In vitro percutaneous absorption and in vivo protoporphyrin IX accumulation in skin and tumors after topical 5-aminolevulinic acid application with enhancement using an erbium:YAG laser

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Abstract

5-Aminolevulinic acid (ALA) is used as a precursor of protoporphyrin IX (PpIX) for photodynamic therapy (PDT) of superficial skin cancers and subcutaneous metastases of internal malignancies. The permeability of ALA across intact skin is always low, making it difficult to achieve the desired therapeutic benefits. Hence new methods for enhancing ALA permeation are urgently needed. The aim of this study was to determine the in vivo kinetics of PpIX generation in mouse tissues after topical ALA application enhanced by an erbium (Er):yttrium-aluminum-garnet (YAG) laser. The in vitro permeation of ALA was also used to screen the optimal method for the in vivo study. The efficacy of the improved drug delivery was determined as a function of various laser fluences and cancer models. ALA applied to laser-treated skin produced a higher accumulations of PpIX within superficial skin and subcutaneous tumors as compared to those of the non-treated group (t-test, $p < 0.05$). The enhancement ratios (ER) of laser-treated skin ranged from 1.7 to 4.9 times as compared to the control depending to the fluences used. The enhanced PpIX level of laser-treated skin was generally more pronounced in normal and lesional skin than in subcutaneous nodular tumors. Confocal laser scanning microscopy (CLSM) of laser-treated skin revealed intense red fluorescence within the epidermis and upper dermis, and a much-weaker fluorescence within the bottom layers of the skin. On the other hand, the fluorescence intensity of the control group was much lower than that of laser-treated group. The barrier properties of the skin irradiated by the laser had completely recovered within 3 days. Pretreatment of skin using an Er:YAG laser was useful in increasing the amount of Pp IX within skin tumors.