

UDK 612.13: [616.36-002.1:578.891]-08-056.83

RYABOKON O.V., FURYK O.O., USHENINA N.S.
Zaporizhya State Medical University, Zaporizhya, Ukraine

INFLUENCE OF VARIOUS SCHEMES OF PATHOGENETIC TREATMENT ON THE STATE OF PROOXIDANT-ANTIOXIDANT HOMEOSTASIS ON PATIENTS WITH ACUTE HEPATITIS B AND CONCOMITANT USE OF ALCOHOL IN HEPATOTOXIC DOSES

Summary. The study involved 133 patients with acute hepatitis B aged from 18 to 60 years. The article shows that in patients with acute hepatitis B and concomitant chronic consumption of alcohol in hepatotoxic doses consumption, the height of disease is characterized by larger disturbances in prooxidant-antioxidant regulation due to the higher level of aldehyde phenylhydrazones of spontaneous oxidative modification of blood proteins and nitrites, which is combined with the low L-arginine content in blood serum. The period of convalescence in these patients is characterized by a higher level of aldehyde phenylhydrazones and ketone phenylhydrazones of spontaneous oxidative modification of blood proteins, a higher content of nitrites in combination with low L-arginine content in the blood serum, as compared with patients without concomitant liver disease. The use of L-arginine hydrochloride (Tivortin) and thiotriazoline in the treatment of patients with acute hepatitis B with chronic consumption of alcohol in hepatotoxic doses improves antioxidant-prooxidant processes by reducing the content of nitrites and ketone phenylhydrazones of spontaneous oxidative modification of blood proteins, increased content of L-arginine and catalase activity in blood serum, contributes to the normalization of alanine aminotransferase activity, and increased frequency of HBeAg – anti-HBe seroconversion compared with patients who are treated using only basic agents.

Key words: acute hepatitis B, prooxidant-antioxidant homeostasis, alcohol, L-arginine hydrochloride, thiotriazoline.

Hepatitis B is one of the major problems in medical science and practical public health, due to its wide distribution, high incidence, pathogenesis complexity, ineffective treatment, severe consequences of the disease. Among the combined lesions of the liver, special attention is currently paid to viral and alcoholic. The development of oxidative stress due to violation of prooxidant-antioxidant homeostasis, leads to the generation of reactive oxygen species that damage cell membranes and is closely related to many pathological changes in the body.

The aim — determine the dynamics of changes in the parameters of prooxidant-antioxidant homeostasis in patients with acute hepatitis B with concomitant chronic use alcohol in doses hepatotoxic during treatment with L-arginine hydrochloride and thiotriazoline.

Material and methods. The observation was 133 patients HBV aged 18 to 60 years. Depending on the presence or absence of chronic use alcohol in hepatotoxic doses in patients with HBV were formed as follows: I group consisted of 52 patients with HBV presence of chronic use alcohol in hepatotoxic doses according to treatment received were divided into groups: IA Group — 25 patients in addition to the basic treatment received L-arginine hydrochloride and thiotriazolin (study group); IB group — 27 patients who received only basic therapy (group). Group II — 81 patients for HBV

without concomitant factor that received traditional basic therapy.

Results and discussion. As a result of biochemical studies of blood in the midst of HBV in patients of group average of total bilirubin in serum was (203.8 ± 11.5) mmol/l and was higher ($p < 0.05$) from this index (170.3 ± 6.6) mmol/l group II patients. When comparing the expression of cytolytic syndrome in the midst of HBV found no statistically significant difference between groups I and II ($p > 0.05$). Comparison of marker profile of patients on admission revealed that all patients in both groups had positive HBsAg, anti-HBcor IgM, and the frequency of positive HBeAg did not differ ($\chi^2 = 1.42$, $p > 0.05$) in the study group.

Analysis of the survey parameters prooxidant-antioxidant homeostasis showed that during the height of the patients of group performance aldehyd fenylylhydrazyn (AFH) and ketone fenylylhydrazyn (KFH) spontaneous oksynaya modification of proteins(OMB) levels were higher ($p < 0.01-0.05$) than in healthy individuals. In Group II patients AFH rate of spontaneous OMB was higher ($p < 0.05$), and the rate of spontaneous KFH OMB had only a tendency ($p > 0.05$) to a

© Ryabokon E.V., Furyk E.A., Ushenina N.S., 2014

© «Актуальна інфектологія», 2014

© Заславський О.Ю., 2014

higher level than in healthy individuals. A comparative analysis of the peak found that the rate of AFH OMB in the serum of patients of group was higher ($p < 0.05$), and the rate KFH OMB had a tendency ($p > 0.05$) to increase compared with those of patients group II.

During the convalescence of the patient IB group performance AFH and KFH spontaneous OMB blood tended to recovery ($p > 0.05$) in the dynamics of the disease, but were significantly higher ($p < 0.05$) with similar rates of healthy people. Patients in Group II performance AFH and KFH spontaneous OMB blood did not differ ($p > 0.05$) from those of healthy options. Comparative analysis showed that at the time of hospital discharge in patients with IB content of AFH and KFH spontaneous OMB were higher ($p < 0.05$) than patients in group II.

Severe combined prooxidative changes in patients with HBV that occurs on a background of chronic use alcohol in hepatotoxic doses of antioxidant protection violation, as evidenced by low, compared with healthy people, catalase activity in serum during the whole observation period in face of the base treatment. In addition, patients I groups, in contrast to patients in Group II, nitrite content in serum was higher ($p < 0.05-0.001$) throughout the observation period.

These changes in performance prooxidant-antioxidant regulation towards activation of free radical oxidation combined with changes in the content of L-arginine in serum that had multidirectional nature of the patients studied groups. Already during hospitalization content of L-arginine in the serum of patients of I group was lower ($p < 0.05$) and II group patients higher ($p < 0.05$) than that of healthy people. In the future, the dynamics in patients with HBV of I group of L-arginine content in serum remained lower ($p < 0.01-0.001$) as compared with healthy people, as patients and group II.

Registered medium strength positive correlation relationship between the activity of ALT in serum and measure spontaneous AFH OMB blood ($r = +0.38$, $p < 0.05$); between bilirubin in serum and maintenance products AFH spontaneous ($r = +0.34$, $p < 0.05$) and KFH spontaneous OMB blood ($r = +0.36$, $p < 0.05$). Correlation analysis showed a strong negative relationship between the activity of ALT in serum and catalase ($r = -0.94$, $p < 0.01$); negative relationship between the average force of bilirubin in serum and catalase ($r = -0.38$, $p < 0.05$).

Comparison of basic biochemical parameters in patients with HBV statement showed that the presence of chronic use alcohol in hepatotoxic doses plays a role in delayed recovery of these patients, which was confirmed continuing more pronounced cytotoxic syndrome of hepatic cells. Amid normalization of total bilirubin in most patients in both groups decreased activity of ALT in serum of patients with IB group was slower than in patients of group II. The activity of this enzyme at discharge remained higher ($p < 0.05$) in patients IB group and was (2.33 ± 0.17) against (1.82 ± 0.07) mmol/h · l patients in Group II.

On delay recovery of I patients and compared with patients in Group II, the results also show the dynamics marker profile of patients. Thus, in patients with IB more frequently ($\chi^2 = 14.21$, $p < 0.01$) remained in the blood circulation of

HBsAg and less ($\chi^2 = 9.67$, $p < 0.05$) was recorded seroconversion HBeAg — anti-HBe.

Given the dynamics of the detected features prooxidant-antioxidant homeostasis to improve basic pathogenetic therapy in patients HBV with chronic use alcohol hepatotoxic in doses applied co-administration of L-arginine hydrochloride (tivortin) and thiotriazoline (IA group).

During the height of HBV average basic biochemical parameters prooxidant-antioxidant homeostasis in patients with I-A group for purpose of treatment was not statistically different ($p > 0.05$) from that of patients with IB group received traditional basic therapy.

In analyzing the dynamics indexes content prooxidant-antioxidant homeostasis in the serum of patients and group A detected at the time of completion of therapy, compared with those before treatment, decreased ($p < 0.05$) concentrations of AFH and KFH spontaneous OMB blood, while these indicators in this period did not differ ($p > 0.05$) from those of healthy options.

Registered increase ($p < 0.001$) content of catalase in the dynamics of the disease, but the impact was significantly higher ($p < 0.05-0.001$) than in patients with IB group and healthy controls. Moreover, in patients with IA group showed a reduction ($p < 0.05$) and nitrite content increase ($p < 0.001$) content of L-arginine in serum in the dynamics of the disease.

Comparative analysis showed that at the time of hospital discharge in patients with IA content of nitrites, KFH OMB blood was lower ($p < 0.05-0.01$), and the content of L-arginine and catalase higher ($p < 0.001$), than in patients IB group.

Comparison of expression of cytolytic syndrome during convalescence showed lower ($p < 0.05$) activity in serum ALT in patients IA group, in addition to the basic treatment treated with L-arginine hydrochloride and thiotriazoline. The activity of this enzyme during this period was (1.84 ± 0.09) against (2.33 ± 0.17) mmol/hod · l according to the patients IA and IB groups.

The analysis of marker profile in patients with HBV discharge that occurs on a background of chronic alcohol in hepatotoxic doses consumption showed preservation of circulating HBsAg levels in all patients in both groups. However, seroconversion HBeAg — anti-HBe often ($\chi^2 = 8.75$, $p < 0.01$) occurred in patients IA group — in 21 (84.0 %) versus 12 (45.0 %) patients I Group. It was found that the content of anti-HBe in the serum of patients IA group was higher ($p < 0.05$) than in patients IB group, and made (0.69 ± 0.09) from (0.38 ± 0.07) units, respectively.

Conclusions

1. In patients with acute hepatitis B from chronic use alcohol in hepatotoxic doses during the height of disorders characterized by greater prooxidant-antioxidant regulation by higher level aldehydifenilhidrazoniv spontaneous oxidative modification of blood proteins ($p < 0.05$) and nitrite ($p < 0.01$), combined with low L-arginine ($p < 0.05$) in serum.

2. The period of convalescence in patients with acute hepatitis B from chronic use alcohol in hepatotoxic doses

characterized by higher levels of aldehydifenilhidrazoniv ($p < 0.05$) and ketonfenilhidrazoniv ($p < 0.05$) spontaneous oxidative modification of blood proteins that are correlated with the activity of alanine aminotransferase ($r = +0.34$, $p < 0.05$, respectively), higher content of nitrates ($p < 0.01$), combined with low L-arginine ($p < 0.05$) in serum, compared with patients with acute hepatitis B without concomitant liver disease.

3. Involvement of L-arginine hydrochloride and thiotriazolone to the treatment of patients with acute hepatitis B from chronic use alcohol in hepatotoxic doses improves prooxidant-antioxidant processes by reducing the amount of nitrites and ketonfenilhidrazoniv spontaneous oxidative modification of blood proteins, increasing the content of L-arginine and catalase activity in serum blood, which eventually contributes to the normalization of alanine aminotransferase ($p < 0.05$) and increased frequency of seroconversion HBeAg — anti-HBe (84 vs. 45 %, $\chi^2 = 8.75$, $p < 0.01$) compared with patients in which treatment using only basic tools.

References

1. Дубинина Е.Е. Окислительная модификация протеинов, ее роль при патологических состояниях / Е.Е. Дубинина, А.В. Пустыгина // Укр. біохім. журн. — 2008. — № 6. — С. 5-18.
2. Зайцев И.А. Естественное течение вирусного гепатита В / И.А. Зайцев, Л.С. Бондарев, В.А. Мирошниченко // Сучасна гастроентерологія. — 2007. — № 1. — С. 81-86.
3. Мовчан А.В. Особенности эпидемического процесса вирусного гепатита В и организации мер борьбы в современных условиях / А.В. Мовчан, Л.В. Маслова // Питання експериментальної та клінічної медицини. Збірник статей. — 2011. — № 15. — С. 97-102.
4. Назар П.С. Зміни біохімічних показників та загального аналізу крові в осіб із алкогольним ураженням печінки / П.С. Назар, О.І. Осадча, М.М. Левон // Буковинський мед. вісник. — 2012. — № 1. — С. 59-62.
5. Олещук О.М. Протективна роль оксиду азоту при ішемії-реперфузії печінки / О.М. Олещук // Фармакологія та лікарська токсикологія. — 2010. — № 6. — С. 41-45
6. Пат. 67226 Україна, МПК (2012.01) А 61 К 31/00. Спосіб комплексного лікування гострого вірусного гепатиту В на тлі супутнього алкогольного ураження печінки / Фурик О.О., Рябоконт О.В.; заявники та патентовласники Запорізький держ. мед. ун-т, О.О. Фурик, О.В. Рябоконт. — № U201108411; заявл. 04.07.11; опубл. 10.02.12, Бюл. № 3.

7. Савченкова Л.В. Клиническая фармакология тиотриазолина / Л.В. Савченкова, Д.А. Филатов, И.П. Белоусова // Укр. мед. альманах. — 2008. — № 3. — С. 212-217.

8. Соціальна медицина та організація охорони здоров'я / За ред. Ю.В. Вороненка, В.Ф. Москаленка. — Тернопіль: Укрмедкнига, 2000. — 680 с.

9. Association of pro-inflammatory cytokines, adipokines & oxidative stress with insulin resistance & non-alcoholic fatty liver disease / R. Kumar, S. Prakash, S. Chhabra [et al.] // Indian J. Med. Res. — 2012. — Vol. 136. — P. 229-236.

10. Ethanol potentiates hepatitis B virus replication through oxidative stress-dependent and -independent transcriptional activation / B.Y. Min, N.Y. Kim, E.S. Jang [et al.] // Biochem. Biophys. Res. Commun. — 2013. — Vol. 431. — P. 92-97.

11. Gao B. Alcoholic liver disease: pathogenesis and new therapeutic targets / B. Gao, R. Bataller // Gastroenterology. — 2011. — Vol. 141. — P. 1572-1585.

12. Ijaz S. The effect of consecutively larger doses of L-arginine on hepatic microcirculation and tissue oxygenation in hepatic steatosis / S. Ijaz, M.C. Winslet, A.M. Seifalian // Microvascular Research. — 2009. — Vol. 78. — P. 206-210.

13. L-arginine supplementation reduces cardiac noradrenergic neurotransmission in spontaneously hypertensive rats / C.W. Lee, D. Li, K.M. Channon [et al.] // J. M. Cell. Cardiol. — 2009. — Vol. 47. — P. 149-155.

14. Light alcohol drinking and cancer: a meta-analysis / V. Bagnardi, M. Rota, E. Botteri [et al.] // Oncol. — 2013. — Vol. 24. — P. 301-308.

15. Oxidative stress and antioxidants in hepatic pathogenesis / Hye-Lin, Hye-Jun Shin, Mark A. Feitelson et al. // World Journal of Gastroenterology. — 2010. — Vol. 16. — P. 6035-6043.

16. The characteristic of T cells response to HBV-specific antigen proteins in patients with HBV infection / X. Feng, H.P. Yan, H.Y. Liao [et al.] // Zhonghua Shi Yan He Lin Chuang Bing Du Xue Za Zhi. — 2012. — Vol. 26. — P. 253-255.

17. The effect of chronic alcohol intoxication and smoking on the activity of oral peroxidase / N. Waszkiewicz, A. Zalewska, S.D. Szajda [et al.] // Folia Histochem. Cytobiol. — 2012. — Vol. 50. — P. 450-455.

Получено 29.09.14 ■

Рябоконт О.В., Фурик О.О., Ушеніна Н.С.
Запорізький державний медичний університет

ВПЛИВ РІЗНИХ СХЕМ ПАТОГЕНЕТИЧНОГО ЛІКУВАННЯ НА СТАН ПРООКСИДАНТНО-АНТИОКСИДАНТНОГО ГОМЕОСТАЗУ У ХВОРИХ НА ГОСТРИЙ ГЕПАТИТ В ІЗ СУПУТНІМ ХРОНІЧНИМ ВЖИВАННЯМ АЛКОГОЛЮ В ГЕПАТОТОКСИЧНИХ ДОЗАХ

Резюме. Обстежені 133 хворі на гострий гепатит В віком від 18 до 60 років. У роботі показано, що у хворих на гострий гепатит В із супутнім хронічним вживанням алкоголю в гепатотоксичних дозах розпал захворювання характеризується більшими порушеннями прооксидантно-антиоксидантної регуляції за рахунок вищого рівня альдегідфенілгідразонів спонтанної окисної модифікації білків крові та нітритів, що поєднується з низьким умістом L-аргініну в сироватці крові. Період реконва-

лесації в цих хворих характеризується вищим рівнем альдегідфенілгідразонів й кетонфенілгідразонів спонтанної окисної модифікації білків крові, вищим умістом нітритів у поєднанні з низьким умістом L-аргініну в сироватці крові порівняно з хворими без супутнього ураження печінки. Залучення L-аргініну гідрохлориду (Тівортін) та тиотриазоліну до лікування хворих на гострий гепатит В із хронічним вживанням алкоголю в гепатотоксичних дозах сприяє поліпшенню прооксидантно-ан-

тиоксидантних процесів за рахунок зниження вмісту нітритів і кетонфенілгідрозонів спонтанної окисної модифікації білків крові, підвищення вмісту L-аргініну й активності каталази в сироватці крові, сприяє нормалізації активності аланінаміно-трансферази та збільшенню частоти сероконверсії HBeAg —

anti-HBe порівняно з хворими, у лікуванні яких використовували лише базисні засоби.

Ключові слова: гострий гепатит В, прооксидантно-антиоксидантний гомеостаз, алкоголь, L-аргініну гідрохлорид, тіотриазолін.

Рябокоть Е.В., Фурик Е.А., Ушенина Н.С.
Запорожский государственный медицинский университет

ВЛИЯНИЕ РАЗЛИЧНЫХ СХЕМ ПАТОГЕНЕТИЧЕСКОГО ЛЕЧЕНИЯ НА СОСТОЯНИЕ ПРООКСИДАНТНО-АНТИОКСИДАНТНОГО ГОМЕОСТАЗА У БОЛЬНЫХ ОСТРЫМ ГЕПАТИТОМ В С СОПУТСТВУЮЩИМ ХРОНИЧЕСКИМ УПОТРЕБЛЕНИЕМ АЛКОГОЛЯ В ГЕПАТОТОКСИЧЕСКИХ ДОЗАХ

Резюме. Обследованы 133 больных острым гепатитом В в возрасте от 18 до 60 лет. В работе показано, что у больных острым гепатитом В с сопутствующим хроническим употреблением алкоголя в гепатотоксических дозах разгар заболевания характеризуется большими нарушениями прооксидантно-антиоксидантной регуляции за счет высокого уровня альдегидфенилгидразонов спонтанной окислительной модификации белков крови и нитритов, что сочетается с низким содержанием L-аргинина в сыворотке крови. Период реконвалесценции у этих больных характеризуется высоким уровнем альдегидфенилгидразонов и кетонфенилгидразонов спонтанной окислительной модификации белков крови, высоким содержанием нитритов в сочетании с низким содержанием L-аргинина в сыворотке крови по сравнению с больными без сопутствующего поражения печени. До-

бавление L-аргинина гидрохлорида (Тивортин) и тиотриазолина к лечению больных острым гепатитом В с хроническим употреблением алкоголя в гепатотоксических дозах способствует улучшению прооксидантно-антиоксидантных процессов за счет снижения содержания нитритов и кетонфенилгидразонов спонтанной окислительной модификации белков крови, повышению содержания L-аргинина и активности каталазы в сыворотке крови, способствует нормализации активности аланинаминотрансферазы и увеличению частоты сероконверсии HBeAg — anti-HBe по сравнению с больными, в лечении которых использовали только базисные средства.

Ключевые слова: острый гепатит В, прооксидантно-антиоксидантный гомеостаз, алкоголь, L-аргинина гидрохлорид, тиотриазолин.
