Medical University of Graz

TRANSPLANTATION RESEARCH

ANTITUMORIGENIC EFFECT OF GLYCINE IN A COMBINED COLORECTAL LIVER METASTASIS AND FOLFOX MODEL

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Background & Aims

FOLFOX chemotherapy is indicated for colorectal liver metastases prior to the resection. Chemotherapy effect may be limited due to chemoresistance or chemotoxicity and it may prevent from aggressive surgery needed in some cases. Novel hepatoprotective and antitumorigenic substances are needed to improve treatment results. Hepatoprotective glycine has been shown to have anti-tumorigenic properties in various cancers. Therefore, this study aimed to evaluate the effects of glycine combined with FOLFOX on colorectal liver metastases (CRLM).

Materials and methods

The effect of glycine combined with 5-fluorouracil and oxaliplatin was investigated in vitro on colorectal cancer (CC531) by MTT test. To test glycine in vivo: Wag/Rij rats with CRLM were treated with 5% dietary glycine ± FOLFOX. Tumor volume by µCT, anti-Ki67 for tumor proliferation, and anti-CD31 for microvascular density (MVD) were compared.

Results

Glycine alone and combined with FOLFOX has no effect on both CC531 viability in vitro and tumor proliferation in vivo. Although, glycine significantly decreased tumor volume to about 42-35% of controls in vivo ($p<0.05$) with a 60% decreased tumor MVD ($p=0.004$). Further glycine doesn't counteract anti-tumor properties of FOLFOX (Figure 1).

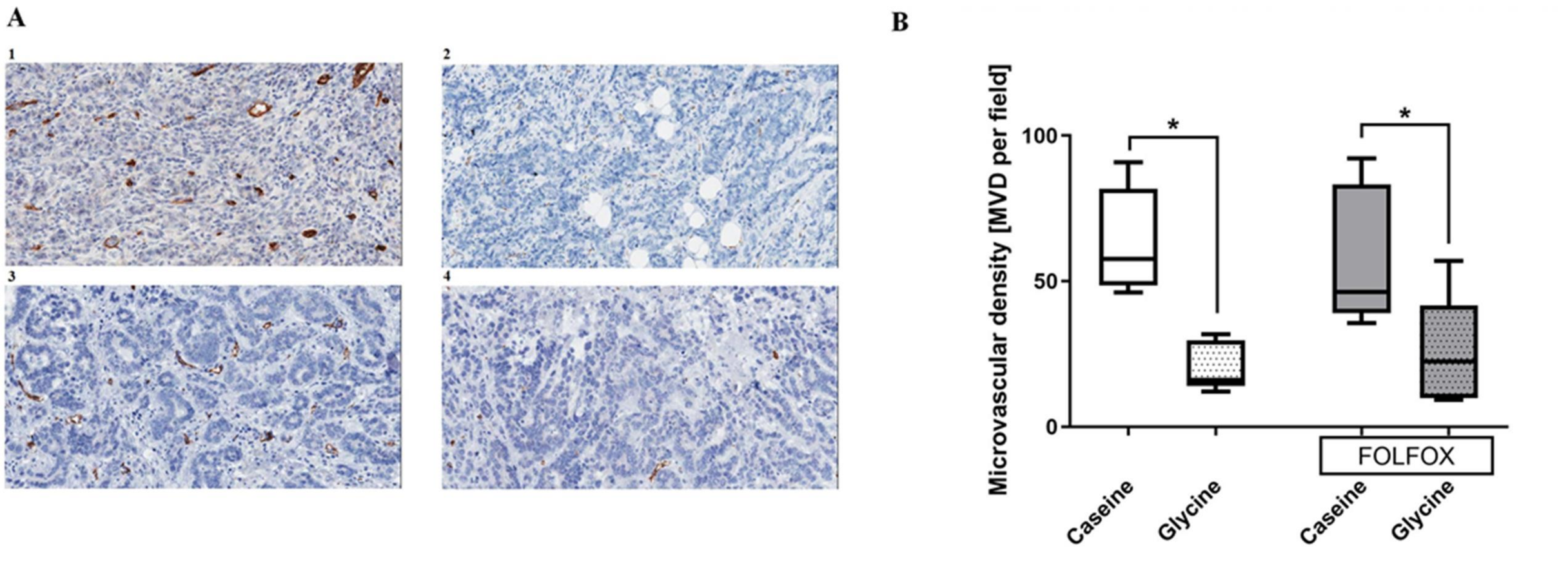

Figure 1. ***Tumor microvascular density (MVD) in different treatment groups.*** *A; representative pictures of tumors stained with anti-CD31 antibody in (1) casein, (2) glycine, (3) FOLFOX+casein and (4) FOLFOX+glycine. B; comparison of MVD between groups. Glycine significantly reduced the MVD irrespective of FOLFOX; * for significance with $p<0.05$.*

Conclusions

Glycine inhibits the growth of colorectal liver metastasis and does not impair effectiveness of conventional chemotherapy. Underlying mechanisms most likely include a decreased tumor MVD. Clinical trials are warranted to implement non-toxic hepatoprotective glycine in novel anti-cancer strategies in humans.

The text and figures are published in the manuscript by Maneikyte et al. "Dietary glycine decreases both tumor volume and vascularization in a combined colorectal liver metastasis and chemotherapy model". Int J Biol Sci. 2019 Jun 4;15(8):1582-1590