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Need for Speed: Topical Roflumilast for Rapid Control of Seborrheic Dermatitis Flares

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ABSTRACT

Seborrheic dermatitis is a common chronic inflammatory skin condition historically treated with topical antifungals and anti-inflammatory agents. While topical corticosteroids are frequently used to quickly control severe disease or flare-ups, efficacy is limited. Topical roflumilast 0.3% foam is the most recent treatment for seborrheic dermatitis approved by the US Food and Drug Administration (FDA); however, its speed of action in controlling flares has not been fully explored. Herein, a case of severe seborrheic dermatitis with significant treatment response to topical roflumilast 0.3% cream, within 24 hours, is described, and the literature reviewed. This case suggests that topical roflumilast may work even faster than topical corticosteroids in controlling flares, and further investigation is warranted to thoroughly assess roflumilast's onset of action and leverage its clinical potential.

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INTRODUCTION

Seborrheic dermatitis is a chronic inflammatory skin condition with an estimated global prevalence of 4.38%.[1] The pathophysiology is not fully elucidated, though it involves lipid secretion by sebaceous glands, *Malassezia* proliferation, and a subsequent inflammatory response. Accordingly, primary treatment options include topical antifungals as well as steroidal and nonsteroidal anti-inflammatory agents. Topical roflumilast 0.3% foam, a phosphodiesterase-4 (PDE-4) inhibitor, was approved by the US Food and Drug Administration (FDA) in December 2023 for the treatment of seborrheic dermatitis in patients aged 9 years and older. Prior to its approval for seborrheic dermatitis, topical roflumilast 0.3% cream was approved for plaque psoriasis, and the oral formulation was approved for severe chronic obstructive pulmonary disease. Most recently, roflumilast 0.15% cream was also approved for atopic dermatitis.[2] Although the safety and efficacy of topical roflumilast for seborrheic dermatitis have been demonstrated in two clinical trials, its onset of action and role in managing active flares remain unclear. Our case documents the rapid improvement in clinical appearance and symptoms after one day of twice-daily treatment with topical roflumilast 0.3% cream in a patient with severe seborrheic dermatitis.

CASE HISTORY

A 25-year-old female with no significant past medical history was urgently referred for rapid escalation of a facial rash associated with significant flaking and itching, believed to be contact dermatitis by the referring physician. The patient reported significant worsening over the past 24 hours after using a new facial wash; however, in the past experienced less severe, though similar, eruptions managed with triamcinolone 0.1% cream with some success. Physical exam was notable for broad white to faint pink thin, scaly petaloid plaques extending from the nasolabial folds to the forehead, glabella, bilateral cheeks, and chin with some peripheral hyperpigmentation. The patient was provided with samples of roflumilast 0.3% cream to be used twice daily, to then be followed by tacrolimus 0.1% topical ointment once daily, as well as pulse fluconazole 300 mg once weekly for 3 weeks. However, after one day of roflumilast use alone, the patient experienced significant improvement in scaling, erythema, and itch (Figure 1). The patient did not use tacrolimus and fluconazole and continues to use roflumilast 0.3% cream as needed.

FIGURE 1. (A) Initial presentation of the patient's seborrheic dermatitis prior to initiation of roflumilast 0.3% topical cream, (B) and images after 1 day of twice-daily treatment with roflumilast 0.3% topical cream.

DISCUSSION

While there are a range of treatment options for seborrheic dermatitis, most are off-label, limiting the data supporting their use. Common treatments include topical antifungals, topical corticosteroids, and topical calcineurin inhibitors. Topical antifungals are postulated to function by reducing *Malassezia* burden and the consequent inflammatory response, though azole antifungals also have known anti-inflammatory effects. Antifungals commonly used in seborrheic dermatitis include topical azoles, ciclopirox, and topical terbinafine.[3] Low-to-mild potency topical corticosteroids, including hydrocortisone, betamethasone dipropionate, and desonide, are also effective in clearing scale, erythema, and pruritus both alongside antifungals and when used alone. However, prolonged use of topical corticosteroids, especially on the face, is limited by their side effects, which include telangiectasias and atrophy. Topical calcineurin inhibitors, including tacrolimus and pimecrolimus, which are FDA-approved for atopic dermatitis, have also proven to be effective and comparable to topical steroids in treating seborrheic dermatitis.[3,4] Compared with topical corticosteroids, they have the important benefit of sparing patients from long-term side effects and thus can be safely used on the face and neck even for longer periods of time.

PDE-4 inhibitors are another, relatively newer, non-steroidal treatment option for inflammatory skin disease, including seborrheic dermatitis. The exact mechanism of PDE-4 inhibitors in seborrheic dermatitis is not fully understood. It is known that PDE-4 inhibition leads to increased levels of cyclic adenosine monophosphate (cAMP), a secondary messenger that triggers protein kinase A (PKA), which ultimately leads to suppression of pro-inflammatory mediators and production of anti-inflammatory mediators.[5]

The efficacy of PDE-4 inhibitors was initially demonstrated in smaller studies evaluating off-label use of crisaborole and apremilast for the treatment of seborrheic dermatitis. Most recently, roflumilast, which is between 25 and 300-fold greater in potency than crisaborole and apremilast, was approved for seborrheic dermatitis.[6] In a phase 2A clinical trial comparing once-daily roflumilast 0.3% foam to vehicle in adults with seborrheic dermatitis, 74% of roflumilast-treated patients achieved Investigator Global Assessment (IGA) success compared with 41% in the vehicle-treated group at 8 weeks (P<0.001).[7] In addition to clinical appearance, this study also observed a statistically significant improvement in itch, based on improvements in Worst Itch Numeric Rating Scale (WI-NRS) score. Another important finding was the low rate of adverse events associated with roflumilast over the 8-week study period. In particular, there was an extremely low rate of application site pain, which occurred in only two of 154 roflumilast-treated patients.[7] This is especially pertinent in the context of the other frequently used treatment options, such as topical calcineurin inhibitors, which have been associated with high rates of local tolerability issues. One study evaluating topical calcineurin inhibitors found that 47% and 37% of patients experienced burning and pruritus, respectively.[8]

Following the phase 2 clinical trial, a larger phase 3 clinical trial, which included adolescents in addition to adults, showed similar results in efficacy and safety, further providing support for topical roflumilast as a reliable treatment option for seborrheic dermatitis across a wide age range of patients.[9] An additional finding in the phase 3 clinical trial was that roflumilast-treated patients had a significant reduction in WI-NRS score within 48 hours after the first application.[9] While a fast reduction in itch was demonstrated in this clinical trial, our case is unique in that it demonstrates an unexpected, rapid speed at which topical roflumilast can impact both clinical signs and symptoms, negating the need for other therapies. Improvement in seborrheic dermatitis with roflumilast in as little as 24 hours has not yet been reported in the literature. This is important because practitioners frequently turn to topical corticosteroids to efficiently and expeditiously control seborrheic dermatitis flare-ups. However, this case suggests that topical roflumilast may work even faster than topical corticosteroids in regard to the onset of action and controlling seborrheic dermatitis flare-ups. Furthermore, topical roflumilast has the added benefit of limited adverse effects when used up to 8 weeks, with more studies underway to assess longer-term adverse effects. More research is needed to fully assess the onset of action and capitalize clinically on this finding.

DISCLOSURES

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