DERMATOLOGICA SINICA 34 (2016) 177–179

Contents lists available at ScienceDirect

Dermatologica Sinica

journal homepage: http://www.derm-sinica.com

BRIEF REPORT

Comparison of the efficacy and safety of 0.1% tacrolimus ointment and 0.1% mometasone furoate cream for adult vitiligo: A single-blinded pilot study

Narumol Silpa-Archa, Sunatra Nitayavardhana, Kanchalit Thanomkitti, Leena Chularojanamontri, Supenya Varothai, Chanisada Wongpraparut*

Department of Dermatology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

ARTICLE INFO

Article history:
Received: Sep 8, 2015
Revised: Jan 13, 2016
Accepted: May 30, 2016

Keywords:
calcineurin inhibitor
corticosteroids
mometasone
tacrolimus
vitiligo

ABSTRACT

Topical tacrolimus has demonstrated efficacy in vitiligo. This study compared the efficacy and safety of 0.1% tacrolimus ointment with 0.1% mometasone furoate cream in adult vitiligo. We enrolled patients with symmetrical, nonacral vitiligo, and the patients on each side were randomized to receive either 0.1% tacrolimus ointment or 0.1% mometasone furoate cream, applied twice daily for 6 months. Repigmentation outcome at 6 months was compared with baseline. Of 18 cases, 22% and 33% in tacrolimus and mometasone groups, respectively, displayed more than 50% repigmentation ($p > 0.05$). Telangiectasia was presented in one-third of cases on the mometasone-treated side. Both treatments were effective in vitiligo; however, 0.1% tacrolimus ointment has fewer adverse effects.

Introduction

Vitiligo is an acquired depigmentation disorder with challenging management.[1] Usually, it takes several months or years for noticeable repigmentation. The therapeutic options depend on vitiligo type and disease severity. For localized vitiligo, topical corticosteroids remain the standard treatment. However, cutaneous side effects from long-term applications of corticosteroids, which included skin atrophy and telangiectasia, are of major concern. The use of topical tacrolimus, a topical calcineurin inhibitor, in vitiligo was first reported in 2002.[2] It is an immunomodulator that affects activation and maturation of T cells, including enhancement of melanocyte migration and differentiation, which explain its effect on repigmentation of vitiligo.[2] In the past 13 years, the efficacy of topical tacrolimus in the treatment of childhood and adult vitiligo has been reported.[2–4] Mometasone furoate is a nonfluorinated Class IV corticosteroid with a good safety profile. It has a much greater vasoconstriction property than hydrocortisones, but similar adverse effects.[5] Mometasone furoate 0.1% demonstrated excellent efficacy in the treatment of childhood vitiligo.[6] For adult vitiligo, mometasone is generally prescribed by physicians; however, the data of its efficacy in vitiligo are still lacking. Herein, the authors reported the outcome of a comparison study using 0.1% tacrolimus ointment and 0.1% mometasone furoate cream for adult vitiligo vulgaris in terms of their efficacy and safety profiles.

Methods

This study was approved by the Ethical Committee on Research Involving Human Subjects of Siriraj Hospital, Mahidol University, Bangkok, Thailand. The ClinicalTrials.gov identifier is NCT01333410.

As this was a pilot study, 20 patients aged >18 years with symmetrical nonacral vitiligo were enrolled. The acral areas included hands, feet, fingers, and toes. Vitiliginous sites were selected by a simple randomization method to receive either 0.1% tacrolimus ointment or 0.1% mometasone furoate. The participants were asked to apply both agents twice daily for 6 months. Repigmentation and adverse events were recorded every 2 months.

Repigmentation outcome was assessed by two independent dermatologists, using blinded comparative photographs taken at baseline and 6 months. The improvement was graded as follows:

Conflicts of interest: The authors declare that they have no financial or non-financial conflicts of interest related to the subject matter or materials discussed in this article.

* Corresponding author. Department of Dermatology, Faculty of Medicine Siriraj Hospital, Mahidol University, 2 Wanglang Rd., Bangkoknoi, Bangkok 10700, Thailand.

E-mail address: chanisada@hotmail.com (C. Wongpraparut).

http://dx.doi.org/10.1016/j.dsi.2016.05.005

no change, and 1–25%, 26–50%, 51–75%, and 76–100% repigmentation.[7] Repigmentation above 50% is indicated as successful repigmentation.

Statistical analysis

All statistical calculations were performed by the statistical software package SPSS, version 17.0 (SPSS Inc., Chicago, IL, USA). The grading of improvements by two dermatologists was subjected to inter-rated reliability assessment and paired sample *t* test. Descriptive statistics were assessed using the Chi-square test.

Results

Eighteen participants completed the study. Two dropped out because of inconveniences in the follow-up schedule. Demographic data including those of age, gender, duration of vitiligo, treated location, underlying diseases, and repigmentation outcome are given in Table 1. In the tacrolimus group, successful repigmentation (> 50%) was demonstrated in 22%, with 11% achieving > 75% repigmentation, while ~50% of cases showed 1–25% repigmentation. In the mometasone group, 33% of cases gained successful repigmentation, with 11% achieving > 75% repigmentation, while 33% of cases had 1–25% repigmentation. There was no statistically significant difference in the grading of repigmentation in both groups ($p = 0.13$); however, repigmentation of lesions on the mometasone-treated side was achieved earlier. At 2 months, repigmentation was seen in eight cases on the mometasone-treated side and in three cases on the tacrolimus-treated side (Figure 1). There was an agreement of grading improvement evaluated by two independent dermatologists using inter-rated reliability assessment. With respect to the location, a higher percentage of repigmentation in both groups was achieved on the neck, followed by on the trunk and extremities. At the end of the study, telangiectasia was found in six cases on the mometasone-treated sites, while no case of telangiectasia was observed on the tacrolimus-treated side ($p = 0.03$). No striae or skin atrophy was detected in both groups. Eight (44.4%) cases and five (27.7%) cases reported slight burning and stinging sensation on the tacrolimus- and mometasone-treated sides, respectively. However, both agents were well tolerated by these patients.

Table 1 Characteristics of the 18 vitiligo patients.

Variable	Data ($n = 18$)				
Age (y)					
Mean ± SD	46.8 ± 15.60				
Gender					
Male:female	1:17				
Duration of vitiligo (mo)					
Mean ± SD	25 ± 18				
Underlying disease (*n*)					
Hypothyroidism	3				
Diabetes mellitus	1				
Treated location (*n*) for each group					
Neck	6				
Trunk	4				
Axilla	4				
Wrist	3				
Knee	1				
Repigmentation (tacrolimus group) (*n*)	None	1–25%	26–50%	51–75%	76–100%
Neck (6)	2	1	1	1	1
Trunk (4)		3		1	
Axilla (4)		4			
Wrist (3)	1	2			
Knee (1)					1
Repigmentation (mometasone group) (*n*)	None	1–25%	26–50%	51–75%	76–100%
Neck (6)	2	1		2	1
Trunk (4)		2		2	
Axilla (4)	1	2	1		
Wrist (3)		1	2		
Knee (1)					1

SD = standard deviation.

Discussion

Long-term treatment is usually required based upon the clinical course of vitiligo; the ideal topical agent should have good clinical efficacy with a better safety profile. Topical tacrolimus is a topical calcineurin inhibitor derived from the bacteria *Streptomyces tsukubaensis*. Since 2002, several studies have shown this agent to have promising results in vitiligo. The response rates vary between 63% and 89% depending on the type and location of vitiligo, with good results for face and neck lesions.[3,8,9]

Lepe et al[10] conducted a double-blinded randomized trial of 0.1% tacrolimus versus 0.05% clobetasol propionate in childhood vitiligo. After a 2-month period, the mean repigmentation was 41.3% for tacrolimus and 49.3% for clobetasol. Although clobetasol achieved better repigmentation, 10% of cases had telangiectasia and 15% skin atrophy. Mometasone furoate is one of the commonest topical corticosteroids prescribed by physicians due to its safety profile. Kose et al[6] conducted an open comparative study of topical mometasone cream and pimecrolimus cream for childhood vitiligo. Mometasone cream was effective on all parts of the body; however, pimecrolimus was effective only for the facial lesions but not for lesions on the body areas.

To the best of our knowledge, this is the first study comparing the efficacy and safety of 0.1% tacrolimus ointment and 0.1% mometasone furoate cream in adult generalized vitiligo. At the end of this study, 15 of 18 cases (83%) achieved repigmentation in both groups, with the majority achieving 1–25% repigmentation at 6 months. Low successful response should be from the anatomical locations that we selected in this study, which included the trunk and wrist. Vitiligo is a difficult condition to treat and usually needs long-term treatment. A 6-month period might not be long enough to see the maximum response to the medication. A few years may be required to observe the maximal outcome. In addition, topical treatments demonstrated the optimum benefit in vitiligo when combined with other treatment modalities.[8,11] Moreover, topical treatment might be considered in the maintenance phase of vitiligo. Cavalie et al[12] reported a significantly low relapse rate in successfully repigmented vitiligo with twice-weekly applications of 0.1% tacrolimus ointment. Occlusive treatment may have a role in enhancing repigmentation. Hartmann et al[9] reported increasing the efficacy of topical tacrolimus in vitiligo using occlusive dressing in areas beyond the head and neck. However, we need to be aware of the side effects of topical steroid occlusive treatment for vitiligo.

Considering treatment response and the location of lesions, the head and neck areas usually show a more favorable response than the trunk and extremities because of the presence of more melanocyte reservoirs.[1] Similar to other studies, our cases achieved a higher percentage of repigmentation at the neck area. We had three cases with vitiligo on the wrist area; all these cases had no or minimal response to tacrolimus or mometasone treatment. As the wrists are close to the hands that are known to be refractory to treatment, a surgical method or camouflage might be the appropriate option for this area.

Although it has been shown that mometasone has minimal adverse events, we still observed the occurrence of telangiectasia in one-third of cases, which is a local effect. This might be caused by frequent applications of mometasone (twice daily). In the normal use of mometasone in vitiligo, once-daily applications might help reduce this adverse event. Regarding financial aspects, mometasone is inexpensive compared with tacrolimus, which is not

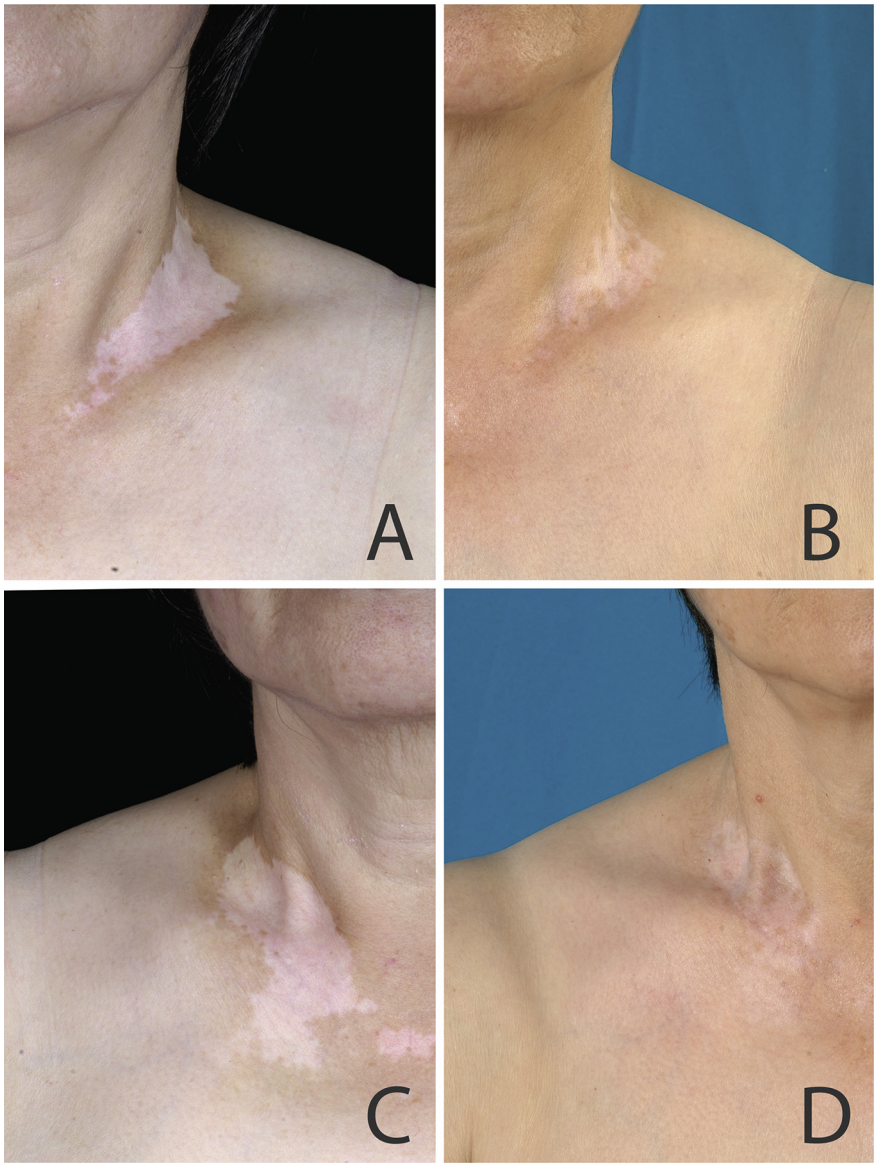

Figure 1 Tacrolimus-treated side at (A) baseline and (B) 6 months' follow-up. Mometasone furoate cream-treated side at (C) baseline and (D) 6 months' follow-up.

covered by insurance in some patients. Based on these results, mometasone appears to be an appropriate choice in patients for whom tacrolimus is unaffordable.

As this is a pilot study, the limitation included the small number of participants. A larger group is essential to confirm the efficacy and safety of both agents for adult vitiligo.

In conclusion, 0.1% tacrolimus ointment and 0.1% mometasone furoate cream are effective in the treatment of adult nonacral vitiligo; however, topical tacrolimus has fewer adverse effects.

Acknowledgments

Funding was not received for this study.

References

1. Ezzedine K, Eleftheriadou V, Whitton M, van Geel N. Vitiligo. *Lancet* 2015;**386**:74–84.
2. Grimes PE, Soriano T, Dytoc MT. Topical tacrolimus for repigmentation of vitiligo. *J Am Acad Dermatol* 2002;**47**:789–91.
3. Silverberg NB, Lin P, Travis L, et al. Tacrolimus ointment promotes repigmentation of vitiligo in children: a review of 57 cases. *J Am Acad Dermatol* 2004;**51**:760–6.
4. Kanwar AJ, Dogra S, Parsad D. Topical tacrolimus for treatment of childhood vitiligo in Asians. *Clin Exp Dermatol* 2004;**29**:589–92.
5. Hoffmann K, Auer T, Stucker M, Hoffmann A, Altmeyer P. Comparison of skin atrophy and vasoconstriction due to mometasone furoate, methyl prednisolone and hydrocortisone. *J Eur Acad Dermatol Venereol* 1998;**10**:137–42.
6. Kose O, Arca E, Kurumlu Z. Mometasone cream versus pimecrolimus cream for the treatment of childhood localized vitiligo. *J Dermatol Treat* 2010;**21**:133–9.
7. Eleftheriadou V, Thomas K, van Geel N, et al. Developing core outcome set for vitiligo clinical trials: international e-Delphi consensus. *Pigment Cell Melanoma Res* 2015;**28**:363–9.
8. Fai D, Cassano N, Vena GA. Narrow-band UVB phototherapy combined with tacrolimus ointment in vitiligo: a review of 110 patients. *J Eur Acad Dermatol Venereol* 2007;**21**:916–20.
9. Hartmann A, Brocker EB, Hamm H. Occlusive treatment enhances efficacy of tacrolimus 0.1% ointment in adult patients with vitiligo: results of a placebo-controlled 12-month prospective study. *Acta Derm Venereol* 2008;**88**:474–9.
10. Lepe V, Moncada B, Castanedo-Cazares JP, Torres-Alvarez MB, Ortiz CA, Torres-Rubalcava AB. A double-blind randomized trial of 0.1% tacrolimus vs 0.05% clobetasol for the treatment of childhood vitiligo. *Arch Dermatol* 2003;**139**:581–5.
11. Nordal EJ, Guleng GE, Ronnevig JR. Treatment of vitiligo with narrowband-UVB (TL01) combined with tacrolimus ointment (0.1%) vs. placebo ointment, a randomized right/left double-blind comparative study. *J Eur Acad Dermatol Venereol* 2011;**25**:1440–3.
12. Cavalie M, Ezzedine K, Fontas E, et al. Maintenance therapy of adult vitiligo with 0.1% tacrolimus ointment: a randomized, double blind, placebo-controlled study. *J Invest Dermatol* 2015;**135**:970–4.