

UDC 616.33/36:616.72-007.24]-085-092

*K.A. Chympoy, N.V. Pashkovska, O.I. Fediv, N.M. Pavlibroda***PATHOGENETIC SUBSTANTIATION TO CORRECT DISORDERS OF THE BLOOD PLASMA FIBRINOLYTIC SYSTEM IN PATIENTS WITH CHRONIC DIFFUSE LIVER DISEASES AND DISORDERS OF THYROID HOMEOSTASIS**

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Abstract. The dynamics of the indices of fibrinolysis and cellular adhesion in patients with chronic diffuse liver diseases against the ground of administration of "Triovit", a selenium-containing drug, has been studied. The administration of "Triovit" in a comprehensive therapy of patients with chronic diffuse liver diseases was found to improve

the indices of the blood plasma fibrinolytic system, to reduce adhesive cellular properties and to increase total enzymatic activity of the blood plasma.

Key words: chronic diffuse liver diseases, cellular adhesion, fibrinolysis, Triovit.

Introduction. Disorders of the endothelial participation in the regulation of fibrinolysis are an important link in pathogenesis of many diseases including chronic diffuse liver diseases (CDLD) [1, 2, 4]. Disorders of the local fibrinolysis are an important factor in the development and progressing of CDLD which can be caused by disorders of the liver circulation, and results in an increased release of thromboplastin, a powerful triggering factor of blood clotting, into the blood [5, 6].

In its turn, endothelial dysfunction causes occurring and progressing of thyroid homeostasis disorders [3], which is indicative of the necessity to elaborate effective methods of its correction.

Objective: to examine the dynamics of indices of the blood fibrinolytic activity and cellular adhesion in patients with chronic diffuse liver diseases against the ground of administration of Triovit, a selenium-containing drug.

Materials and methods. 28 CDLD patients were examined. 20 practically healthy individuals of a corresponding age and sex were included in the group for comparison. Patients with chronic hepatitis and liver cirrhosis of a viral etiology, Wilson's disease, congenital α -antitripsin insufficiency (α -inhibitor of proteinase), idiopathic (genetic) hemochromatosis, autoimmune hepatitis were not included into the study.

All the patients were divided into two groups represented by their age, sex, degree of cytotoxicity activity and liver cirrhosis compensation. The first group (a comparative group) included 12 individuals afflicted with CDLD receiving a generally accepted therapy (diet No 5), hepatoprotectors, diuretics and detoxicants in case of need. The main group included 16 patients with CDLD receiving two Triovit capsules in the morning and in the evening against the ground of basic therapy during one month. The diagnosis of CDLD was made on the basis of carefully collected anamnesis, generally accepted complex of clinical-laboratory and instrumental methods of examination, detection of serum markers of viral hepatitis B and C, USD of the abdominal organs and thyroid gland.

The content of soluble intercellular adhesive molecule of the 1st type (ICAM-1) was detected by

means of immune-enzymatic method using the commercial test-system of the "Diaclone" firm (France).

The total (TFA), non-enzymatic (NFA) and enzymatic fibrinolytic activity (EFA) of the citrate blood plasma was detected by means of azofibrinolysis (Simko Ltd., Ukraine).

Peculiarities of thyroid homeostasis were studied by the content of free thyroxine (fT₄), free triiodothyronine (T₃) and thyrotrophic hormone (TTH) by means of immune-enzymatic method using the reagents "ImmuneFa-TTH", "IFA-SvT₃" and "IFA-SvT₄-1" (JSC "Immunotech") on the analyzer of immune-enzymatic reactions "Uniplan" calculating the coefficients fT₃/fT₄, fT₄/fT₃.

The results obtained were processed by means of Biostat program using Student t-criterion.

Results and discussion. The level of ICAM-1 in the blood plasma of CDLD patients was 34,6 % higher (P<0,001).

Examination of blood fibrinolytic activity detected a reliable decrease of TFA index on 20,2 % (P<0,001) at the expense of reduced enzymatic portion of fibrinolysis (EFA on 45,5 %, P<0,001). The index of non-productive NFA, being 35,2 % higher (P<0,001) that of the control, increased against this ground.

Thus, CDLD patients demonstrate inhibition of fibrinolytic blood plasma activity occurring at the expense of inhibition of enzymatic fibrinolysis as well as compensatory increase of non-enzymatic fibrinolytic activity.

According to the data of correlation analysis the development of fibrinolytic system disorders in patients with dysmetabolism of thyroid hormones against the ground of CDLD is connected with hypotriiodothyroninemia and conversion disorders of free thyroid hormones.

Thus, endothelial dysfunction caused by pathological mechanisms such as oxidant stress and increased cellular adhesion is likely to inhibit fibrinolytic blood activity in the examined patients.

The results of Triovit effect upon the indices of cellular adhesion and fibrinolytic blood plasma activity of CDLD patients are presented in the table.

Examination of the dynamics of ICAM-1 content in the blood serum detected more considerable

Table

Homeostasis indices of patients with chronic diffuse liver diseases in the dynamics of treatment with Triovit (M±m)

Indices	Control group (n=20)	Patients with chronic diffuse liver diseases (n=28)			
		Basic treatment (n=12)		Basic treatment+Triovit (n=16)	
		Before treatment	After treatment	Before treatment	After treatment
ICAM-1, ng/ml	259,6±10,324	377,7±16,08 P ₁ <0,001	338,7±10,64 P ₁ <0,001 P ₂ <0,05	374,1±14,68 P ₁ <0,001	307,5±9,54 P ₁ <0,01 P ₂ <0,01 P ₃ <0,05
Total fibrinolytic activity, azofibrin mkmol/ 1 ml per 1 hour	1,63±0,041	1,30±0,042 P ₁ <0,001	1,52±0,079 P ₁ >0,05 P ₂ <0,01	1,31±0,031 P ₁ <0,001	1,58±0,055 P ₁ >0,05 P ₂ <0,001 P ₃ >0,05
Non-enzymatic fibrinolytic activity, azofibrin mkmol/1 ml per 1 hour	0,51±0,019	0,72±0,010 P ₁ <0,001	0,63±0,016 P ₁ <0,001 P ₂ <0,01	0,69±0,028 P ₁ <0,001	0,58±0,011 P ₁ <0,001 P ₂ <0,01 P ₃ <0,05
Enzymatic fibrinolytic activity, azofibrin mkmol/ 1 ml per 1 hour	1,12±0,051	0,57±0,052 P ₁ <0,001	0,88±0,077 P ₁ <0,05 P ₂ <0,001	0,61±0,052 P ₁ <0,001	0,98±0,035 P ₁ <0,05 P ₂ <0,001 P ₃ >0,05

Notes. n – number of observations; P₁ – probability of changes considering the control; P₂ – probability of changes concerning the index before treatment; P₃ – probability of changes concerning the comparative group

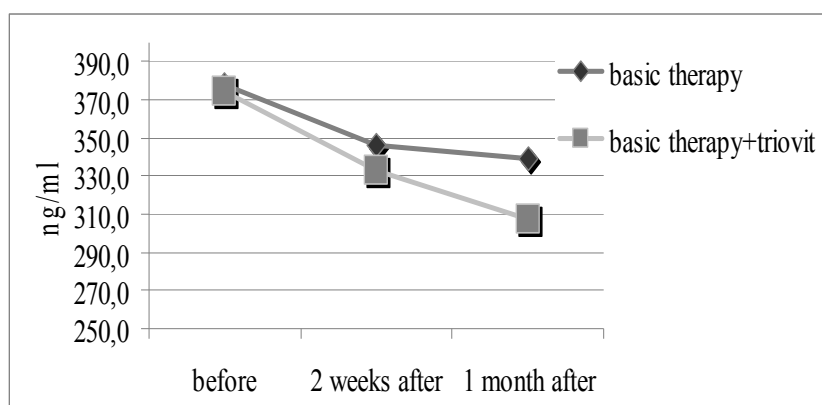


Fig. 1 Dynamics of the content of the 1st type intercellular adhesion molecules (ICAM-1) in the blood serum of patients with chronic diffuse liver diseases in the course of treatment

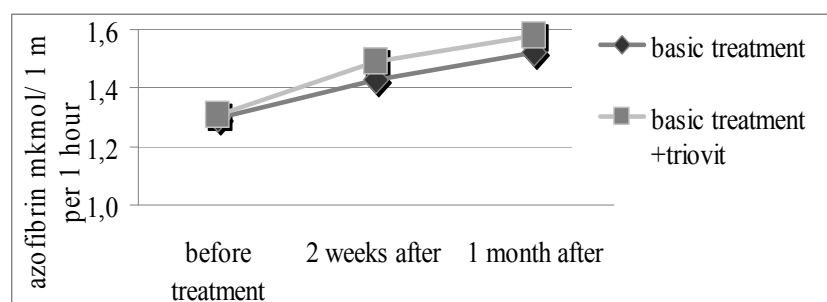


Fig. 2. Dynamics of the total fibrinolytic activity of the blood plasma in patients with chronic diffuse liver diseases in the course of treatment

decrease of the cellular adhesive properties in the main group. This index was 10,3 % lower (P<0,001) in a month against the basic therapy, and 17,8 % lower (P<0,01) against Triovit administration (fig. 1).

In 14 days the patients of the main group demonstrated a reliable increase of TFA index on 13,7 %

(P<0,01), in a month – on 20,6 % (P<0,001), at the same time in the comparative group these changes were reliable only in a month after the treatment (P<0,01) (fig. 2).

After Triovit use NFA reduction on 10,0 % (P<0,05) and 15,9 % (P<0,01) was registered 2

weeks and 1 month after the treatment, in the patients treated by means of basic therapy only – on 8,1 % and 12,5 % ($P < 0,01$).

The result of the therapy conducted was a reliable increase of EFA in the main group 2 weeks after the initiation of therapy on 42,6 % ($P < 0,001$) and on 60,7 % ($P < 0,001$) in a month, in the comparative group – on 36,8 % ($P < 0,01$) and 54,4 % ($P < 0,001$) respectively.

Thereby, administration of Trioivit, a selenium-containing drug, in a comprehensive treatment of CDLD patients promotes decrease of cellular adhesive properties which is proved by reduced ICAM-1 expression. TFA increases against this ground at the expense of EFA increase.

Conclusions

1. Chronic diffuse liver diseases are accompanied by disorders of the blood plasma fibrinolytic system, functional endothelial state with inhibition of enzymatic fibrinolysis against the ground of increased expression of the 1st type intercellular adhesion molecule.

2. Addition of Trioivit into the therapeutic complex of patients with chronic diffuse liver diseases results in the reduction of adhesive cellular properties (expression of the 1st type intercellular adhesion molecule) and the signs of disorders of the blood plasma fibrinolytic system (increase of enzymatic fibrinolytic activity).

The prospects of proceeding investigations will be further studies of pathogenetic peculiarities

of thyroid homeostasis disorders under conditions of chronic diffuse liver diseases with the aim to find the mechanisms of their occurrence and progress and substantiation of the improved methods to correct and prevent the given pathology.

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ПАТОГЕНЕТИЧЕСКОЕ ОБОСНОВАНИЕ КОРРЕКЦИИ НАРУШЕНИЙ СИСТЕМЫ ФИБРИНОЛИЗА ПЛАЗМЫ КРОВИ У БОЛЬНЫХ ХРОНИЧЕСКИМИ ДИФФУЗНЫМИ ЗАБОЛЕВАНИЯМИ ПЕЧЕНИ С НАРУШЕНИЕМ ТИРЕОИДНОГО ГОМЕОСТАЗА

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Резюме. Изучена динамика показателей фибринолиза и клеточной адгезии у больных хроническими диффузными заболеваниями печени на фоне использования селенсодержащего препарата «Триовит». Установлено, что триовит в комплексной терапии больных хроническими диффузными заболеваниями печени способствует оптимизации показателей фибринолиза плазмы крови, позволяет существенно уменьшить адгезивные свойства клеток и повысить суммарную ферментативную активность плазмы крови.

Ключевые слова: хронические диффузные заболевания печени, тиреоидный гомеостаз, клеточная адгезия, фибринолиз, триовит.

ПАТОГЕНЕТИЧНЕ ОБҐРУНТУВАННЯ КОРЕКЦІЇ ПОРУШЕНЬ СИСТЕМИ ФІБРИНОЛІЗУ ПЛАЗМИ КРОВІ У ХВОРИХ НА ХРОНІЧНІ ДИФУЗНІ ЗАХВОРЮВАННЯ ПЕЧІНКИ З ПОРУШЕННЯМ ТИРЕОЇДНОГО ГОМЕОСТАЗУ

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Резюме. Вивчено динаміку показників фібринолізу та клітинної адгезії у хворих на хронічні дифузні захворювання печінки на тлі використання селеновмісного препарату «Триовіт». Встановлено, що триовіт у комплексній терапії хворих на хронічні дифузні захворювання печінки сприяє оптимізації показників системи фібринолізу плазми крові, дозволяє істотно зменшити адгезивні властивості клітин та підвищити сумарну ферментативну активність плазми крові.

Ключові слова: хронічні дифузні захворювання печінки, тиреоїдний гомеостаз, клітинна адгезія, фібриноліз, триовіт.

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Buk. Med. Herald. – 2014. – Vol. 18, № 2 (70). – P. 113-115

Надійшла до редакції 29.01.2014 року