

Research Article

# Peculiarities of Hepatic Encephalopathy in Patients with Alcohol Liver Cirrhosis Against the Background of Chronic Bronchitis Exacerbation

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## Abstract

**Objective.** To evaluate the clinical manifestations of hepatic encephalopathy (HE) in patients with alcohol liver cirrhosis (ALC) in exacerbation of chronic bronchitis (CB).

**Materials and methods.** 100 patients with ALC class B and C according to Child-Pugh, 82.00% of men and 18.00% of women aged ( $47.2 \pm 3.9$ ) years, were examined: 48 patients without combination with CB (group I); 52 patients on the background of CB exacerbation (group II). Clinical-laboratory and instrumental examination was performed. The West-Haven criteria were used to assess the HE.

**Results.** In 54.17% of patients in group I, the I degree of HE was determined, in 35.42% - the II degree, in 10.42% - the III degree. In patients of group II the HE of the I degree was found in 17.31%, the II degree - in 50.0%, the III degree - in 32.69% ( $p < 0.05$ ). In patients with ALC and ALC in combination with CB, respectively, clinically HE was manifested by drowsiness in the daytime and the inversion of sleep (58.33%; 75.00%), lengthening the duration of the TMT-time test ( $61.59 \pm 2.38$  sec;  $72.84 \pm 3.03$  sec), mood disorders (20.83%; 28.85%), appearance of asterixis (54.17%; 76.92%), constructive apraxia (41.67%; 55.77%).

**Conclusions.** 1. Exacerbation of CB in patients with ALC contributes to the increase in the degree of HE, worsening the prognosis. 2. The relationship between the hyponatremia and the degree of HE is revealed.

## Keywords

alcoholic liver cirrhosis; chronic bronchitis; hepatic encephalopathy; hyponatremia

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## Problem statement and analysis of the recent research

According to the WHO, worldwide chronic liver diseases in 2020 could cause more than 2.5 million deaths, predicting about 1 million deaths from liver cirrhosis (LC). According to the statistics, in 2015 in Ukraine [5], among all fatal cases more than 4% were due to the diseases of the digestive system, among which about half - were due to the decompensation of liver cirrhosis. The main etiological factors of the LC are hepatotropic viruses B, C, D and alcohol [12].

Hepatic insufficiency is clinically manifested by hepatic encephalopathy, jaundice, ascites, edema of tissues, hemorrhagic syndrome, hyperdynamic type of circulation, palmar erythema, telangiectasia, liver odor (feto hepaticus), endocrine changes, fever, septicemia [3, 7]. Hepatic encephalopathy (HE) is the most indicant and sensitive clinical manifestation of liver failure, which clearly reflects its positive or negative dynamics. One of the most important prognostic criteria, which allows assess the severity of the patients' condition with alcoholic liver cirrhosis (ALC), is the appearance and progression of hepatic encephalopathy (HE). According

to the latest accepted definitions by the International Organization for the Study of Hepatic Encephalopathy and Nitrogen Exchange (IOSHENE), the emergence of disorientation or asterixis is considered the beginning of the HE [4].

Hepatic encephalopathy (HE) - is a complex of potentially reverse mental and neuromuscular disorders caused by severe hepatic insufficiency. HE in patients with LC can develop under the influence of trigger factors, which include gastrointestinal bleeding, infections such as bacterial ascites-peritonitis, and also infectious-associated conditions of other organs and systems, including the respiratory tract, intake of sedative drugs and tranquilizers, alcohol, excessive use of animal proteins, surgical intervention because of other diseases, paracentesis with the removal of a large amount of ascitic fluid [3].

Another independent predictor of mortality in patients with LC is the low serum sodium concentration, but its prevalence and clinical significance are not fully studied. Hyponatremia is defined when serum sodium level is  $< 135$  mmol/l, and in LC - is  $< 130$  mmol/l [11, 14]. It is proved that hyponatremia is an independent predictor of an adverse prognosis, and often it combines with refractory ascites, spontaneous

bacterial peritonitis, and HE [9]. A greater incidence of these complications was observed in patients with serum sodium level <130 mmol/l, and also significantly increased in patients with moderate serum sodium level - up to 131-135 mmol/l [6, 14]. In patients without LC, hyponatremia, depending on severity, can lead to a number of symptoms, including mild cognitive dysfunction, convulsions, coma occasionally death [11]. Hyponatremia in the LC is a chronic process and it allows the brain to adapt to the hypo-osmolality of the extracellular fluid. The most important factor in determining the severity of the HE in patients with hyponatremia is the rate of reduction of sodium in blood serum [8]. However, hyponatraemia may trigger brain edema, which, along with the effect of ammonia in ALC patients, can accelerate the HE [6, 8].

The objective of the study was to evaluate the clinical manifestations of the HE in ALC patients in the presence of exacerbation of chronic bronchitis.

## 1. Materials and methods of the research

100 patients with diagnosed alcoholic cirrhosis of the liver (ALC), 82.00% of men and 18.00% of women aged (47.2±3.9) years, were examined: 48 patients with ALC, class B and C according to Child-Pugh without a combination with CB (group I); 52 ALC patients, class B and C according to Child-Pugh in combination with CB in the phase of exacerbation (group II). The control group consisted of 20 practically healthy persons. Diagnosis of ALC was established according to the Adapted clinical guideline "Alcoholic liver disease" (2014) and the protocols of medical care provision on the specialty "Gastroenterology" (Order of the Ministry of Health of Ukraine # 271 dated 13.06.2005), "Alcoholic Hepatitis" (Order of the Ministry of Health of Ukraine # 826 dated 06.11. 2014).

A general clinical examination (analysis of complaints, anamnesis of the disease, anamnesis of life, objective status), ultrasound examination (US) of the abdominal cavity organs, esophagogastroduodenoscopy were performed. CAGE and AUDIT questionnaires were used to confirm the LC of the alcoholic genesis. The severity of the LC was assessed according to the Child-Pugh criteria (Engl. Child-Pugh, Child-Turcotte, Child-Turcotte-Pugh, and sometimes Child-Paquet).

For the comparison of manifestations of hepatic encephalopathy (HE), there was used index, which was based on: the patient's mental status, TMT-time ("exit from the labyrinth" test), asterixis (flapping-tremor). The criteria proposed by West-Haven [2] were used to estimate the HE. The functional state of the liver was evaluated according to the activity of aspartate aminotransferase (AsAT), alanine aminotransferase (ALAT), gammaglutamyltranspeptidase (GGTP), alkaline phosphatase (AP), content of total bilirubin and protein. Serum creatinine, urea, sodium, and INR were determined.

The exclusion criteria were liver cirrhosis of the viral, toxic genesis; chronic hepatitis, steatosis of various geneses; metabolic liver diseases; decompensated somatic pathology, oncological diseases, bronchial asthma; chronic obstructive

pulmonary disease; lack of individual consent of the patient to perform the study.

The statistical processing of the received results was carried out using the software - Microsoft Excel spreadsheet and Statistica v. 10.0 StatSoft, USA. The assessment of the probability of differences in the mean values was performed using the Student's paired t-criterion.

## 2. Results of the research and their discussion

Among the examined patients, in the presence of CB exacerbation, ALC class C was more often diagnosed according to Child-Pugh - in 36.53% of cases in group II compared with 14.58% of cases in group I (Table 1).

**Table 1.** Division of patients with alcoholic liver cirrhosis according to the Child-Pugh criteria

Class of LC	Patients			
	Group I, n=48		Group II, n=52	
	n	%	n	%
Class B	41	85.42	33	63.47
Class C	7	14.58	19	36.53*
Totally	48	100.00	52	100.00

Note. \* – the reliability of the difference in the indicators in the groups I and II,  $p < 0.05$ .

In 54.17% of patients with ALC there was established the first degree of the hepatic ecephalopathy (HE) according to West-Haven, in 35.42% - the second degree of the HE and in 10.42% - the third degree of the HE. ALC with an exacerbation of CB in patients of the group II the third degree of the HE 1.9-fold ( $p < 0.05$ ) was found more often; that indicated the aggravating effect of the exacerbation of CB on the course of ALC with the development of complication in the form of the HE (Table 2).

In patients with ALC and ALC in combination with CB clinically HE was manifested as sleep disturbance, daytime sleepiness and sleep inversion (58.33%; 75.00% respectively), decreased mnemonic functions, ability to logical thinking and attention concentration (52.08%; 73.08%), including lengthening the duration of the TMT-time test (61.59±2.38 sec; 72.84±3.03 sec), mood impairment due to depression, aggressiveness, irritability (20.83%; 28.85%), euphoria, inadequate assessment of their own condition (43.75%; 57.69%), asterixis in the form of slapping movements (54.17%; 76.92%), constructive apraxia (41.67%; 55.77% respectively).

In patients with ALC, exacerbation of CB was accompanied by an increase of liver failure in 86.54% of cases with a deterioration of the indicators of the functional state of the liver with an increase in the content of bilirubin at 59.53% ( $p < 0.05$ ), the activity of AsAT, ALAT and GGTP at 72.41%, 194.64%, 47.45% respectively ( $p < 0.05$ ), (Table 3).

Patients of the group I have significantly increased serum creatinine and urea levels at 76.34% and 26.85% ( $p < 0.05$ )

**Table 2.** Characteristics of manifestations of hepatic encephalopathy in patients with alcoholic liver cirrhosis depending on the presence of chronic bronchitis in the degree of exacerbation

Manifestations of hepatic encephalopathy	Group I, n=48		Group II, n=52	
TMT-time (sec)	65.28±2.33		72.84±4.71	
	Abs.	%	Abs.	%
Asterixis (flapping-tremor)	41	85.42	47	90.38
Degree of hepatic encephalopathy according to West-Haven criteria:				
- degree I	26	54.17	9	17.31●
- degree II	17	35.42	26	50.0
- degree III	5	10.42	17	32.69●

Note. ● – the reliability of the difference in the indicators in group II compared to the group I,  $p < 0.05$ .

**Table 3.** Laboratory indices in patients with alcoholic liver cirrhosis against the background of exacerbation of chronic bronchitis

Indices	Healthy, n=20	Group I, n=48	Group II, n=52
Bilirubin total, mcmol/l	15.03±0.47	55.13±3.25*	87.95±1.95*●
AsAT, mmol/hour*1	0.31±0.01	0.87±0.05*	1.50±0.09*●
ALAT, mmol/hour*1	0.29±0.01	0.56±0.04*	1.65±0.08*●
GGTP, mmol/hour*1	4.99±0.023	19.07±0.64*	28.12±0.92*●
Urea, mmol/l	4.99±0.03	6.33±0.41*	8.98±0.53*●
Creatinine, mcmol/l	75.28±3.17	132.75±51.6*	182.79±8.06*●
Total protein, g/l	78.18±2.26	64.28±2.43*	57.22±2.64*●
Albumin, g/l	41.73±2.23	33.27±1.94*	27.34±2.05*●
Na blood serum, mmol/l	146.28±3.02	138.86±3.35	131.47±4.05
INR	1.19±0.06	1.35±0.09*	2.39±0.015*●

Note.

\* – the reliability of the differences in the indicators in groups I and II compared with the healthy ones,  $p < 0.05$ ;

● – the reliability of the difference in the indicators in group II compared to the group I,  $p < 0.05$ .

compared with the healthy persons. In patients of the group II the disorders of nitrogen exchange tended to have a more pronounced tendency, and respectively, were accompanied by the increased levels of creatinine and urea compared with the control group at 142.81% and at 79.96% respectively ( $p < 0.05$ ) and compared to patients in group I - at 37.69% and at 41.86% respectively ( $p < 0.05$ ). Direct correlations between the HE degree and the content of bilirubin in the blood and the INR index were found ( $r = + 0.63$ ;  $r = + 0.45$ ; respectively,  $p < 0.05$ ).

The proportional increase in the concentration of serum creatinine and diuresis control over many years and up to this day remains important indicators of decreased renal function in the LC. However, in patients with LC, due to the decrease in the mass of muscular tissue, and therefore the synthesis of creatinine, even a sharp decrease in glomerular filtration may be accompanied by a normal or slightly elevated creatinine level. Instead, hyponatremia is a more accurate marker for predicting the probable complications of the LC [10]. In patients of groups I and II, the mean values of serum sodium at 5.07% ( $p > 0.05$ ) and at 10.12% ( $p < 0.05$ ) were lower than in the control group. The serum sodium level  $> 135$  mmol/l,

$\leq 135$  mmol/l,  $\leq 130$  mmol/l was 57.92%, 36.67%, and 5.41% respectively in group I - against 26.92%, 43.85%, and 29.23% respectively in group II. The reverse correlations between the HE degree and the serum sodium level ( $r = -0.65$ ,  $p < 0.05$ ) were found.

According to the results of the study, it was found that a more unfavorable prognosis for the ALC course according to the MELD index was in patients of the group II in the presence of CB exacerbation. In particular, the MELD index for patients of the group I was  $12.52 \pm 0.61$  points, while the second group was  $16.34 \pm 0.75$  points. The correlations between the MELD index and the HE degree, the INR index ( $r = + 0.70$ ,  $+ 0.56$ ,  $p < 0.05$ ) and the hyponatremia by the serum sodium level ( $r = -0.52$ ,  $p < 0.05$ ) were determined.

### 3. Conclusions

1. Exacerbation of CB in patients with ALC contributes to the increase of the HE degree, which is accompanied by a deterioration of the prognosis by the MELD index and requires timely adequate therapy.
2. Hyponatremia is observed more often in patients with

ALC with an exacerbation of CB; an inverse correlation between serum sodium level and HE degree was found.

#### 4. Prospects for further research

Prospects of further research – it is the study of pathogenetic links in the development of hepatic encephalopathy in patients with ALC in exacerbation of CB for the choice of effective integrated therapy.

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