Off-Label Drug Uses

Oxymetazoline (Topical): Rosacea

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This *Hospital Pharmacy* feature is extracted from *Off-Label Drug Facts*, a publication available from Wolters Kluwer Health. *Off-Label Drug Facts* is a practitioner-oriented resource for information about specific drug uses that are unapproved by the US Food and Drug Administration. This new guide to the literature enables the health care professional or clinician to quickly identify published studies on off-label uses and determine if a specific use is rational in a patient care scenario. References direct the reader to the full literature for more comprehensive information before patient care decisions are made. Direct questions or comments regarding *Off-Label Drug Uses* to jgeneral@kumc.edu.

BACKGROUND

Rosacea, a chronic skin disorder of the central face, is characterized by symmetrical facial flushing, erythema, and edema often accompanied by acne (papular or pustular). Although the exact cause is not known, it has been suggested to be of vascular origin; more recent data have indicated an exacerbated immune response, possibly caused by bacteria or an overproduction of inflammatory proteins.¹ Traditional therapy has centered on reducing symptoms and facial redness through the use of oral tetracyclines and/or topical metronidazole, which is effective in the majority of cases. However, in patients who do not respond or who are unable to tolerate tetracyclines, other oral antibiotics have been tried (eg, macrolides).^{2,3} The use of vasoactive drugs, including topical oxymetazoline, may be beneficial for symptoms of flushing and erythema associated with rosacea.

PATIENT POPULATION

Adult patients (age range, 55 to 70 years) with acne rosacea accompanied by symptoms of erythema and flushing.

DOSAGE AND DURATION

Intranasal oxymetazoline 0.05% solution applied topically once daily to affected facial areas for up to 17 months.

RESULTS

The topical use of oxymetazoline 0.05% solution in the management of rosacea has been primarily

limited to data from case series involving fewer than 10 patients and demonstrating sustained improvements in both erythema and flushing. Although oxymetazoline is not recognized in national guidelines, an international consensus statement recognizes the possible therapeutic role of oxymetazoline in the management of rosacea, despite the limited evidence.

Guidelines

American Acne and Rosacea Society

The American Acne and Rosacea guidelines provide an overview of the fundamental issues associated with the disease and outline the pharmacological and behavioral management. The discussion of pharmacological management is provided as a review of all therapies and does not suggest a tiered approach to therapy. Included in this guideline are the 3 US Food and Drug Administration (FDA)–approved topical products, sulfacetamide/sulfur, azelaic acid, and metronidazole. Other topical agents addressed have varying levels of evidence, including calcineurin inhibitors (eg, tacrolimus and pimecrolimus), benzoyl peroxide/clindamycin, and retinoids. Topical permethrin has also been noted as effective in case reports of refractory rosacea that were related to demodex folliculitis. Oral anti-inflammatory agents include low-dose controlled release doxycycline, which is FDA approved. Doses greater than 50 mg of oral doxycycline are considered off-label, as is the use of other oral antibiotics (eg, tetracyclines, minocycline, and oral isotretinoin).

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It should be noted that there has been increased concern regarding the promotion of antibiotic resistance with the use of antibiotics in the management of rosacea. Thus, these guidelines recommend that antibiotic use be limited and directed at a specific pathogen when present. Oral antibiotics should be reserved for cases that are poorly responsive or refractory to topical or anti-inflammatory therapies.

Topical oxymetazoline is not mentioned in these guidelines.⁴

International Consensus (Rosacea International Expert Group)

This international consensus statement notes that oral tetracyclines (tetracycline, doxycycline, and minocycline) and topical agents are the mainstay of rosacea treatment, with the 3 primary topical drugs having FDA approval (eg, azelaic acid, metronidazole, and sodium sulfacetamide/sulphur). Other topical agents with noted efficacy include antibiotics (eg, erythromycin, clindamycin) and retinoids (eg, adapalene, tretinoin). This guideline also notes that other topical agents have been evaluated but are supported by variable evidence in the treatment of rosacea, including permethrin, tacrolimus, pimecrolimus, and oxymetazoline. Oxymetazoline has resulted in improvement in erythema and erythematous flares with relief in stinging and burning.

For symptoms of periodic flushing, vasoactive drugs are also recommended, including topical oxymetazoline and oral nadolol, ondansetron, or clonidine, despite limited evidence. The FDA-approved topical therapies are suggested as first-line treatment for persistent erythema or rosacea characterized by papules and pustules. The addition of oral antibiotics may be warranted. For nodular or plaque type rosacea, first-line therapy consists of oral antibiotics, oral isotretinoin, intralesional corticosteroids, or combined topical agents with low-dose doxycycline. In refractory cases, the addition of high-dose antibiotics may be combined with topical agents. Topical antibiotics (fusidic acid and metronidazole) and oral antibiotics (doxycycline) are recommended for ocular symptoms. Topical maintenance therapy may be required to maintain remissions after relapses with systemic therapy.⁵

Case Reports

In 2 case reports of adults (aged 55 and 70 years) with a history of refractory erythema and flushing related to rosacea for several years, topical oxymetazoline 0.1% solution was applied once daily to

affected facial areas. A decrease in facial erythema was noted within 1 hour after application, and a dramatic improvement was observed within 2 to 3 hours. The effects were sustained throughout the day. Continued use for several months was associated with marked improvement in erythema without episodes of flushing or flares. Both patients experienced sustained effects with prolonged use of 8 and 17 months.⁶

SAFETY

This is a limited safety profile. Refer to package labeling for complete prescribing information (eg, warnings/precautions, adverse reactions, drug interactions).

Concerns with the use of intranasal alpha-agonist decongestants include the loss of efficacy with prolonged use (tachyphylaxis) and possible rebound vasodilation, although these effects have not occurred in the limited number of patients studied. No stinging or burning was noted with application.⁶

THERAPY CONSIDERATIONS

Published data regarding the use of topical oxymetazoline to treat the flushing and erythema associated with rosacea are limited, but they suggest improvements in these symptoms with chronic use. Larger controlled trials are needed to establish the role of this agent in therapy.

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