

Evaluation of the effectiveness of the use of “Hepa-Merz” in burn disease

Abstract

A burn affects the structure and function of almost every organ including the liver. This study received approval from Samarkand Centre of Emergency Medical Care (RCSUMA), Uzbekistan. The research program included complex treatment and examination of 82 patients with IIIAB-IV degree burns from 30% to 60% of the body surface and included: a general clinical and instrumental examination, biochemical and clinical blood tests. The analysis of the results of the study showed the effectiveness of the use of Hepa-Merz in the complex treatment of severely burned patients. The use of Hepa-Merz allows to enhance the targeted therapeutic effect on the functional and morphological state of the liver and is indicated for the prevention and treatment of post-burn intoxication hepatitis.

Introduction

The liver is the organ where nutrients absorbed in the digestive tract are processed and stored for later use by other body systems. Therefore, the liver is the link between the digestive and circulatory systems [1]. The position of the liver in the vascular system is optimal for the collection, modification and filling of metabolites, for the neutralization and elimination of toxic substances [2, 3]. A burn affects the structure and function of almost every organ. Therefore, organ failure (whether single or multiple) is a significant factor in the survival of patients with extensive and deep burns [4]. Hypermetabolic processes, an inflammatory reaction associated with protein catabolism, amino acid degradation, insulin resistance, hyperglycemia, and lipolysis, make a significant contribution to the development of organ failure, primarily the liver [5-7]. The liver plays a central role as a distant target organ due to the "systemic" inflammatory component of burn disease. Patients with liver pathology prior to burn injury are 2 times more likely to die compared to patients who did not have liver pathology prior to injury [8]. Of undoubted interest may be the drug Hepa-Merz,

the pharmacological action of which is based on the ornithine- aspartate complex, which stimulates the neutralization of ammonia, which is currently of great importance in the pathogenesis of hepatic encephalopathy (9,10). In addition, its blocking effect on muscle catabolism has been described. In this case, this is of particular importance, because. it is known that under conditions of protein deficiency in severely burned patients, endogenous reserves are consumed, primarily muscle proteins.

Material and methods

This study received approval from Samarkand Centre of Emergency Medical Care (RCSUMA), Uzbekistan. The research program included complex treatment with Hepa-Merz and examination of 82 patients with IIIAB-IV degree burns from 30% to 60% of the body surface and included: a general clinical and instrumental examination, biochemical and clinical blood tests.

In 61 severely burned patients, Hepa-Merz was administered intravenously at a daily dose of 20 g per 400 ml of infusion solution. 21 severely burned patients underwent traditional complex treatment, the scheme of which did not include the use of " Hepa-Merz " (comparison group). Indication for the appointment of the drug Hepa-Merz in most cases was post-burn hepatitis, which developed against the background of extensive burns, burn intoxication, dystrophy of internal organs with the development of multiple organ failure and metabolic exhaustion. When examining patients, the characteristic laboratory signs indicating functional and morphological damage to the liver were:

1. Hepatomegaly (enlargement of the liver by 3-5 cm or more);
2. An increase in the level of bilirubin to $53.6 \mu\text{mol} / \text{l}$;
3. Fermentemia (AST and ALT up to 70 units / l);
4. An increase in the activity of alkaline phosphatase (AP) up to 700 units / l;
5. Hypoproteinemia (total protein 45-50 g/l);
6. Increasing the level of urea (up to $10\text{-}17 \text{ mmol} / \text{l}$);
7. Increase in creatinine content (up to $200\text{-}300 \mu\text{mol} / \text{l}$);
8. Coagulopathy (hypercoagulability, DIC).

In all patients, a shift in the blood formula to the left to young forms, lymphopenia was observed. Clinically noted hyperthermia up to 39°C , tachyarrhythmia (HR 100-120/min), shortness of breath (RR 25-30/min). Clinical and laboratory control to assess the effectiveness of the drug was carried out 1 time in 2-3 days.

Results and discussion

Dynamic observation showed that Hepa-Merz patients tolerated it well, no side effects were observed. For most patients, the minimum period of use of the drug should be considered 7 days.

In 47 (77%) of 61 patients, by day 6 after the start of using Hepa-Merz, the main laboratory parameters normalized, including improved indicators indicating the restoration of liver functions (prothrombin -forming, synthetic, detoxification, etc.).

At the same time, in 14 (23%) of the most severe patients, in whom the course of burn disease was complicated by the development of sepsis, according to clinical and laboratory data, the functional recovery of the liver was "delayed", which served as the basis for continuing the intravenous course of treatment up to 12-13 days. In addition, taking into account the severity of the patients' condition, in order to prevent possible further complications from the liver, associated both with massive drug exposure and with burn disease continuing until the restoration of the integrity of the skin, the use of Hepa-Merz in 6 patients continued in oral form for another within 14 days.

Against this background, we did not notice manifestations of functional liver failure, and nutritional indicators (total protein, albumin, total hemoglobin, lymphocytes, etc.) tended to further improve or stabilize. In another 9 cases, in patients with deep, but limited in area burns up to 10% of the body surface, Hepa-Merz was administered orally due to the development of alcohol intoxication delirium or the threat of its development (in patients suffering from chronic alcoholism). In these cases, Hepa-Merz was included in the scheme of ongoing detoxification and sedative therapy, which made it possible to reduce the manifestations of delirium and its duration, to normalize liver function tests already on the 7th day after the start of treatment.

Hepa-Merz, whose pharmacological action is based on the ornithine- aspartate complex, stimulates the neutralization of ammonia. In addition, its blocking effect on muscle catabolism has been described. As is known, under conditions of protein deficiency in severely burned patients, endogenous reserves are consumed, primarily muscle proteins.

As part of a comprehensive survey, more than 50 determinations of the ammonia content in the blood serum of severely burned patients during the acute period were carried out. As a result, initially and in dynamics, fluctuations in the value of the indicator were within the normal range (0.20-0.80 mg/ml). In this category of patients, this indicator was not pathognomic of the severity of the condition, because All patients received intensive care.

At the same time, we consider it expedient to continue these studies in patients who are in a delirious state, as well as to conduct a detailed study of the nitrogen balance of urea nitrogen and amino acids under treatment with Hepa-Merz.

The accumulation of end products of protein metabolism is a well-known criterion for multiple organ failure, as well as hypercatabolism and increased exogenous administration of AA.

In the group of intravenous use of Hepa Merz, a decrease in the level of urea after the course was clearly observed, while in the comparison group, a continuing accumulation of this metabolite was observed.

As already mentioned, in severely burned patients, functional liver failure is polyetiologic. One of its manifestations is an increase in the activity of alkaline phosphatase (AP). We traced and compared the dynamics of this indicator in different groups (Table 1).

As a result of the use of this drug, there is a decrease in congestion in the liver in a short time. On the contrary, in the comparison group there is a persistent increase in the activity of alkaline phosphatase for a long time (up to a month).

It should be noted that in 3 patients there was a single increase in enzyme activity immediately after drug administration, which is quite understandable: against the background of pronounced microcirculation disorders, increased membrane permeability and intracellular hydration, any metabolic stimulation can cause additional stress to these processes. This fact must be taken into account in severely burned patients in the acute period and in order to achieve the desired effect, a longer course should be preferred to an increase in the daily dose.

One of the manifestations of functional liver failure is bilirubinemia, which is quite often observed in severely burned patients in the acute period. Also, an increase in the level of bilirubin is observed in patients who have previously had a viral infection. According to our data, Hepa-Merz has an impact on this indicator (Table 2).

Conclusion

Thus, the analysis of the results of the study showed the effectiveness of the use of Hepa-Merz in the complex treatment of severely burned patients. The use of Hepa-Merz allows to enhance the targeted therapeutic effect on the functional and morphological state of the liver and is indicated for the prevention and treatment of post-burn intoxication hepatitis. In this case, Hepa-Merz should be administered parenterally at a maximum daily dose of 20 g per 400 ml of saline. The course of treatment is determined individually and

ranges from 7 days to 3 weeks. It is possible to sequentially prescribe the drug in different forms (intravenous administration, the use of Hepa-Merz per os).

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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Table. 1 Changes in the activity of alkaline phosphatase in severely burned patients (normal alkaline phosphatase 80-295E/l)

Hepa-Merz treatment		Traditional treatment	
Before treatment	After 7 days	Before treatment	After 7 days
790.6	413.0	495.0	472.0

584.2	243.0	296.1	250.0
534.0	253.0	354.0	472.0
300.0	76.0	377.6	374.6
495.6	103.2	354.0	539.0
354.0	183.0		
438.9	198.2		
236.0	136.8		
Avg. value 466.6	Avg. value 200.8	Avg. value 375.0	Mean value 421.5

Table 2 Dynamics of the level of bilirubin $\mu\text{mol.}$ in severely burned Patients during treatment with Hepa - Merz for 7 day)	
Before treatment	After treatment
17.5	9.6
53.3	47.5
33.0	7.9
18.5	10.5
53.6	12.9
16.5	12.0
Mean value 32.1	Mean value 20.0