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11931 Barlow Pl Philadelphia, PA 19116, USA

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THE EFFECT OF ENDOTOXICOSIS AND ENDOGENOUS INTOXICATION SYNDROME ON THE FUNCTIONAL STATE OF THE LIVER IN PATIENTS WITH DIABETES MELLITUS COMPLICATED BY THE DIABETIC FOOT SYNDROME

Ibragimov Nematjon Komildjonovich
Department of Anesthesiology and Resuscitation of Tashkent Medical Academy, Uzbekistan

Abstract: Objective: to study the effect of endogenous intoxication on the liver in patients with diabetes mellitus (DM) complicated by purulent - necrotic soft tissue lesion (PNSFL). Materials and methods: 110 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 liver failure. Patients were divided into 2 groups: 52 (control), 58 (study), which, in addition to traditional therapy, included hepatoprotectors and drugs that stop transaminase activity. Conclusions. The inclusion of hepatoprotectors, antioxidants and drugs blocking transaminase activity in complex therapy is pathogenetically justified and optimizes the outcomes of such a formidable complication of diabetes as PNSFL.

Keywords: endotoxicosis, endotoxemia, intoxication, diabetes mellitus, liver.

Introducrion. Diabetes mellitus (DM) is one of the most common diseases that affects from 3 to 15% of the population of economically developed countries, with an annual increase in newly detected cases from 6 to 10% [5, 8, 9, 12]

To date, the treatment of surgical diseases developing against the background of diabetes mellitus remains one of the most important issues of modern surgery [2, 29, 30]. Up to 47% of hospitalizations of diabetic patients are associated with foot lesions [15, 27]. The prevalence of diabetic foot syndrome (DFS) among patients with diabetes is on average 4-10% [13, 16, 22, 24]. Despite the fact that the prevalence of DM in various countries ranges from 1.5 to 6%, patients with diabetes mellitus with DFS account for 40-60% of all lower limb amputations of a non-traumatic nature. Purulent - necrotic lesions of the foot can develop in patients with DM of various age groups, but most often at the age of 50-75 years, as a rule, suffering from various concomitant diseases [10, 14, 28].

The problems of treating such patients are far from being resolved. Timely treatment of trophic ulcers, purulent-necrotic wounds in patients with diabetes mellitus avoids the spread of infection leading to limb amputation [11, 18, 31].

This clearly indicates the urgent need for further scientific research aimed at early diagnosis of DM and its complications, effective methods of DF therapy.

According to recent estimates, liver damage is one of the most common pathologies in DM [1, 19]. The fact of liver damage in DM is beyond doubt.

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. L. A. Kamerdina [3] emphasizes that the diagnosis of liver pathology in patients with DM is difficult because clinical manifestations of this complication are often asymptomatic, erased, the absolute majority of authors hold the same opinion [6, 7, 33]

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 [4]. Therefore, it is not always possible to detect functional liver disorders using conventional clinical and laboratory methods, even with decompensated DM [26].

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 in clinical settings [20].

Generalized lesions of the vascular system, pronounced endotoxemia in DM patients with diabetic foot syndrome, 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 [17, 21, 25, 32].

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, and even acute liver failure. Ideal treatment regimens for various complications of DM with liver pathology have not yet been developed [23, 34]. In this regard, in daily practice, the doctor, first of all, should focus on the underlying cause of the disease.

The aim of the study was to study the effect of endogenous intoxication on the liver in patients with diabetes mellitus (DM) complicated by purulent - necrotic soft tissue lesion (PNSFL).

Materials and methods of research.

We examined 110 patients with purulent - necrotic soft tissue lesions complicated by diabetes mellitus. Depending on the nature of the treatment measures, all patients were divided into two groups. Group 1 (control) - 52 (47.3%) patients receiving complex conventional therapy: correction of hypo- and dysproteinemia, anemia, hypovolemia, dyshydria and dyselectrolythemia, depending on the degree of their disorders.

The 2nd (main) group consisted of 58 (52.7%) patients who underwent surgical and conservative therapy. In order to prevent and combat the generalization of infection, as well as to improve liver functions, primarily detoxification, patients received additional hepatoprotectors, drugs that improve hepatic blood flow and stop the septic cascade (transaminase and free radical activity).

The patients of the study group (the main one) differed from the patients of the 1st severity and extent of the lesion of the lower limb. All patients showed signs of pronounced endogenous intoxication, and hepatic encephalopathy was registered in 72.2%.

In 67.8% of the patients we examined, the picture of PNL of the foot developed in the late stages of DM suffering (6-15 years). In 13.8% of cases, DPNL developed within less than 5 years from the onset of the disease. Group 1 patients had a shorter duration of diabetic history.

All patients of both groups received complex treatment, including surgical treatment of a purulent focus of non-viable tissues and /or amputation of a limb according to indications, as well as treatment aimed at normalizing carbohydrate, protein and fat metabolism, water-electrolyte and acid-base state. Detoxification, antibacterial and immunotherapy, anticoagulants were prescribed.

Clinical and biochemical parameters of blood, liver function, and the degree of endotoxemia were evaluated in all patients.

Statistical processing of the results was carried out using the Microsoft Office Excel-

2012 software package, including the use of built-in statistical processing functions. The methods of variational parametric and nonparametric statistics were used with the calculation of the arithmetic mean of the studied indicator (M), the mean square deviation ( ), the standard error of the mean (m), relative values (frequency, %). The statistical significance of the measurements obtained when comparing the average values was determined by the Student's criterion (t) with the calculation of the probability of error (P) when checking the normality of the distribution (by the kurtosis criterion) and the equality of general variances (F - Fisher criterion). The level of confidence $P<0.05$ was taken as statistically significant changes.

The results of the study. Patients were admitted to the hospital in a serious condition due to the underlying pathology, endotoxemia, anemia.

The relationshi p between the state of detoxifying liver and kidney function and SEI indicators was determined by the results of their study in 8 patients with satisfactory liver and kidney values, and in 12 patients (the same group) with impaired their functions. We have established a correlation between the severity of endotoxemia and the frequency of liver and kidney damage, in which the values of MSM > 0.400 mg/ml, LVL <12 min., BFM conductivity> 4 ohms-1 cm-2 10-8 , and DC <30%.

In 18.7% of patients, an increased content of bilirubin and serum transaminases was detected, which indicated cholestatic syndrome and necrobiotic processes in hepatocytes.

The study of hemostasis showed activation of the coagulation system, hyperfibrinogenemia, an increase in PDF with a simultaneous decrease in the prothrombin index. These were direct signs of DIC syndrome and indirect violations of liver function responsible for hemostasis.

Hypovolemia was detected in almost all patients of the control group. The CBV was 33% lower than normal values due to both ingredients. But mainly due to the globular volume.

These disorders were reflected in the indicators of hepatic blood flow, as indicated by the RGG data, a decrease in rheographic indices - RSI and RDI - by 10.6 and 5.9%, respectively. In addition, deviations in the ratio of anacrota and catacrota indicated a decrease in hepatic blood flow.

In general, the treatment improved the condition of patients. But at discharge, anemia and hypoproteinemia were also diagnosed. The levels of ammonia and bilirubin in the blood significantly decreased, indicating an improvement in the urea-synthesizing function of the liver and a decrease in cholestasis. But hemostasis, despite the decrease in PTI, remained elevated. Correction of hypovolemia contributed to the improvement of hepatic circulation, although it did not recover to normal, judging by the values of rheographic indices and the ratio of anacrota to catacrota.

Consequently, traditional therapy, subjectively improving the patient's condition, does not normalize liver function by discharge (10th - 12th day). It should be assumed that monitoring of blood circulation and liver function and early diagnosis of generalization of the process in such a contingent of patients will allow them to promptly diagnose emerging disorders and carry out timely treatment.

The main group consisted of 58 patients who, in addition to traditional therapy, were prescribed hepatotropes, drugs that stop the septic cascade. In 70.3%, the duration of DM disease was up to 10 years, and PNLNA - in 64.8% developed within 30 days. A high percentage were patients with fluffed forms (35.2%). They were received after 31 - 61 days.

Changes in SEI indicators were somewhat more pronounced in patients of this group. According to all parameters characterizing the degree of endogenous intoxication, more pronounced shifts were detected in patients of group II than in group 1

Determination of the relationshi p between the values of ammoniaand the severity of SEI in the dynamics of complex treatment of PNLNA with the use of hepatoprotectors in 22 patients showed a direct correlation with a positive clinical effect. Thus, on the 4th day of treatment, the concentration of ammonia in the blood of patients decreased by 0.4 mmol/ 1 (28.4%), which indicated an improvement in the urea-synthesizing, and, consequently, detoxifying functions of the liver. The concentration of MSM decreased by 26.6%, the VPJP lengthened by 44.1%, DC increased by 148.6%, and the conductivity of BFM decreased by 18.7%.

Consequently, ammonia plays an important role in the development of intoxication in patients, the growth of which indicates a violation of the urea-synthesizing function of the liver. Therefore, we consider the use of hepatoprotectors in the complex therapy of such patients to be exclusively pathogenetically justified and a priority.

Indicators of volemia and regional (hepatic) blood flow also showed negative trends.

Hepatography revealed a significant slowdown in the accumulation of the drug in hepatocytes, an extension of the plateau time and the timing of radionuclide excretion into the intestine.

Table
Rheohepatography and hepatoscintigraphy indicators by groups M±m

Indicators	Control group (n=52)	Main group (n=58)	P
RDI	0,608±0,020	0,610±0,032	>0,05
RSI	1,002±0,020	1,008±0,033	>0,05
α , with	0,076±0,002	0,079±0,002	>0,05
β, with	0,738±0,070	0,740±0,041	>0,05
α/β	0,178±0,028	0,130±0,009	<0,05
Total clearance	0,36±0,01	0,35±0,02	>0,05
Share of liver, %	84,3±0,7	83,3±2,2	>0,05
Share of spleen, %	4,8±0,3	4,9±0,3	>0,05
Hepatic clearance	0,37±0,03	0,35±0,01	>0,05
Retention coefficient in the blood	0,71±0,04	0,73±0,21	>0,05
Retention coefficient in the liver	1,50±0,09	1,47±0,05	>0,05
Hepatic seizure Index	2,48±0,14	2,41±0,04	>0,05

The scans showed a more pronounced decrease in the intensity of radiopharmaceutical accumulation and uneven image texture than in the control. All this clearly indicated a violation of the absorption-excretory function of the liver.

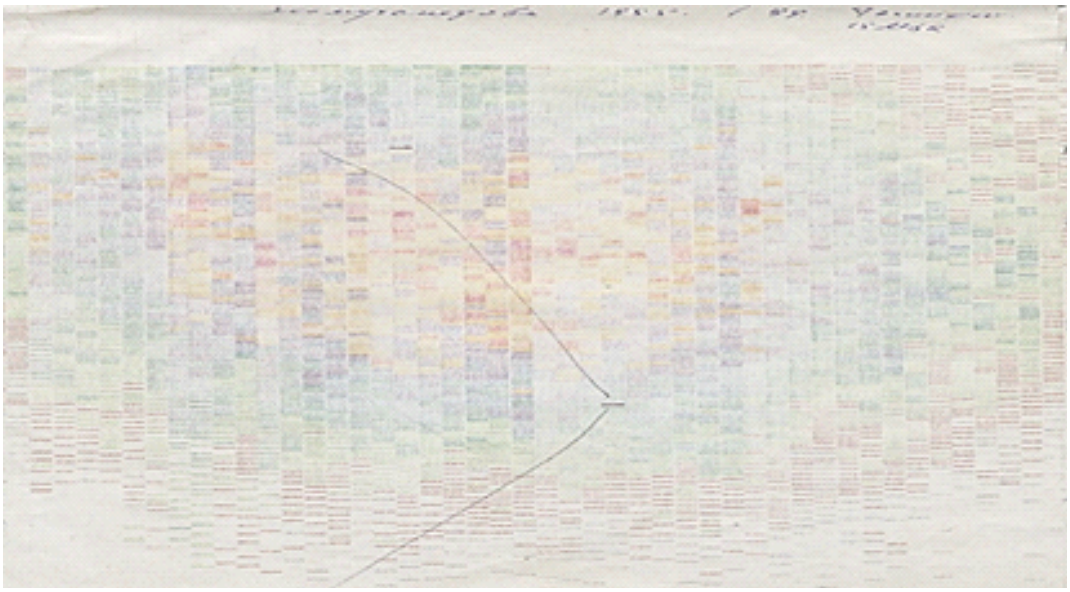

Figure 1. Hepatoscintigraphy.

Slowing down the accumulation of the drug in hepatocytes, prolonging the plateau time and slowing down the period of radionuclide excretion in the intestine.

In addition to traditional therapy, one of the main drugs of treatment was L - ornithine L-aspartate, which reduces ammonia intoxication, converts ammonia into urea and prevents the development of HE. An important place in the treatment was occupied by antioxidants (ascorbic acid, thioctacid, tocopherol) and drugs that stop transaminase activity (magnesium preparations).

The complex of therapy had a positive effect on the normalization of liver function, improving the overall results of treatment. By the 4th day of treatment, the level of ammonia decreased in all patients, ahead of clinical symptoms. The performance of psychometric tests in HE I and II degrees improved by the end of the week-long course. By the 12th day, the execution time of the TL, TL and the number of errors in TL significantly decreased. At the same time, in 69.2% of patients with grade I PE and in 41.6% with grade II PE, the performance of psychometric tests normalized.

The indicators of the functional state of the liver also improved, however, radioisotope hepatography on the 7th day still continued to state a decrease in the absorption and excretory function of the liver in all patients, but it was less pronounced than after traditional therapy.

61% of high limb amputations were performed. In control - 85%. Complications that occurred in patients of the main group (pneumonia - in 3 patients, acute hepatic insufficiency - in 2, acute hepatic-renal insufficiency - in 1, PE - in 39, suppuration of the stump, sepsis - in 6 patients) were stopped during complex therapy. Consequently, the generalization of the infectious process with the development of sepsis was noted in 10.3%.

Thus, the examination of patients with DM complicated by PNLNA showed that almost all of them have impaired liver function, the degree and severity of which directly depends on the duration of PNLNA, the nature of gangrene and inflammatory reaction, the severity of SEI, the level of ammonia in the blood. The inclusion of hepatoprotectors, antioxidants and drugs blocking transaminase activity in complex therapy is pathogenetically justified and optimizes the outcomes of such a formidable complication of diabetes as PNSFL.

Conclusions:

1.Decompensated DM, complicated by PNLNA, disrupts numerous liver functions, the degree of which is directly proportional to the duration of the purulent - inflammatory process, the severity of endogenous intoxication.

2.Monitoring of hepatic functions in patients with DM complicated by PNLNA makes it possible to promptly register emerging disorders.

3.The timely use in therapy of drugs that improve hepatic blood flow, hepatoprotectors and stop the septic cascade, contributes to the regression of disorders of hepatic functions.

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