

CHANGES IN FIBROSIS UNDER THE INFLUENCE OF TREATMENT OF PATIENTS WITH ALCOHOLIC CIRRHOSIS OF THE LIVER IN COMBINATION WITH OBESITY USING ADEMETHYANINIUM AND ARGININE GLUTAMATE

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Summary

Aim: to study the changes in liver parenchymal fibrosis under the influence of treatment of patients with alcoholic liver cirrhosis in combination with obesity using ademethionine and arginine glutamate.

Material and methods. 215 patients, diagnosed with alcoholic liver cirrhosis (ALC), took part in the study, including 66 women and 149 men aged (48.1 ± 9.7) years and a median disease duration (5.8 ± 2.6) years. 109 people had ALC with obesity (group I) and 106 people had ALC without obesity (group II). Patients were divided into subgroups depending on the stage of decompensation according to Child-Pugh: class A – group IA ($n=40$), class B – group IB ($n=39$), class C – group IC ($n=30$) and IIA ($n=39$), IIB ($n=36$), IIC ($n=31$) groups, respectively. Depending on the treatment protocol (b protocol – basic therapy, h protocol – basic therapy in combination with ademethionine and arginine glutamate), all patients were divided into subgroups.

Results. In patients with ALC in combination with obesity, the elasticity of the liver parenchyma according to shear wave elastography and the FIB-4 index were higher than classes A, B and C compared to those in patients with ALC without obesity. According to the study results, obese patients with ALC had a more severe course of ALC according to the Child-Pugh and MELD scores. There is a direct relationship between the level of fibrosis in patients with ALC in combination with obesity according to elastography and the FIB-4 index with the severity of the disease according to the Child-Pugh and MELD scores. The inclusion of ademethionine and arginine glutamate in the treatment regimen has improved the general condition of patients, compensated for clinical and laboratory parameters and reduced the rate of progression of liver fibrosis.

Conclusion. In patients with ALC in combination with obesity, the inclusion in the treatment of ademethionine and arginine glutamate has improved the course of the disease, as evidenced by changes in the parameters of the disease severity by Child-Pugh and MELD scores, and helped to reduce the rate of progression of liver fibrosis according to elastography and the FIB-4 index.

Key words: alcoholic liver disease, liver cirrhosis, obesity, fibrosis

INTRODUCTION

The increase in the overall mortality rate is due to endogenous (diseases of the circulatory system and neoplasms) and exogenous (respiratory, digestive, infectious and parasitic diseases, external) causes. The proportion of deaths from diseases of the digestive system is gradually increasing. The most important contributors to mortality from this class of causes of death belong to liver fibrosis and cirrhosis, vascular lesions of the intestines, alcoholic liver disease, which account for 70% of deaths from diseases of the digestive system, and this share tends to increase. The causes of this tendency are the progressive growth of the quantitative and qualitative components of such patients, frequent chronic diseases, long and severe course, adverse

short-term and long-term consequences of the disease, the predominant affection of people of working age due to medical and socio-economic factors [1].

The leading causes of liver damage are alcohol, viruses, non-alcoholic fatty liver disease [2]. Alcohol abuse causes about 3.3 million deaths annually, which is 5.9% of the total mortality rate. About 5% of all morbidity and disability are alcohol-related cases. Among the diseases of the gastrointestinal tract, the main share belongs to alcoholic liver cirrhosis (ALC). In developed countries, alcohol, along with the hepatitis C virus and metabolic syndrome, are the leading causes of hepatocellular carcinoma. In Ukraine, mortality due to ALD takes the second place in the structure of causes of death from digestive diseases [1].

Taking into account the increasing prevalence of obesity, metabolic syndrome, and nonalcoholic fatty liver disease (NAFLD), special attention is being paid to studying their potential impact on the progression of ALD [3, 4, 5]. The most important risk factor for diet-related liver fibrosis is obesity, which determines the risk of liver cirrhosis (LC) in heavy drinkers [6]. The combined effects of alcohol and obesity increase the risk of liver damage. The synergy between obesity and chronic alcohol consumption in large quantities probably reflects similar disease mechanisms for both ALC and NAFLD, as well as the direct fibrogenic effect of increased adipose tissue mass [7].

Liver biopsy is considered to be the “gold standard” for the diagnosis of diffuse liver diseases. However, this method is invasive and carries considerable risks and costs [8, 9]. Non-invasive techniques are alternative solution, which will allow to evaluate the condition of the liver as a whole but not the particular samples of liver tissue [10, 11]. Non-invasive methods for assessing the degree of liver fibrosis include ultrasound liver elastography and laboratory panels that are widely used in practical medicine. FIB-4 is a laboratory panel comprising four indicators (age, platelet count, alanine aminotransferase and aspartate aminotransferase levels); they are available at primary and secondary medical care and not expensive. According to many studies, the use of FIB-4 score is recommended for assessment of the degree of liver fibrosis. Its noninvasiveness and simplicity should be taken into account [12, 13, 14, 15].

The aim of the study was to evaluate the changes in liver parenchymal fibrosis under the influence of treatment of patients with alcoholic liver cirrhosis in combination with obesity using ademethionine and arginine glutamate.

MATERIAL AND METHODS

215 patients, diagnosed with alcoholic liver cirrhosis (ALC), took part in the study, including 66 women and 149 men aged (48.1 ± 9.7) years and a median disease duration (5.8 ± 2.6) years. 109 people had ALC with obesity (group I) and 106 people had ALC without obesity (group II). Patients were divided into subgroups depending on the stage of decompensation according to Child-Pugh: class A – group IA (n=40), class B – group IB (n=39), class C – group IC (n=30) and IIA (n=39), IIB (n=36), IIC (n=31) groups, respectively. Depending on the treatment protocol used (b protocol – basic therapy, h protocol – basic therapy in combination with intravenous administration of ademethionine and subsequent oral administration of ademethionine and arginine glutamate): patients receiving basic therapy were included in IAb (n=19), IBb (n=20), ICb (n=15), IIAb (n=22), IIBb (n=18), IICb (n=16) groups; patients who additionally received ademethionine and arginine glutamate were included in IAh (n=21), IBh (n=19), ICh (n=15) та IIAh (n=17), IIBh (n=18), IICH (n=15) groups.

Groups Ih and IIAh, in addition to the basic treatment, received intravenously 500 mg of ademethionine per

day during two weeks, followed by oral administration of 500 mg of ademethionine and 1500 mg of arginine glutamate per day for 12 weeks.

Groups IBh and IIBh, in addition to the basic treatment, received intravenously 1000 mg of ademethionine per day for two weeks, followed by oral administration of 1000 mg of ademethionine and 3000 mg of arginine glutamate for 12 weeks.

Groups ICh and IICH, in addition to their basic treatment, received intravenously 1000 mg of ademethionine per day for two weeks, followed by oral administration of 1500 mg of ademethionine and 4500 mg of arginine glutamate per day for 12 weeks.

ALC was diagnosed according to the Adapted Clinical Guideline “Alcoholic Liver Disease” (the Ministry of Health of Ukraine, 2014). NAFLD was diagnosed according to the Adapted Clinical Guideline “Non-Alcoholic Fatty Liver Disease” (the Ministry of Health of Ukraine, 2014). The severity of LC was evaluated by the Child-Pugh score. The MELD score (Mayo Endstage Liver Disease, 2001) was calculated with electronic calculator: $\text{MELD score} = 3.8 \times \log_e \text{ serum bilirubin level (mg/dL)} + 11.2 \times \log_e \text{ serum creatinine level (mg/dL)}$. The diagnosis was verified using general clinical and instrumental methods of examination.

The degree of liver parenchyma fibrosis was assessed by calculating the FIB-4 (FibroIndex-4) and the liver parenchyma elasticity (kPa) determined by the shear wave elastography method on the GE Logiq E8 with assessment of the degree of fibrosis on METAVIR scale. The confirmation of the degree of F4 fibrosis by the method of elastography was the value of the elasticity of the liver parenchyma more than 11.9 kPa. The FIB-4 index was calculated by the formula: $(\text{patient age [years]} \times \text{ASAT level [U/L]} : \text{platelet level} [\times 10^9 / \text{L}] \times \text{ALAT level [U/L]})$. The control group consisted of 20 healthy individuals, who were age and gender matched. Assessment of patients was performed before and after 3 months from the beginning of treatment.

Statistical processing of the obtained results was carried out using the software package Statistica v. 12.0 (StatSoft, USA, trial) and Microsoft Excel. The average values are presented in the form ($M \pm m$), where “M” is the average value of the indicator (mean value), “m” is the standard error of mean. Student’s t-test was used to determine the significance of differences between groups in a distribution close to normal. Differences at $p < 0.05$ were considered statistically significant.

RESULTS

Patients with signs of astheno-vegetative, painful, dyspeptic, hepatorenal, hepatopulmonary syndromes, jaundice, drug-induced ascites, manifestations of hepatic encephalopathy were more common in group I of the

corresponding classes, which was accompanied by a more severe course of the ALC according to the the Child-Pugh and MELD scores. In patients of both groups, they increased with increasing ALC decompensation. However,

in patients of group I these values were higher compared to group II by 7.23% and 28.42%, 13.62% and 17.14%, 14.62% and 18.57% of classes A, B, C, respectively ($p<0.05$), (Tables 1, 2, 3).

Table 1

Dynamics of fibrosis, severity and MELD score in patients suffering from alcoholic cirrhosis of the liver with stage A according to Child-Pugh depending on the combination with obesity, $M\pm m$

Values	Control, n=20	ALC with obesity				ALC			
		IAb, n=19		IAh, n=21		IIAb, n=22		IIAh, n=17	
		Before treatment	After 3 month treatment	Before treatment	After 3 month treatment	Before treatment	After 3 month treatment	Before treatment	After 3 month treatment
Elasticity of the liver parenchyma, kPa	3.25±0.09	19.45±0.65*	19.63±0.87**	19.53±0.82**	16.14±0.96	15.84±0.92	15.94±0.83#	15.92±0.59*	14.48±0.67
Index FIB-4	0.92±0.03	3.88±0.10*	3.96±0.08**	3.92±0.05**	3.45±0.08	3.52±0.06	3.59±0.05*	3.53±0.05*	3.34±0.06
Child-Pugh score	-	5.76±0.11*	5.94±0.12**	5.81±0.09**	5.32±0.11	5.38±0.08	5.51±0.07#	5.39±0.09*	5.19±0.08
MELD score	-	13.64±0.92*	14.79±0.95**	13.47±0.84**	8.17±0.75	10.36±0.71	10.94±0.68#	10.54±0.86*	7.41±0.57

Notes: 1) * – statistical significance of difference between groups I and II ($p<0.05$); 2) • – statistical significance of difference before and after treatment ($p<0.05$); 3) # – statistical significance of difference between groups a and ah with treatment protocols ($p<0.05$).

Table 2

Dynamics of fibrosis, severity and MELD score in patients suffering from alcoholic cirrhosis of the liver with stage B according to Child-Pugh depending on the combination with obesity, $M\pm m$

Values	Control, n=20	ALC with obesity				ALC			
		IBb, n=20		IBh, n=19		IIBb, n=18		IIBh, n=18	
		Before treatment	After 3 month treatment	Before treatment	After 3 month treatment	Before treatment	After 3 month treatment	Before treatment	After 3 month treatment
Elasticity of the liver parenchyma, kPa	3.25±0.09	26.37±1.24**	29.23±1.21**	25.93±1.19**	23.27±1.23	19.27±1.22*	21.91±1.22#	19.46±1.25*	16.79±1.17
Index FIB-4	0.92±0.03	4.43±0.12**	4.73±0.11**	4.47±0.16**	3.51±0.17	4.10±0.13*	4.39±0.12#	4.15±0.16*	3.39±0.11
Child-Pugh score	-	8.73±0.19**	9.17±0.15**	8.82±0.12**	5.47±0.14	7.69±0.17*	8.08±0.16#	7.81±0.11*	5.24±0.13
MELD score	-	19.74±0.72**	21.86±1.15**	19.95±1.12**	8.65±0.43	16.76±1.16*	19.64±1.27#	16.98±1.20*	7.92±0.56

Notes: 1) * – statistical significance of difference between groups I and II ($p<0.05$); 2) • – statistical significance of difference before and after treatment ($p<0.05$); 3) # – statistical significance of difference between groups a and ah with treatment protocols ($p<0.05$).

Table 3

Dynamics of fibrosis, severity and MELD score in patients suffering from alcoholic cirrhosis of the liver with stage C according to Child-Pugh depending on the combination with obesity, $M\pm m$

Values	Control, n=20	ALC with obesity				ALC			
		ICb		ICb		IICb		IICb	
		Before treatment, n=15	After 3 month treatment, n=12	Before treatment, n=15	After 3 month treatment, n=15	Before treatment, n=16	After 3 month treatment, n=14	Before treatment, n=15	After 3 month treatment, n=15
Elasticity of the liver parenchyma, kPa	3.25±0.09	33.65±1.26**	36.45±1.35**	34.15±1.42**	31.34±1.15	25.34±1.03*	27.88±1.25#	26.41±1.13*	23.16±1.32
Index FIB-4	0.92±0.03	5.86±0.07**	6.73±0.06**	5.93±0.09**	5.59±0.07	4.37±0.08*	5.28±0.05#	4.43±0.06*	4.11±0.08
Child-Pugh score	-	13.98±0.61**	15.38±0.52**	14.21±0.64**	7.84±0.41	12.52±0.67*	13.97±0.65#	12.81±0.53*	7.44±0.38
MELD score	-	27.43±1.19**	30.13±1.21**	28.13±1.23**	17.52±1.15	23.65±1.02*	25.43±1.26#	23.71±1.11*	16.83±1.18

Notes: 1) * – statistical significance of difference between groups I and II ($p<0.05$); 2) • – statistical significance of difference before and after treatment ($p<0.05$); 3) # – statistical significance of difference between groups a and ah with treatment protocols ($p<0.05$).

These results indicate a more severe course and more pronounced progression of liver failure in patients with a combination of ALD and obesity due to a more pronounced increase in inflammatory-necrotic process and fibrosis in the liver and accompanied by significant systemic changes in blood flow, more severe systemic immunoinflammatory response, which ultimately leads to the development of multiple organ failure with fatal consequences.

According to the results of shear wave elastography, the elasticity of the liver parenchyma in all patients corresponded to stage F4 according to the METAVIR classification. In patients of both groups, this indicator rose with increasing decompensation of the disease.

In group I patients, the elasticity index of the liver parenchyma in class B exceeded that in class A by 1.37 times, and class C exceeded the values of class B by 1.28 times ($p < 0.05$). The values of the elasticity of the liver parenchyma were higher in patients of group I compared with patients of group II. In particular, in IA, IB and IC patients they were higher than in IIA, IIB and IIC by 1.24, 1.35 and 1.34 times, respectively ($p < 0.05$). In group II, the index of elasticity of the liver parenchyma in class B exceeded that in class A by 1.24 times, and class C exceeded these values in class B by 1.31 times ($p < 0.05$).

The FIB-4 index in patients of both groups increased depending on the stage of decompensation. This indicator was higher in group IIB compared to group IIA by 16.43%, in group IIB compared to group IIB – by 7.31%, in group IB compared to group IA – by 14.26%, in patients of group IC compared to group IB – by 31.12% ($p < 0.05$). FIB-4 values in patients of group I were higher than in classes A, B and C compared to those of group II by 10.76%, 8.27% and 33.42%, respectively ($p < 0.05$).

The elasticity of the parenchyma according to the results of shear wave elastography and the FIB-4 index in patients with ALC in combination with obesity were higher than classes A, B and C compared to those in patients with ALC without obesity.

Higher values of liver parenchymal elasticity and FIB-4 index in patients of group I compared with patients of group II show more pronounced processes of fibrogenesis in patients with a combination of ALC and obesity. These results indicate the effect of a combination of ALD and obesity on increasing the intensity of fibrogenesis in the liver, especially in those who are at the stage of subcompensation and decompensation.

In patients with ALC in combination with obesity, direct correlations were found between the Child-Pugh score and the elasticity of the liver parenchyma ($r = 0.63$; $p = 0.0007$), the value of the MELD score and the elasticity of the liver parenchyma ($r = 0.63$; $p = 0.0005$), the Child-Pugh score and FIB-4 index ($r = 0.65$; $p = 0.0007$), the MELD score and FIB-4 index ($r = 0.56$; $p = 0.0006$), FIB-4 index and liver parenchyma elasticity ($r = 0.69$;

$p = 0.0006$). These correlations suggest a direct relationship between the fibrosis level in patients with ALC in combination with obesity according to elastography and the FIB-4 index with the indicator of the severity of LC according to Child-Pugh and the prognostic MELD score.

Three months after the prescribed course of treatment, clinical and laboratory manifestations improved in most patients receiving the h protocol, whereas in patients with the b protocol, deterioration was observed, especially at the stages of subcompensation and decompensation. In patients receiving basic treatment, the Child-Pugh and MELD scores deteriorated, indicating further disease progression and, consequently, a worsening of the mortality prognosis. Within 3 months from the beginning of treatment, 3 people died in group ICb and 2 people – in group IICb due to deterioration of patients' condition and the development of complications (in 2 patients of group IICb and 1 patient of group ISb liver failure was developed, 1 patient of group ICb group had mesenteric thrombosis, 1 patient of group IICb had bleeding from varicose veins).

After the onset of treatment, patients in groups I and II who received the h protocol, at the stage of compensation the elasticity of the liver parenchyma and FIB-4 index significantly improved ($p < 0.05$), and in patients receiving basic treatment, such indicators increased, however no significant difference was observed before and after treatment ($p > 0.05$), (Table 1). At the stage of subcompensation and decompensation, the elasticity of the liver parenchyma and the FIB-4 index significantly improved in patients of groups I and II who received h protocol ($p < 0.05$), and in patients receiving basic treatment, such indicators increased significantly ($p < 0.05$), which was accompanied by deterioration of patients' condition and increased the risk of 3-month mortality.

The indicators of elasticity of the liver parenchyma on the basis of shear wave elastography and FIB-4 index were used to assess the degree of fibrosis and the effectiveness of a three-month treatment regimen including ademethionine and arginine glutamate for patients with ALC in combination with obesity. In patients with ALC in combination with obesity, they were higher than classes A, B and C compared to those in non-obese patients with ALC. According to the study results, obese patients with ALC had a more severe course of ALC according to the Child-Pugh and MELD scores. There is a direct relationship between the level of fibrosis in patients with ALC in combination with obesity according to elastography and the FIB-4 index with the severity of the disease according to the Child-Pugh and MELD scores.

The inclusion of ademethionine and arginine glutamate in the treatment regimen for 3 months improved the general condition of patients, compensated for clinical and laboratory parameters and reduced the rate of progression of liver fibrosis, which is reflected in a decrease in Child-Pugh and MELD scores of the severity of the disease and 3-month mortality.

CONCLUSIONS

1. According to elastography and the FIB-4 score, patients with ALC had higher fibrosis rates in the case of obesity at all stages of liver cirrhosis.
2. The level of fibrosis in patients with ALC in combination with obesity according to elastography and the FIB-4 score correlates with Child-Pugh classification of the severity of LC and the prognostic MELD score.
3. In patients with ALC in combination with obesity, the inclusion in the complex treatment of ademethionine and arginine glutamate helps to improve the course of the disease according to Child-Pugh classification of the severity of LC and the MELD score.
4. Inclusion of ademethionine and arginine glutamate in the complex treatment of obese patients with ALC helps

to reduce the progression of liver fibrosis according to elastography and the FIB-4 score.

The perspective for the further scientific research is to study the effect of ademethyaninium and arginine glutamate on changes in biochemical parameters in patients with alcoholic liver disease at the stage of cirrhosis associated with obesity.

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Conflicts of interest: authors have no conflict of interest to declare.

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*Резюме***ЗМІНИ ПОКАЗНИКІВ ФІБРОЗУ ПІД ВПЛИВОМ ЛІКУВАННЯ ХВОРИХ НА АЛКОГОЛЬНИЙ ЦИРОЗ ПЕЧІНКИ У ПОЄДНАННІ З ОЖИРІННЯМ З ВИКОРИСТАННЯМ АДЕМЕТІОНІНУ ТА АРГІНІНУ ГЛУТАМАТУ****Н. Р. Матковська**

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Мета дослідження. Вивчення змін показників фіброзу паренхіми печінки під впливом лікування хворих на алкогольний цироз печінки в поєднанні з ожирінням з використанням адеметіоніну та аргініну глутамату.

Матеріал і методи. У дослідженні взяли участь 215 пацієнтів з діагнованим алкогольним цирозом печінки (АЦП), серед яких було 66 жінок та 149 чоловіків віком $(48,1 \pm 9,7)$ років та середньою тривалістю захворювання $(5,8 \pm 2,6)$ років. У 109 осіб діагновано АЦП з ожирінням (І група) та у 106 осіб був АЦП без ожиріння (ІІ група). Пацієнтів було поділено на підгрупи залежно від стадії декомпенсації за Чайльд-П'ю. Залежно від застосованого протоколу лікування (b протокол – базова терапія, h протокол – базова терапія в поєднанні з адеметіоніном та аргініну глутаматом) пацієнти були поділені на підгрупи.

Результати. У хворих на АЦП у поєднанні з ожирінням показники еластичності паренхіми печінки за результатами зсувнохвильової еластографії та показники індексу FIB-4 були вищі за класів А, В та С порівняно з такими показниками у хворих на АЦП без ожиріння. Відповідно до результатів роботи у хворих на АЦП поєднання з ожирінням супроводжувалося більш тяжким перебігом АЦП за показниками шкали Чайльд-П'ю та прогностичного індексу MELD. Виявлено прямий зв'язок величини фіброзу у хворих на АЦП у поєднанні з ожирінням за даними еластографії та індексу FIB-4 з показником тяжкості ЦП Чайльд-П'ю та прогностичним індексом MELD. Включення в схему лікування адеметіоніну та аргініну глутамату дозволило покращити загальний стан пацієнтів, компенсувати клініко-лабораторні показники та зменшити темпи прогресування фіброзу печінки.

Висновки. У хворих на АЦП в поєднанні з ожирінням включення в комплексне лікування адеметіоніну та аргініну глутамату дозволило поліпшити перебіг захворювання, про що свідчать зміни показників індексів Чайльд-П'ю та MELD та сприяє зменшенню темпів прогресування фіброзу печінки за даними еластографії та індексу FIB-4.

Ключові слова: алкогольна хвороба печінки, цироз печінки, ожиріння, фіброз

*Резюме***ИЗМЕНЕНИЯ ПОКАЗАТЕЛЕЙ ФИБРОЗА ПОД ВЛИЯНИЕМ ЛЕЧЕНИЯ БОЛЬНЫХ С АЛКОГОЛЬНЫМ ЦИРРОЗОМ ПЕЧЕНИ В СОЧЕТАНИИ С ОЖИРЕНИЕМ С ИСПОЛЬЗОВАНИЕМ АДЕМЕТИОНИНА И АРГИНИНА ГЛУТАМАТА****Н. Р. Матковская**

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Цель исследования. Изучение изменений показателей фиброза паренхимы печени под влиянием лечения больных алкогольным циррозом печени в сочетании с ожирением с использованием адеметионина и аргинина глутамата.

Материал и методы. В исследовании приняли участие 215 пациентов с диагностированным алкогольным циррозом печени (АЦП), среди которых было 66 женщин и 149 мужчин в возрасте $(48,1 \pm 9,7)$ лет и средней продолжительностью заболевания $(5,8 \pm 2,6)$ лет. В 109 пациентов диагностирован АЦП с ожирением (I группа) и в 106 пациентов был АЦП без ожирения (II группа). Пациенты были разделены на подгруппы в зависимости от стадии декомпенсации по Чайльд-Пью. В зависимости от примененного протокола лечения (b протокол – базовая терапия, h протокол – базовая терапия в сочетании с адеметионином и аргинина глутаматом) пациенты были разделены на подгруппы.

Результаты. У больных с АЦП в сочетании с ожирением показатели эластичности паренхимы печени по результатам сдвиговолновой эластографии и показатели индекса FIB-4 были выше с классами А, В и С по сравнению с такими показателями у больных с АЦП без ожирения. Согласно результатам работы у больных с АЦП сочетание с ожирением сопровождалось более тяжелым течением АЦП по показателям шкалы Чайльд-Пью и прогностического индекса MELD. Обнаружена прямая связь величины фиброза у больных с АЦП в сочетании с ожирением по данным эластографии и индекса FIB-4 с показателем тяжести цирроза печени Чайльд-Пью и прогностическим индексом MELD. Включение в схему лечения адеметионина и аргинина глутамата позволило улучшить общее состояние пациентов, компенсировать клинико-лабораторные показатели и уменьшить темпы прогрессирования фиброза печени.

Выводы. У больных с АЦП в сочетании с ожирением включение в комплексное лечение адеметионина и аргинина глутамата позволило улучшить течение заболевания, о чем свидетельствуют изменения показателей индексов Чайльд-Пью и MELD и способствует уменьшению темпов прогрессирования фиброза печени по данным эластографии и индекса FIB-4.

Ключевые слова: алкогольная болезнь печени, цирроз печени, ожирение, фиброз

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