conservative therapy were examined. They had pronounced endogenous intoxication and hepatic encephalopathy. The duration of diabetic gangrene of the lower extremities in these patients was from 2 to 8 weeks.

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In addition to traditional therapy, for the prevention and control of generalized infection, to improve liver functions and, above all, detoxification, patients also received hepatoprotectors, drugs aimed at improving hepatic blood flow and stopping the septic cascade (transaminase and free radical activity).

The patients had moderate and severe degrees of DM, but the number of patients with severe DM with manifestations of hepatic - renal insufficiency and signs of encephalopathy prevailed.

Unfortunately, the main contingent of patients was admitted at a late date from the moment of occurrence of purulent-necrotic lesion. Thus, the majority of patients (69.2%) were hospitalized 3-4 weeks after the development of gangrene, and in the main group 75.9% of patients were admitted to the hospital after 3-6 weeks.

General characteristics of research methods

From the first day of hospitalization, the patients underwent laboratory and instrumental examination methods – a general examination of blood and urine.

The degree of endogenous intoxication was judged by indicators of endotoxemia and endotoxicosis, i.e. multiple organ disorders.

The severity of endotoxemia was determined by the content of medium-weight molecules (MWM) in the blood (spectrophotometric method according to N.G. Gabrielyan), [11].

Plasma toxicity was also judged by the lifetime of the paramecium (LOP), the change in the conductivity of biomolecular phospholipid membranes (BFM) and the respiratory coefficient (RC).

To judge the severity of endotoxicosis, we examined:

а) Research of CBV and its ingredients. The degree of hypovolemia was determined by the indicators of the of circulating blood volume (CBV) and its ingredients according to the method of A. T. Staroverov.

After studying the indicators of central hemodynamics, MWM, Hb, Ht, CVP, hourly diuresis, subjective feelings of patients, we calculated the volume and tactics of ITT in order to combat SEI.

In addition, all patients underwent ultrasound of the main arteries of the lower extremities, percutaneous determination of partial oxygen tension, microbiological studies. 41 patients with PNSTL underwent radiopaque angiography.

б) Methods for assessing liver function. Liver function was studied using radioisotope scanning and hepatography. The state of the liver parenchyma and bile ducts was assessed by ultrasound, and the visualization of blood flow in the liver vessels was assessed by color Doppler scanning. At the same time, magnetic resonance imaging was performed in 14 patients with severe SEI and manifestation of encephalopathy.

Additionally, for a more complete judgment on the functional state of hepatocytes, 22 patients with DM complicated by PNSTL underwent dynamic hepatoscintigraphy with technetium – 99 m.

в) The degree of encephalopathy was studied by psychometric tests: the number connection test (NCT) and the line test (LT). Estimated the execution time and the number of errors.

The test of the connection of numbers, somewhat modified, was as follows: the patient was given the task - to connect the numbers from 1 to 25 sequentially with a line, which were randomly printed on a piece of paper. Estimated execution time (Fig. 1, 2).

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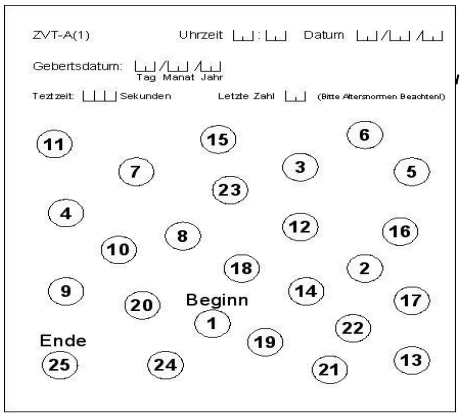

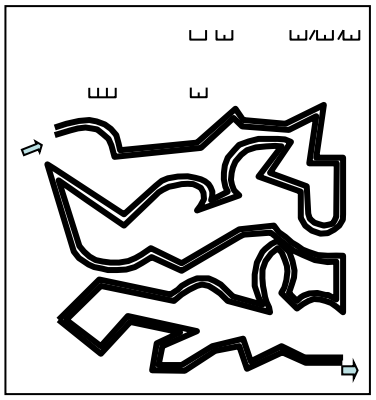

Number connection test., Line test: The patient must draw a long line without touching the two already drawn, and not intersect them. The execution time, the number and degree of errors were evaluated.

RESEARCH RESULTS

The results of the study were compared with the indicators of 30 healthy volunteers (control): 15 men (19-65 years old) and women (20-68 years old).

The test results were evaluated in points from: + 2 to – 4. A result below 2 points was considered a deviation from the norm. Latent HE was diagnosed in cases when the total score was lower than - 3 and there was at least one test result equal to - 2.

The tests were performed at the patient's admission and during the implementation of hepatotropic therapy.

Infusion - transfusion therapy.

Taking into account the pronounced endogenous intoxication in the patients we examined, as well as the fact that the detoxification effect of ITT is possible only when there are prerequisites for strengthening the natural detoxification pathways with the help of an injected infusion drug, we used innovative drugs "Reosorbilact" and "Sorbilact" as the main means of IT carried out by us during the treatment of patients, due to which they significantly increase the flow of fluid from the interstitium into the vascular bed, which improves microcirculation and tissue perfusion [8]. This solved the first task of detoxification therapy. The movement of fluid from the intercellular space into the vascular bed leads to an increase in CBV due to an increase in plasma volume, which leads to hemodilution.

Considering the above, we used these solutions at a dose of 2-4 ml / kg / day, which were administered alternately in / in drip at a rate of 60-80 drops / min.

Therapeutic measures aimed at eliminating endotoxicosis (detoxification) were based on the following principles:

- enhancement of tissue perfusion in order to create conditions for the diffusion of toxins from affected tissue cells and organs into the general bloodstream;

- hemodilution accompanied by a decrease in the concentration of toxins in the blood plasma;

- forcing diuresis, as a result of which toxins and metabolites are excreted from the body.

The main principle that guided us when choosing a drug for infusion therapy in the patients we examined with manifestations of endotoxicosis against the background of DM with micro- and macroangiopathies

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was the principle of low-volume infusion therapy, i.e. therapy based primarily on the redistribution of endogenous fluid without the introduction of significant volumes of endogenous "solvent", which corresponded to our goals – the leaching of toxins from cells, interstitial into the vascular bed and their elimination.

In addition to traditional therapy, patients were supplemented with hepatoprotectors and drugs that stop and prevent the development of a septic cascade. It was pointed out that the liver under "DS syndrome" is exposed to massive and comprehensive effects, and it is natural that a violation of its function in patients with severe "DS syndrome" significantly complicates the clinical course of the latter, worsening its results.

It should be noted that despite the importance of hemorheological disorders in the pathogenesis of a significant number of diseases, including DS, the arsenal of medications that can affect the rheological properties of blood is extremely limited.

One of the main ones in the treatment of patients was the drug L-ornithine L-aspartate, which reduces ammonia intoxication by converting it into urea and prevents the development of hepatic encephalopathy.

L-ornithine L-aspartate in the complex treatment of severe forms of diabetic foot syndrome had a positive hepatotropic effect, contributing to the improvement of the functional ability of the liver.

The patients' well-being improved by the 3rd - 4th days of treatment, which was expressed in normalization of sleep rhythm, reduction of drowsiness, irritability, asthenic syndrome, tremor of the hands, improvement of memory.

By discharge, a positive clinical effect was achieved in all patients with SEI caused by diabetic foot syndrome with stage I HE, and stage II HE. With the improvement of clinical indicators, the concentration of ammonia in the blood decreased. By the 4th day of treatment, the concentration of ammonia decreased in most patients with HE of stages I and II. Moreover, the degree of its decrease was higher than the degree of improvement in clinical symptoms. In five patients with grade II HE and one with grade III HE, due to complications associated with surgical status, we did not observe an improvement in hepatic functions, a decrease in signs of hepatic encephalopathy.

Indicators (Fig. 3, 4) of psychometric tests for HE of stages I and II improved by the end of a week-long course of treatment. By the 12th day, the execution time of the LT, and the number of errors in LT were significantly reduced.

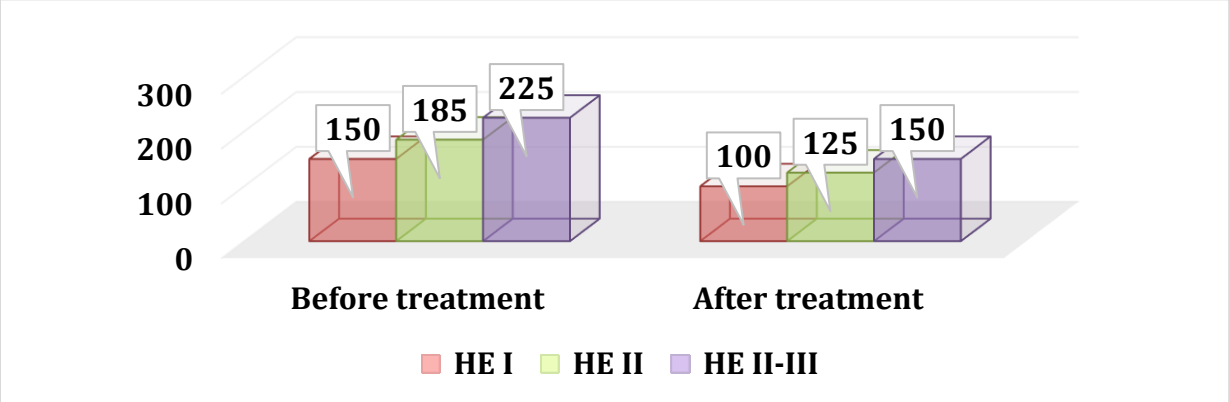

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Fig. 3. Number connection test

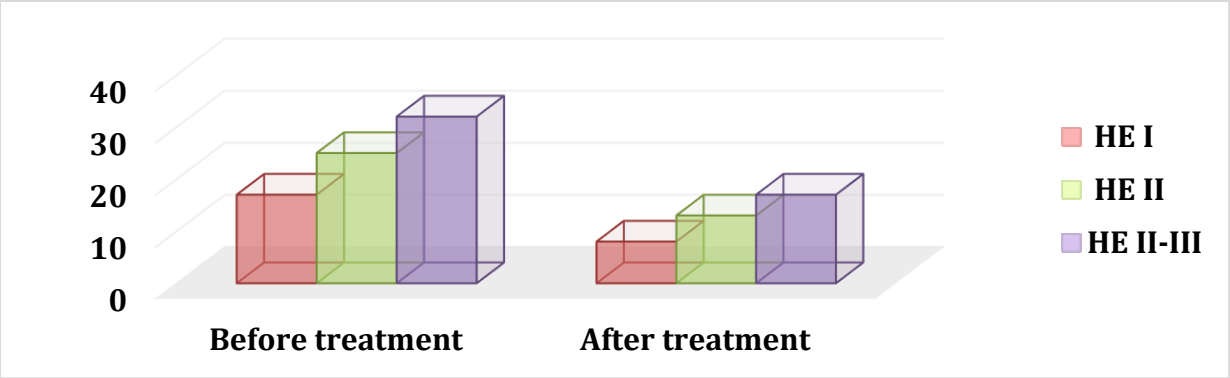

Fig. 4. Line test

In 69.2% of patients with stage I HE and in 41.6% of patients with stage II, the indicators of psychometric tests by day 12 did not differ from similar indicators of healthy people.

The determination of the correlation between the values of ammonia and the severity of SEI in the dynamics of complex treatment of PNSTL with the use of hepatoprotectors and drugs that stop tranaminase activity in 46 patients with a positive clinical effect clearly showed (Table 4.19) a direct relationship between the content of ammonia in the blood and other SEI indicators. So, already on the 4th day of treatment of patients, the concentration of ammonia in the blood decreased by 0.4 mmol/l (28.4%), which indicated an improvement in the urea-synthesizing and, consequently, detoxification function of the liver; The concentration of MWM decreased by 26.6%, the LOP lengthened by 44.1%, BC increased by 148.6%, and the conductivity of BFM shortened by 18.7%. These data indicate a significant role in the intoxication of ammonia in patients with PNSTL, which is the result of a violation of the urea-synthesizing function of the liver.

Table 4.19

Indicators of ammonia and SEI in patients with PNSTL in the course of complex therapy with the use of hepatoprotectors, M±m

Indicator	Treatment, days		
	1st	4th	12th
Ammonia, mmol/l	1,41±0,04	1,01±0,01	0,978±0,022
WMW, mg/ml	0,422±0,010	0,310±0,011	0,268±0,021
LOP, min	10,4±0,7	14,6±0,3	17,2±0,36

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RC %	26,0±0,8	63,9±0,8	70,4±1,3
Bfm, $ом^{-1}\ см^{-2}\cdot10^{-8}$	4,28±0,07	3,05±0,04	2,79±0,05

Note: Significant difference of all indicators from the beginning of treatment (1-day)

Along with the improvement of the studied parameters, by the end of the course of treatment, the indicators of the functional state of the liver improved in patients: the prothrombin index, the concentrations of albumin, fibrinogen and bilirubin in the blood, which also reduced the severity of the disease.

Summing up, after the completion of treatment, its effectiveness, expressed in the disappearance of HE symptoms and normalization of the results of psychometric tests, was achieved in 73.1% of patients with stage I HE and in 50% of patients with stage I HE.

Thus, the study of patients with DM complicated by PNSTL showed that in almost 100% of cases there are violations of the functional state of the liver. The degree and severity of these disorders directly depend on the duration of PLSTL, the nature of gangrene and inflammatory reaction, the severity of SEI, the level of ammonia in the blood. Especially the protein-synthesizing, detoxifying functions of the liver (urea-synthesizing), absorption-excretory functions are disrupted. Almost all of these disorders are potentially reversible, despite an increase in transaminase activity indicating necrobiotic changes in the liver. The inclusion of hepatoprotectors, antioxidants, and drugs that stop transaminase activity in complex therapy is pathogenetically justified and contributes to the regression of liver disorders.

CONCLUSION

1. Endogenous intoxication, with DM complicated by PNSTL, disrupts numerous liver functions, in particular urea-synthesizing, which is the cause of severe hepatic encephalopathy.

2. Monitoring of liver functions in patients with endogenous intoxication, allows you to quickly register emerging disorders.

3. Use in therapy of agents that improve hepatic blood flow, hepatoprotectors and stop the septic cascade, contributes to the prevention of hepatic encephalopathy and coma.

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