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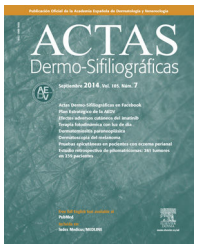

RESIDENTS FORUM

RF-Oral Nonsteroidal Anti-inflammatory Drug Use May Reduce the Risk of Cutaneous Squamous Cell Carcinoma☆

FR-El consumo oral de antiinflamatorios no esteroideos podría disminuir el riesgo de aparición de carcinoma espinocelular cutáneo

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A causal relationship has been demonstrated between UV radiation and cutaneous squamous cell carcinoma (SCC) due to, among other factors, the induction of the cyclooxygenase 2 (COX-2) enzyme,[1] which stimulates the production of prostaglandin E2, which in turn promotes carcinogenesis.[2] The same also occurs in other organs (colon, breast, and prostate) in association with various stimuli that induce COX-2, and research has demonstrated the potential of nonsteroidal anti-inflammatory drugs (NSAIDs) to prevent carcinogenesis in those organs.[3] The prevention of cutaneous SCC is of great importance because the incidence of this disease has continued to increase.[2] Because COX-2 is overexpressed in cutaneous SCC, NSAIDs are thought to be useful in preventing the disease.[1]

On the basis of this evidence, several epidemiologic studies are currently being carried out to determine the true utility of NSAID use in the prevention of nonmelanoma skin cancer, with variable results. Muranushi et al.[1] carried out a meta-analysis with the aim of unifying and evaluating all current evidence on the relationship between NSAID use and cutaneous SCC. This study found, with statistical significance, that NSAID use reduces the risk of cutaneous SCC by 18% and that the use of nonaspirin NSAIDs reduces the same risk by 15%.[2] The use of aspirin alone yielded similar percentages, but with borderline statistical significance.[2] The decrease in risk is thought to be caused by the inhibition of COX-2 activity in promoting cutaneous carcinogenesis.

The meta-analysis has multiple limitations, including the heterogeneity of the NSAID dosage measurements (which makes it impossible to analyze the relationship between dose and effect) and the failure to consider the confounding effect of sun exposure. Dosage is especially important in the study of aspirin because at low doses it would inhibit COX-1 and the preventive effect would be negligible but at high doses it would inhibit COX-2 and have an antitumor effect.[2] In addition, the study considered NSAIDs as a group, despite the differences between their mechanisms of action, which

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are quite probably related to their preventive effects. The variability of the prevalence of NSAID use among the studies could reflect differences in the health status of the patients and, therefore, in their immune function. Collecting data on NSAID use is complex because patient interviews lead to greater memory bias in sporadic users, whereas prescription database searches do not detect people who use NSAIDs without a prescription.

The synthesis of the data published to date therefore provides evidence for a significant inverse association between oral NSAID use and the incidence of cutaneous SCC, especially in patients with a high prevalence of actinic keratoses or a personal history of other keratinocytic tumors.[4] However, further studies that consider other confounding factors besides sun exposure—such as type of NSAID, dose, reason for use, etc.—are needed. Despite its limitations, this study provides a basis for conducting further research into effective new lines of prevention.

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