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Comparative study of the treatment of large actinic keratoses with glycolic acid peeling and 5-fluorouracil vs. cryopeeling

Estudo comparativo do tratamento de ceratoses actínicas extensas com peeling de ácido glicólico + 5-fluoracil x criopeeling

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ABSTRACT

Introduction: *Chronic and intense photodamage usually produces numerous actinic keratoses, with early and global treatment of the affected skin being of paramount importance.*

Objective: *To evaluate the effectiveness of two different treatments for multiple actinic keratoses.*

Methods: *Five patients were selected Were selected five patients with diffuse, with diffuse actinic keratoses on the dorsum of the hands and forearms. The patients underwent the following protocol: Side A (right): biweekly superficial chemical peeling with 70% glycolic acid in gel, followed by the subsequent application of 5% 5-fluorouracil solution; Side B (left): monthly sessions of cryopeeling. The number of sessions ranged from four to six in Side A and two to three in Side B, according to the degree of photodamage.*

Results: *All patients had a satisfactory clinical response, with improvement of actinic keratoses throughout the whole area of actinic damage, and good tolerance of the treatment among patients. The only exception was that a more intense and persistent erythema arises after the cryopeeling.*

Conclusions: *Both treatments are valid and effective alternatives for the treatment of the field cancerization.*

Keywords: *keratosis, actinic; therapeuctics; fluorouracil; cryotherapy.*

RESUMO

Introdução: O fotodano intenso e crônico geralmente produz inúmeras queratoses actínicas, sendo importante o tratamento precoce e global da pele acometida.

Objetivo: Avaliar a efetividade de dois tratamentos distintos para ceratoses actínicas múltiplas.

Métodos: Foram selecionados 5 pacientes com ceratoses actinicas difusas no dorso de mãos e antebraços foram submetidos ao seguinte protocolo: lado A (direito) peeling químico superficial quinzenal com ácido glicólico 70% em gel seguido de solução de 5-fluoracil 5%; lado B (esquerdo) criopeeling mensal. O número de sessões variou de quatro a seis no lado A e de duas a três no lado B, de acordo com o grau de fotodano.

Resultados: Todos os pacientes apresentaram resposta clínica satisfatória, com melhora das ceratoses actínicas e de toda área de dano actínico, com boa tolerância dos pacientes ao tratamento, apenas com a ressalva de que ao criopeeling segue-se eritema mais intenso e persistente.

Conclusões: As duas terapêuticas utilizadas constituem-se em alternativas válidas e eficazes para tratamento do "campo de cancerização".

Palavras-chave: ceratose actínica; terapêutica; fluoruracila; crioterapia.

INTRODUCTION

Actinic keratoses (AKs), solar keratosis, or senile keratoses constitute some of the clinical signs of advanced photoaging, and are considered markers of risk for development of malignant lesions, especially squamous cell carcinoma (SCC).[1,2] They are also intraepithelial neoplasias consisting of atypical proliferation of keratinocytes. [3]

AKs are mainly induced by chronic exposure to ultraviolet radiation, occurring in sun-exposed areas, especially in adults of advanced age and individuals with a low photoype.[1,3] UVA spectrum (320-400nm) induces photooxidative stress and causes characteristic mutations in the keratinocytes' DNA. On the other hand, UVB radiation (290-320nm) results in the formation of cyclobutane dimers (thymidine) in the DNA and RNA, leading to mutations in the telomerases' genes and in the tumor suppressor gene p53.[3-5] Thus, UVB radiation is the most harmful wavelength to the keratinocytes' DNA, and UVA radiation acts as a facilitator of the deleterious action of UVB.[3,4]

AKs are some of the most commonly found conditions in the clinical practice. According to a Brazilian survey on a series of cases carried out in 2006, AKs were the fourth most frequently found clinical diagnosis among 57,343 dermatological consultations, being present in 5.1% of cases, with a predominance in the southern region of the country.[3,6]

AK patients in general have multiple lesions due to actinic damage inflicted on the entire sun-exposed area, constituting a "field cancerization." Faced with the impossibility of anticipating which lesions will undergo malignant transformation during clinical development, it is necessary to carry out a global treatment of the affected skin, as opposed to a limited treatment focusing on punctual lesions only.[3,7]

Different therapies have already been established for the treatment of AKs.[4] Isolated, well-delimited or hyperkeratotic lesions can be treated with cryotherapy, electrocautery, or curettage.[1,8] For patients with widespread AKs, a viable treatment is with the topical application of 5-fluorouracil, cryopeeling, dermabrasion, medium depth chemical peel (70% glycolic acid or the combination of Jessner Solution with 35% trichloroacetic acid), and photodynamic therapy.[1]

Marrero and Katz introduced a peeling modality combining 70% glycolic acid gel and 5% 5-fluorouracil solution for treating extensive AKs areas.[9] The mechanism involves the removal of the stratum corneum and the decohesion of keratinocytes by the glycolic acid, allowing the penetration of 5-fluorouracil up to the atypical cells.[1,9]

Cryopeeling is a technique that employs cryotherapy across all photodamaged skin aimed at inducing scaling and cell renewal, and is also used to treat multiple KAs.[2]

Due to the extensive therapeutic possibilities and the potential risk of malignization of the "field cancerization", the present study was aimed at evaluating the effectiveness of two different treatments for multiple AKs, looking at the maximum or complete disappearance of lesions in clinical terms.

METHODS

A non-randomized open clinical trial comparing therapeutic modalities in the same patient was carried out with voluntary samples. The study lasted three months. Eight volunteers with a clinical picture of diffuse AKs on the dorsum of the hands and forearms were recruited at the Dermatology Outpatient Clinic of the Universidade de Mogi das Cruzes. Patients of both genders, between the ages of 55 and 75 years were included. Those with decompensated systemic diseases were excluded. In total, five of the patients previously selected took part in the study, which was approved by the Research Ethics Committee of the institution, with patients signing a term of free and informed consent. The volunteers underwent initial photographic documentation, which was repeated fortnightly and at the end of the study. The right hand side (Side A) was standardized for use of the combination of 70% glycolic acid gel, followed by 5% 5-fluorouracil solution as a superficial peeling, performed fortnightly. The left hand side (Side B) was standardized for the monthly application of cryopeeling. The number of sessions varied according to the intensity and severity of the clinical manifestations of each patient.

The treatment on Side Awas carried out with the initial cleansing and degreasing of the skin with acetone; next, a layer of 70% glycolic acid gel (Drogaderma™, São Paulo SP, Brazil) was applied up until the appearance of erythema or frosting of the AKs, with a subsequent neutralization achieved with sodium bicarbonate solution. The last step consisted of applying the 5% 5-fluorouracil solution (Drogaderma™, São Paulo SP, Brazil), which remained in contact with the skin for 12 hours. Patients were instructed to remove the substance at home by washing the site.

Side B underwent treatment with a liquid nitrogen spray applied in "brushing" movements up to the skin became whitened.

The patients were instructed to use solid petrolatum and sunscreen after the procedure, and to avoid direct exposure to the sun.

The researchers evaluated the methods' effectiveness through clinical observation and photographs (Figures 1 and 2).

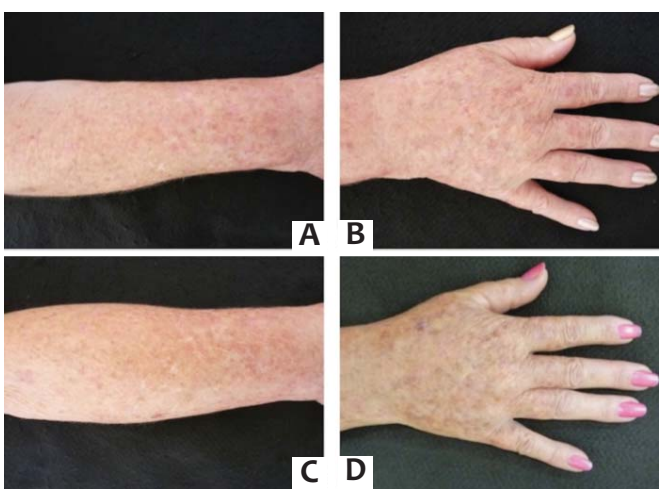

Figure 1: A and B: Pre-treatment of Side A; C and D: After six sessions

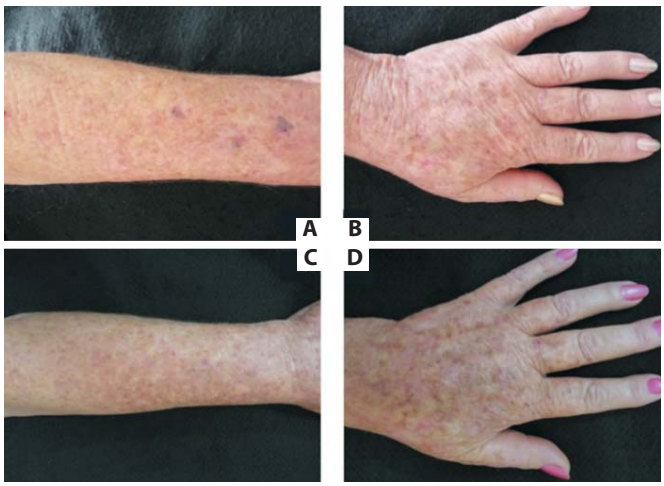

Figure 2: A and B: Pre-treatment of Side B; C and D: After three sessions

RESULTS

Of the five patients studied, four were female and one male, between the ages of 56 and 72 (average = 63-years-old). The degree of photoaging of the treated areas was considered mild in three patients and moderate in two patients. Local erythema, which was more pronounced and persistent on Side B, was observed immediately after each session (Figure 3). Both methods were well tolerated and considered effective, however the authors noted that the treatment with cryopeeling was more aggressive and offered more evidence of side effects, but without difference in the clinical improvement of AKs when compared to the superficial peeling at the end of treatment. In total four sessions were performed in three patients with a mild form of AK and six sessions in two patients with moderate AKs on Side A. Regarding Side B, the three patients with a mild AK picture underwent two sessions while the two cases with a moderate AK picture underwent three sessions.

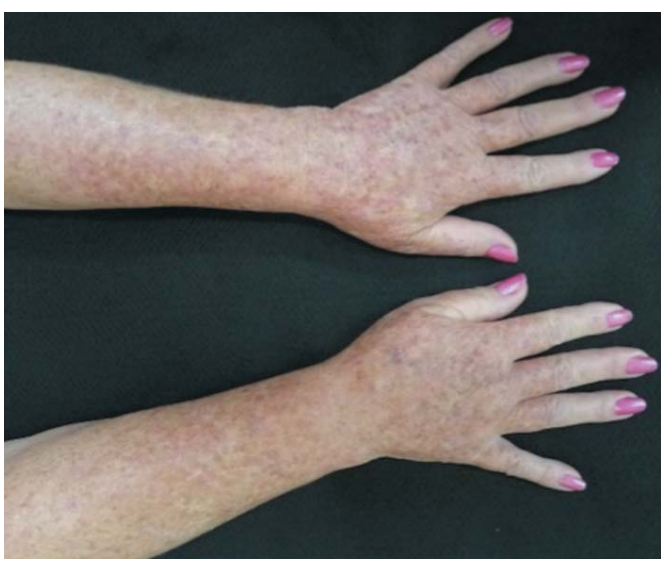

Figure 3: More pronounced and persistent erythema on Side B after the treatment

DISCUSSION

AKs are an important indicator of cumulative and uncontrolled exposure to UV radiation, with pre-malignant potential.[1] There are various treatment types available for the various clinical forms of the condition. The therapy must begin with changes in the patient's behavior regarding exposure to the sun, the daily application of sunscreens, as well as the use of physical barriers to the sun. A few decades ago, there was not knowledge about the harmful effects of UV radiation or general guidance on habits of protection from the sun—currently a significant demand has been noticed at dermatological outpatient clinics for the treatment of cutaneous effects resulting from chronic damage caused by sun exposure. In this manner, it is important to implement early on a global treatment of the photodamaged area, focusing on the potential malignant transformation of the "field cancerization."

5-fluorouracil is an effective antimetabolite that inhibits the synthesis of RNA and DNA, presenting a cytotoxic effect, which induces the destruction of AKs. Cryopeeling aims at improving the skin's clinical appearance and preventing the appearance of new lesions.

The present study's results were similar to the literature, having nevertheless varied the number of sessions per patient depending on the degree of actinic damage and the method chosen (two to six sessions).

CONCLUSION

The authors believe that both techniques studied can be successfully used in the treatment of extensive AKs, with good tolerance on the part of patients, the only exception being that after cryopeeling there is an occurrence of more intense and persistent erythema. Therefore, they constitute two valid alternatives for the treatment of the "field cancerization". ●

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