N.N. Evlukhina (II place)
Scientific Center of Children's Health, Moscow, Russian Federation

STRUCTURAL AND FUNCTIONAL LIVER INFRINGEMENTS IN CHILDREN WITH CHRONIC LIVER PATHOLOGY

Relevance. Up to now there is no objective assessment system for violations of the liver structure and function based on the International Classification of Functioning, Disability and Health (ICF), which could be used to assess the severity of organ damage, changes in the dynamics during therapy and medical-social examination. There is no criteria used to establish the category of "child with disabilities", even if addressing the need for liver transplantation.

Object: To develop a method for determining the degree of liver function and structure impairment based on the ICF, to establish the dependence of the dysfunction degree on the liver structure violation and portal hypertension severity degree.

Materials and methods. A retrospective analysis of 282 cases of patients aged 1 to 17 years (average age 10.8 ± 4.1): 72 children with autoimmune hepatitis (AIH), 117 - with Wilson's disease (WD) and 93 - with chronic hepatitis C (CHC); ultrasound evaluation procedure, fubroelastometry, morphological examination of the liver tissue. In 171 patients, fibrosis severity was determined by Desmet, and the histological activity index - by Knodell. Of these, 48 patients (average age 12,6 ± 3,9 years) with liver cirrhosis (LC) in the outcome of WD (62.5%) and AIH (37.5%) underwent liver transplantation (TA). The degree of liver dysfunction (DLD), degree of liver structure impairment (DLSI) and severity of portal hypertension was determined by point scales developed and patented at the FSBI "SCCH". DLSI evaluation was carried out during the analysis of 10 indicators characterizing a liver structure impairment (fibrosis severity according to elastometry and morphological study of the liver) and severity of portal hypertension (the diameter of the portal and splenic veins, length of spleen, esophageal varices, recanalization of the umbilical vein, ascites, hydropericardium, hydrothorax). DLD evaluation was carried out with the analysis of 14 indicators characterizing the role of the liver in the metabolism of proteins, fats and carbohydrates (ALT, AST, de Rytis coefficient, urea, ammonia, albumin, ceruloplasmin, transferrin, fibrinogen, prothrombin by Quick, cholesterol, bilirubin, glucose, and lactate). When designing a system of DLD and DLSI definition, we accepted the indicators of 95 patients (average age 10.6 ± 4.5 years), who had no liver disease and were evaluated "4" points, as the absence of violations. As absolute DLD impairments were considered indexes of 15 patients who died from liver failure, As absolute DLSI impairments – indexes of 26

patients with DLSI > 50% and > 20 points on a MELD / PELD scale, separated from 48 patients who underwent TP, and evaluated in "0" points, according to the ICF.

Results. It was found that during the first hospitalization DLSI was more pronounced in case of LC in the outcome of AIH (24.8 ± 8.3%; $p < 0.001$) or WD (32.7 ± 9.2%; $p < 0.001$) than in the absence of a AIH (13.2 10,5 ± 2,5 and ± 4.0%, respectively). At CHC DLSI during the first hospitalization was 6.8 ± 4.4%. After 12 months of therapy in children with LC, DLSI dropped to 15.6 ± 5.3% ($p < 0.001$) for up to 18.8 in AIH and ± 6.1% ($p < 0.001$) in WD. DLD during the first hospitalization with LC in the outcome of AIH was 33.3 ± 12.6% (in the absence of the LC - 21.9 ± 8.9%; $p= 0.001$), in the outcome of WD - 48.1 ± 12.9% (in the absence of the LC - 37 8 ± 11.6%; $p < 0.001$). After 12 months of therapy in children with LC, DLD decreased to 18,9 ± 10,1% at AIH ($p < 0.001$) and to 35.4 ± 8.8% at the WD ($p < 0.001$). In children with AIHG, not taking immunosuppressive therapy during the first hospitalization, DLD was reduced by 35.3 ±14,8 against 26,5 ± 10.7% in patients treated with immunosuppressive therapy for more than 2 weeks ($p = 0.035$). In children with CHC during the first hospitalization, DLD was reduced by 19.1 ± 7.8%. In the dynamics during the therapy after 12 months, DLD decreased to 17.3 SNFP ± 5.9% ($p = 0.012$). It was found that in case of liver fibrosis 3-4 DLD points were 40.3 ± 13.0%, and fibrosis 0-2 points - 32.6 ± 10.9% ($p = 0.015$). The study has determined a significant association between fibrosis and DLD ($r = 0.561$; $p < 0.001$) and a weak link between the histological activity index and DLD ($r = 0.320$; $p < 0.001$). Correlation analysis of DLSI and DLD determined the average correlation between these parameters ($r = 0.542$; $p < 0.001$). We discovered that at the optimum sensibility of 72.2% and specificity of 64.4%, as well as at the optimal sensitivity of 72.2% and specificity of 94.4%, the threshold DLSI value was ≥ 40%. We also noted a fair significance of the DLD definition system (AUC 0.776) and high importance of the DLSI definition system (AUC 0.927) in the prediction of a planned liver transplantation.

Conclusion. The developed scoring systems determining DLSI and DLD can be an objective criterion for assessing the severity of liver diseases, their changes in dynamics during therapy, during the medical and social expertise to establish the category of "child with disabilities", as well as to influence the decision of liver transplantation in children.