Imiquimod creme a 5% no tratamento do carcinoma basocelular superficial – experiência em Porto Alegre – RS

Imiquimod 5% cream in the treatment of superficial basal cell carcinoma – experience in Porto Alegre – RS

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RESUMO

Em um estudo aberto, quatro pacientes foram selecionados para avaliação da eficácia do imiquimod creme 5% no tratamento do carcinoma basocelular superficial. Os pacientes utilizaram o medicamento no regime de uma aplicação diária, por 12 semanas. A taxa de resposta foi avaliada pela remissão clínica e histológica. O uso do imiquimod creme a 5% no tratamento do carcinoma basocelular resultou na remissão completa dos tumores neste estudo.

UNITERMOS: Carcinoma Basocelular, Neoplasias Cutâneas, Terapêutica.

ABSTRACT

In an open label study 4 patients were selected in order to evaluate the efficacy of imiquimod cream 5% in the treatment of superficial basal cell carcinoma. The patients applied the medication once a day for 12 weeks. The response rate was evaluated through the clinical and histological response. The use of imiquimod cream 5% in the treatment of basal cell carcinoma resulted in complete remission of tumors in this trial.

KEYWORDS: *Basal Cell Carcinoma, Cutaneous Neoplasms, Therapeutics.*

INTRODUCTION

Imiquimod is an immune response modifier that has been shown to induce a local immune response when applied topically. Imiquimod stimulates the production of interferon and other cytokines important in cell-mediated local immune responses and has been shown to promote antitumor and antiviral effects (1, 2, 3, 4).

Basal cell carcinoma (BCC) is the most common malignancy in the white human population worldwide, and its incidence has been increasing in the last decade. Basal cell carcinoma tends to grow slowly and rarely metastasizes. Additionally, BCC can spontaneously regress, exhibiting a shift in immune response toward a Th1 profile, which in turn suggests that the immune system plays an active role in BCC surveillance (1, 4).

Imiquimod has been shown to promote histological clearance of basal cell carcinoma on clinical studies for treatment of BCC. The most promising dosing schedule has been 5x/week and 7x/week regimens. Moreover, 6 and 12-week-treatment durations have been evaluated, as well as the use of occlusion. High cure rates (>70%) have been achieved in most clinical trials concluded until now (5, 6, 7, 8, 9).

We report our experience with topical imiquimod therapy in a small cohort of 4 patients with either superficial or nodular BCC.

MATERIALS AND METHODS

Four patients with histological evidence of low risk BCC and at least 18 years old were offered imiquimod therapy as a no surgical treatment for their skin cancers. The lesions were no recurrent primary tumors and had not undergone previous treatment. The study was approved by the local ethic and research committee. Informed consent was ob-

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TABLE 1 – Patients' features

Patient No.	Sex	Age (y)	Type of cancer (dimensions)	Location	Fitzpatrick skin type	Previous skin tumors
1	M	62	Superficial BCC (1,5 × 1,0 cm)	Left anterior thorax	III	Yes, BCC (7)
2	M	46	Nodular BCC Left (2,5 × 2,0 cm)	shoulder	II	No
3	M	56	Superficial BCC (1,3 × 1,5 cm)	Right shoulder	II	Yes, BCC (6), SCC (1)
4	M	72	Superficial BCC (1,0 × 1,1 cm)	Right scapular region	II	Yes, BCC (1)

BCC: basal cell carcinoma; *SCC:* squamous cell carcinoma.

tained. The patients features are described in Table 1. The lesion in Patient number 3 can be seen in Figure 1.

All 4 patients were treated with one-dose-imiquimod 5% cream daily for 12 weeks. Patients continued the treatment until the 12 weeks were completed. For safety evaluation, patients returned to the ambulatory for designed visits for evaluation, photographs and documentation of tumor appearance, local skin reactions and adverse effects. They were weekly evaluated during the first month and twice a month on the second and third months of treatment. At the 6-week and the 12-week post treatment visit, the investigator made a clinical assessment to determine any visible evidence of tumor. After 3 months of the completion of imiquimod therapy, a histological sample was examined for histological evidence of residual BCC.

This open-label study of a small cohort of 4 patients was not amenable to statistical analysis.

RESULTS

All 4 patients treated with imiquimod presented complete resolution of their skin cancers in 12 weeks. Assessment of the presence or absence of residual tumor was based on a clinical and histological end point, at 12 weeks after the end of the treatment. In Figure 2, we can see no clinical evidence of tumor in Patient number 3.

All 4 patients experienced application site reactions as shown in Table 2. These application site reactions usually began during the second week of treatment. None of these patients experienced systemic flu-like symptoms or lymphadenopathy.

In all the patients, the application site reactions were mild to moderate. These mild to moderate reactions consisted of erythema, pruritus, scaling, vesicles, tenderness and mild crusting. In one patient, a secondary bacterial infection of the application site reaction responded to 7 days of

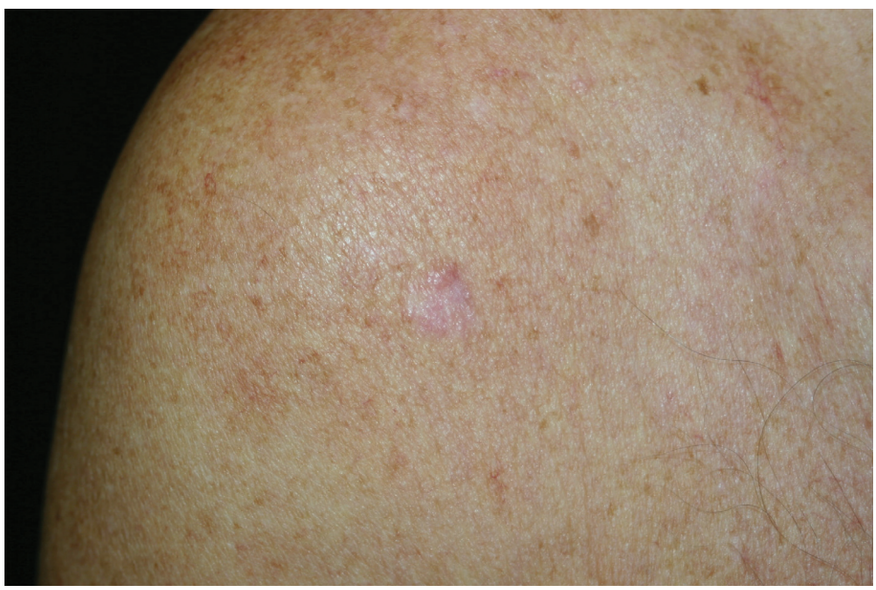


FIGURE 1 – Patient No.3: Superficial BCC (1.3 × 1.5 cm) on the right shoulder.

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TABLE 2 – Treatment outcomes

No. Patient	Duration of therapy	ASR	Clinical outcome at and of treatment	Post-Tx follow up	Recurrence during observation interval	Histological outcome at 12 weeks after the end of treatmen
1	12wk, once daily	Moderate	No tumor	3 months	ND	No tumor
2	12wk, once daily	Mild	No tumor	3 months	ND	No tumor
3	12wk, once daily	Mild	No tumor	3 months	ND	No tumor
4	12wk, once daily	Mild	No tumor	3 months	ND	No tumor

Grading of ASR: mild: erythema, vesicles, accompanied by edema and mild scaling, with little or no pruritus; moderate: more severe erythema, vesicles, edema accompanied by crusting and superficial erosions, and accompanying pruritus.
ASR, Application Site Reactions; *ND*: not detected.

oral and 14 days of topic antibiotic therapy and a 2-week-break period without imiquimod therapy. All reactions were limited to the application site, without any distant remote-site reactions.

DISCUSSION

Immune response modifiers are substances that directly influence a specific immune function or modify one or more components of the immunoregulatory network to achieve an indirect effect on specific immune function. Although Imiquimod´s mechanism of action is not fully understood, its clinical benefits are likely to be related to its immunomodulatory properties. In this case series, topical immunotherapy with imiquimod 5% cream resulted in complete clearance of all 4 BCCs.

The tumors selected for treatment were considered relatively low risk in terms of histological appearance, location and size. Up to present, larger or high-risk lesions have not been studied.

There are many approaches to the treatment of BCC. Excisional or Mohs surgery or ablative treatments are currently the standards of care. The literature suggests that this no surgical, biologic approach is promising. If clinical trials of imiquimod therapy for low-risk BCC indicate that this treatment has response and recurrence rates comparable to those of existing treatments, no surgical biologic could be a good approach to selected BCC. (5)Recurrent BCC, incomplete resection and the presence of residual BCC in excisional margins continue to present a treatment challenge. Although curettage before excision decreased margin positivity after excision by 24%, this procedure still results in a failure rate with positive histological margin in 13% of



FIGURA 2 – No.3: No clinical evidence of BCC after 3 months of the end of treatment.

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such excisions. The potencial use of imiquimod as an adjuvant treatment to surgery may warrant consideration. It may be beneficial to determine whether imiquimod could reduce the size of the larger tumors before surgery, and to see whether the immune system could induce a specific Th1 immune response that would perhaps decrease the risk for recurrence of high risk and recurrent tumors. (6)Yet, imiquimod may have some advantages over surgical procedures, especially when good cosmetic outcome is paramount (7), and can be an option in areas where surgical approaches would be limited for other reasons.

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