

# Comparative Evaluation of Tacrolimus Ointment and Pimecrolimus Cream in the Management of Vitiligo in Children: Assessing Clinical Efficacy and Prognosis Implications

LI WENG AND HUAN XING\*

Department of Dermatology, Beijing Children's Hospital, Capital Medical University, National Center for Children's Health, Xicheng, Beijing 100045, China

## Weng *et al.*: Tacrolimus Ointment and Pimecrolimus Cream in Vitiligo Treatment

By evaluating the clinical efficacy of tacrolimus ointment and pimecrolimus cream in treating childhood vitiligo, this study aims to determine their prognostic implications. A cohort of 120 children with vitiligo, who underwent treatment at our hospital over the period of June 2021 to June 2022, was chosen as the subjects for this study. They were divided into an observation group (tacrolimus ointment+308 nm excimer laser) and a control group (pimecrolimus cream+308 nm excimer laser). The two groups received continuous treatment for 12 w. The overall effective rate, time to appearance of pigmented spots, pre and post treatment pigmentation scores, and occurrence of adverse reactions were compared between the two groups. Observation group had a higher effective rate (91.67 %) than the control group (88.33 %), but the difference was not significant ( $p>0.05$ ). The duration for pigmented spots to manifest was significantly shorter in the observation group ( $9.01\pm 2.20$  d) compared to the control group ( $11.13\pm 2.96$  d) ( $p<0.05$ ). No significant difference in pre-treatment pigmentation scores ( $p>0.05$ ). After treatment, both groups had increased pigmentation scores, with observation group showing significantly higher scores ( $p<0.05$ ). No notable difference in the incidence of adverse reactions between the observation group (6.67 %, 4/60) and the control group (10.00 %, 6/60) ( $p>0.05$ ) was identified. Tacrolimus ointment and pimecrolimus cream had similar efficacy in childhood vitiligo. The observation group showed faster pigmented spot appearance and higher pigmentation scores, favoring tacrolimus ointment

**Key words:** Tacrolimus ointment, pimecrolimus cream, vitiligo, clinical efficacy, calcineurin inhibitors

The occurrence of vitiligo involves an acquired pigmentary disorder that primarily impacts the skin and mucous membranes. It commonly presents as depigmented or lightly pinkish patches on exposed areas such as the extremities, neck, and face, with clear borders and a smooth surface<sup>[1,2]</sup>. This pigmentary dysregulation not only affects physical appearance but can also pose challenges to patients' psychological well-being, social interactions, and overall quality of life<sup>[3,4]</sup>. Children with vitiligo are particularly vulnerable, as their growth, development, learning and social environments may be affected. Consequently, research on the treatment of childhood vitiligo is of paramount importance<sup>[5]</sup>. Currently, treatment options for childhood vitiligo are limited, with medication being a common choice. This includes

topical agents and systemic drugs<sup>[6-8]</sup>. Tacrolimus ointment and pimecrolimus cream are commonly used topical agents and belong to the class of calcineurin inhibitors. They inhibit the transcription of pro-inflammatory cytokines and affect the function of white blood cells and mast cells, thereby exerting immunosuppressive effects and showing potential for improving vitiligo symptoms<sup>[9]</sup>. However, direct comparative studies on the two medications in pediatric patients with vitiligo are still limited. Tacrolimus ointment, as a topical agent, is widely used in the treatment of vitiligo by suppressing immune responses and regulating the function of melanocytes. Its effectiveness has been demonstrated in some studies, but further research is still needed to assess its efficacy and safety in pediatric patients.

---

\*Address for correspondence

E-mail: xh09032023@126.com

Pimecrolimus cream, on the other hand, is a newer topical agent with a similar mechanism of action to tacrolimus but with a milder profile. While pimecrolimus has shown promising results in adult patients, research on its efficacy and safety in pediatric patients is still limited. This study aims to compare the treatment outcomes of tacrolimus ointment and pimecrolimus cream in childhood vitiligo, with a specific focus on evaluating their impact on prognosis. We will focus on comparing the treatment efficacy, recurrence rate and potential adverse reactions during the treatment process for the two medications. Through this study, we aim to provide more scientific and effective guidance for the treatment of childhood vitiligo, improving the quality of life and prognosis for affected children. Included in this study were 120 pediatric patients diagnosed with vitiligo during their hospitalization period from June 2021 to June 2022 in our hospital. The research protocol received official ethical approval from the hospital's ethics committee. Informed consent forms, signed by the guardians of the patients, were obtained to ensure their understanding and agreement to participate in the study. Inclusion criteria, pediatric patients aged between 2 y and 14 y old; clinical features of vitiligo in accordance with international standards, including the presence of depigmented patches and the exclusion of other skin diseases; the area of vitiligo patches should be  $\geq 1\%$ ; patients who were receiving tacrolimus ointment or pimecrolimus cream for the first time; and patients and their families agreed to a 12 w treatment observation period were included. In exclusion criteria, the presence of other serious underlying diseases, such as autoimmune diseases or malignancies; presence of other serious skin diseases or infectious skin diseases commonly associated with vitiligo; female patients who were not suitable for medication during pregnancy or lactation; patients with allergies to tacrolimus, pimecrolimus, or other related components and patients who had previously received treatment with tacrolimus ointment or pimecrolimus cream were excluded. The patients were evenly allocated into the observation group and the control group (60 in each group) randomly. The control group consisted of 33 male patients and 27 female patients, with an age range of 2 y to 14 y old (mean age  $6.9 \pm 2.4$  y), a disease duration of 2 w to 24 mo (mean duration  $9.8 \pm 2.9$  mo), and a distribution of

18 cases of localized type, 16 cases of scattered type, 13 cases of acral type, and 13 cases of segmental type. The observation group consisted of 35 male patients and 25 female patients, with an age range of 2 y to 13 y old (mean age  $7.7 \pm 2.4$  y), a disease duration of 2 w to 23 mo (mean duration  $9.4 \pm 2.7$  mo), and a distribution of 19 cases of localized type, 16 cases of scattered type, 15 cases of acral type, and 10 cases of segmental type. The general characteristics of the two groups showed no statistically significant differences ( $p > 0.05$ ), suggesting that they were comparable in terms of demographics and baseline characteristics. In observation group, the patients were treated with tacrolimus ointment (protopic 0.03 %) applied twice daily on the affected areas, along with 308 nm excimer laser treatment twice a week. In control group, the patients were treated with pimecrolimus cream (Elidel 1 %) applied twice daily on the affected areas, along with 308 nm excimer laser treatment twice a week. The clinical efficacy was evaluated after 12 w of treatment, following the "Diagnosis and Treatment Criteria for Melasma and Vitiligo"<sup>[10]</sup>. Cure means complete disappearance of depigmented patches; significant improvement has  $>50\%$  restoration of skin lesions; in improvement,  $10\% - 49\%$  restoration of skin lesions; ineffective means  $<10\%$  restoration of skin lesions. Overall effective rate = (cure + significant improvement + improvement) / total number of patients  $\times 100\%$ . The measurement of lesion area was performed by marking the edge of the depigmented patches and using a  $1\text{ mm} \times 1\text{ mm}$  transparent grid paper, with rounding. Appearance time of pigmented spots was noted. Pigment score of the lesions before and after treatment including the assessed using a 4 point grading scale, where 0 indicates no pigment deposition and white color; 1 indicates slight pigment deposition; 2 indicates the formation of multiple pigment islands and 3 indicates gradual restoration of yellow-brown or normal skin color. Adverse reactions include the comparison of local redness, mild itching, burning sensation, blisters and acne occurrence after treatment in the two groups. Statistical Package for the Social Sciences (SPSS) 25.0 software was employed to analyze the collected data. Continuous variables will be reported as mean and standard deviations ( $\bar{x} \pm s$ ) and analyzed using t-tests. Categorical variables will be presented as frequencies and percentages [ $n$  (%)] and analyzed

using Chi-square ( $\chi^2$ ) tests. To establish statistical significance, a significance level of  $p < 0.05$  will be employed. The comparison outlined in Table 1 reveals that the observation group achieved an overall effective rate of 91.67 %, which was higher compared to the control group's rate of 88.33 %. Nonetheless, no statistical difference was identified between the two groups ( $p > 0.05$ ). As displayed in Table 2, the appearance of pigmented spots occurred more rapidly in the observation group, with a mean duration of  $9.01 \pm 2.20$  d, compared to the control group's mean duration of  $11.13 \pm 2.96$  d. This difference was without significance ( $p < 0.05$ ). In Table 3, it can be seen that no notable distinction in the lesion pigment score was found prior to treatment ( $p > 0.05$ ). However, after treatment, both groups demonstrated an improvement in the lesion pigment score. Notably, statistical analysis revealed a significant difference in the lesion pigment score between the observation and control groups ( $p < 0.05$ ), with the observation group exhibiting a higher score. Regarding the incidence of adverse reactions, the observation group exhibited a rate of 6.67 % (4/60), in comparison to 10.00 % (6/60) in the control group, as indicated in Table 4. Importantly, the statistical analysis indicated no significant distinction in the occurrence of adverse reactions between the two groups ( $p > 0.05$ ). Vitiligo is a primary skin and mucous membrane disorder characterized by melanocyte dysfunction, resulting in pigment loss. It may be associated with various factors such as genetics, neuro-mental factors, melanocyte self-destruction, immune response, cytokines and oxidative stress<sup>[11,12]</sup>. Currently, immune dysfunction is believed to be closely related to the pathogenesis of vitiligo. The purpose of this research was to compare the clinical effectiveness and prognostic impact of tacrolimus ointment and pimecrolimus cream in managing pediatric vitiligo. In the comparison between the two groups, the overall effective rate was slightly higher in the observation group than in the control group (91.67 % vs. 88.33 %), but the difference was not significant ( $p > 0.05$ ). This suggests that both drugs may have similar efficacy in treating pediatric vitiligo. Further observation revealed that the appearance time of pigmented spots was notably shorter in the observation group than in the control group ( $9.01 \pm 2.20$  d vs.  $11.13 \pm 2.96$  d,  $p < 0.05$ ). This indicates that tacrolimus ointment

may achieve pigment restoration more quickly. No significant difference in the pre-treatment pigment score between the two groups was observed ( $p > 0.05$ ). However, after treatment, both groups showed an increase in lesion pigment score, with the observation group showing a greater increase compared to the control group, and the difference was significant ( $p < 0.05$ ). This indicates that tacrolimus ointment may play a more active role in promoting pigment restoration. Although calcineurin inhibitors, such as tacrolimus, do not cause adverse reactions associated with steroids, they can still cause or exacerbate local infections such as folliculitis, acne and herpes simplex<sup>[13]</sup>. In our study, adverse reactions such as local skin erythema, burning sensation, acne and blisters occurred during treatment. When considering the overall incidence of adverse reactions, the observation group exhibited a rate of 6.67 % (4/60), while the control group had a slightly higher rate of 10.00 % (6/60). Nonetheless, the statistical analysis concluded that the difference between the two groups was not statistically significant ( $p > 0.05$ ). This indicates that both drugs have good safety profiles, and the frequency of adverse reactions is relatively low, which is consistent with a study by Alshiyab *et al.*<sup>[14]</sup> on tacrolimus. However, this research is not without limitations. Firstly, the sample size was limited, which may affect the stability and generalizability of the results. Secondly, we only considered single indicators such as the overall effective rate, appearance time of pigmented spots, and lesion pigment score, without comprehensive consideration of other factors that could influence treatment outcomes, such as patient age, severity of the disease and treatment compliance. Notwithstanding these limitations, the results of this study offer valuable insights into the potential use of tacrolimus ointment and pimecrolimus cream for treating pediatric vitiligo. Further research with larger sample sizes and consideration of other relevant factors is needed to validate these findings and provide more accurate and reliable evidence for clinical practice. In conclusion of this study, tacrolimus ointment and pimecrolimus cream showed similar clinical efficacy in the treatment of pediatric vitiligo. However, it was observed that the appearance time of pigmented spots was shorter and the increase in lesion pigment score was greater in the observation

group, suggesting a potential advantage of tacrolimus ointment over pimecrolimus cream in treatment. Further research considering more factors and with larger sample sizes is needed to validate these results.

**TABLE 1: COMPARISON OF CURATIVE EFFECT (n %)**

Group	n	Cured	Remarkable effective	Effective	Invalid	Overall effective rate
Observation	60	19 (31.67)	21 (35)	15 (25.00)	5 (8.33)	55 (91.67)
Control	60	15 (25.00)	22 (36.67)	14 (23.33)	7 (11.67)	53 (88.33)
$\chi^2$						0.37
p						0.543

**TABLE 2: COMPARISON OF OCCURRENCE TIME OF PIGMENTATION SPOTS (x±s)**

Group	n	Time of appearance of pigmented spots (d)
Observation	60	9.01±2.20
Control	60	11.13±2.96
t		5.533
p		0.021

**TABLE 3: COMPARISON OF PIGMENT SCORES IN SKIN LESIONS (x±s)**

Group	n	Skin lesion pigment score	
		Before	After
Observation	60	0.17±0.04	2.34±0.27*
Control	60	0.16±0.03	1.86±0.23*
t		0.787	2.533
p		0.442	0.001

**TABLE 4: COMPARISON OF THE OCCURRENCE OF ADVERSE REACTIONS (n %)**

Group	n	Local erythema	Burning sensation	Acne	Blisters	Overall incidence
Observation	60	1 (1.67)	2 (3.33)	1 (1.67)	0 (0)	4 (6.67)
Control	60	2 (3.33)	2 (3.33)	1 (1.67)	1 (1.67)	6 (10)
$\chi^2$						0.436
p						0.509

**Conflict of interests:**

The authors declared no conflict of interests.

**REFERENCES**

- Sun M, Chen X, Liu X. Clinical effect of CO<sub>2</sub> dot matrix laser combined with tacrolimus in the treatment of localized vitiligo. *J Jilin Univ* 2018;44(5):4.
- Dillon AB, Sideris A, Hadi A, Elbuluk N. Advances in vitiligo: An update on medical and surgical treatments. *J Clin Aesthetic dermatol* 2017;10(1):15.
- Handjani F, Aghaei S, Moezzi I, Saki N. Topical mycophenolate mofetil in the treatment of vitiligo: A pilot study. *Dermatol Pract Concept* 2017;7(2):31.
- Yang L, He T, Ma H. Clinical analysis of 243 cases of vitiligo. *J Dermatol Venereal* 2019;26(5):4.
- Ucuz I, Altunisik N, Sener S, Turkmen D, Kavuran NA, Marsak M, *et al.* Quality of life, emotion dysregulation, attention deficit and psychiatric comorbidity in children and adolescents with vitiligo. *Clin Exp Dermatol* 2021;46(3):510-5.
- Hu W, Xu Y, Ma Y, Lei J, Lin F, Xu AE. Efficacy of the topical calcineurin inhibitors tacrolimus and pimecrolimus in the treatment of vitiligo in infants under 2 y of age: A randomized, open-label pilot study. *Clin Drug Investig* 2019;39:1233-8.
- Wada-Irimada M, Tsuchiyama K, Sasaki R, Hatchome N, Watabe A, Kimura Y, *et al.* Efficacy and safety of IV methylprednisolone pulse therapy for vitiligo: A retrospective study of 58 therapy experiences for 33 vitiligo patients. *J Dermatol* 2021;48(7):1090-3.
- Liu X, Yao Z, Wang Y, Chai L, Zhou X. Vitamin D analogs combined with different types of phototherapy in the treatment of vitiligo: A systematic review of randomized trials and within-patient studies. *Int Immunopharmacol* 2022;109:108789.
- Xu X. Characteristics and treatment progress of vitiligo in children. *J Dermatopathol* 2022;29(3):275-9.
- Pigmentology group, dermatological and venereal diseases committee, Chinese association of integrated traditional and western medicine. Diagnosis and treatment criteria of melasma and vitiligo. *Chin J Dermatol* 2010;6:1.
- Zhou H, Wu Y. Research progress of pathogenesis of vitiligo. *Dermatol Venereal Dis* 2019;41(2):5.
- Zhao V. Chinese clinical dermatology. *Chin Clin Dermatol* 2010;5:15-8.
- Pigmentology group, dermatological and venereal diseases committee, Chinese association of integrated traditional and western medicine. Consensus of diagnosis and treatment of vitiligo. *Chin J Dermatol* 21;54(2):5.
- Alshiyab DM, Al-Qarqaz FA, Muhaidat JM, Alkhader YS, Al-Sheyab RF, Jafaar SI. Comparison of the efficacy of tacrolimus 0.1 % ointment and Tacrolimus 0.1 % plus topical pseudocatalase/superoxide dismutase gel in children with limited vitiligo: A randomized controlled trial. *J Dermatol Treat* 2022;33(1):146-9.

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms

This article was originally published in a special issue, "Drug Development in Biomedical and Pharmaceutical Sciences" *Indian J Pharm Sci* 2023;85(5) Spl Issue "233-237"