

Tacrolimus 0,1% ointment in the treatment of vitiligo: a series of cases *

Pomada de tacrolimo 0,1% no tratamento de vitiligo: série de casos

Carla Tamler ¹

Patrícia Azevedo Oliveira ²

Bruna Duque-Estrada ¹

João Carlos R. Avelleira ³

Abstract: Vitiligo is a dermatosis of difficult treatment and significant psychosocial impact. The objective of this study was to evaluate the response to tacrolimus 0,1% ointment for vitiligo treatment. Ten patients took part in the present study: six patients with lesions on the cephalic and cervical regions had more than 75% of repigmentation. As for extremities and trunk results varied from good to excellent in 27% of the cases. The association with other therapeutic options could possibly increase the efficacy of the treatment.

Keywords: Tacrolimus; Treatment outcome; Vitiligo

Resumo: O vitiligo é dermatose de difícil tratamento e de significativo impacto psicossocial. O objetivo deste estudo foi avaliar a resposta do tacrolimo 0,1% pomada no vitiligo. Dez pacientes completaram o estudo: seis com lesões nas regiões cefálica e cervical obtiveram mais de 75% de repigmentação. Nas extremidades e no tronco, os resultados variaram de bons a excelentes em 27% dos casos. A associação com outras formas de tratamento possivelmente aumentará a eficácia da terapêutica.

Palavras-chave: Resultado de tratamento; Tacrolimo; Vitiligo

Vitiligo is characterized by achromatic spots related to the loss of melanocytes in the epidermis and the hair follicle. It happens at any age, affects both sexes and in some regions, affects up to 2% of the population. It influences considerably the quality of life of the patients. None of the therapeutic alternatives is fully satisfactory either because its improvement is unpredictable and the treatment is long or because of the side effects and operational difficulty of application of the medication. For these reasons we carried out an open study, not controlled, assessing the response to tacrolimus 0,1%, 2 b.i.d., in lesions on the face, neck and limbs. Twelve patients, phototypes III-VI and with lesions simultaneously on the head and extremities were treated for 120 days, with clinical evaluation every 15 days. For the trunk and limbs it

was used, as ipsilateral control, the lesions on the right side which did not have the ointment applied on them (Picture 1A). Exclusion criteria were: report of spontaneous repigmentation or treatment in the last 6 months. Therapeutic response was observed according to the evaluation of both doctor and patient. The medical evaluation was based on standardized digital photos and it was considered a score of 0% of repigmentation at the beginning of the treatment and classified, at the end of the study, according to the levels of repigmentation as follows: none (0%), regular repigmentation (1-25%), moderate (26-50%), good (51-75%) and excellent (>75%). All patients signed a consent form and the study was approved by the CEP (Ethic Commission of Research) of SCMRJ. Ten patients took part in the study (4 women and 6

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¹ Dermatologist member of the Brazilian Society of Dermatology - Preceptress at the Professor Rubem David Azulay Dermatology Institute from the Santa Casa de Misericórdia Hospital of Rio de Janeiro (SCMRJ) - Rio de Janeiro (RJ), Brazil.

² Dermatologist member of the Brazilian Society of Dermatology - Post graduate course from the Professor Rubem David Azulay Dermatology Institute from the Santa Casa de Misericórdia Hospital of Rio de Janeiro (SCMRJ) - Rio de Janeiro (RJ), Brazil.

³ PhD from the Federal University of Rio de Janeiro (UFRJ) - Associate Professor from the post graduation course at the Professor Rubem David Azulay Dermatology Institute from the Santa Casa de Misericórdia Hospital of Rio de Janeiro (SCMRJ) and from the post graduation Medical School from the Catholic University of Rio de Janeiro (PUC-RJ) - Rio de Janeiro (RJ), Brazil.

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men) and two were excluded for noncompliance. In the final evaluation (16th week), the best answer were observed in patients with phototypes varying from IV to VI. Six patients with lesions on the cephalic region showed excellent response / more than 75% of repigmentation (Picture 1B and 1C). As for extremities and chest, results varied from good to excellent in 27% of the cases (Table 1). According to patients evaluation the level of repigmentation of 50 % was considered cosmetically satisfactory. The only adverse effect observed in 2 patients was mild burning that regressed spontaneously. Among the established therapies phototherapy (UVB-NB) and photochemotherapy (PUVA) have limited use for reasons such as adverse reactions¹, difficult access to the sources of light and time spent during treatment. Recent study evaluated the effectiveness and tolerability of UVB-NB, pimecrolimus and topical tacrolimus and the improvement was better using pimecrolimus and tacrolimus for facial lesions and UVB-NB for the cervical² area. Regarding topical corticosteroids a double-blind randomized study compared tacrolimus 0,1% to ointment of clobetasol 0,05%, with repigmentation of 49,3% related to clobetasol and of 41,3% related to tacrolimus. Despite the best answer, the side effects associated with corticosteroids, mainly in the acrofacial lesions, are relevant³. Analogues of Vitamin D3 presented better results when combined with phototherapy.^{4,5} Surgical techniques and *excimer laser* are limited by variables such as activity/extension of the disease, Köebner phenomenon and high cost.⁶ Grimes *et al.* Shwed showed the role of tacrolimus in the repigmentation of lesions² in 2002. Tacrolimus is an immunosuppressant macrolide derived from the fun-

gus *Streptomyces tsukubaensis* that acts through the inhibition of phosphorylation depending of calcineurin, which leads to the inhibition of the production of various inflammatory cytokines derived from T lymphocytes. The hypothesis of increased carcinogenesis associated with the combination of tacrolimus and phototherapy so far has not been proven in humans or animals.^{4,6} Furthermore, the occurrence of skin cancer in patients with vitiligo is unusual suggesting an innate resistance to the development of cutaneous malignancy on the skin affected by the dermatosis.⁷ Grimes *et al.* show the increased expression of cytokines such as interferon γ (IFN- γ), tumor necrosis factor \cdot (TNF- α) and interleukin 10 (IL-10) in vitiligo lesions and adjacencies. The decreased expression of TNF- α in the same areas after the treatment with tacrolimus (FK506), suggests that the suppression of these molecules would be involved in the repigmentation process.⁸ It is probable that the inhibitors of calcineurin beyond blocking the production of inflammatory cytokines by T lymphocyte, interfere in melanogenesis. In 2005, Lan *et al.* observed the growth and migration of melanocytes and melanoblasts *in vitro* under the action of tacrolimus.⁹ Kang *et al* confirmed, in culture of melanocytes, increase of biosynthesis of melanin due to a greater activity of tyrosinase apart from the migration of melanocytes.¹⁰ In the present study, it was observed the effectiveness of topical tacrolimus in the repigmentation of lesions in the cephalic and cervical regions. The possibility of synergy with other therapies will probably increase the effectiveness of the treatments available for vitiligo. □

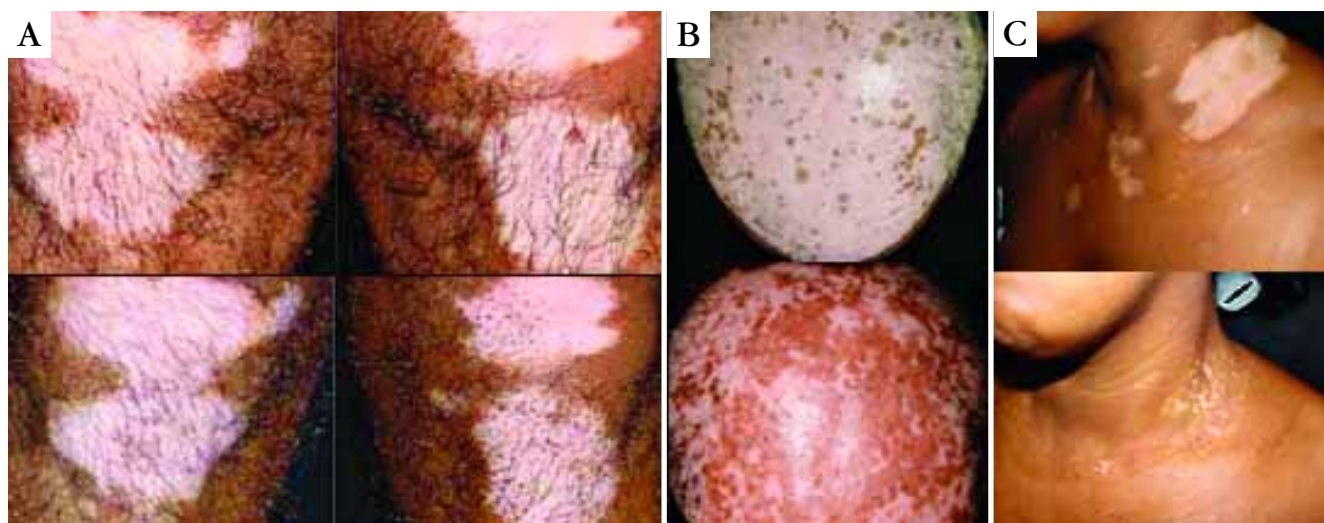


FIGURA 1: Degree of pigmentation: weeks 0 and 16
Knees (A), scalp (B), cervical (C)

TABLE 1: According to sex, phototype, repigmentation and exclusion

Patient	Sex	Phototype	Repigmentation MMSS/MMII	Repigmentation Cephalic/Cervical Regions	Exclusion
1	F	III	None	Excellent	
2	M	III	None	Regular	
3	M	III	None	None	
4	M	III	None	None	
5	F	VI	None	Excellent	
6	F	VI	Excellent	Excellent	
7	M	V	None	Excellent	
8	M	VI	None	Regular	
9	M	VI	None	Excellent	
10	F	VI	None	Excellent	
11	F	III	Good		x
12	M	III	Excellent		x

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MAILING ADDRESS / ENDEREÇO PARA CORRESPONDÊNCIA:

Carla Tamler

Av. Gilberto Amado, 1.020/201

Barra da Tijuca, Rio de Janeiro - RJ, Brazil

Tel./Fax: 21 9615 7667 / 21 2484 3285

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