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Local skin reactions following the administration of topical ingenol mebutate for actinic keratosis

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Abstract

Actinic keratoses are cutaneous lesions that appear as the result of the proliferation of atypical keratinocytes. These lesions are considered pre-malignant and they can progress to squamous cell carcinoma. Ingenol mebutate has been approved as an effective treatment for AK on the face and trunk. We studied the local skin reactions to this therapy. Data about local skin reactions were collected in a series of 5 patients with photographic documentation, a visual analog scale, and a ranking of satisfaction of the patient. Moderate to severe reactions were reported in most of patients, but only one stopped treatment early. The short duration of treatment contributes to high adherence to the therapy.

Keywords: keratoses, actinic, precancerous conditions, skin neoplasms

Introduction

Actinic keratoses (AK) are cutaneous lesions caused by the proliferation of atypical keratinocytes. More common in adults with light colored skin, they are characterized by squamous and erythematous macules and papules. The risk factors for AK include exposure to the sun, possession of Fitzpatrick skin type I or II, baldness, older age, and male gender [1]. Approximately 60% of people over 40 years of age who have experienced long-term sun exposure have at least one AK lesion [2]. Although pre-malignant, there is a reported annual 0.025-16% risk that these lesions will progress to squamous cell carcinoma [3].

Ingenol mebutate is an approved, effective treatment for AK on the face and trunk.

Case Synopsis

We prospectively studied a series of 5 patients treated with this medication (150 mg/day, for 3 days) on the forehead (2 patients), cheek (2 patients), and nose (1 patient) for either isolated AK (1 patient) or for field therapy for this condition (4 patients). Between day 4 and day 8 after initiating treatment, local skin reactions were scored on a 0-10 visual analogue scale (VAS; 0 = no reaction; 10 = extreme reaction). Patient satisfaction with the outcome was noted as low, moderate, or high. All patients but one completed the prescribed treatment. Two patients required further treatment with fusidic acid. Four out of five patients had good adherence to treatment. In reference to the local skin reactions, two of the patients scored 7/10, one of them 8/10, one 4/10, and one 9/10; treatment was not completed in this...
last patient. According to the level of satisfaction, the patient that did not complete treatment had low satisfaction, whereas the remaining four scored high (2 patients) and moderate (2 patients) satisfaction.

Examples of the local skin reactions are shown on Figures 1 (score 8/10) and 2 (score 7/10).

Case Discussion
Different treatments have been approved for AK. A systematic review of their effects noted diclofenac, 5-fluoracil, imiquimod, and ingenol mebutate to provide good field therapy results, but to differ in terms of the cosmetic outcome achieved and their adverse effects [4].

Ingenol mebutate has the drawback of causing local skin reactions. In the present patients, strong irritation was present after 4-8 days. Four of the 5 patients were, however, able to complete the course of treatment. Adherence to therapy is influenced by such side effects, which need to be carefully managed. Longo et al. highlight how good communication between physician and patient can be reassuring [5]. The short duration of treatment, however, facilitates high adherence rates [6].

The significance and severity of LSR when applying ingenol mebutate gel, was analysed by Shelbi C Jim On, et al. As they noted, there seemed to be a direct relation with the LSR score on the day after the last application and the speed of its resolution. Therefore, this score was considered an important predictor of the resolution of LSRs. This same study concluded that the rate of resolution differed depending on the location of the treated area, being greatest for AKs treated on face, then scalp, and finally those on trunk or extremities [7].

Conclusion
Ingenol mebutate can reduce the extension of AK lesions by some 87% [8]. Local reactions are the main adverse event, but these heal in 2-3 weeks and do not greatly hinder adherence to therapy [5].

References
of Ingenol Mebutate Gel for the Treatment of Actinic Keratoses. 
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