Tumori, 97: 660-665, 2011

The effect of 2-methoxyestradiol liposome on growth inhibition, angiogenesis and expression of VEGF and Ki67 in mice bearing H_{22} hepatocellular carcinoma

Bin Du, Shu-yu Wang, Xiu-fang Shi, Chao-feng Zhang, and Zhen-zhong Zhang

School of Pharmacy, Zhengzhou University, Zhengzhou, China

ABSTRACT

Aims and background. 2-methoxyestradiol (2-ME), an endogenous metabolite of estrogen, has very low water solubility. It is currently in phase II clinical trials as both a chemopreventive and chemotherapeutic agent and has been orally administered to cancer patients. However, the poor oral absorption of the compound is one of the major obstacles for 2-ME development. Based on the molecular features of 2-ME, liposome can be considered an attractive formulation approach. Our purpose in this study is to research the antitumor efficacy of 2-methoxyestradiol liposome (2-ME-L) in mice bearing H_{22} tumors.

Methods. Murine H_{22} hepatocarcinoma served as an ectopic solid tumor model. The effects of antitumor therapy were evaluated by testing tumor growth, measuring the tumor inhibition rates in terms of weight and volume, and staining the tissues by hematoxylin and eosin. The synergistic mechanism of 2-ME-L therapy was elucidated by detecting changes in the expression of pathognostic factors in the tumor microenvironment.

Results. 2-ME-L significantly suppressed tumor growth. The morphological changes in the tumors indicated that the tumors in the treatment groups were effectively confined with little surrounding angiogenesis. Tumor cells of the treatment groups had abundant areas of necrosis with few nuclei in the mitotic phase. It was found that there was less immunohistochemical expression of vascular endothelial growth factor (VEGF), Ki67 and CD31 in the treatment groups and the efficacy of 2-ME-L was better than that of 2-ME solution (2-ME-S). This research demonstrated that 2-ME-L inhibited the growth of H_{22} tumors in a concentration-dependent manner and was more effective than 2-ME-S.

Conclusions. 2-ME-L can suppress the growth of H_{22} solid tumors and has antiproliferative, proapoptotic and antiangiogenic activity. 2-ME-L could be of potential use in the treatment of hepatocellular carcinoma.

Key words: 2-methoxyestradiol, liposome, H_{22}, pharmacodynamics.

Correspondence to: Professor Zhen-zhong Zhang, School of Pharmacy, Zhengzhou University, 100 Science Road, Zhengzhou, 450001, China.
Tel +86-371-67781910;
fax +86-371-67781908;
e-mail zzupaper@sina.com

Received January 7, 2010;
accepted February 23, 2011.