Summary

Cholestatic liver disease in a rat model and the possibilities for its control

Cholestatic liver disease is accompanied with oxidave stress. That it the reason why decreases antioxidative capacity of liver and increases leaky gut. It causes endotoxemia and expansion of production of cytokines and then forming multiorgan failure. Statins can be the way to protect liver cause of their anti-inflammatory efects. **Aims:** Aims of this study was to verify effect of statines. The questions are if the statin can be medicament which could prevent to increase of liver disease. The reason of this it will be in the oxidative and inflammatory damage, and if may depent on the time of filling statines and dose of statine. **Methods:** We have defined four groups of rats. We compared between the rats with laparotomy and with or without ligation of choledochus and with taking fluvastatin or not. We rated the tissue of liver and blood sample, or serum. We rated the degree of demage of liver tissue, the degree of cholestasis and proteosyntetic function of the liver. The rating of effects of fluvastatin depends on quantity of the dose (1 and 5 mg/kg of body weight) and the time of dosing of fluvastatin (1 and 2 weeks). Next scale in the studying of processing in cholestatic liver tissues is studium of mechanism of effects fluvastatin to changes which were transformed by cholestasis. We observed the effects of fluvastatin to the intensity parameters of oxidative stress, functions of mitochondries. It was chosen the transporters, its expression changes by cholestasis. **Results:** Within 14 days by taking fluvastatin the increasing lethality of rats with ligation of choledochus and taking fluvastatin it observed. It does not apply to the group of rat with ligation of choledochus but without fluvastatin. There is no complications during the study. The changes of parameter which rated the degree of liver damage were not found by the application of 1mg/kg of doses fluvastatin. When we applicated the dose of fluvastatin by 14 days in the group of rats with ligation choledochus and application fluvastatin, there were the increase of activity of enzymes for progress of liver damage. With application of the dose 5 mg/kg the liver damage was faster (it depends on the changes of ALT and AST).

Conclusion: The application of fluvastatin to rats with cholestasis caused by ligation of choledochus did not lead to decreasing diminish the development of cholestatic liver disease but rather to progression. Fluvastatin without ligation was not led to liver damage. The tempo of increasing the liver disease depended on the dose of fluvastatin and the time of application of fluvastatin. The oxidative stress and mitochondrial dysfunction will be increased as a consequence of failure of metabolism and transportation the potential toxic substances. We could respect high caution cause of changes in metabolism and transporting potential toxic substances.