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USE OF PROTON PUMP INHIBITORS IN PATIENTS WITH LIVER CIRRHOSIS AND THEIR IMPACT ON THE MENTAL STATUS OF PATIENTS

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Abstract:

Chronic liver diseases have recently occupied the leading place as the most common cause of mortality in many developed countries. One of the manifestations caused by liver failure is hepatic encephalopathy syndrome, which is a disorder of brain function that manifests itself in a wide range of neurological or psychiatric disorders from minimal cognitive impairment to coma. Researchers have found evidence that the use of proton pump inhibitors (PPIs) may cause changes in gut bacteria that may contribute to liver disease and, when pathogenic bacteria multiply in the intestines, may cause hepatic encephalopathy and/or worsen the stage.

Keywords: Hepatic encephalopathy, liver cirrhosis, gastropathy, proton pump inhibitors, intestinal microbiome .

INTRODUCTION. Chronic liver diseases have recently occupied the leading place as the most common cause of mortality in many developed countries. One of the manifestations caused by liver failure is hepatic encephalopathy (HE) syndrome, which is a disorder of brain function that manifests itself in a wide range of neurological or psychiatric disorders from minimal cognitive impairment to coma. Chronic diseases of the liver and biliary tract are often combined with inflammatory and degenerative-dystrophic changes in the mucous membrane of the stomach and duodenum . There are portal hypertensive gastropathy and gastric antral vascular ectasia, against which ulcerative lesions of the stomach and duodenum occur [1,4,6]. With decompensated liver cirrhosis, gastric ulcers are detected in 15% of patients , with compensated cirrhosis - in 3.3%, in the general population - in 1.7% [2,7,9, 15]. Duodenal ulcers are found in 9.5% of patients with liver cirrhosis and in 4% of the general population; however, the relationship between the incidence of ulcers and the severity of cirrhosis has not been established [11,15]. Most often (in 60% of cases) ulcer is localized in the antrum of the stomach and the ampulla of the duodenum (in 10%) [12,14]. Gastric hyperplasia occurs against the background of pronounced venous stagnation [11]. The main cause of ulcer formation is considered to be hemodynamic disturbances that occur during liver cirrhosis [15,18]. Due to morphological changes in the liver, resistance in the portal vein system increases, which causes venous hypertension and the opening of natural portocaval shunts. In addition, the hyperdynamic state of blood flow with the opening of arteriovenous shunts, an increase in cardiac output and a decrease in peripheral vascular resistance plays an important role in the occurrence and maintenance of portal hypertension. Intraorgan blood flow increases due to an increase in the level of circulating vasodilators and a decrease in the sensitivity of blood vessels to endogenous vasoconstrictors [9].

Researchers have found evidence that use of proton pump inhibitors (PPIs) may cause changes in gut bacteria that may contribute to liver disease. In recent years, it has become clear that in addition to clearly expressed HE, there is also a subclinical or latent form of HE, called minimal hepatic encephalopathy (MHE). Patients with MHE do not have subjective symptoms of the disease, but with special psychometric tests (for example, a number connection test for reaction speed) they demonstrate obvious impairments in brain function: a decrease in the speed of cognitive activity and the accuracy of fine motor skills. Most often, attention deficit and motor disorders are detected, which can result in the inability to provide proper control, for example, when managing complex mechanisms, as well as sleep disorders. The prevalence of minimal HE among patients with liver cirrhosis varies from 30 to 84% [6,15].

MATERIALS AND RESEARCH METHODS. A total of 98 patients participated, including 52 men and 46 women. The average age was 48±2.4 years. Your patients were diagnosed with liver cirrhosis of various Child -Pugh classes. All patients were divided into 2 groups: 1st group of patients, these were patients who, due to the presence of lesions of varying severity of the gastrointestinal tract (GIT), received drugs from

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the proton pump inhibitor group (n = 40) ; and group 2 of patients who were treated with basic therapy for liver cirrhosis and did not take PPI drugs (n = 58). The study also involved practical healthy individuals who formed a control group consisting of 21 people.

When selecting patients, the exclusion criteria were:

1. Patients with neuropsychic disorders not caused by liver diseases.
2. Patients with severe somatic diseases
3. Patients with a history of taking psychotropic drugs.
4. Patients with alcohol and drug intoxication.
5. Patients with primary and secondary brain tumors.
6. Patients with severe hepatic encephalopathy (hepatic coma).

The leading role in the diagnosis of HE is played by the assessment of clinical data, primarily the assessment of the patient's mental state. Although diagnosing severe HE is not particularly difficult, at earlier stages it is not easy to verify this syndrome, since no symptom is absolutely sensitive and specific. However, it is the early stages of HE, especially MHE, that are of particular clinical importance; on the one hand, they affect the quality of life of patients with liver cirrhosis, and on the other hand, they are amenable to drug correction. Instrumental examination methods play a secondary role and only allow one to suspect HE. We assessed the severity of clinical manifestations of HE using the West -Haven criteria.

The patients underwent the following research methods, including : a questionnaire containing subjective information was carried out , and a neurological condition was examined Using psychometric tests, conducting a question and answer session with the patient, cognitive impairment and degree of depression were determined using the MMSE test and using the Beck Inventory. All patients underwent the following instrumental research methods, such as EEG, Transcranial Dopplerography (TCDG), MRI examination of the brain, to exclude tumors and neoplasms. General clinical laboratory research methods were carried out, such as a general blood and urine test, biochemical blood parameters, ELISA and PCR tests to determine the quantitative and qualitative determination of viral hepatitis B, C, D, determination of sodium and ammonia in the blood.

RESULTS. Upon admission to the hospital on the first day and upon discharge of patients from the hospital, all patients with liver cirrhosis were administered several types of subjective questionnaires and psychometric testing. **MMSE** (Mini-Mental State Examination) - a brief scale for assessing mental status consists of 22 points and is assessed by point.

Table 1.

Dynamics of results in groups before and after treatment of patients according to the MMSE questionnaire

Groups / Before and/or after treatment	Control group (n=21) Average overall score	Main group	
		1-group (n =40) Average overall point	2-group (n =58) Average overall score
Before treatment	**29.8** ±1.3*	25.5± 1.4 **	2 3.8 ±1.4*
After treatment		20.4±1.2*	27.3±0.8**

Note : **- p< 0.05 - differentiation _*
***- p < 0.01 - level of static significance of differences*

As the disease progresses, the patient's personality changes, and family members report apathy, irritability, and incontinence, in addition to obvious changes in consciousness and motor function. Patients with PE are poorly oriented in time and space, behave inappropriately and are in a clearly confused state, characterized by agitation or drowsiness, stupor and subsequently coma. The development of overt HE leads to persistent problems with working memory and learning objects.

Table 2.

Results of psychometric testing before and after treatment in patients receiving PPIs at different stages of hepatic encephalopathy with liver cirrhosis (group 1)

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Stages of HE	**Number connection test (sec)**	
	Before treatment	**After treatment**
Patients without HE	39.8 ± 0.3 sec	44.6 ± 0.33 ***
0-I stage	55.6 ± 0.78 sec	56.2 ± 1.7 sec***
Stage II	101.8 ± 2.3 sec	95.2 ± 3.04 sec***
Stage III	126.0 ± 0.9 sec	1 38.3 ± 1.05 sec ***
Control group (total = 21)	37.09±0.72sec	

Note: ** ** - p< 0.0 01 - level of static significance of differences.*

Based on the results of the test of the connection of numbers in the first group according to the table, we can say that after treatment, patients who took PPI drugs associated with damage to the gastrointestinal tract, the general mental status was depressed to one degree or another. After treatment, the duration of the number connection test was increased by an average of 6.8 ± 1.2 seconds.

Table 3.
Results of psychometric testing before and after treatment in patients receiving PPIs at different stages of hepatic encephalopathy with liver cirrhosis (group 2)

Stages of HE	**Number connection test (sec)**	
	Before treatment	**After treatment**
Patients without HE	41.06±0.18 sec	39.18±0.14 sec *
0-I stage	54.56±0.79 sec	53.16±2.46 sec*
Stage II	89.72±2.36 sec	86.15 ±2.17 sec*
Stage III	132.38±3.54 sec	95.2±4.2 sec*
Control group (total = 21)	37.09±0.72sec	

Note: ** - p<0.05 - - level of static significance of differences.*

On the above table and according to the results of the number connection test in the second group, we can say that after treatment in patients who did not take drugs from the PPI group, but only took basic drugs for the treatment of liver cirrhosis, the general mental status and psycho-neurological disorders were changed to better side. After treatment, the duration of the number connection test was reduced by an average of 12.8 ± 2.9 seconds.

CONCLUSIONS. In patients with liver cirrhosis, a risk factor for developing PE may be taking proton pump inhibitors. We recommend diagnosing overt HE based on the clinical picture, noting that its leading diagnostic symptoms are the detection/presence of disorientation and asterixis in the patient. Based on the available data, we recommend that PPIs be used with caution in patients with cirrhosis, and when strictly indicated, not for long-term treatment. We have provided recommendations for safety and dosage for oral PPI use in patients with cirrhosis that can be used in daily practice.

REFERENCES:

1. Bajaj JS, Ratliff SM, Heuman DM, et al. Proton pump inhibitors are associated with a high rate of serious infections in veterans with decompensated cirrhosis . *Aliment Pharmacol Ther* 2012; 36 :866–74 . [PMC free article] [PubMed] [Google Scholar]
2. Bian J, Wang A, Lin J, Wu L, Huang H, Wang S, Yang X, Lu X, Xu Y, Zhao H. Association

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between proton pump inhibitors and hepatic encephalopathy: A meta-analysis. Medicine (Baltimore). 2017.
3. Bian J, Wang A, Lin J, Wu L, Huang H, Wang S, Yang X, Lu X, Xu Y, Zhao H. Association between proton pump inhibitors and hepatic encephalopathy: A meta-analysis. Medicine (Baltimore). 2017 Apr;96(17):e 6723. Doi: 10.1097/MD.0000000000006723. PMID: 28445288; PMCID: PMC5413253.
4. Bekmuradova M. S., Shodieva G. R. Helicobacter pylori worsening factor of the patient's condition in patients with liver encephalopathy. – 2021.
5. Dam G, Vilstrup H, Watson H, et al. Proton pump inhibitors as a risk factor for hepatic encephalopathy and spontaneous bacterial peritonitis in patients with cirrhosis with ascites . *Hepatology* 2016; 64 :1265–72 .
6. Jackson MA, Goodrich JK, Maxan ME, et al. Proton pump inhibitors alter the composition of the gut microbiota. Gut 2016; 65:749-56.
7. Khabibovna YS, Salkhidinovna BM Effects of proton pump inhibitors on hepatic encephalopathy in patients with cirrhosis //World Bulletin of Public Health. – 2022. – T. 9. – S. 230-233.
8. Min YW, Lim KS, Min BH, et al. Proton pump inhibitor use significantly increases the risk of spontaneous bacterial peritonitis in 1965 patients with cirrhosis and ascites: a propensity score matched cohort study . *Aliment Pharmacol Ther* 2014; 40 : 695–704.
9. Quigley EM, Stanton C, Murphy EF. The gut microbiota and the liver. Pathophysiological and clinical implications . *J Hepatol* 2013; 58 :1020 –7. [PubMed] [Google Scholar]
10. Salhiddinovna B. M. , Alisherovna , KM ., Tashtemirovna , EM ., & Tatlibayevich , YS . (2023). Hepatic Encephalopathy and Quality of Life of Patients With Viral Cirrhosis of the Liver. *Miasto Przyszłości* , *35* , 1–5. Retrieved from https://miastoprzyszlosci.com.pl/index.php/mp/article/view/1323
11. Salkhidinovna BM, Rabimkulovna SG, Totliboevich YS Comparative assessment of the effect of omeprazole and pantaprazole on the degree of development of hepatic encephalopathy in the patients with liver cirrhosis //E-Conference Globe. – 2021. – S. 149-152.
12. Salkhidinovna B. M., Nizomitdinovich K. S. ASSESSMENT OF THE DYNAMICS OF HEPATIC ENCEPHALOPATHY IN PATIENTS WITH CIRRHOSIS BEFORE AND AFTER IN-HOSPITAL TREATMENT.
13. Tsung- Hsing Hung, Hsing -Feng Lee, Chih -Wei Tseng, Chih -Chun Tsai, Chen-Chi Tsai. Effect of proton pump inhibitors in hospitalization on mortality of patients with hepatic encephalopathy and cirrhosis but no active gastrointestinal bleeding, Clinics and Research in Hepatology and Gastroenterology, Volume 42, Issue 4, 2018, 353-359.
14. Vilstrup H., Amodio P., Bajaj J. et al. Hepatic encephalopathy in chronic liver disease: 2014 practice guideline by the American association for the study of liver diseases and the European association for the study of the liver. Hepatology . 2014; 60: 715–735.
15. Weissenborn K, Ennen JC, Schomerus H, et al. Neuropsychological characterization of hepatic encephalopathy . *J Hepatol* 2001; 34 :768–73 .
16. Yang YX, Lewis JD, Epstein S, et al. Long-term proton pump inhibitor therapy and risk of hip fracture . *JAMA* 2006; 296 :2947–53 .
17. Ziyadullaev Shukhrat Khudoyberdievich , Bekmuradova Makhsuda Salkhidinovna , Toirov Doston Rustamovich , Effect of Proton Pump Inhibitors on Hepatic Encephalopathy in Cirrhotic Patients with Concomitant Gastroduodenal Disorders, *American Journal of Medicine and Medical Sciences* , Vol. 13 No. 2, 2023, pp. 112-118. Doi: 10.5923/j.ajmms.20231302.18.
18. Bekmuradova M. S. Effect of proton pump inhibitors on hepatic encephalopathy in patients with liver cirrhosis and concomitant gastroduodenal pathology // Science and Education . – 2022. – T. 3. – No. 12. – pp. 280-287.
19. Bekmuradova M. S., Gaffarov Kh. Kh., Yarmatov S. T. Oshkozon-ichak tracts zararlanishi ustunliga Bilan kechgan coronavirus infectionsidan keyings holatni Davolashning Uziga hosliclari // Scientific progress . – 2021. – T. 2. – No. 1. – S. 489-493.
20. Bekmuradova M. S., Normatov M. B. Comparative assessment of the dynamics of hepatic encephalopathy in patients with liver cirrhosis // Scientific progress . – 2022. – T. 3. – No. 2. – S. 895-899.
21. Ivashkin V.T., Mayevskaya M.V., Pavlov Ch.S., Fedosina E.A., Bessonova E.N., Pirogova I.Yu., Garbuzenko D.V. Clinical recommendations of the Russian Society for the Study of the Liver and the Russian Gastroenterological Association for the treatment of complications

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of liver cirrhosis. Russian journal of gastroenterologists, hepatologists , coloproctologists . 2016; 26(4): 71–102.
22. Maksimova E.V., Klyaritskaya I.L. "Hepatic encephalopathy, diagnosis, differential diagnosis and therapy with ornithine" 2018. Art. 110-116.
23. Moiseeva E.O. "Modern clinical and instrumental methods for diagnosing hepatic encephalopathy." Bulletin of the Smolensk State Medical Academy. 2010.78-83.