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Research Article

Liver Fibrosis in Non-Alcoholic Fatty Liver Disease: Motor Function of the Gastrointestinal Tract and Biliary Tract

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Abstract

Introduction: Non-alcoholic fatty liver disease encompasses a spectrum of pathological conditions, including fatty steatosis, which has a benign course, non-alcoholic steatohepatitis, characterized by the potential to progress to liver fibrosis, and hepatocellular carcinoma.

Aim: To identify violations of the motor function of the gastrointestinal tract and biliary tract (BIT) in liver fibrosis as an outcome of NAFLD.

Materials and Methods: The study was conducted on 12 patients with liver fibrosis in the outcome of NAFLD, which constituted the main group of patients. The motor function of the gastrointestinal tract and GI was examined by electromyography (EMG). EMG registration was carried out using a Nihon Kohen multichannel electromyograph (Japan). The amplitude-frequency characteristics of slow waves and spikes, the power of phase and tonic contractions, and propulsive activity were determined on the EMG curve.

Results: With the development of liver fibrosis in the outcome of NAFLD, hypermotor dyskinesia of the stomach and left sections of the colon was revealed - by 47.8% and 26.6%, respectively.

With the development of liver fibrosis, hypomotor dyskinesia of the choledochus was revealed - by 88.9% and jejunum - by 45%.

The development of liver fibrosis is accompanied by slight fluctuations in the motor function of the gallbladder and duodenum.

Keywords: *Non-Alcoholic Fatty Liver Disease; Liver Fibrosis; Hepatocellular Carcinoma; NAFLD; Electromyography (EMG)*

Introduction

Non-alcoholic fatty liver disease combines a spectrum of pathological conditions, including fatty steatosis, which has a benign course, non-alcoholic steatohepatitis, characterized by the potential for progression to liver fibrosis (F) hepatocellular carcinoma [1].

Up to 80 - 90% of patients with NAFLD have isolated hepatic steatosis, which is predominantly benign, but 10 - 30% of patients develop steatohepatitis (SH), a progressive form of NAFLD associated with hepatocellular damage and inflammation.

In 25 - 40% of patients with FH, hepatic fibrosis subsequently develops, gradually leading to the development of organ fibrosis in 20 - 30% of cases. Individuals with F3-4 liver fibrosis have a significantly higher mortality rate than those with less severe fibrosis. Mortality over a 10-year period in patients with Chaid-Pugh F liver fibrosis is as high as 20%. In patients with liver fibrosis in the outcome of SH, there is a high risk of developing hepatocellular carcinoma with a frequency of 2.6% per year.

In the etiology and pathogenesis of the development of liver fibrosis, there is an initial disturbance in the metabolism of free fatty acids, which leads to the formation of liver stasis, contributing to an increase in the sensitivity of hepatocytes to initiate inflammation. The latter, in turn, leads to necrosis of hepatocytes, which activates the processes of fibrogenesis, leading to the development of liver fibrosis.

Pathogenetic factors in the development of NAFLD and its progression include specific genetic polymorphisms (for example, the PLPKA3 gene and epigenetic modifications), the nature of the diet (high intake of saturated fatty acids and fructose), obesity, insulin resistance [2], dysregulation of adipokines production, bacterial overgrowth syndrome (SIBR).

Under conditions of increased formation of free fatty acids (FFA) in hepatocytes, the role of beta-peroxisomal and omega-microsomal oxidation increases, which occurs with the participation of CYP2E1 and CYP4A isoenzymes, which is accompanied by the accumulation of reactive oxygen species. FFA, being a highly active substrate of LPO, activate this process, which leads to disruption of the integrity of hepatocyte membranes and their subsequent death. There is apoptosis of hepatocytes and activation of Ito stellate cells, which play a key role in the processes of fibrogenesis.

Given the deep study of the pathogenetic mechanisms of the development of liver fibrosis, it should be noted that the motor function of the hollow organs of the digestive system in liver F has not been studied enough.

Aim of the Study

The aim to identify violations of the motor function of the gastrointestinal tract and biliary tract (BIT) in liver fibrosis as an outcome of NAFLD.

Materials and Methods

The study was conducted on 12 patients with liver fibrosis in the outcome of NAFLD, which constituted the main group of patients. The control group consisted of 10 patients suffering from gastritis C. The exclusion criteria were patients with cancer, mental illness, patients who refused to conduct electromyography.

The motor function of the gastrointestinal tract and biliary tract was studied electromyographically (EMG) by placing cutaneous bipolar silver electrodes on the anterior abdominal wall in the region of the projection of the organ onto the anterior abdominal wall. EMG registration was carried out using a Nihon Kohen multichannel electromyograph (Japan). On the EMG curve, the amplitude-frequency characteristics of slow waves and spikes, the power of phase and tonic contractions, and propulsive activity were determined.

Statistical analysis was performed using the Mann-Whitney small sample method at $p < 0.05$.

Results

The results of EMG of the esophagus in patients with liver fibrosis are shown in table 1.

Research Group	Slow waves			Spike activity			Propulsive activity
	Frequency	Wave amplitude	Power of tonic contractions	Frequency	Wave amplitude	Power of phase contractions	
Fibrosis of the liver	15,6 ± 0,13	0,09 ± 0,0015	1,404 ± 0,13	3,5 ± 0,12	0,03 ± 0,0012	0,105 ± 0.011	13,3 ± 1,8
Control	14,0 ± 0,1	0,1 ± 0,003	1,4 ± 0,11	1,0 ± 0,02	0,1 ± 0,003	0,1 ± 0,004	14,0 ± 1,5

Table 1: *Electromyogram parameters of the esophagus in various conditions.*

From table 1 shows that mild hypomotor esophageal dyskinesia was detected in liver fibrosis (5%, $p < 0.05$).

The results of the study of EMG of the stomach in patients with liver fibrosis are shown in table 2.

Research Group	Slow waves			Spike activity			Propulsive activity
	Frequency	Wave amplitude	Power of tonic contractions	Frequency	Wave amplitude	Power of phase contractions	
Fibrosis of the liver	10,3 ± 0,4	0,12 ± 0,001	1,308 ± 0,12	4,3 ± 0,2	0,025 ± 0,003	0,1075 ± 0.009	12,2 ± 1,1
Control	5,5 ± 0,3	0,15 ± 0,003	0,825 ± 0,007	1,0 ± 0,04	0,1 ± 0,002	0,1 ± 0,002	8,25 ± 0,7

Table 2: *Indicators of electromyography of the stomach in various conditions.*

Thus, moderate hypermotor dyskinesia of the stomach (47.8%, $p < 0.05$) was revealed in liver fibrosis due to a significant increase in the power of tonic contractions of the longitudinal and partially oblique muscles of the stomach by 32.3% ($p < 0.05$).

The results of studies of EMG choledochus in liver fibrosis are shown in table 3.

Research Group	Slow waves			Spike activity			Propulsive activity
	Frequency	Wave amplitude	Power of tonic contractions	Frequency	Wave amplitude	Power of phase contractions	
Fibrosis of the liver	12,12 ± 0,22	0,14 ± 0,02	1,7 ± 0,03	5,9 ± 0,5	0,05 ± 0,001	0,295 ± 0.0021	5,8 ± 0,6
Control	9,0 ± 0,5	0,1 ± 0,001	0,9 ± 0,0073	1,0 ± 0,03	0,1 ± 0,002	0,1 ± 0,004	9,0 ± 0,6

Table 3: *Choledoch electromyogram parameters in various conditions.*

From table 3 it follows that the power of tonic contractions of the choledochus in fibrosis is increased by 88.9% ($p < 0.05$), the power of phase contractions is increased by 195% (p 0.001), propulsive activity is increased by 35.6% ($p < 0.05$). That is, a significant spasm of the circular muscles of the common bile duct was revealed in liver fibrosis in NAFLD.

The results of studies of EMG of the gallbladder with liver fibrosis are shown in table 4.

From table 4 it follows that the power of tonic contractions of the gallbladder in liver fibrosis increased by 93.13% ($p < 0.05$), the power of phase contractions increased by 100% ($p < 0.001$), the propulsive activity of the gallbladder decreased by 3, 4% ($p > 0.1$). That is, a significant spasm of both longitudinal and circular muscles of the gallbladder was revealed in liver fibrosis.

Research Group	Slow waves			Spike activity			Propulsive activity
	Frequency	Wave amplitude	Power of tonic contractions	Frequency	Wave amplitude	Power of phase contractions	
Fibrosis of the liver	10,3 ± 0,4	0,15 ± 0,005	1,545 ± 0,13	5,0 ± 0,3	0,04 ± 0,0012	0,2 ± 0.0015	7,725 ± 0,82
Control	8,0 ± 0,5	0,1 ± 0,001	0,8 ± 0,003	1,0 ± 0,1	0,1 ± 0,003	0,1 ± 0,004	8,0 ± 0,7

Table 4: *Indicators of the electromyogram of the gallbladder in various conditions.*

The results of the study of the motor function of the duodenum in liver fibrosis are shown in table 5.

Research Group	Slow waves			Spike activity			Propulsive activity
	Frequency	Wave amplitude	Power of tonic contractions	Frequency	Wave amplitude	Power of phase contractions	
Fibrosis of the liver	21,0 ± 0,5	0,11 ± 0,02	2,31 ± 0,14	4,12 ± 0,2	0,025 ± 0,003	0,102 ± 0.011	22,6 ± 0,45
Control	22,0 ± 1,0	0,1 ± 0,002	2,2 ± 0,007	1,0 ± 0,1	0,1 ± 0,001	0,1 ± 0,0013	22,0 ± 0,3

Table 5: *Indicators of electromyography of the duodenum in various conditions.*

From table 5 it follows that in liver fibrosis, the propulsive activity of the duodenum is slightly increased - by 2.8% ($p > 0.1$), the power of tonic contractions of smooth muscles of the duodenum is reduced by 5% ($p < 0.05$), the power of phase contractions increased by 2% ($p < 0.05$). That is, the propulsive activity of the duodenum is slightly changed, apparently due to the developing bacterial overgrowth syndrome.

The results of the study of the motor function of the jejunum in liver fibrosis in NAFLD are shown in table 6.

Research Group	Slow waves			Spike activity			Propulsive activity
	Frequency	Wave amplitude	Power of tonic contractions	Frequency	Wave amplitude	Power of phase contractions	
Fibrosis of the liver	19,5 ± 0,5	0,12 ± 0,003	2,34 ± 0,13	3,5 ± 0,4	0,035 ± 0,005	0,1225± 0,015	11,0 ± 0,45
Control	20,0 ± 1,0	0,1 ± 0,002	2,0 ± 0,007	1,0 ± 0,03	0,1 ± 0,002	0,1 ± 0,004	20 ± 0,3

Table 6: *Indicators of electromyography of the jejunum in various conditions.*

From table 6 it follows that in liver fibrosis, the propulsive activity of the jejunum is reduced by 45% ($p < 0.05$), the power of tonic contractions of the smooth muscles of the jejunum is reduced by 17% ($p < 0.05$), the power of phase contractions is increased by 22.5% ($p < 0.05$). That is, the propulsive activity of the duodenum is reduced, apparently due to the developing syndrome of excessive bacterial growth.

The results of the study of the right sections of the colon with liver fibrosis are shown in table 7.

Research Group	Slow waves			Spike activity			Propulsive activity
	Frequency	Wave amplitude	Power of tonic contractions	Frequency	Wave amplitude	Power of phase contractions	
Fibrosis of the liver	11,0 ± 0,6	0,14 ± 0,003	1,54 ± 0,12	3,6 ± 0,4	0,33 ± 0,002	1,188 ± 0.11	1,3 ± 0,2
Control	11,0 ± 0,3	0,1 ± 0,002	1,1 ± 0,15	1,0 ± 0,03	0,1 ± 0,003	0,1 ± 0,004	11,0 ± 1,4

Table 7: *Electromyogram parameters of the right sections of the colon in various conditions.*

From table 7 it follows that the propulsive activity of the right sections of the colon is reduced by 88.1% ($p < 0.05$), the power of tonic contractions is increased by 40% ($p < 0.05$), the power of phasic contractions is increased by 88% ($p < 0.05$). The results obtained indicate the presence of hypomotor dyskinesia of the right colon, which is a consequence of the development of dysbiosis in liver fibrosis.

The results of the study of the left sections of the colon with liver fibrosis are shown in table 8.

Research Group	Slow waves			Spike activity			Propulsive activity
	Frequency	Wave amplitude	Power of tonic contractions	Frequency	Wave amplitude	Power of phase contractions	
Fibrosis of the liver	10,1 ± 0,5	0,13 ± 0,004	1,313 ± 0,11	4,3 ± 0,5	0,04 ± 0,008	0,172 ± 0.0021	7,6 ± 0,15
Control	6,0 ± 0,5	0,1 ± 0,002	0,6 ± 0,003	1,0 ± 0,02	0,1 ± 0,012	0,1 ± 0,004	6,0 ± 0,3

Table 8: *Electromyogram parameters of the left sections of the colon in various conditions.*

From table 8 it follows that the propulsive activity of the left sections of the colon is increased by 26.6% ($p < 0.05$), the power of tonic contractions is increased by 118.8% ($p < 0.001$), the power of phasic contractions is increased by 72% ($p < 0.05$). The results obtained indicate the presence of hypermotor dyskinesia of the left sections of the colon, which is the basis for the development of diarrhea in liver fibrosis.

Figure 1 shows the morphological picture of the biopsy material of patients with liver fibrosis.

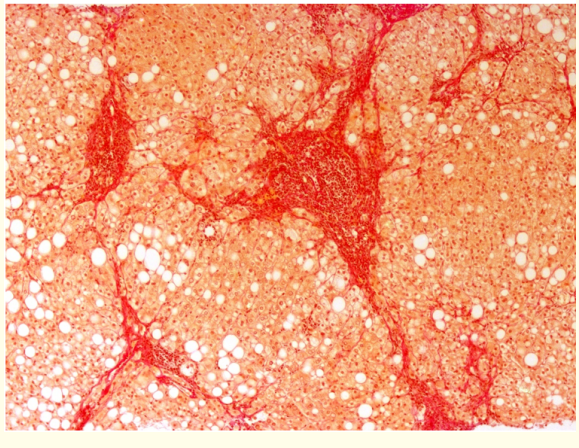

Figure 1: *Severe liver fibrosis on the background of steatohepatitis. Connective tissue septa connect adjacent portal tracts. Stained with picrofuchsin according to Van Gieson. Magnification x120.*

Discussion

The results of the study showed that with liver fibrosis, hypomotor dyskinesia of the esophagus was detected, while, as the researchers note, gastroesophageal disease is detected in NAFLD. It is possible that variations in the direction of esophageal motility are due to the presence or absence of increased abdominal pressure in patients with different body mass index. At the same time, most authors point to the positive effect of weight correction on the clinical and endoscopic picture of reflux disease. Jacobson., *et al*. (2006) demonstrated that a 3 kg/m^2 weight loss was associated with a 40% change in the frequency and intensity of heartburn [3].

Attention is drawn to a significant increase in the propulsive activity of the stomach in liver fibrosis against the background of NAFLD, which may be associated with an increase in the sensitivity of parietal cells to gastrin and pentagastrin, which stimulate the motor function of the stomach and intestines.

A sharp decrease in the motility of the choledochus was revealed, due to the fact that in NAFLD there is a change in the synthesis of bile acids and a decrease in the stimulating effect of cholecystokinin on the secretory activity of the pancreas and motility of the biliary tract [4].

There is a decrease in the motility of the jejunum, the development of pancreatic insufficiency, a decrease in the stimulating effect of bile. On the other hand, these factors create conditions for the development of a syndrome of excessive bacterial growth and a decrease in the motor function of not only the jejunum, but also the development of dysbiosis of the right sections of the colon.

Conclusion

1. With the development of liver fibrosis in the outcome of NAFLD, hypermotor dyskinesia of the stomach and left sections of the colon was detected - by 47.8% and 26.6%, respectively.
2. With the development of liver fibrosis, hypomotor dyskinesia of the choledochal tract was revealed by 88.9% and of the jejunum by 45%.
3. The development of liver fibrosis is accompanied by slight fluctuations in the motor function of the gallbladder and duodenum.

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