

### FREQUENCY OF HEMATOLOGIC DISORDERS IN PATIENTS WITH CHRONIC HEPATITIS C RECEIVING ANTIVIRAL THERAPY

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During antiviral therapy patients with chronic hepatitis C of the most important side effects are hematological disorders.

**The purpose of the study:** were evaluate hematological disorders in patients with chronic hepatitis C during antiviral therapy.

**Material and methods.** 26 patients with chronic hepatitis C who received standard antiviral treatment with pegylated interferon alpha and ribavirin were examined. Among them 16 men (61.5%), 8 women (38.5%). The average age was 31,2±2,9 years. HCV genotype 1 was detected in 14 patients (53.8%) patients, HCV genotype 2 or 3 was detected in 12 patients (46.2%). The level of hepatic fibrosis F0-F2 detected in 17 (65.4%) patients, F3-F4 – in 9 patients (34.6%). We used usual clinical, biochemical, virological and instrumental methods. Fibrosis and the level of activity were determined by FibroTest (Biopredictive, France) in the system METAVIR.

**The results.** Hematologic abnormalities were detected in 20 (76.9%) patients during antiviral therapy, among them anemia in 8 (38.5%) patients, neutropenia - in 20 (76.9%), thrombocytopenia - in 12 (46.1%). Combined cytopenia detected in 14 (53.8%) patients. More severe hematologic abnormalities were detected in all patients with fibrosis F3-F4.

**Conclusions.** Haematological disorders during chronic hepatitis C antiviral treatment registered in 20 (76.9%) patients and were more marked in patients with advanced fibrosis that requires careful monitoring and correction.

### THE CLINICAL SIGNIFICANCE OF DIFFERENT TYPES OF LIVER ELASTOGRAPHY

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**Objective:** To determine the optimal modes of different types of liver elastography using. During 2007 - 2013 years 7005 transit elastography were conducted (Fibroscan F - 504, France), during 2012 - 2013 - 47 compression elastography with endosonography were conducted (Hitachi Prerius-Pentax); in 2013 23 trials with shear wave elastography were conducted (AngiodinSono - M Ultra, Russia).

**Materials and Methods.** Elastography was performed in patients with diffuse liver disease: chronic viral hepatitis B, C - 6201 patients, alcoholic steatohepatitis (ASN) - 243 patients, nonalcoholic steatohepatitis (NASN) - 537 patients with cirrhosis of liver - 178 patients. Reference method was a needle biopsy under ultrasound control.

**Results.** Segments were evaluated: maximum efficiency of transit elastography (Fibroscan) – is noted in VII, VI segments ( $r=0,83$ ); moderate efficiency – in IV, III segments ( $r=0,67$ ); minimum efficiency - in V and II ( $r=0,44$ ). During compression elastography at endosonography maximum efficiency was observed in I, II, III segments ( $r=0,91$ ); moderate data were marked in segments IV, V ( $r=0,72$ ); minimally informative data in the segments VIII, VII, VI ( $r=0,57$ ). In elastography shear wave maximum efficacy was observed in VIII, VII, VI, V, IV segment ( $r=0,94$ ); good results in marked segments I, II, III ( $r=0,84$ ).

**Conclusions:** Elastograph «card» of liver segments in diffuse liver disease was developed, which defines an optimal diagnostic effectiveness of various types of elastography in comparing with liver biopsy data: for transit elastometry - VII, VI segments, for compression elastography at endosonography - I, II, III segments. Shear wave elastography - a method of optimal choice, because its performance, expressed in kPa, have a maximum correlation with the histology data of liver biopsy.

### THE IMPACT OF POLYMORPHISM OF CPX4 (718C/T) AND GSTP1 (Ile105Val) GENES ON COURSE OF CHRONIC HEPATITIS C

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**Aims:** to evaluate impact of polymorphic variants of glutathione peroxidase CPX4 (718C/T) and glutathione-S-transferase GSTP1 (Ile105Val) on course of chronic hepatitis C (CHC).

**Materials and methods:** 180 residents in Perm were surveyed (80 healthy (control group) and 100 patients with CHC). The enzyme activity of serum glutathione peroxidase (GIPer) as a marker of free radical oxidation (FRO) was evaluated by the rate of oxidation of reduced glutathione using photometer (wavelength 340 nm). Polymorphism of CPX4 (718C/T) and GSTP1 (Ile105Val) genes was investigated by analysis of melting curves obtained by PCR. The distribution of genotypes was tested for compliance with the Hardy-Weinberg equilibrium using the  $\chi^2$  criterion.

**Results.** Reduced blood saturation with GIPer enzyme occurred in CHC group compared with the control group ( $n=26$ ) ( $8,88\pm3,95$  and  $24,91\pm6,62$  mmol/l respectively,  $p<0.0001$ ). The overall prevalence of genotypes and alleles of CPX4 (718C/T) in CHC patients did not differ from the control group ( $\chi^2=0,1$ ;  $p=0.76$ ). But the minor T allele of the CPX4 (718C/T) gene in patients with CHC showed an inverse relationship with GIPer activity ( $p=0.04$ ). Restructuring of the promoter region of the gene leads to a deficiency of GIPer production, activation of FRO, accumulation of toxic free radicals in the liver and progression of CHC. Analysis of polymorphism of gene GSTP1 (Ile105Val) showed a higher prevalence of heterozygous AG in CHC patients (41% vs 31% in control group,  $\chi^2 = 4,05$ ;  $p = 0.03$ ). The frequency of the minor allele G in GSTP1 (Ile105Val) gene was 31% and 24% in CHC and control groups respectively ( $\chi^2 = 1,75$ ;  $p = 0.19$ ).

**Conclusions.** Polymorphic variants of CPX4 (718C/T) and GSTP1 (Ile105Val) genes may serve as a hereditary risk factors for FRO process in the liver and progression of CHC.

### HBV AND HCV INFECTION AND FREQUENCY OF AUTOANTIBODIES TO PANCREATIC $\beta$ -CELLS IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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**Background and aims.** In patients with chronic viral hepatitis the high prevalence of diabetes mellitus (DM) is observed. Hepatitis viruses B and C (HBV and HCV) are considered as triggers in the development of autoimmune reactions in diabetic patients. The goal was to study the frequency of autoantibodies to pancreatic  $\beta$ -cells in patients with type 2 DM, infected and uninfected by HBV and HCV.

**Materials and methods:** 221 patients with type 2 DM (62 male – 28%; middle age  $59.8\pm0.6$  year, average DM duration  $9.1\pm1.4$  years) were surveyed. Patients were distributed into five groups: first group ( $n=19$ ) – diabetic patients with HBV infection in replicative phase; second ( $n=75$ ) – HBV infected in nonreplicative phase; third ( $n=32$ ) – HCV infected in replicative phase; fourth ( $n=24$ ) – HCV infected in nonreplicative phase; fifth ( $n=71$ ) – noninfected type 2 diabetic patients. Markers of a viral hepatitis B and C, glutamic acid decarboxylase antibodies (GADA) and islet cells antibodies (ICA) were studied by immune-enzyme assay, viral DNA and RNA – by polymerase chain reaction. Statistical data processing is carried out using Yates corrected Chi-square test.

**Results.** GADA was revealed more often in HBV and HCV infected type 2 DM patients in comparison with noninfected: in group 1 – 57.9% ( $\chi^2=15.21$ ;  $p<0.001$ ); in 2 – 37.3% ( $\chi^2=10.45$ ;  $p=0.0012$ ); in 3 – 37.5% ( $\chi^2=6.91$ ;  $p=0.009$ ); in 4 – 54.2% ( $\chi^2=15.1$ ;  $p<0.001$ ) vs. group 5 – 12.7%. ICA in infected patients also met more often, than in noninfected: in group 1 – 31.6% ( $\chi^2=11.97$ ;  $p=0.0005$ ); in 2 – 28.0% ( $\chi^2=15.58$ ;  $p=0.0001$ ); in 3 – 18.8% ( $\chi^2=5.75$ ;  $p=0.017$ ); in 4 – 20.8% ( $\chi^2=6.09$ ;  $p=0.014$ ) vs group 5 – 2.8%. GADA and ICA revealing frequency did not depend on a virus replication. In 18.2% HBV- and HCV-infected patients both kinds of antibodies were determined. In noninfected patients simultaneously ICA and GADA didn't revealed.

**Conclusion.** In type 2 diabetic HBV and HCV infected patients antibodies to pancreatic  $\beta$ -cells are found out statistically significantly more often, than in non-infected DM patients.