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LETTER TO THE EDITOR

Does nicotine effectively protect against hand-foot syndrome?

Dear Editor,

Hand-foot syndrome (HFS), characterized by erythema, pigmentation, xerosis, and desquamation on hands and feet, is a well-known adverse effect of 5-fluorouracil (5-FU) and capecitabine, a systemic prodrug of 5-Fu. These drugs are widely used for the treatment of various cancers. HFS is also induced by the newly developed kinase inhibitors such as sorafenib and sunitinib. Because of the progress in the development of such molecular targeted agents, dermatologists face the increasing demand to manage HFS. In our recent search for measures to prevent HFS, we encountered the study of Kingsley[1] who reported that nicotine patches protect against 5-FU dermatitis. The patient was a 65-year-old woman with metastatic colorectal carcinoma who received a weekly 24-hour continuous infusion of 5-FU. A few months after the inception of this treatment, she noticed hyperpigmentation and desquamating erythema involving her palms. These symptoms were completely resolved when a 7-mg nicotine skin patch was applied 1 hour before starting and removed 1 hour after completing each 24-hour infusion. Kingsley suggested that her skin lesions were improved because the vasoconstrictive property of nicotine decreased the delivery of 5-FU to the skin. Although we are intrigued by this finding, nicotine-induced vasodilation has been reported in humans and experimental animals. In dogs, nicotine stimulated the release of epinephrine from nerve terminals and promoted vasodilation in the hindlimbs [2] and the topical and systemic administration of nicotine increased their gingival blood flow.[3] In frogs, the immersion of a hindlimb in a nicotine solution resulted in a blood flow increase in the webs.[4] Using laser blood flowmetry and thermography, we previously demonstrated that nicotine chewing gum increased the cutaneous blood flow and elevated the skin temperature in human fingers.[5] We obtained similar results with a 5-mg transdermal nicotine patch. In line with these findings, a meta-analysis for management of capecitabine-induced HFS failed to reveal the significant efficacy of nicotine patch.[6]

According to Goodman and Gilman's textbook on the pharmacological basis of therapeutics, nicotine exerts biphasic action on peripheral nervous and vascular systems that is time- and concentration-dependent.[7] The major action of nicotine consists initially of transient stimulation followed by a more persistent depression of autonomic ganglia. This produces initial vasoconstriction and subsequent vasodilation. Small doses of nicotine evoke a discharge of catecholamines including epinephrine; larger doses prevent their release. Based on the above considerations, we propose that nicotine patch could be a tool for HFS prophylaxis with precise evaluation in terms of the timing and dose of administration. Prospective, randomized, and controlled studies are warranted for clinical use.

CONFLICT OF INTEREST

The author declares no conflict of interest.

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