1. SUMMARY

Liver regeneration after partial hepatectomy in rats suffering from non-alcoholic fatty liver disease

Non-alcoholic fatty liver disease (NAFLD) is currently the most frequent chronic liver disease in economically developed countries with prevalence of about 30 %. Liver resection from different reasons is nowadays common surgical procedure. Successful recovery and renewal of liver functions depend on regenerative capacity of liver remnant. The course of liver regeneration could be profoundly influenced by concomitant liver pathological processes including NAFLD.

The aim of this work has been study of early phase of liver regeneration after partial hepatectomy (PHx) in rats with nutritionally induced simple steatosis. At the beginning we introduced a model of NAFLD by a high-fat diet giving to Wistar or Sprague-Dawley rats for 3 and 6 weeks, resp. This regimen induced simple steatosis without signs of inflammation, necrosis or fibrotic changes in both strains.

In the second part of our study we followed if liver regeneration after PHx in rats with NAFLD is altered. Liver regeneration was assessed by bromodeoxyuridin incorporation into DNA of hepatocytes. Regeneration of liver with simple steatosis induced by 2/3 PHx was not significantly influenced in comparison to non-steatotic liver. The only difference in regenerative response we have observed in steatotic liver was delay in proliferation onset in centrilobular zones of liver acinus.

In the last part of our work we tried to find out, if the hepatocytes isolated from steatotic liver show changes in sensitivity towards oxidative stress in *in vitro* conditions. Non-treated steatotic hepatocytes *in vitro* have higher production of reactive oxygen species, higher degree of lipoperoxidation, lower redox level of glutathione, and decreased state 3 respiration in presence of Complex I substrates in comparison to non-fatty control group. Steatotic hepatocytes are more sensitive towards oxidative damage induced by tert-butylhydroperoxid. This supports widely accepted hypothesis that steatosis increases susceptibility of hepatocytes to other insults.