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Condition of Renal Excretory Function in Patients with Chronic Liver Diseases

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Abstract

This study examined 37 patients with hepatitis and cirrhosis of the liver and 30 healthy individuals, assessing liver function indicators and renal function under conditions of daily diuresis and after a load of drinking water and a 0.5% sodium chloride solution, at 0.5% of body weight.

The study showed that hepatitis and cirrhosis of the liver lead to signs of hepatorenal syndrome development, particularly in patients with cirrhosis, primarily manifested by a reduction in glomerular filtration rate (GFR). The extent of reduction correlated with the severity of liver damage. Simultaneously, it was independent of blood pressure, plasma protein, and renal sodium exchange mechanisms. The primary dysfunction in hepatorenal

syndrome was determined to be a reduction in GFR, evidenced by the rise in creatinine concentration, although urea increased only in cirrhosis, requiring further explanation.

The results showed that liver diseases, especially cirrhosis, can lead to kidney problems, mainly by reducing the kidney's ability to filter blood, which was shown by higher creatinine levels in the blood.

Keywords: hepatitis, liver cirrhosis, kidneys, hepatorenal syndrome, glomerular filtration rate.

Introduction

It is known that chronic liver diseases can be accompanied by the development of hepatorenal syndrome (HRS) [1, 2, 3, 4]. It has been established that the involvement of the kidneys in the pathological process is not due to morphological changes but is associated with disturbances in microcirculation due to the activation of the renin-angiotensin system (RAS) [5, 6, 7]. The main manifestation of HRS is a decrease in glomerular filtration rate (GFR), which leads to renal failure [5, 8]. Among its manifestations, the primary one is intoxication, which is related to the impairment of the excretory function. The markers for this are the concentrations of creatinine and urea in the blood plasma, but the ratio between them in various severities of chronic liver diseases has not been studied.

Chronic liver diseases can lead to a condition called hepatorenal syndrome (HRS), where the kidneys are affected not by structural changes but by issues in blood flow due to the activation

of the renin-angiotensin system (RAS). The main problem in HRS is a decrease in the glomerular filtration rate (GFR), which can cause kidney failure and lead to the buildup of toxins in the body.

The study aims to investigate how the kidney's ability to regulate fluid volume is affected in chronic liver diseases of different severities, focusing on the relationship between liver damage and kidney function.

The aim of the study was to examine the condition of renal excretory function in chronic liver diseases of varying severity in relation to the volume-regulating function of the kidneys.

Materials and Methods

To achieve the study's objective, 12 patients with chronic hepatitis (CH), 10 patients with subcompensated liver cirrhosis (SC), and 15 patients with decompensated liver cirrhosis (DC) were examined. Diagnoses were established based on the Ukrainian Ministry of Health Order No. 271 from June 13, 2005 (Clinical Protocol for Providing Medical Care in the Specialty "Gastroenterology") using common clinical, laboratory, biochemical, and instrumental research methods. The disease duration ranged from 2 to 10 years. The main etiological factors causing the diseases were alcohol, medications, and other toxic factors. The average age of patients was 43-56 years. The control group for comparison consisted of 25 practically healthy individuals of the corresponding age. The severity of cirrhosis was assessed using the Child-Pugh diagnostic complex. The frequency of main clinical symptoms is shown in Table 1, indicating a characteristic pathology picture. The liver function state depending on the disease stage is shown in Table 2, indicating typical pathology characteristics such as increased bilirubin, both indirect and direct, along with increased ALT activity.

Table 1: Frequency of Clinical Symptoms in Patients with Chronic Hepatitis and Liver Cirrhosis

Symptoms	Disease Forms		
	Chronic Hepatitis (CH)	Subcompensated Cirrhosis (SC)	Decompensated Cirrhosis (DC)
Asthenovegetative	100%	100%	100%
Dyspeptic	85.2%	73%	53.2%
Weight Loss and Muscle Atrophy	14.7%	35%	70%
Skin Itching	16.39%	26%	25%
Fever	49%	11%	48%
Hemorrhagic	0%	26%	29%
Jaundice (Sclera and Skin)	34.4%	55.8%	67.7%
Peripheral Edema	18%	29.7%	95.16%
Ascites	0%	41.17%	100%
Hepatomegaly	91%	97%	100%
Blood Pressure (mm Hg)	128.1±21.1/79.75±14.8	125.7±34.2/77.3±20.6	125.16±26.5/78.3±14.1

Functional Status of the Kidneys

Renal function was studied using the clearance method under conditions of 12-hour spontaneous nocturnal and induced 2-hour diuresis: on the first day with distilled water and on the second day with a 0.5% sodium chloride solution at 0.5% of body weight. The unification of study conditions during the load standardizes the impact on the body's water-salt homeostasis and allows a fairly accurate study of renal function, excluding external influences [7, 9, 10]. Patients with organic kidney damage in their history or with significant changes in the general urine analysis were not included in the study.

The study was conducted in accordance with the Helsinki Declaration of 1975 and its revised version of 1983. For statistical analysis of the obtained results, the Statistica for Windows 6.0 software package (Stat Soft Inc., USA) was used. The critical significance level when testing statistical hypotheses was taken as 0.05.

Table 2: Characteristics of Liver Function State in Patients with Chronic Hepatitis and Liver Cirrhosis (M±m)

Studied parameters	Control n=30	Patients		
		Chronic Hepatitis (CH) (n=12)	Subcompensated Cirrhosis (SC) (n=12)	Decompensated Cirrhosis (DC)
Total Protein (g/l)	78.17±0.54	76.28±0.83	74.99±1.54 p<0.05	73.23±0.91 p<0.001
Total Bilirubin (µmol/l)	18.77±1.03	35.72±2.48**	32.54±4,49 p<0.001	59.18±6,67 p<0.001
Direct Bilirubin (µmol/l)	3.76±0.19	13.83±1.74**	11.87±2.04 p<0.001	13.75±2.63 p<0.001
Indirect Bilirubin (µmol/l)	15.01±1.12	21.89±2.49**	20.75±2.86 p<0.05	45.42±6.47 p<0.001
AST (µmol/g·l)	0.43±0.02	0.87±0.11**	0.68±0.03 p<0.001	0.69±0.02 p<0.001
ALT (µmol/g·l)	0.68±0.03	1.13±0.16**	0.87±0.04 p<0.001	0.90±0.06 p<0.01

Notes:

p: Significance of differences compared to the healthy group

p1: Significance of differences in indicators before and after treatment within the same patient group

n: Number of observations

Results

The results of the study of renal function in patients with chronic diffuse liver diseases (CDLD) indicate that during the spontaneous 12-hour nocturnal diuresis, the diuresis slightly increased in patients with CH, subcompensated and decompensated cirrhosis. This increase was also observed when calculating standardized diuresis per 1 kg of body weight, but it was not significant. Simultaneously, plasma creatinine concentration increased (Table 3, Figure 1). Parallelly, blood urea levels increased, reaching significant values in decompensated cirrhosis (Table 3, Figure 2).

Figure 1: Plasma Creatinine Levels in Patients with Chronic Hepatitis and Liver Cirrhosis Depending on Disease Stage

Plasma Creatinine Levels (µmol/l):

Practically Healthy	Chronic Hepatitis	Subcompensated Cirrhosis	Decompensated Cirrhosis
75.2	108.6	98.7	106.41

Figure 2: Blood Urea Levels in Patients with Chronic Hepatitis and Liver Cirrhosis Depending on Disease Stage

Blood Urea Levels (mmol/l):

Practically Healthy	Chronic Hepatitis	Subcompensated Cirrhosis	Decompensated Cirrhosis
5.48	5.83	5.89	6.08

When calculating GFR, its significant reduction was found in CH and a slight decrease in subcompensated cirrhosis, especially in decompensated cirrhosis. Changes in the ion-regulating function of the kidneys were also observed. In patients with CH and decompensated cirrhosis, there was a tendency to reduce sodium excretion. It is important to note that sodium excretion decreased due to reduced GFR, while standardized sodium excretion/100 ml GFR tended to increase. In all patient groups, plasma sodium concentration significantly decreased. Overall, sodium clearance tended to decrease, most significantly in patients with CH (Table 3).

Table 3: Characteristics of Renal Function in Patients with Chronic Hepatitis and Liver Cirrhosis During Spontaneous Nocturnal Diuresis (M±m)

Renal Function Indicators	**Practically Healthy Individuals (n=18)**	**Chronic Hepatitis (CH) (n=12)**	**Subcompensated Cirrhosis (SC) (n=10)**	**Decompensated Cirrhosis (DC) (n=15)**
12-hour Diuresis (ml)	627.92±85.41	730±81.19	720±174.47	734±91.67
Standardized Diuresis (ml/kg)	9.62±1.45	11.9±2.94	11.77±3.18	11.52±1.97
Urine Specific Gravity	1.018±0.152	1.013±0.122*	1.011±0.413	1.011±0.208*
Urea (mmol/l)	5.48±0.19	5.83±0.15	5.89±0.15	6.08±0.22*
Plasma Creatinine Concentration (μmol/l)	75.20±5.86	108.61±8.32*	98.70±6.41*	106.41±13.19*
Glomerular Filtration Rate (GFR) (ml/min)	132.71±13.44	98.83±4.36*	111.09±19.94	59.1±7.2
Plasma Sodium Concentration (mmol/l)	144.35±1.26	135.51±3.39*	138.20±1.42*	131.89±2.07*
Sodium Excretion (mmol/12 hr)	12.9±0.35	9.4±0.26	11.2±1.1	9.7±0.38
Standardized Sodium Excretion (mmol/100 ml GFR)	0.79±0.15	0.93±0.25	1.06±0.28	0.79±0.33
Sodium Clearance (ml/12 hr)	9.17±2.41	6.31±1.76	7.73±3.8	8.42±2.78

Notes: * - significant differences compared to the healthy group.

Study of Renal Function Under Standard Water Load

The study revealed more significant changes under standard water load (Table 4). In healthy individuals, two hours after the load, diuresis increased, calculated per hour, to twice the 12-hour value, averaging more than 80% of the water load. However, in patients with chronic diffuse liver diseases (CDLD), diuresis increased only in subcompensated cirrhosis, remaining close to control values. In chronic hepatitis and decompensated cirrhosis, diuresis significantly decreased, both in absolute and relative terms. In response to standard load, diuresis in subcompensated cirrhosis reached only 70%, and in chronic hepatitis and decompensated cirrhosis, it was only about one-third of the load volume.

Table 4: Some Indicators of Renal Function in Patients with Chronic Hepatitis and Liver Cirrhosis During Water Load (M±m)

Indicators Studied	Practically Healthy Individuals (n=18)	Chronic Hepatitis (CH) (n=12)	Subcompensated Cirrhosis (SC) (n=10)	Decompensated Cirrhosis (DC) (n=15)
Diuresis (ml/2 hr)	257.50±28.05	104.75±36.58*	214.6±59.99	129±44.87*
Standardized Diuresis (ml/kg)	4.17±0.41	1.62±0.56*	3.47±1.11	1.89±0.57*
Plasma Creatinine Concentration (μmol/l)	73.50±3.61	105.53±4.49*	102.75±9.76*	121.82±14.07*
Glomerular Filtration Rate (GFR) (ml/min)	108.57±13.64	30.01±1.75*	43.79±6.02*	33.01±11.68*
Plasma Sodium Concentration (mmol/l)	134.11±3.42	136.25±5.57	140.62±6.95	132.52±2.31
Sodium Excretion (mmol/2 hr)	3.8±0.04	1.9±0.08*	4.4±1.5	1.6±0.08*
Standardized	0.45±0.08	0.61±0.26	0.82±0.15*	0.62±0.29

Indicators Studied	Practically Healthy Individuals (n=18)	Chronic Hepatitis (CH) (n=12)	Subcompensated Cirrhosis (SC) (n=10)	Decompensated Cirrhosis (DC) (n=15)
Sodium Excretion (mmol/100 ml GFR)				
Sodium Clearance (ml/2 hr)	33.6±4.3	20.1±1.31	29.8±14.5	12.1±4.9*

Notes: * - significant differences compared to the healthy group.

Changes in Renal Function with Salt Load

The study also showed that diuresis values in healthy individuals decreased compared to the water load. The changes in patients were similar but significantly different in magnitude, particularly in patients with chronic hepatitis and decompensated cirrhosis ($p<0.05$) (Table 5). Simultaneously, there was a significant increase in plasma creatinine levels in all study groups ($p<0.05$). The reduction in diuresis was primarily due to a decrease in GFR in all groups ($p<0.05$). The decrease in GFR followed a similar dynamic during water load and was most pronounced in patients with chronic hepatitis and decompensated cirrhosis. Significant disturbances in the ion-regulating function of the kidneys were observed with salt load. While plasma sodium concentration remained normal in all groups, sodium excretion significantly decreased in patients with chronic hepatitis and decompensated cirrhosis. Notably, in healthy individuals, sodium excretion increased by 50% compared to spontaneous diuresis, while in CDLD patients, it decreased, indicating reduced adaptive renal response to sodium intake. Sodium-regulating function disturbances were primarily due to reduced GFR. Sodium clearance significantly decreased in chronic hepatitis and decompensated cirrhosis groups, but sodium excretion per 100 ml GFR tended to increase.

Table 5: Some Indicators of Renal Function in Patients with Chronic Hepatitis and Liver Cirrhosis During Salt Load (M±m)

Indicators Studied	Practically Healthy Individuals (n=18)	Chronic Hepatitis (CH) (n=12)	Subcompensated Cirrhosis (SC) (n=10)	Decompensated Cirrhosis (DC) (n=15)
Diuresis (ml/2 hr)	136.5±14.6	51.66±6.64*	130.6±14.1	93±84.3*
Standardized Diuresis (ml/kg)	2.1±0.25	0.88±0.12*	2.01±0.45	1.43±0.11*
Plasma Creatinine Concentration (μmol/l)	67.30±3.32	105.12±9.06*	107.81±19.79*	118.45±13.29*
Glomerular Filtration Rate (GFR) (ml/min)	106.10±17.04	30.79±5.05*	54.79±9.03*	26.41±2.78*
Water Reabsorption (%)	99.81±0.01	99.76±0.02*	99.59±0.10*	99.49±0.08*
Plasma Sodium Concentration (mmol/l)	138.6±5.42	143.33±6.48	141.66±15.56	145.5±21.39
Sodium Excretion (mmol/2 hr)	3.4±0.05	1.4±0.07*	4.1±1.2	1.5±0.06*
Standardized Sodium Excretion (mmol/100 ml GFR)	0.36±0.03	0.43±0.16	1.03±0.58	0.59±0.19
Sodium Clearance (ml/2 hr)	26.4±4.2	10.14±0.54*	28.7±6.7	13.5±3.9*

Notes: * - significant differences compared to the healthy group.

Future Works Suggested in This Paper Further Investigation on Urea Levels: The study found that urea levels increased significantly only in patients with cirrhosis, and this phenomenon requires further investigation to understand the underlying mechanisms and implications. Exploring Microcirculation Disturbances: Since the involvement of kidneys in hepatorenal syndrome is linked to disturbances in microcirculation due to the activation of the renin-angiotensin system (RAS), future research should focus on exploring these microcirculatory changes in more detail. Longitudinal Studies on Disease Progression: Future studies should include longitudinal research to track the progression of kidney dysfunction over time in

patients with chronic liver diseases, providing a clearer picture of how these conditions evolve. Impact of Different Treatments: Investigating the impact of various treatments for chronic liver diseases on kidney function could provide insights into how to better manage hepatorenal syndrome and improve patient outcomes.

Conclusion

1. In patients with chronic liver diseases, especially with cirrhosis, signs of hepatorenal syndrome were detected, indicated by a decrease in GFR under both spontaneous and salt load diuresis conditions. The reduction in GFR was not related to blood protein concentration, blood pressure, or renal sodium exchange mechanisms. The result of the decreased GFR was azotemia, evidenced by an increase in plasma creatinine concentration, with urea levels rising only in cirrhosis.
2. Hepatorenal Syndrome Development: The study found that patients with chronic liver diseases, especially those with cirrhosis, showed signs of hepatorenal syndrome, which is a condition where the kidneys start to fail due to severe liver disease. Reduction in Glomerular Filtration Rate (GFR): The primary issue in these patients was a significant reduction in the glomerular filtration rate (GFR), which is a measure of how well the kidneys are filtering blood.
3. This reduction was not linked to blood pressure, plasma protein levels, or sodium exchange in the kidneys. Increased Creatinine and Urea Levels: As a result of the decreased GFR, there was an increase in plasma creatinine levels, indicating kidney dysfunction. Urea levels also increased, but this was mainly observed in patients with cirrhosis.
4. Severity Correlation: The extent of kidney dysfunction correlated with the severity of liver damage, meaning that more severe liver disease led to more significant kidney issues.
5. Contributions of the Paper Assessment of Kidney Function in Liver Disease: The paper studied how chronic liver diseases like hepatitis and cirrhosis affect kidney function, focusing on how well the kidneys filter blood, which is measured by the glomerular filtration rate (GFR).
6. Correlation with Liver Disease Severity: It found that the severity of kidney dysfunction is linked to how severe the liver disease is, meaning worse liver conditions lead to more significant kidney problems. Independent of Other Factors: The study showed that the

reduction in GFR was not related to blood pressure, plasma protein levels, or sodium exchange in the kidneys, indicating a direct impact of liver disease on kidney function.
7. Increased Creatinine and Urea Levels: The research highlighted that patients with liver disease had higher levels of creatinine and urea in their blood, which are markers of kidney dysfunction, especially in those with cirrhosis.

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