PHARMACOLOGY OF BLEOMYCIN, IMPLICATIONS IN LOWERING THE DOSE

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According to the standard operating procedure for electrochemotherapy (ECT), a bleomycin dose of 15 000 IU/m^2 body surface area should be injected intravenously and, after an interval of 8 minutes, electric pulses are delivered to the tumor. However, most of the patients treated with electrochemotherapy are older than 65 years, with the age-dependent body changes resulting in a decrease lean body mass and total body water. Consequently, the distribution of water-soluble drugs, such as bleomycin, is reduced and higher plasma or serum levels of the drugs that is more than expected might be achieved.

On the basis of the pharmacokinetics of bleomycin in the elderly patients, which was analyzed by using a newly developed analytical method for determination of bleomycin in serum samples, a lower dose of bleomycin of 10 000 IU/m^2 was recommended. Recently published clinical studies confirm that ECT performed with reduced dose of bleomycin could be as effective as currently recommended dose. Especially older patients, patients with impaired renal function and candidates for multiple ECT cycles could have the benefit from reduced dose protocol.

Recently, a study on animal models, based on the comparison of the carcinoma and melanoma models, implicate the differences in bleomycin pharmacokinetics in various histological types of malignant tumors as a possible explanation of differences in response rates to ECT. Alterations in bleomycin pharmacokinetics in histologically different tumors could be due to variations in tumor vascularization, which has an impact on bleomycin accumulation at the time of electroporation. According to these findings, tumor vascularization might be used as a predictive factor for the tumor response to ECT.