Ukrainian Scientific Medical Youth Journal
Issue 2 (131), 2022
ISSN 1996-353X
ISSN 2311-6951

**PHARMACY, INDUSTRIAL PHARMACY /
ФАРМАЦІЯ, ПРОМИСЛОВА ФАРМАЦІЯ**

UDC: 616.36-002-06:616-001.45]-08
https://doi.org/10.32345/USMYJ.2(131).2022.61-69

Received: March 12, 2022
Accepted: May 17, 2022

Effectiveness of reactive hepatitis therapy in injured with ballistic wounds

Savichan Kyrylo
Military Therapy Department, Ukrainian Military Medical Academy, Kyiv, Ukraine

Address for correspondence:

Savichan Kyrylo

E-mail: k.savichan@gmail.com

Abstract: *Reactive hepatitis complicates the treatment of ballistic wounds. The aim of our study was to study the clinical and pharmacoeconomic effectiveness of the treatment of reactive hepatitis in the wounded. A prospective study of 112 wounded servicemen with increased transaminase activity was randomized into three groups: group I received arginine glutamate intravenously for 10 days, group II received phosphatidylcholine intravenously for 10 days, and group III received standard treatment. In the presence of hypoalbuminemia, the wounded received intravenous infusions of albumin to normalize its level in serum. The initial level of alanine aminotransferases was 62.5 in group I patients [50.5; 80.0] IU / l, in the second group - 64.0 [48.5; 83.0] IU / l and 62.0 [47.0; 85.5] IU / l, respectively, in group III (p> 0.05 according to the Mann-Whitney test). In the period up to 14 days after injury, alanine aminotransferase levels decreased significantly in all groups (p <0.05 according to Wilcoxon's test) and amounted to 38.5 in group I [34,0; 63.5] IU / l, in the second group 46.0 [32.0; 62.5] IU / l, in group III 50.0 [40.0; 78.0] IU / l (p = 0.014 according to the Mann-Whitney test compared to group I). In 14 and more days after injury in all groups the average concentration of alanine aminotransferases was significantly lower compared to the previous study period (p <0.05 according to Wilcoxon's test): in group I the concentration of alanine aminotransferases was 33.0 [29,8; 40.0] IU / l (p = 0.048, p <0.001 according to the Mann-Whitney test in comparison with group II and III, respectively), in group II - up to 38.0 [31.0; 62.0] and in group III to 48.0 [39.5; 69.0] (p = 0.014 according to the Mann-Whitney test compared to group II). Also, there was a tendency to reduce the frequency of complications from internal organs: in 13% (8 of 63) patients of groups I and II, compared with 27% (13 of 49) of group III (p = 0.063). Significantly decreased both the duration of treatment in the intensive care unit: in group I (4.2 ± 1.8) days, compared with group III (7.4 ± 6.0) days, p = 0.012, and the duration of total hospital stay (20.4 ± 11.1) days for group I, compared with (29.7 ± 3.5) days for group III, p = 0.022. In the cost-effectiveness analysis of arginine glutamate and phosphatidylcholine regimens, a 2-fold better cost-effectiveness ratio was found in the group of reactive hepatitis wounded who received arginine glutamate.*

Key words: hepatitis, liver, pharmaceutical economics, therapeutics, transaminases.

ISSN 1996-353X
ISSN 2311-6951

Introduction

One of the serious complications of ballistic wounds is reactive hepatitis (RH) due to primary liver damage (Osyodlo et al., 2022), or secondary lesions resulting from systemic disorders in critically ill patients (Horvatits, Trauner, & Fuhrmann, 2013; Soleimanpour et al., 2015; Horvatits, Drolz, Trauner, & Fuhrmann., 2019; Yang, 2015). Almost 40% of those injured in the anti-terrorist operation showed an increase in transaminases (alanine aminotransferase - ALT and aspartate aminotransferase – AST (Kazmyrchuk, Miasnykov, Sydorova N.M., & Sydorova L.L., 2014). In a retrospective study, 2 weeks or more after a gunshot wound, the proportion of ALT patients above 80 IU / l was more than 20% (Savichan, 2022a). There is a gradual increase in the incidence of chronic diffuse liver disease of predominantly non-viral aetiology, which ranks second in the structure of digestive diseases among officers and servicemen of the contract service (Osyodlo, 2013; Osyodlo et al., 2015).

Preventing the development of chronic liver pathology is possible with timely diagnosis and pathogenetic treatment (Horvatits et al., 2013). A special place in the treatment of hepatitis of various origins is occupied by hepatoprotectors - a large group of drugs that restore hepatocyte metabolism, prevent the development of degenerative-dystrophic processes and stimulate regeneration in the liver. In patient`s treatment are used essential phospholipids (EFL) - essentiale, phosphogliv, essliver, enlir, lesfal, etc., which help to restore hepatocyte membranes, reduce the accumulation of free fatty acids in the liver, protect cell organelles and reduce the intensity of oxidative stress (Belovol, & Kniazkova, 2019; Palii, 2009). According to several studies, the use of essential phospholipids accelerates the reduction of subjective symptoms and clinical manifestations of liver pathology, which is confirmed by the results of histological and ultrasound examinations, and the positive dynamics of hepatic cytolysis markers. The therapeutic effect of EFL is associated with the effect on membrane-dependent cell functions, as well as with anti-inflammatory, antioxidant, antiseptic, membrane-protective and lipid-regulating actions of drugs (Gundermann et al., 2016). Modulators of nitric oxide, in particular arginine glutamate, also have a hepatotropic effect. Arginine is part of many proteins and is one of the precursors in the synthesis of creatine and an intermediate in the synthesis of urea in the liver. (Oleshchuk, 2014). It is known that arginine is a replaceable amino acid, but against the background of traumatic or metabolic stress, this amino acid becomes indispensable due to the inability to meet the requirements of the body due to only endogenous arginine (Patel et al., 2016; Hsu et al., 2021). The consequences of a lack of arginine in a critical disease can be a decrease in NO production, poor wound healing, impaired microcirculatory blood flow, immunosuppression (T-cell dysfunction) and impaired muscle function (Patel et al., 2016; Morris et al., 2017; Hsu et al., 2021). Parenteral administration of arginine to rats with polymicrobial sepsis not only reduced inflammation of the liver tissue, but also improved the condition of CD4+ T lymphocytes (Yeh et al., 2020). The positive effect of this drug was also found with clinical use. Adding arginine to standard therapy in patients after injury or hemorrhagic shock improved wound healing (Shi et al., 2007; Debats et al., 2009), and in postoperative patients significantly reduced the incidence of infectious and non-infectious complications and hospital stay time (Osland et al., 2014; Marimuthu et al., 2012). Also recommended are arginine glutamate, ornithine aspartate, mixtures of amino acids and other hepatotropic drugs (Osyodlo et al., 2022).

Aim

study of clinical and pharmacoeconomic effectiveness of reactive hepatitis treatment in wounded by firearms.

Methods

To verify the clinical advisability of early hepatotropic therapy, a prospective study of 112 prehealthy wounded servicemen, who underwent regular medical examinations, was undertaken. They were hospitalized at the National Military Medical Clinical Center (NMMCC) (clinical base of the Military Therapy Department of the Ukrainian Military Medical Academy) with increased transaminase activity and a high risk of reactive hepatitis occurrence (Savichan, 2022b), received standard wound treatment according to existing protocols and were randomized into 3 groups:

ISSN 1996-353X
ISSN 2311-6951

- Group I (main) - 30 wounded received arginine glutamate from the first day of inpatient treatment, 2 g / day in 200 ml of isotonic sodium chloride solution intravenously by drop infusion;

- Group II (main) - 33 wounded as hepatotropic therapy from the first day of inpatient treatment received phosphatidylcholine 500 mg (10 ml) 1 g / day intravenously on autologous blood).

Treatment was prescribed from the first day of hospital stay for 10 days.

Group III (comparison) - 49 wounded who received standard wound treatment according to existing protocols with the appointment of hepatotropic therapy in the presence of clinical and laboratory signs of hepatic dysfunction. For the treatment of clinically significant hepatic dysfunction, arginine glutamate was prescribed immediately after diagnosis (5-7 days after admission) for at least 10 days with correction of hypoalbuminemia according to the indications.

General clinical characteristics of the injured on admission to the hospital did not reveal a significant difference between the groups (Table 1).

Injured with preceding persistent or acute liver disease were not included in the study.

Most of the wounded suffered mine injuries and were in a state of shock, the most common being abdominal trauma and multiple soft tissue injuries, and in half of the cases, anaemia was observed on the first day after the injury. Only one indicator showed a significant difference - in groups I and II the frequency of liver injuries was higher than in the comparison group III ($p < 0.05$ by criterion $\chi 2$), in cases of significant primary liver damage. But in general, the groups were similar in severity and type of injuries.

All victims underwent surgical treatment with the necessary surgical intervention for the wound and the necessary postoperative conservative treatment. All wounded servicemen received other necessary types of treatment, such as antibacterial, blood transfusion, detoxification, gastroprotective, symptomatic, etc., in accordance with approved current industry standards and clinical guidelines.

All injured were examined in the laboratory with the use of unified methods of laboratory tests on the basis of the department of laboratory diagnostics of the NMMCC. Biochemical analysis of blood was performed on the 5th, and 10th day of therapy and as needed using an automatic biochemical analyzer AU480 from Beckman Coulter (USA), which defines the concentration of total protein and its fractions, bilirubin and its fractions, electrolytes, urea, creatinine, amylase, Alanine aminotransferase (ALT), blood and Aspartate aminotransferase (AST).

The obtained data were processed taking into account the recommendations for biomedical research (Glanz, 1987) using the package of statistical programs PSPP (ver. 1.4.1) (an open program that does not require a license). Quanti-

Table 1. General clinical characteristics of the wounded included in the prospective study - n (%).

Indicator	Group I n=30	Group II n=33	Group III n=49
Average age	38,6±8,2	37,4±9,1	38,2±11,4
Mining and explosion wound	25 (83%)	27 (82%)	40 (82%)
Shock (I-III grades)	25 (83%)	26 (79%)	38 (78%)
Abdominal trauma	16 (53%)	18 (60%)	24 (49%)
Liver injuries	5 (17%)[1]	5 (15%)[2]	2 (4%)
Skeletal trauma	11 (37%)	13 (39%)	20 (41%)
Thoracic trauma	8 (27%)	9 (27%)	14 (28%)
Multiple soft tissue injuries	17 (57%)	18 (54%)	28 (57%)
Combined injury	11 (37%)	12 (36%)	19 (39%)
Anaemia on the first day after injury	16 (53%)	17 (51%)	24 (49%)

Note. 1 - the difference between I and III subgroups is significant - $p < 0.05$ by criterion $\chi 2$. 2 - the difference between subgroups II and III is significant - $p < 0.05$ according to the criterion $\chi 2$.

ISSN 1996-353X
ISSN 2311-6951

tative indicators were tested for normality of the distribution using the Kolmogorov-Smirnov test. In the normal distribution, the data are described as standard deviation arithmetic averages, and the t-test (Student's) for independent samples and the paired Student's test for dependent samples are used to compare the data. In the case of an abnormal distribution, the data were described by the median (M) with 25 (Q_{25}) and 75 (Q_{75}) quartiles, and the nonparametric Mann-Whitney test (for two independent samples) was used for comparison. Conjugation tables with the definition of the $\chi 2$ criterion or the Fisher criterion (for small samples and four-pole tables) were used to compare qualitative indicators. Differences were considered significant when the probability of the null hypothesis is less than 5% ($p < 0,05$).

Additionally, a pharmacoeconomic analysis (PEA) of the effectiveness of arginine glutamate therapy and phosphatidylcholine in patients with reactive hepatitis with an assessment of the cost of hepatoprotective therapy and cost-effectiveness. For this purpose, 15 patients from the I (I-A) and II (II-A) groups had equable trauma and comparable changes in transaminase activity on the first day after trauma before the start of hepatotropic drugs prescription. To use the method of "cost-effectiveness" was calculated the value of the coefficient "cost-effectiveness" for each drug:

CER = Cost / Ef, where CER is the value of the cost-effectiveness ratio, Cost - is the cost of drugs, UAH, Ef - is the value of drug efficiency according to the relevant efficiency criterion.

The criterion of efficacy was the duration and frequency of normalization of transaminase activity with the use of arginine glutamate and phosphatidylcholine during 10 days of treatment in the relevant groups of patients. The value of the effectiveness of drugs on the relevant criterion of effectiveness was calculated by the formula:

$$Ef = K_1 \times Xe_1 + K_2 \times Xe_2,$$

where Ef - is the value of the effectiveness of the drug in terms of normalization of the level of transaminase activity, X_{e1} is the efficiency index (1 to 10 points), inverse to the period of normalization of the level of transaminase activity, X_{e2} is the efficiency index (1 to 10 points), directly proportional to the frequency of normalization ALT. K_1, K_2 - the corresponding coefficients of significance. For reactive hepatitis, the significance coefficients were $K_1 = 0.5$, $K_2 = 0.5$, respectively, as they were specified by similar criteria.

The main criterion for the effectiveness of treatment was the normalization of transaminase activity of serum during 10-day treatment.

Results

According to the results of the analysis of the level of transaminases, it was found that the initial level of ALT in the subgroups had no significant differences, amounting to 62.5 in group I [50.5; 80.0] IU / l, in the second group - 64.0 [48.5; 83.0] IU / l and 62.0 [47.0; 85.5] IU / l, respectively ($p > 0.05$ according to the Mann-Whitney test). After treatment, the ALT content significantly decreased in all subgroups ($p < 0.05$ according to Wilcoxon's test): in group I on average to 38.5 [34,0; 63.5] IU / l, which did not differ significantly from the same indicator in group

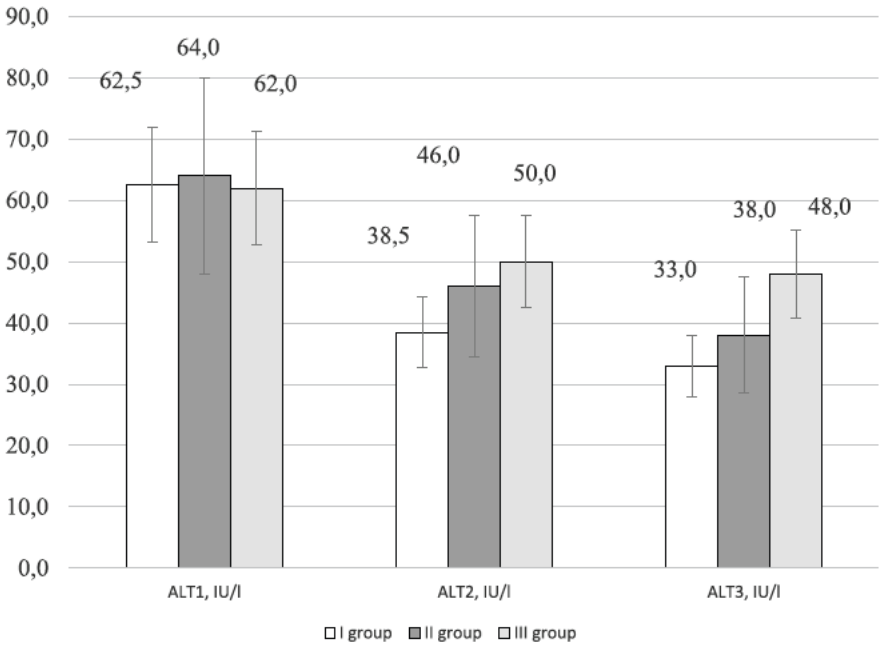

Fig. 1. Dynamics of ALT concentration in patients with reactive hepatitis depending on the timing of hepatotropic therapy.

ISSN 1996-353X
ISSN 2311-6951

II ($p > 0.05$ according to the Mann-Whitney test) and was significantly lower than in group III ($p = 0.014$ according to the Mann-Whitney test). In group II, the average ALT level decreased to 46.0 [32.0; 62.5] IU / l, and in group III – it up to 50.0 [40.0; 78.0] IU / l (the difference between groups II and III is not statistically significant - $p = 0.087$ according to the Mann-Whitney test) (Fig. 1).

In 14 and more days after injury in all subgroups, the average ALT concentration was significantly lower compared to the previous study period ($p < 0.05$ according to Wilcoxon's test): in group I the ALT concentration was 33.0 [29,8; 40.0] IU / l, in the second group - up to 38.0 [31.0; 62.0] and in group III to 48.0 [39.5; 69.0]. In group I this indicator was significantly lower than in group II ($p = 0.048$ according to the Mann-Whitney test) and in group III ($p < 0.001$ according to the Mann-Whitney test), and in group II significantly less than in group III ($p = 0.014$ according to the Mann-Whitney test). In the second period of observation, the most significant decrease in transaminase activity was observed in group I (Fig. 1).

The dynamics of AST were almost similar (Fig. 2). The initial level of AST in the subgroups did not differ: in group I 73.0 [62.0; 82.3] IU / l, in the second group - 75.0 [58.5; 91.5] IU / l and 70.0 [59.0; 95.5] IU / l, respectively ($p > 0.05$ according to the Mann-Whitney test). During treatment, the concentration of AST gradually decreased, reaching 3-13 days after the injury: in group I on average to 38.8 [35.7; 78.0] IU / l, in the second group - 56.0 [36.5; 76.0] IU / l and in group III - 69.0 [57.0; 88.0] IU / l ($p < 0.05$ according to Wilcoxon's test compared to the previous period). 14 or more days after the injury, the concentration of ACT in group I was 36.0 [28.0; 68.3] IU / l, in the second group - 39.0 [36.0; 65.0] IU / l and in group III - 64.0 [46.5; 82.0] IU / l. The difference between groups I and II 3-13 days after injury is not significant ($p > 0.05$ according to the Mann-Whitney test), and compared to group III is significant ($p = 0.049$ according to the Mann-Whitney test). At 14 days or more after the injury, in group I the mean average AST concentration was significantly lower than in groups II and III, and significantly lower in group II than in group III ($p < 0.05$ according to the Mann-Whitney test) (Fig. 2).

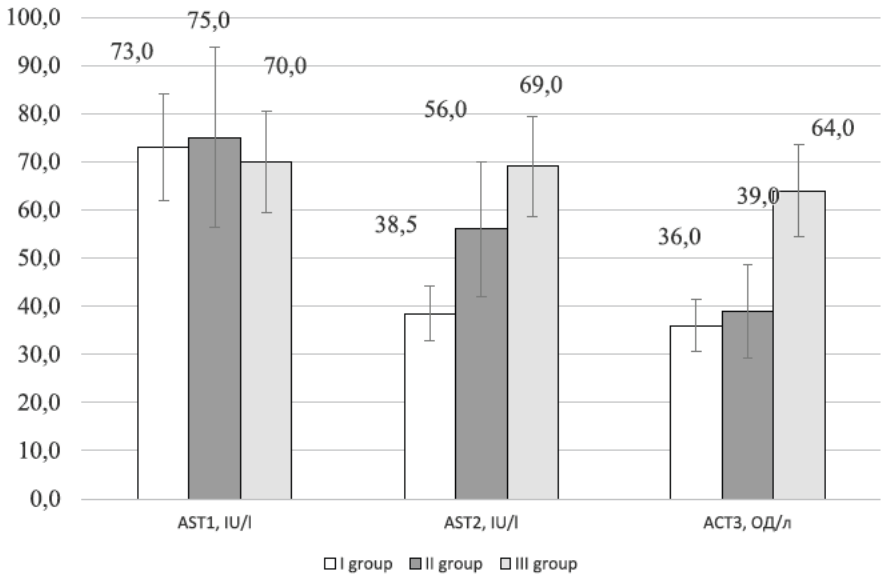

Fig. 2. Dynamics of AST concentration in patients with reactive hepatitis depending on the timing of hepatotropic therapy.

Thus, the positive dynamics of aminotransferase concentration in the post-traumatic period indicate the effectiveness of early hepatotropic therapy, which was higher with the use of arginine glutamate compared with phosphatidylcholine. At the same time, the dynamics of ALT and AST in the wounded with early hepatotropic therapy are better than in the wounded with traditional management in the post-traumatic period.

In addition, the appointment of early RH treatment with arginine glutamate, phosphatidylcholine and albumin (according to indications) contributed to a faster normalization of transaminases and albumin in comparison with the traditional approach to treatment: 9.3 ± 1.4 days and 13.6 ± 2,1 day, respectively ($p < 0.05$ according to Student's test).

This also has an effect on other indicators of the post-traumatic period. Thus, there was a tendency to reduce the frequency of complications from internal organs (general and/or local complications that caused an increase in the duration

ISSN 1996-353X
ISSN 2311-6951

Indicator	Group I and II, n=63	Group III, n=49	p
Frequency of complications	8 (13%)	13 (27%)	=0,063
Treatment at the ICU (number of cases)	46 (73%)	38 (78%)	=0,583
Duration of treatment in the ICU, days	4,2±1,8	7,4±6,0	=0,012
Duration of inpatient treatment, days	20,4±11,1	29,7±3,5	=0,022

Table 2. The course of the post-traumatic period in patients with reactive hepatitis depending on the appointment of early hepatotropic therapy.

of treatment in ICU and inpatient treatment and/or indications for repeated surgical interventions): in 13% (8 of 63) patients of groups I and II, compared with 27% (13 of 49) of group III (p = 0.063).

There was a tendency to reduce the frequency of treatment in the intensive care unit (ICU) - 73% (46 of 63) of groups I and II wounded, compared with 78% (38 of 49) of group III wounded. Significantly decreased both the duration of treatment in the ICU in groups I and II (4.2 ± 1.8) days, compared with group III (7.4 ± 6.0) days, p = 0.012, and the duration of total hospital stay (20.4 ± 11.1) days for groups I and II, compared with (29.7 ± 3.5) days for group III, p = 0.022 (Table 2).

According to the results of PEA, the cost of treatment with phosphatidylcholine (group II-A) was increased compared to the treatment with arginine glutamate (group I-A) 1.8 times: UAH 13,800.00. against UAH 7,501.80. (Table 3). Since the main disadvantage of the total cost method is not taking into account the clinical effectiveness of the studied drugs, for further analysis we used the method of "cost-effectiveness".

The analysis of the rate and frequency of transaminase decrement in wounded servicemen with reactive hepatitis showed that the clinical effectiveness (Ef) of arginine glutamate was 6.5 points, and for phosphatidylcholine - 6.0 points, and the cost-effectiveness ratio CER - 1154 UAH / point and 2300 UAH / point, respectively (Table 3).

From this perspective, the cost-effectiveness analysis of arginine glutamate and phosphatidylcholine regimens revealed a higher clinical efficacy rate (6.5 points) and a 2-fold cost-effectiveness ratio in the group of reactive hepatitis patients receiving arginine glutamate.

Discussion

The data obtained on the effectiveness of arginine glutamate in RH are consistent with the results of other studies. In particular, it was shown that the use of nitric oxide precursors L-arginine and L-arginine-L-glutamate helped to normalize liver function in experimental peritonitis, reduce the intensity of lipid peroxidation, increase the level of renewed glutathione and activity of antioxidant and mitochondrial enzymes (Cherniashova, 2015). Also in the experiment it was found that the administration of L-arginine L-glutamate in rats with experimental chronic hepatitis led to a slowing of fibrotic processes in the liver (Shevchenko, 2015). The positive effect of this drug was found in clinical use. Inclusion in the complex therapy of L-arginine helped to reduce

Table 3. The results of the analysis by the methods of total cost and "cost-effectiveness" of different options for reactive hepatitis hepatoprotective therapy.

Indicator	Arginine glutamate, n=15	Phosphatidylcholine, n=15
Total costs (Cost), UAH	7,501.80	13,800.00
The ratio of the cost of treatment of arginine glutamate and phosphatidylcholine		1.8
Clinical Efficacy Index (Ef), points	6.5	6.0
Cost-effectiveness ratio (CER), UAH / point	1154	2300
The cost-effectiveness ratio of arginine glutamate and phosphatidylcholine therapy		1.99

ISSN 1996-353X
ISSN 2311-6951

the level of total bilirubin by 26.3%, ALT - by 48.5%, alkaline phosphatase - by 33%, as well as the normalization of parenchymal echogenicity and vascular pattern of the liver (Semenchuk, 2017).

The effectiveness of hepatotropic therapy with essential phospholipids has also been confirmed by other studies. It was found that the institution of these drugs accelerates the elimination of subjective symptoms and clinical manifestations of liver pathology, which is confirmed by the results of histological and ultrasound examinations, and the positive dynamics of markers of hepatic cytolysis. The therapeutic effect is associated with the effect on membrane-dependent cell functions and with anti-inflammatory, antioxidant, antiapoptotic, membrane-protective and lipid-regulating effects of drugs (Gundermann et al., 2016).

Conclusions

Early hepatotropic therapy with arginine glutamate from the first day of inpatient treatment promotes faster normalization of transaminase activity compared to the traditional approach to treatment: 9.3 ± 1.4 days and 13.6 ± 2.1 days, respectively ($p < 0.05$ according to Student's test).

Early hepatotropic therapy helps to reduce the incidence of internal diseases complications (13% vs. 27%, $p = 0.063$) by reducing the duration of treatment in ICU to 4.2 ± 1.8 days compared to traditional treatment 7.4 ± 6.0 days ($p = 0.012$), the duration of the total stay in the hospital up to 20.4 ± 11.1 days compared to traditional treatment 29.7 ± 3.5 days ($p = 0.022$).

Hepatotropic therapy with arginine glutamate in wounded servicemen is effective and pharmacologically cost-effective not only in terms of treatment cost (1.8 times) but also cost-effectiveness (2 times) compared to phosphatidylcholine.

Financing

This study did not receive external financing.

Conflict of interest

The authors state that there is no actual or potential conflict of interest regarding the results of this work with pharmaceutical companies and other organizations whose products and services may be related to the subject of the provided materials.

Consent to publication

The authors have agreed to publish this work from all patients related to the manuscript.

ORCID ID and AUTHORS CONTRIBUTION

0000-0002-8650-3383 (A,B,C,D,E,F) Savichan Kyrylo

A – Research concept and design, B – Collection and/or assembly of data, C – Data analysis and interpretation, D – Writing the article, E – Critical revision of the article, F – Final approval of the article

REFERENCES

Belovol, A. N., & Kniazkova, Y. Y. (2019). Clinical pharmacology of hepatoprotectors. *Medicines of Ukraine*, (5-6), 231-232.

Chernyashova, V. V. (2015). Peculiarities of metabolic processes in the liver of animals with acute experimental peritonitis and with the use of L-arginine and L-arginine-L-glutamate. *Bulletin of Scientific Research*, (3). https://doi.org/10.11603/2415-8798.2015.3.5212

Debats, I. B., Wolfs, T. G., Gotoh, T., Cleutjens, J. P., Peutz-Kootstra, C. J., & van der Hulst, R. R. (2009). Role of arginine in superficial wound healing in man. *Nitric oxide : biology and chemistry*, *21*(3-4), 175–183. https://doi.org/10.1016/j niox.2009.07.006

Glantz, S. A. (1987). *Primer of biostatistics*. New York: McGraw-Hill.

Gundermann, K. J., Gundermann, S., Drozdzik, M., & Mohan Prasad, V. G. (2016). Essential phospholipids in fatty liver: a scientific update. *Clinical and experimental gastroenterology*, *9*, 105–117. https://doi.org/10.2147/CEG.S96362

Horvatits, T., Drolz, A., Trauner, M., & Fuhrmann, V. (2019). Liver Injury and Failure in Critical Illness. *Hepatology (Baltimore, Md.)*, *70*(6), 2204–2215. https://doi.org/10.1002/hep.30824

Horvatits, T., Trauner, M., & Fuhrmann, V. (2013). Hypoxic liver injury and cholestasis in critically ill patients. *Current Opinion in Critical Care*, *19*(2), 128–132. https://doi.org/10.1097/mcc.0b013e32835ec9e6

Hsu, C. C., Sun, C. Y., Tsai, C. Y., Chen, M. Y., Wang, S. Y., Hsu, J. T., Yeh, C. N., & Yeh, T. S. (2021). Metabolism of Proteins and Amino Acids in Critical Illness: From Physiological Alterations to Relevant Clinical Practice. *Journal of multidisciplinary healthcare*, *14*, 1107–1117. https://doi.org/10.2147/JMDH.S306350

ISSN 1996-353X
ISSN 2311-6951

Kazmyrchuk, A. P., Miasnykov, H. V., Sydorova, N. N., & Sydorova, L. L. (2014). Pathology of internal organs in combat trauma. Register of victims from the zone of the Antiterrorist operation. *Current aspects of military medicine*, (21), 44-48.

Marimuthu, K., Varadhan, K. K., Ljungqvist, O., & Lobo, D. N. (2012). A meta-analysis of the effect of combinations of immune modulating nutrients on outcome in patients undergoing major open gastrointestinal surgery. *Annals of surgery*, *255*(6), 1060–1068. https://doi.org/10.1097/SLA.0b013e318252edf8

Morris, C. R., Hamilton-Reeves, J., Martindale, R. G., Sarav, M., & Ochoa Gautier, J. B. (2017). Acquired Amino Acid Deficiencies: A Focus on Arginine and Glutamine. *Nutrition in clinical practice : official publication of the American Society for Parenteral and Enteral Nutrition*, *32*(1_suppl), 30S–47S. https://doi.org/10.1177/0884533617691250

Oleshchuk, O. M. (2014). The impact of modulators of nitric oxide synthesis on biochemical indices of the liver in rats. *Fiziolohichnyĭ zhurnal*, *60*(2), 57–62. https://doi.org/10.15407/fz60.02.057

Osland, E., Hossain, M. B., Khan, S., & Memon, M. A. (2014). Effect of timing of pharmaconutrition (immunonutrition) administration on outcomes of elective surgery for gastrointestinal malignancies: a systematic review and meta-analysis. *JPEN. Journal of parenteral and enteral nutrition*, *38*(1), 53–69. https://doi.org/10.1177/0148607112474825

Osyodlo, G. V., Trykhlib, V. I., Tkachuk, S. I., Haida, I. M., Maidaniuk, V. P., Antonenko, L. P., ... & Poda, N. V. (2015). Epidemiological and therapeutic aspects of non-combat pathology in mobilized servicemen and anti-terrorist operation participants. *Military health service problems*, (43), 225-234.

Osyodlo, G. V. (2013). Epidemiological and therapeutic aspects of chronic diffuse liver disease in servicemen. *Gastroenterology*, *50*(4), 50-56.

Osyodlo, G. V. et al. (2022). *Military-field therapy (textbook, 2nd edition)*. Kyiv: SPD Chalchynska N.V.

Palii, I. H. (2009). Essential phospholipids: realities and prospects. *Ukrainian medical magazine,* (70), 43-46.

Patel, J. J., Miller, K. R., Rosenthal, C., & Rosenthal, M. D. (2016). When Is It Appropriate to Use Arginine in Critical Illness?. *Nutrition in clinical practice : official publication of the American Society for Parenteral and Enteral Nutrition*, *31*(4), 438–444. https://doi.org/10.1177/0884533616652576

Savichan, K. (2022a). Blood serum concentration of aminotransferases in the gunshot victims. *Emergency Medicine*, *18*(1), 54–58. https://doi.org/10.22141/2224-0586.18.1.2022.1460

Savichan, K. V. (2022b) Risk and Forecasting Factors of Liver Dysfunction in Military Persons with Gunshot Wounds. *Journal of Medicine, Biology and Sport,* 7(2): 129–135. https://doi.org/10.26693/jmbs07.02.129

Semenchuk, S. A. (2017). Effect of l-arginine l-glutamate on the morphofunctional condition of the heart and liver in patients with postinfarction cardiosclerosis. *Bulletin of Scientific Research*, (3). https://doi.org/10.11603/2415-8798.2017.3.8080

Shevchenko, O. P. (2015). Pathomorphological changes in rats in an experimental model of chronic viral hepatitis. *Morphologia*, *9*(3), 111-116. https://doi.org/10.26641/1997-9665.2015.3.111-116

Shi, H. P., Wang, S. M., Zhang, G. X., Zhang, Y. J., & Barbul, A. (2007). Supplemental L-arginine enhances wound healing following trauma/hemorrhagic shock. *Wound repair and regeneration : official publication of the Wound Healing Society [and] the European Tissue Repair Society*, *15*(1), 66–70. https://doi.org/10.1111/j.1524-475X.2006.00186.x

Soleimanpour, H., Safari, S., Rahmani, F., Nejabatian, A., & Alavian, S. M. (2015). Hepatic Shock Differential Diagnosis and Risk Factors: A Review Article. *Hepatitis Monthly*, *15*(10). https://doi.org/10.5812/hepatmon.27063

Yang, M. (2015). Systemic inflammation and multiple organ injury in traumatic hemorrhagic shock. *Frontiers in Bioscience*, *20*(6), 927–933. https://doi.org/10.2741/4347

Yeh, C. L., Tanuseputero, S. A., Wu, J. M., Tseng, Y. R., Yang, P. J., Lee, P. C., Yeh, S. L., & Lin, M. T. (2020). Intravenous Arginine Administration Benefits $CD4^+$ T-Cell Homeostasis and Attenuates Liver Inflammation in Mice with Polymicrobial Sepsis. *Nutrients*, *12*(4), 1047. https://doi.org/10.3390/nu12041047

Ukrainian Scientific Medical Youth Journal
Issue 2 (131), 2022
ISSN 1996-353X
ISSN 2311-6951

Ефективність гепатотропної терапії при реактивному гепатиті у постраждалих з вогнепальними пораненнями

Савічан Кирило
Кафедра військової терапії, Українська військово-медична академія, м. Київ, Україна

Address for correspondence:
Savichan Kyrylo
E-mail: k.savichan@gmail.com

Анотація: Реактивний гепатит ускладнює лікування вогнепальних поранень. Метою нашого дослідження було вивчення клінічної та фармакоекономічної ефективності лікування реактивного гепатиту при вогнепальній травмі. Проведено проспективне дослідження 112 поранених військовослужбовців із збільшенням трансаміназної активності, які були рандомізовані на три групи: I група отримувала аргініну глутамат внутрішньовенно протягом 10 діб, II група отримувала фосфатидилхолін внутрішньовенно протягом 10 діб, III група отримувала стандартне лікування. При наявності гіпоальбумінемії поранені отримували внутрішньовенні інфузії альбуміну до нормалізації його рівня в сироватці крові. Вихідний рівень аланінамінотрансфераз склав в I групі хворих 62,5 [50,5; 80,0] ОД/л, в II групі – 64,0 [48.5; 83,0] ОД/л та 62,0 [47,0; 85,5] ОД/л відповідно у III групі (p>0,05 за критерієм Мана-Уітні). У період до 14 днів після травми рівень АЛТ достовірно зменшився у всіх групах (p<0,05 за критерієм Уілкоксона) і склав у I групі 38,5 [34,0; 63,5] ОД/л, у II групі 46,0 [32,0; 62,5] ОД/л, у III групі 50,0 [40,0; 78,0] ОД/л (p=0,014 за критерієм Мана-Уітні у порівнянні з I групою). Через 14 та більше діб після травми у всіх групах середня концентрація аланінамінотрансфераз була достовірно менше у порівнянні з попереднім терміном дослідження (p<0,05 за критерієм Уілкоксона): в I групі концентрація аланінамінотрансфераз складала 33,0 [29,8; 40,0] ОД/л (p=0,048, p<0,001 за критерієм Мана-Уітні у порівнянні з II та III групою відповідно), в II групі – до 38,0 [31,0; 62,0] та в III групі до 48,0 [39,5; 69,0] (p=0,014 за критерієм Мана-Уітні у порівнянні з II групою). Також, мала місце тенденція до зменшення частоти ускладнень з боку внутрішніх органів: у 13% (8 із 63) хворих групи I, порівняно з 27% (13 із 49) групи II (p=0,063). Достовірно зменшувалася як тривалість лікування у ВРІТ у групі I (4,2±1,8) л./днів, порівняно з групою III (7,4±6,0) л./днів, p=0,012, так і тривалість загального перебування в стаціонарі (20,4±11,1) л./днів для групи I, в порівнянні з (29,7±3,5) л./днів для групи III, p=0,022. При аналізі за методом «витрати-ефективність» схем терапії з аргініну глутаматом та фосфатидилхоліном, встановлено у 2 рази кращий коефіцієнт витратної ефективності у групі поранених з реактивним гепатитом, які отримували аргініну глутамат.

Ключові слова: вогнепальні, гепатит, економіка, лікування, печінка, поранення, трансамінази, фармацевтична.