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Original Research Article

Evaluation of the effectiveness of the use of "Hepa-Merz" in burn disease

Abstract

Introduction: A burn affects the structure and function of almost every organ including the liver. **Material and Methods:** 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 (deep burns) degree burns from 30% to 60% of the body surface and included: a general clinical and instrumental examination, biochemical and clinical blood tests. **Results:** The results of the study showed the effectiveness of the use of Hepa-Merz in the complex treatment of severely burned patients. Conclusions: 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.

Keywords: Burns, Liver, Hepa-Merz

Introduction

A severe burn, represents a devastating injury affecting nearly every body organ system and leads to significant patient morbidity and mortality. 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). Hepa-Merz International name: ornithine, active substance: L-ornithine-L-aspartate 3 g. 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

The research program included complex treatment with Hepa-Merz and examination of 82 patients with IIIAB-IV (deep burns) 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 μmol / 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 10-17 mmol / l);
7. Increase in creatinine content (up to 200-300 μmol / 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 39C, 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

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).

Discussion

Severe burn injuries represent a critical health care challenge. In the United States, 1.1 million burn-victims require medical attention yearly (11). In adult victims, the overall mortality rate reaches as high as 50% when the total body surface area (TBSA) of burn injury is over 60% (12). Mortality in severe burn victims results from a consequence of systemic complications and multiple organ failure. Extensive burn represents a devastating traumatic injury and leads to high mortality rates in affected patients (13,14). The last decades have witnessed a number of advances in burn research and therapeutic strategies for the treatment of severely burned patients, including improved fluid resuscitation, infection control, would healing, new grafting materials, the management of inhalation injuries, and life support techniques for the clinical care for burns, which have significantly improved post-burn clinical outcomes. The liver plays an important role in the body's response to thermal injury. It is the principal organ responsible for producing acute-phase proteins and modulating the systemic inflammatory response. After major trauma, such as a severe burn, hepatic protein synthesis shifts from hepatic constitutive proteins, such as albumin, prealbumin, transferrin, and retinol-binding protein, to acute phase proteins, which serve as mediators of the inflammatory process, function as transport proteins, and participate in burn wound healing.

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).

Ethical Approval

This study received approval from Samarkand Centre of Emergency Medical Care (RCSUMA), Uzbekistan.

Consent

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

Conflicts of interest

None

References

1. Czaja AJ, Rizzo TA, Smith WR Jr, Pruitt BA Jr //Acute liver disease after cutaneous thermal injury// J Trauma. 1975 Oct;15(10):887-94.
2. Maev I.V., Vyuchnova E.S., Lebedeva E.G., Yakovenko E.I., Dicheva D.T.//Evaluation of the effectiveness of complex therapy for hepatic encephalopathy in patients with cirrhosis of the liver// Klin. medical, 2002, №5. p.23-27.
3. Prelack K. Practical guidelines for nutritional management of burn injury and recovery Burns 2007-Vol.33, Issue 6, p.14-24.
4. Bukowska W, Szarzewski A, Szumera M, Raczkowska-Kozak J, Korzon M //Acute hepatic insufficiency acute liver failure in five children// Med Sci Monit , 1998, 4.
5. Feher J, Lang I, Gogl A, Varga L, Tompos G, Pronai L //Effect of ornithine-aspartate infusion on elevated serum ammonia concentration in cirrhotic patients — results of a randomized, placebo-controlled double-blind multicentre trial// Med sci Monit, 1997; 3(5).
6. Jeshke MG, Low JF, Spies M, Vita R, Hawkins HK, Herndon DN, Barrow RE// Cell proliferation, apoptosis, NF- kappa B expression, enzyme, protein, and weight changes in livers of burned rats// Am J Physiol Gastrointest Liver Physiol. 2001 Jun;280(6): p.1314-20.
7. Kaiser S, Gerok W, Heusinger D //Ammonia and glutamine metabolism in human liver slices: new aspects in the pathogenesis of hyperammonemia in chronic liver diseases// Eur. J. Clin. Invest. 1988; 18:535-42.
8. Kong F, Guo X, Noel JG, Wells DA, Lovell GJ, Ogle CK //Thermal injury-induced increases of hepatocyte SOCS3 leading to decreases in STAT3// Shock. 2002 Oct;18(4):374-9.
9. Tadros T, Traber DL, Herndon DN // Hepatic blood flow and oxygen consumption after burn and sepsis// J Trauma. 2000 Jul;49(1):101-8.
10. Nuguent N., McCormick P.A. Orr D.J.// Severe Acute hepatitis in a burns patients// Burns.2004, - vol.30, Issue 6, p.610-611.

11. Association AB. *Burn incidence fact sheet*. Chicago, IL: The ABA; Available online at: http://ameriburn.org/who-we-are/media/burn-incidence-fact-sheet. 2016.
12. Taylor SL, Lawless M, Curri T, Sen S, Greenhalgh DG, Palmieri TL. Predicting mortality from burns: the need for age-group specific models. Burns. 2014;40(6):1106–15.
13. Kallinen O, Maisniemi K, Böhling T, Tukiainen E, Koljonen V. Multiple organ failure as a cause of death in patients with severe burns. Journal of Burn Care & Research. 2012;33(2):206–11.
14. Jeschke MG. The hepatic response to thermal injury: is the liver important for postburn outcomes? Molecular medicine. 2009;15(9):337–51.

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 µmol. 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