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Hepatic progenitor cells as a source of adipokines and glucagon-like peptide-1 in pediatric nonalcoholic fatty liver disease

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Background & aims. nonalcoholic fatty liver disease (NAFLD) is one of the most important causes of liver-related morbidity and mortality in children. NAFLD includes a spectrum of diseases ranging from simple fatty liver to nonalcoholic steatohepatitis (NASH)1. NASH development is characterized by intricate interactions between resident and recruited cells2. The aim of our study was to evaluate the involvement of Hepatic Progenitor Cells (HPCs) in pediatric NAFLD.

Methods. 20 untreated, consecutive children and adolescents with biopsy-proven NAFLD (12 NASH, 8 NO-NASH) were studied by immunohistochemistry/fluorescence. HPCs and intermediate hepatocytes were counted and correlated with steatosis, inflammation, hepatocyte ballooning, fibrosis and the NAFLD activity score (NAS). Finally, the expression of adipokines (adiponectin, resistin, GLP-1) in liver cells was assessed.

Results. HPC compartment was markedly expanded in pNAFLD and especially in childrens with NASH and this was independently associated with the degree of fibrosis. NASH livers were also characterized by the appearance of intermediate hepatocytes. Adiponectin expression in HPCs of NAFLD patients appears to be down-regulated with respect to the normal liver and this was correlated with lobular inflammation and steatosis. Resistin expression increases in pNAFLD in relation with the expansion of HPCs pool and with the degree of fibrosis. GLP-1 was overexpressed in HPCs of pNAFLD patients in relation with the degree of steatosis and NAS.

Conclusions. HPCs activation takes part of liver response to oxidative stress in pediatric NAFLD and is correlated with the setting of fibrosis and the progression towards NASH. Adiponectin, resistin and GLP-1 become available to liver resident cells not only through the bloodstream but, possibly, through local production by paracrine mechanisms. The intra-hepatic expression of these proteins is strongly associated with the severity of pediatric NAFLD and may have relevant implications both in diagnosis and therapy.

1. Alisi A et al. J Pediatr 2009;155:469-74
2. Gaudio E et al. Dig Liver Dis 2009;41:455-62

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