Quality of etiotropic therapy efficacy of chronic hepatitis C patients in accordance of toll-like receeceptor 4 +3725G/C gene polymorphisms variety

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Background and Aims: Antiviral therapy is considered to be the only method that can stop the progression HCV infection, the development of hepatocellular carcinoma and death. The end point of antiviral therapy is the achievement of a sustained virologic response (SVR), which in 99% of cases is associated with the possibility of complete elimination of the virus. The aim of our study was to assess the dependence of the frequency of obtaining a SVR to antiviral therapy on the +3725G/C polymorphism of the toll-like receptor 4 (TLR4) gene.

Method: 111 chronic hepatitis C (1b genotype), patients (78 males, 33 females) were observed. All participants received antiviral treatment with Sofosbuvir/Ledipasvir. The duration of antiviral therapy was 12 weeks in patients without cirrhosis and 24 weeks in patients with liver cirrhosis.

Results: The vast majority of treated patients archived a SVR (91.89%), the antiviral therapy was ineffective for 9 patients (8.11%). The number of non-RSVs was significantly (p<0.05) higher among patients with the +3725C allele of the TLR4 gene (GC and CC genotypes) - 77.8% of all those who did not respond to treatment were carriers of this allele. It was established that among patients with the GG genotype, only 2.41% of patients with chronic hepatitis C did not have a SVR. According to the results of the genotypes distribution comparison according to variants of the TLR4 gene +3725G/C allelic polymorphism by the exact two-tailed Fisher test among patients with chronic hepatitis C who had received antiviral therapy, the significantly higher frequency of carriers of the +3725G allele (genotypes GG and GC) was detected (p < 0.001) in the group of patients with RSV vs. the group of patients who did not receive a SVR. According to the odds ratio calculations, it was established that individuals carrying the +3725G allele of the TLR4 gene have a 13 fold higher chance of obtaining a SVR during antiviral therapy use (OR = 13.5; CI 2.61, 69.81). It was established that in the vast majority of patients (68.63% [n = 70]) with chronic hepatitis C, whom a SVR was obtained in, absent liver fibrotic changes (F0) or initial stages of liver fibrosis were observed in 2.26 fold higher number of patients vs. ones with liver fibrosis/cirrhosis (F3 - F4). Among non-RSV patients, the degree of liver fibrosis F0 - F2 were not detected.

Conclusion: Among patients with chronic hepatitis C who did not have a SVR to administered antiviral therapy, there were 3.2 fold higher number of patients with severe liver fibrosis/cirrhosis (F3 - F4). Most of the patients (77.8%) who did not achieve a SVR were carriers of the +3725C allele of the TLR4 gene (p < 0.05). The odds ratios of achieving a SVR in patients with chronic hepatitis C with the 1b genotype were 13 fold higher among carriers of the +3725G allele of the TLR4 gene than among carriers of the +3725C allele.