

Efficacy and safety of tacrolimus ointment 0.03% treatment in a 1-month-old "red baby": A case report

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ABSTRACT

Several trials have indicated that topical tacrolimus is safe and effective for several immunologic-based skin disorders. We report a child <2 months old, who was admitted to our pediatric department because of generalized erythroderma. We started tacrolimus ointment 0.03% therapy by applying the ointment to the skin once daily, on a limited surface of 10 cm², changing the skin areas only after the disappearance of inflammation. After only one application we observed a marked improvement of the treated area and after another application the localized erythroderma disappeared. We changed the site of application and continued this treatment regime for 4 weeks. After 2 weeks we reduced treatment application once every other day and after an additional 2 weeks we discontinued therapy because of complete resolution of erythroderma. No adverse clinical effect was recorded and tolerance to the treatment was good. We conclude that 0.03% tacrolimus ointment is efficacious and safe even in an infant <2 months of age.

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Several trials have indicated that topical tacrolimus is safe and effective for treatment of atopic eczema in both adults and children and may be an alternative to corticosteroids.^{1,2} To date, reports of its efficacy in treating several immunologically based skin disorders, including psoriasis, lichen planus, vitiligo, and seborrheic dermatitis³ are based on phase IV clinical trials and on case reports or series.³ We report successful tacrolimus ointment 0.03% treatment of a 1-month-old infant with neonatal erythroderma-like appearance.

A 45-day-old male infant was admitted to our pediatric department because of generalized erythroderma. The baby was breast-feeding and showed a regular growth (height, 57 cm; weight, 4.500 kg). Approximately 20 days before admission eyelid edema and erythema on the face had been noted. His pediatrician initially treated him with oral antihistamines and a few days later with topical corticosteroids in addition. Because of worsening of his clinical condition and the appearance of generalized erythroderma, he added to the treatment regimen oral betametasone and topical antifungal on the folds of groin and neck with poor efficacy.

On admission to our hospital the child was very restless, cried frequently, and often refused breast-feeding. On physical examination erythroderma affected the whole body and there were scattered, scaly

patches on his forehead, scalp, trunk, and lower and upper limbs (Fig. 1, A and B).

Normal values were recorded for hematocrit, platelet count, inflammatory markers, glucose, electrolytes, creatinine, creatine kinase, pancreas and liver enzyme levels, serum immunoglobulins, C3, C4, total IgE, and specific IgE immunoglobulin levels. Blood, urinary, and fecal cultures were negative. Chest radiograph was normal. Serological test for cytomegalovirus, herpes simplex type I and II viruses, and rubella virus were negative with the presence of maternal IgG. The clinical picture was compatible with a neonatal erythroderma presentation related to seborrheic dermatitis.

We started antibiotic therapy using amoxicillin and continued oral antihistamines (oral cetirizine at dosage of 2.5 mg once daily), oral corticosteroids (betametasone at a dosage of 0.025 mg/day twice daily), and topical antifungals (miconazole) for 3 days. As we observed a worsening in his condition, we decided to stop this therapy and to start tacrolimus ointment 0.03% therapy.

Although the Food and Drug Administration advisory panel has expressed concerns regarding the potential for carcinogenesis of topical calcineurin inhibitors, recently, a Task Force of the American College of Allergy, Asthma and Immunology and the American Academy of Allergy, Asthma and Immunology has underlined that there is no scientific evidence to justify this concern.⁴

However, because it is not licensed for children under 2 years of age and to avoid the risk of systemic absorption, we decided to use 0.5 g of the ointment on the skin to a limited surface area of 10 cm² once daily. Initially, we applied a thin layer of 1 cm once daily over a defined area of the forearm (Fig. 2 A). After only

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Figure 1. (A and B) Front and back view of infant's body before starting therapy.



Figure 2. (A–C) View of the left forearm (A) before tacrolimus application, (B) after 24 hours, and after 48 hours.

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one application we observed a marked improvement of the treated area (Fig. 2 B) and after a second application the localized erythroderma disappeared (Fig. 2 C). We changed the site of application and continued this regimen for 4 weeks.

Improvement of erythema was less marked and slower on the trunk than on upper and lower limbs. In the same zone we observed a partial relapse during the treatment. No adverse clinical effects were recorded and tolerance to treatment remained good. After 4 weeks we reduced the frequency of treatment application to once every other day. We stopped tacrolimus application after the disappearance of erythroderma 2 weeks later (Fig. 3, A and B). Full blood count and renal and liver functions remained normal at the end of this treatment. After 1 month of follow-up the patient showed a mild flare-up on the neck, which disap-

peared after a single application of 0.5 cm of tacrolimus ointment.

Erythroderma is defined as an inflammatory skin disorder affecting >90% of the body surface.⁵ In 1908 Carl Leiner, a pediatrician from Vienna, first described a series of young infants with desquamative erythroderma, sparse hair, diarrhea, and failure to thrive⁶ Since then, several diseases have been associated with erythroderma presentation. In adults it may be either drug induced or secondary to preexisting pathologies.⁷

In newborns and infants only a few studies have been published, usually isolated case reports; it has an incidence of 0.11%^{8,9} and it can be the primary manifestation of several conditions.¹⁰ Because of this factor, the choice of initial treatment becomes difficult, especially in the neonatal period when the etiologic diagnosis of erythroderma is usually delayed.



Figure 3. (A and B) Front and back view of infant's body after finishing therapy.

Topical antifungal and corticosteroid preparations may be started if this uncommon presentation is related to seborrhoeic dermatitis diagnosis.^{8,9} Although these therapies are effective in most cases, there are potential side effects to consider. For this reason, steroids are used with reluctance on the face, axillae, and groin, all common sites for seborrhoeic dermatitis.

The pediatric population also is at increased risk for systemic absorption because of their high ratio of skin surface to body mass, especially in the presence of a wide diffusion of skin lesions as in the case of erythroderma. In our case, the diffusion of skin inflammation over the whole body and poor clinical response to both oral and topical corticosteroids led us to start tacrolimus therapy even though the infant was <2 months old.

To date, this is the first reported experience on this rare form of presentation. Data from studies in atopic dermatitis suggest minimal absorption,¹¹ even when application of 0.1 or 0.03% ointment has been performed to an extensive area of atopic eczema. In a few studies on Netherton's syndrome, to avoid the risk of systemic absorption and to reduce blood tacrolimus concentration, the treated surface area or application frequency¹² has been reduced or it has increased the

applications progressively and treated <15% of the body surface.¹³

Our case confirms these data and illustrates the safety of tacrolimus ointment 0.03% in an infant <2 months old and a complete efficacy even using tacrolimus ointment on limited (10 cm²) skin areas. Because few studies off label have been published regarding immunity-based skin disorders other than atopic dermatitis, we believe this report adds new knowledge to possible tacrolimus indications. Although topical tacrolimus may have a place for long-term use on sites where side effects from topical corticosteroids might develop quickly, the usefulness of either treatment in patients who have failed to respond adequately to topical corticosteroids is unclear also.¹⁴

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