# COMPARATIVE ASSESSMENT OF THE EFFECT OF OMEPRAZOLE AND PANTAPRAZOLE ON THE DEGREE OF DEVELOPMENT OF HEPATIC ENCEPHALOPATHY IN THE PATIENTS WITH LIVER CIRRHOSIS

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**Introduction.** Chronic liver disease is becoming one of the first places in terms of prevalence and is currently the fifth most common cause of death in many developed countries[2,3]. One of the manifestations associated with liver failure is hepatic encephalopathy syndrome, which is a dysfunction of the brain, which manifests itself in a wide range of neurological or psychiatric disorders from subclinical changes to coma [1,6,10]. Often, with cirrhosis of the liver due to portal hypertension against the background of pronounced venous stasis, the stomach and duodenum are affected [2,12]. Sometimes due to hemodynamic disturbances in the gastrointestinal tract with cirrhosis of the liver, ulcers are formed, the so-called hepatogenic ulcers [3,7]. In addition, 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. In the genesis of the development of hepatogenic ulcers, a number of authors attach great importance to the acid-peptic factor [8,10]. Duodeno-gastric reflux is considered an important factor in the pathogenesis of gastric ulcer and duodenal ulcer in liver cirrhosis [11,12]. The development of duodenal ulcers in patients with cirrhosis of the liver can be associated with microcirculatory disorders of the gastric mucosa, stagnation of venous blood and functional liver failure [2,6,10]. This condition requires the use of PPIs in patients with cirrhosis of the liver and concomitant gastrointestinal lesions. In recent years, data have appeared in the literature that PPIs can worsen the degree of hepatic encephalopathy in patients with cirrhosis of the liver, and sometimes even can provoke the development of encephalopathy in this category of patients [4,6,9]. Recent studies have shown that these drugs cannot be used without clear indications, since a number of studies have demonstrated a clear relationship between PPIs and the development of conditions such as hepatic encephalopathy, osteoporosis, pneumonia, etc.[5,10]. And it has also been shown that PPIs work by suppressing acid, which can disrupt the gut microbiome, as a result of this, the concentration of ammonia in the blood can increase, that is, hyperammonemia [2,4,12].

**Purpose of the study.** To evaluate in a comparative aspect the effect of Omeprazole and Pantaprazole on the degree of development of hepatic encephalopathy in patients with cirrhosis of the liver accompanying with diseases of the gastrointestinal tract.

**Materials and research methods.** The work was carried out at the Department of Propedeutics of Internal Diseases on the basis of the clinic SamMI №1 in the Department of 2-therapy. We examined 52 patients (24 women and 28 men) with liver cirrhosis (class A, B, C according to

Childe-Pugh), with lesions of the gastrointestinal tract, with the presence of hepatic encephalopathy from a minimal to a pronounced degree, who took proton pump inhibitors. The stages of HE were determined in accordance with the criteria of the International Association for the Study of Liver Diseases (West-Haven modified by Conn).

The grade of hepatic encephalopathy was determined by the West Haven scale to the following grade:

1st degree - drowsiness, sleep disturbance; II-nd degree - lethargy or apathy; III degree - severe confusion of consciousness, incoherent speech, disorientation; IV-th degree - coma. The patients were equally divided into two groups. The first group (26 patients) is patients with cirrhosis of the liver with hepatic encephalopathy, who had concomitant lesions of the gastrointestinal tract from mild lesions of the mucous membranes of the gastrointestinal tract (gastritis, duodenitis) to ulcers. This group of patients took Omeprazole 20 mg / day to prevent various complications from the gastrointestinal tract. And the second group (26 patients), these are patients with cirrhosis of the liver with hepatic encephalopathy, who took Pantaprazole 20 mg / day to treat complications from the gastrointestinal tract.

All patients in both groups were assessed as patients with grade I and II hepatic encephalopathy. Once these patients were identified, a cartographic analysis was performed to determine if these patients had been on omeprazole / pantaprazole for> 30 days prior to their hospitalization. All patients taking PPIs before admission to the hospital were excluded from the examination. All patients underwent a complete clinical, laboratory and instrumental examination, including: questionnaires and diagnostic tests. From laboratory methods, the patients underwent: general analysis of blood, urine; biochemical analyzes - bilirubin, ALT, AST, total protein, creatinine, urea; Prothrombin index, Prothrombin time, as well as in all patients, the concentration of ammonia in the blood was determined (clinical suspicion of the presence of HE can be objectified by determining the concentration of ammonia in the blood serum, however, it should be remembered that there is no clear relationship between the concentration of ammonia in the blood and the degree of HE). And also taking into account hypoglycemia as a marker of more severe liver damage in all patients, blood sugar was measured. Of the instrumental methods, ultrasound, Fibroscan, EEG were used for an additional method for diagnosing hepatic encephalopathy, EGDFS (esofagogastroduodenofibroscopy) for diagnosing complications of liver cirrhosis from the gastrointestinal tract. Patients in both groups took PPI drugs during 28 days or more.

To diagnose and differentiate the degree of hepatic encephalopathy, the Number Link Test was applied to all patients. In many literature studies, it has been proven that the sensitivity of psychometric tests (number connection test, number-symbol test, line test and dashed lines test in detecting hepatic encephalopathy is 70-80%.

In patients with cirrhosis of the liver accompanied by lesions of the stomach and duodenum, who took Omeprazole, the degree of HE was assessed twice, before and after treatment.

And also, the degree of PE was evaluated twice in patients taking Pantaprazole in patients with liver cirrhosis with gastrointestinal lesions before and after treatment.

In the course of treatment, the majority of patients showed a decrease in the intensity of pain in the epigastric region, heartburn stopped, and stomach discomfort decreased.

Along with this, the degree of hepatic encephalopathy was assessed in both groups.

Dynamics of the degree of hepatic encephalopathy before and after treatment in patiens taking Omeprazole and taking pantaprazole

Table 1.

| HE grade | Patients using Omeprazole | | Patients using Pantaprazole | |
|---|---|---|---|---|
| | n= 26 | | n= 26 | |
| | Before using omeprazole | After omeprazole treatment | Before using Pantaprazole | After treatment with pantaprazole |
| 1st degree | 11(42,3%) | 10(38,5%) | 12(46,1%) | 7(26,9%) |
| 2nd degree | 15(57,6%) | 16(61,5%) | 14(38,5%) | 19(73,1%) |

**Research results.** As can be seen from the table, the degree of HE in the 1st group after treatment with Omeprazole, using the West Haven criterion, the degree of hepatic encephalopathy worsened in only one (1) patient, for example, the mental status slightly worsened, dementia progressed slightly, memory worsened, tremor increased hands, etc. In short, the degree of hepatic encephalopathy increased, but not significantly.

And in the second group, after treatment with pantaprazole, the mental status of patients worsened much worse, that is, in 5 patients, the degree of HE worsened. There were observed mental disorders with impaired consciousness, decreased intelligence, tremors with ataxia, nystagmus, rigidity, increased balance disorders, etc. In this way, in the second group, the deterioration in the degree of HE was significant.

**Discussion of the results obtained.** As can be seen from the obtained data, the majority of hospitalized patients with liver cirrhosis who took Pantaprazole had a significant worsening of the degree of HE, in about 20% of patients, which is confirmed by the higher mean West Haven criterion for HE compared to patients who took Omeprazole.

Based on the data obtained, it can be assumed that the use of PPIs can affect patients with cirrhosis by changing the pH of the stomach, which leads to the proliferation of the intestinal microbiome, thereby increasing the production of ammonia and the translation of bacteria, which in turn affects the degree of HE.

Several studies have shown that PPI use can worsen liver failure in patients with cirrhosis. An analysis by Tsai et al, which stratified patients based on duration of PPI use, showed that longer PPI use resulted in higher HE rates. The result remained statistically significant after the correction of the patient's comorbidities. According to our data, patients taking Pantaprazole had a significantly higher rate of HE episodes on the West Haven Criterion scale compared with patients taking Omeprazole. In addition, our study shows that pantaprazole predispose patients with cirrhosis to worsening encephalopathy regardless of age or gender.

This circumstance makes it possible to recommend Omeprazole as the drug of choice in patients with liver cirrhosis with gastro-duodenal pathology.

**Conclusions of the study.** Thus we can conclude, in this study, it was shown that when using Omeprazole in patients with cirrhosis of the liver with gastrointestinal tract damage, the degree of HE changes insignificantly compared to patients taking pantaprazole. In the treatment of patients with cirrhosis of the liver with concomitant gastroduodenal pathology, in order to avoid the development and (or) deterioration of the degree of hepatic encephalopathy, the drug of choice may be omeprazole.

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