

Combination of Topical Tacrolimus, Antioxidants, and Probiotics in the Treatment of Periorbital Vitiligo

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BACKGROUND

- Vitiligo is a chronic depigmenting skin disease.
- Major impact on quality of life, especially in young patients.
- Suggested pathogenesis of vitiligo:
 - Autoimmune theory
 - Biochemical theory
 - Neural theory
- The main characteristic of the disease is the loss of epidermal melanocytes.
- The underlying mechanism:
 - Environmental and genetic factors >>
 - >> leading to infiltration of the skin by CD8+ T lymphocytes >>
 - >> leading to elevated levels of TNF- α and IFN- γ >>
 - >> leading to a chronic inflammatory state and damage to the melanocytes.
- Currently, there is **no approved treatment for vitiligo**.
- Limited off-label options are mainly based on **immunosuppression** and phototherapy.
- The roles of **oxidative stress** and **dysbiosis** have been established in pathogenesis.
- There is evidence that **microbiome changes** play a role in vitiligo pathogenesis, by affecting immune homeostasis, oxidative stress, skin barrier, and even gene expression.
- Topical corticosteroids have shown good repigmentation rates, however, their chronic use is limited due to the risk of skin atrophy, striae, and telangiectasia.
- In lesions of the face, neck, and intertriginous areas and lesions in children, non-steroidal agents are highly preferred.
- Topical calcineurin inhibitors (TCIs) such as **Tacrolimus (to address autoimmunity)**:
 - Good efficacy
 - Better side effect profile
 - Recommended first-line for face and neck vitiligo lesions.
- Antioxidants (to address oxidative stress)**, in conjunction with other treatments, have been shown to be effective and increase the repigmentation rate.
- Probiotics (to address dysbiosis)** have been suggested for vitiligo recently.

In this report, we present a case of facial vitiligo who was treated with a novel combination of topical tacrolimus, antioxidants, and probiotics and reached complete repigmentation after 6 weeks, with no relapse after 52 weeks to date.

REPORT OF A CASE

- 13-year-old male, with no specific past medical history and no history of autoimmune diseases in the family.
- Hypopigmented area of 3x8 millimeters on his right upper eyelid (Fig 1).
- The patient and the family were in severe distress, and especially concerned about the effect of this condition on the patient's quality of life and social interactions.
- The diagnosis of vitiligo was confirmed clinically by a dermatologist.
- A combination of:
 - Topical tacrolimus 0.1% once a day (gently applied on the area of hypopigmentation, avoiding contact with the ocular surface).
 - An antioxidant cocktail containing vitamin A 14320 IU, vitamin C 226 mg, vitamin E 200 IU, Zinc 34.8 mg, and copper 0.8 mg once a day.
 - A probiotic cocktail containing calcium 140 mg and Bacillus coagulans 2 Billion CFUs once a day.
- Following 3 weeks of treatment, the lesion started repigmentation.
- After 6 weeks, the lesion completely disappeared with total repigmentation (Figure 2).
- The patient was closely followed for ophthalmic reactions such as conjunctival injection, follicular reaction, and corneal decompensation, and did not show any reaction or side effects.
- No visual changes were noted after the treatment course compared to before.
- Retinal and fundus exams were normal before and after the treatment.
- The patient is under close follow-up, and to date has been stable for 52 weeks, with no recurrence or other lesions on other locations.



Figure 1: Periorbital vitiligo lesion in a 13-year-old male at presentation.



Figure 2: Lesion reached complete repigmentation after 6 weeks of treatment.

DISCUSSION

- Tacrolimus, a TCI, is widely used off-label for the treatment of vitiligo, especially for facial lesions. Therapeutic role via different mechanisms:
 - Suppress the activation, proliferation, and cytokine production of CD8+ T lymphocytes.
 - Directly stimulate the proliferation, migration, and function of melanocytes.
 - TCIs alone have a greater response rate compared to TCIs combined with UV light therapy in facial vitiligo.
- In a study on monotherapy with Tacrolimus 0.03%, repigmentation was achieved in up to 45% of the cases after 24 weeks, with better response in younger age and head and neck lesions. A **minimum of 8 and 16 weeks** were required to gain some degree of repigmentation and complete response, respectively.
- Another study on monotherapy with Tacrolimus 0.1% showed a complete repigmentation rate of up to 75% after **24 weeks**, with **40% relapse in 48 weeks**.
- The role of **oxidative stress** in vitiligo has been established in many studies. This oxidative stress exerts a **pro-inflammatory effect** and induces **melanocyte damage**. Deregulations in oxidative metabolism most notably include elevated superoxide dismutase, decreased catalase, and increased lipid peroxidation.
- Using Antioxidants as an adjuvant with other treatments has been shown to increase the repigmentation rate.
- When combined with narrowband ultraviolet B light therapy (NB-UVB), they can increase the repigmentation rate up to 75%, compared to 18% in the control.
- Recent studies highlighted the importance of dysregulations in the skin and gut microbiome in vitiligo patients.
- There is an association between dysbiosis, mitochondrial damage, and immunity in vitiligo.
- The mitochondrial alterations in vitiligo lead to increased production of oxygen species, increasing oxidative damage.
- Dysbiosis is also associated with an increase in cytokine production, including IFN- γ (19).
- Based on these, a combination of **Tacrolimus** (the first-line treatment option for facial vitiligo) along with an **antioxidative** and **probiotic** regimen as an **adjuvant** could provide a scientifically reasonable treatment regimen.
- In this report, we presented a case who was treated with this regimen and reached complete repigmentation in a **relatively short period of 6 weeks**.
- No relapse has been noted up to 52 weeks to date**.
- This report could highlight the potential of adjuvant therapy with antioxidants and probiotics to achieve an earlier, effective, and sustained response.

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