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К.Ш. Сатиараджа, А.Ф. Ахамед Фалил

ГЕНДЕРНЫЕ РАЗЛИЧИЯ В ПРОГРЕССИРОВАНИИ И ТЯЖЕСТИ АЛКОГОЛЬНОЙ БОЛЕЗНИ ПЕЧЕНИ: СРАВНИТЕЛЬНОЕ ИССЛЕДОВАНИЕ

Научный руководитель: д-р мед. наук, доц. М.В. Шолкова
Кафедра пропедевтики внутренних болезней
Белорусский государственный медицинский университет, г. Минск

C.S. Sathiarajah, A.F. Ahamed Faleel

GENDER-BASED DIFFERENCES IN THE PROGRESSION AND SEVERITY OF ALCOHOLIC LIVER DISEASE: A COMPARATIVE CASE STUDY

Tutor: MD, associate professor M.V. Sholkova
Department of Propaedeutics of Internal Diseases
Belarusian State Medical University, Minsk

Резюме. Алкогольная болезнь печени (АБП) – это спектр заболеваний печени, возникающих вследствие чрезмерного употребления алкоголя. Она представляет собой глобальную угрозу здоровью, где цирроз печени, вызванный употреблением алкоголя, занимает 8-е место среди наиболее распространенных неинфекционных причин смерти. Чрезмерное употребление алкоголя оказалось наиболее распространенным фактором риска развития и прогрессирования цирроза печени. Цирроз печени остается важной глобальной проблемой здравоохранения, на долю которого ежегодно приходится около 1,2 миллиона смертей, при этом распространенность заболевания заметно варьируется по регионам. В странах Восточного Средиземноморья и Юго-Восточной Азии высокие показатели обусловлены гепатитами С и В соответственно, в то время как в западных странах распространены заболевания печени, связанные с употреблением алкоголя. В 2010 году Беларусь занимала первое место в мире по потреблению 17,5 л чистого алкоголя на душу населения в год. Однако, по данным Всемирной организации здравоохранения (ВОЗ), к 2016 году потребление алкоголя на душу населения в Беларуси снизилось до 11,2 л. Несмотря на эту тенденцию, Беларусь остается в числе стран с наибольшим количеством лет жизни, потерянных из-за алкоголя.

Ключевые слова: алкогольная болезнь печени (АБП), липополисахаридсвязывающий белок (LBP), оценка по шкале Чайлд-Пью, биохимические маркеры, эстроген.

Resume. Alcohol liver disease (ALD) is a spectrum of liver conditions that arises due to excessive alcohol consumption. It poses a global health threat where liver cirrhosis due to alcohol consumption takes the lead as the 8th most common non-communicable cause of death. Excessive alcohol consumption has proven to be the most prevalent risk factor in the development and progression of liver cirrhosis. Liver cirrhosis remains a significant global health issue, accounting for approximately 1.2 million deaths annually, with notable regional variations in prevalence. The Eastern Mediterranean and Southeast Asia experience high rates due to hepatitis C and B, respectively, while alcohol-related liver disease is prominent in Western countries. In 2010, Belarus was rated #1 in the world with 17.5 L of pure alcohol consumption per capita per year. However, according to the World Health Organization (WHO), by 2016, per capita alcohol consumption in Belarus has dropped to 11.2 L. Despite this improved trend, Belarus remains among the countries with the most estimated years of life lost due to alcohol.

Keywords: alcoholic liver disease (ALD), Lipopolysaccharide binding protein (LBP), Child-Pugh's score, biochemical markers, estrogen.

Relevance. Globally, we can see an increasing trend of liver cirrhosis in females compared to males, whereas in the European region, an increasing trend of liver cirrhosis in males can be seen. However, several studies have continued to prove that females are more prone to developing ALD compared to men at the same level of alcohol consumption.

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According to a research study conducted by Nobuhiro et al., it is proposed that excessive alcohol consumption makes the gut permeable, thereby releasing endotoxins (lipopolysaccharides), and the sex difference in alcoholic liver injury may be due to the difference in the induction of CD14 and LBP (lipopolysaccharide binding protein) levels in the liver, which can be influenced by oestrogen. This was determined by an investigation about the effect of oestrogen on the response of Kupffer cells to endotoxins in rats. Serum TNF-a levels were measured, and the levels were almost twice as high in oestrogen-pretreated rats as compared with the controls. Further observations showed that oestrogen sensitises Kupffer cells to endotoxins in vivo and increases both CD14 and LBP in the liver, which leads to the sensitisation of the liver to endotoxin and thereby augments ethanol-induced liver injury in females. Females may also have different alcohol pharmacokinetics and pharmacodynamics compared to males. Females tend to have lower overall water content and smaller stature than males, leading to higher blood alcohol concentrations for the same amount of alcohol consumed. According to Frezza et al., females have less alcohol dehydrogenase activity in the gastric mucosa, which leads to increased alcohol bioavailability.

Aim: confirm sex differences in patients with liver cirrhosis, particularly in the context of alcohol-related liver disease (ALD).

Objectives:

1. Investigate why women are more susceptible to alcohol-related liver disease (ALD) than men at comparable levels of alcohol consumption.
2. Discuss the role of estrogen in increasing liver sensitivity to endotoxins and ethanol-induced injury.
3. To analyze collected clinical data (e.g., biochemical markers, disease severity, alcohol consumption patterns) stratified by gender.

Material and methods. Several cases from the gastrointestinal department at Hospital 6 were reviewed, and just one Female patient met the required diagnosis of isolated ALD was identified from the 6th City Clinical Hospital, and a male patient with a comparable diagnosis was selected from the 3rd City Clinical Hospital.

We evaluated laboratory findings considering the following parameters: AST, ALT, total protein, albumin, total bilirubin, GGT, and CRP. We also took into account cirrhosis, ascites, hepatomegaly, encephalopathy, anaemia, and thrombocytopenia for the evaluation of the severity of the disease. Additionally, we also calculated the Child-Pugh's score to determine the extent of Liver failure.

Results and their discussion. A 59-year-old female patient and a 51-year-old male patient were compared for the severity of ALD. The female drank frequently (diluted wine and beer), and the male was an alcohol abuser (vodka). The male had AST and ALT levels of 518.46 U/L and 479.21 U/L, respectively, with an AST/ALT ratio of 1.08. The female had lower AST, ALT levels (156.1 U/L and 58.8 U), but with a higher AST/ALT ratio of 2.65 (fig. 1).

The male patient had normal ALP and elevated GGT (87.69 U/L), indicating excessive alcohol use. Albumin was lower in the female (24.6 mg/L) compared to the male (36.67 mg/L), with the female also presenting with ascites. CRP was significantly higher in

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the male (505 mg/L) compared to the female (12.52 mg/L). Bilirubin was elevated in both, but higher in the male (101 mmol/L) compared to the female (55 mmol/L) (fig. 2).

Despite these differences, the female progressed to liver cirrhosis with ascites and was classified as Child-Pugh Class C, while the male was categorized as Class B.

PATIENT	ALT (U/L)	AST (U/L)	AST/ALT	GGT (U/L)	CRP (mg/L)	TOT. PROT. (mg/L)	ALB. (mg/L)	TOT. BILI. (mmol/L)	CHILD - PUGH CLASS
F	58.8	156.1	2.65	173	12.5	85	24.6	55.5	C
M	479.2	518.5	1.08	87.7	505	52.8	36.67	101	B

Fig. 1 – Table illustrating the results of the biochemical and instrumental tests

PATIENT	CIRRHOSIS	ASCITES	ENCEPHALOPATHY	ANEMIA	THROMBOCYTOPENIA
F	+	+	-	+	-
M	-	-	-	-	+

Fig. 2 – Table illustrating the concomitant diseases related to their main diagnosis

Conclusion:

1. Lower body water content and smaller stature in women led to higher blood alcohol concentrations for equivalent intake.

2. Reduced gastric alcohol dehydrogenase (ADH) activity in women resulted in poorer first-pass alcohol metabolism and greater systemic exposure.

3. Estrogen-mediated mechanisms (e.g., Kupffer cell sensitization to endotoxins, upregulation of CD14/LBP) exacerbated inflammatory liver injury, accelerating fibrosis even at lower cumulative alcohol exposure.

4. Despite lower alcohol consumption levels, women in our study developed alcoholic liver disease (ALD) at a higher rate than men, supporting the hypothesis of increased biological vulnerability.

Literature

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