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Impact of glycine on liver after chemotherapy with FOLFOX

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Examen am 26.06.2003 an der Kaunas Medicine University, Kaunas, Litauen

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Hepatotoxic side effects of chemotherapy for colorectal liver metastases increase perioperative morbidity and mortality after liver resection. Glycine has been shown to possess hepatoprotective effects in various animal models. Thus, this study was designed to assess its effect on liver after chemotherapy.

Female Sprague-Dawley rats (200 – 220 g) were divided into two groups and received a 5 % glycine or a control diet for 5 days. Subsequently, FOLFOX (Oxaliplatin, Leucovorin, and fluorouracil) chemotherapy was administered at standard doses. Transaminases, histology, immunohistochemistry and in vivo microscopy were used to index hepatic injury, to monitor microperfusion, and activation of Kupffer cells. Analysis of variance (ANOVA) followed by t-test were used as appropriate. Results are presented as mean ± SEM.

Glycine significantly decreased transaminases after chemotherapy to 25-50 % of control values ($p<0.05$). Microvesicular steatosis was significantly reduced from 57.1±8.6 % in controls to 37.7±4.4 % after FOLFOX. Furthermore, phagocytosis of latex beads was reduced by about 50 % while leukocyte adherence in central and midzonal subacinar zones decreased to 60 - 80 % after glycine ($p<0.05$). Glycine significantly reduced expression of inducible nitric oxide synthase (iNOS) after chemotherapy while hepatic microcirculation was increased ($p<0.05$).

In conclusion, this study shows for the first time that glycine reduces chemotherapy-induced liver injury. The underlying mechanisms most likely include Kupffer cells and an improved intrahepatic microperfusion.