CASE SERIES

3-Step Topical Regimen for Rosacea

Zein Obagi, MD
Rachael Eckel, MD

ABSTRACT

Background and Objective:

Marked by flushing, blushing, telangiectasias, erythema and papulopustular eruptions, rosacea can cause patients irritation, discomfort and embarrassment. Results offered by available treatments are often modest, transient and/or fraught with side effects. In a recent case series, a 3-step regimen including a new normalizing serum that incorporates antioxidants, exfoliants and other ingredients showed the ability to soothe and reduce many rosacea symptoms without adverse events.

Methods:

The principal investigator enrolled 25 patients with mild to moderate rosacea diagnosed by a board-certified dermatologist. At baseline and follow-up visits, the investigator assessed each patient's erythema, edema, dryness and telangiectasias. Patients also graded their own facial stinging, burning, flushing and dryness, and underwent standardized photography at each visit. For 6 weeks, patients used a patented facial cleanser and the normalizing serum twice daily (AM and PM) and a sun protection factor (SPF) 50 sunscreen (AM only).

Results:

The regimen led to statistically significant improvement in erythema and telangiectasias at various time points, and in lesion counts at Week 6. Subjective measures that also showed statistically significant improvement included flushing, rosacea severity, redness and susceptibility to environmental factors.

Conclusion:

The 3-step regimen appears effective in reducing symptoms of mild to moderate rosacea.

INTRODUCTION

Despite recent advances in unraveling the pathophysiology of rosacea, this condition remains incompletely understood,[1] and results of commonly used treatments are often modest, transient and/or accompanied by unwanted side effects.

Although rosacea can affect all races, it occurs most frequently in fair-skinned people of Northern and Eastern European descent.[2] The National Rosacea Society estimates that 16 million Americans suffer from rosacea, with the highest prevalence occurring in New England states, which post rates above 10%.[3]

Usually occurring after age 30, and more commonly in women than men, rosacea is a highly heterogeneous but well-recognized skin disease typically characterized by centrofacial erythema with or without pustular eruptions.[4] Additional symptoms can include burning, stinging, edema, dryness/scaling, ocular manifestations and, over time, vascular and phymatous changes.[5]

The array of treatments used for rosacea ranges from oral and topical medications (many of which are available by prescription only) to procedures including laser therapy, photodynamic therapy and botulinum toxin injections. However, these treatments often fail to provide adequate and persistent improvement.[6] The American Acne & Rosacea Society says that, in a climate in which relatively few treatments have robust randomized controlled trials (RCTs) supporting their use, clinicians must combine the best clinical information available with their best clinical judgment, sometimes looking beyond U.S. Food and Drug Administration (FDA)-approved indications and large-scale RCTs.[7]

A recent case series shows that a 3-step twice-daily regimen can provide statistically significant improvements in rosacea symptoms including telangiectasias, erythema, lesion counts and dryness, while reducing susceptibility to environmental triggers. The regimen proved safe and well tolerated.

METHODS

The principal investigator enrolled 25 patients with mild to severe rosacea diagnosed by a board-certified dermatologist. At the baseline visit, the dermatologist noted areas of rosacea and used a 6-point scale (0 = none, 0.5 = barely perceptible, 1 = mild, 2 = moderate, 3 = marked, 4 = severe) to evaluate erythema, edema and dryness. The physician used a similar 5-point scale to evaluate telangiectasias. Patients also used a 5-point scale (0 = none; 4 = severe) to grade their own facial stinging, burning, flushing and dryness.

Additionally, patients underwent standardized digital photography with a commercially available camera system (VISIA-CR, Canfield Scientific, Inc., Fairfield, NJ) at baseline and at follow-up visits occurring at the end of weeks 2, 4 and 6. At the final study visit, patients answered a questionnaire about their experience and skin condition.

The study regimen included a patented cleanser, treatment serum and sunscreen. At the baseline visit, the physician instructed patients to use the study materials for 6 weeks as follows:

1. AM and PM: Wash entire face with cleanser for 60 seconds. Rinse with cool water. Key cleanser ingredients include

3-STEP Topical Regimen for Rosacea

Zein Obagi, MD
Rachael Eckel, MD

salicylic acid (for chemical exfoliation), various antioxidants (vitamin E, Melaleuca alternifolia [tea tree] leaf oil and Spiraea ulmaria [meadowsweet] extract).

2. AM and PM: Apply 2 to 3 pumps of treatment serum to the entire face – 2 pumps for smaller faces, 3 for larger faces (e.g., males). Allow to dry fully for 1 to 3 minutes. With a pH of approximately 6.0, the serum incorporates botanical ingredients (Brassica oleracea italica [broccoli] extract, Marrubium vulgare [horehound] meristem cell culture and Leontopodium alpinum [edelweiss] meristem cell culture) that provide antioxidant and anti-inflammatory properties.[8-10] Additional ingredients include palmitoyl glycine (believed to encourage healthy vascular function and optimize microcirculation); farnesyl acetate, farnesol, and panthenyl triacetate (believed to prevent excess sebum production and provide antimicrobial benefits); papain (an enzymatic exfoliator); hydrolyzed algin (to restore healthy cellular communication); and glycerin.

3. AM only: Apply SPF 50 sunscreen 15 minutes before sun exposure. Avoid excessive or prolonged sun exposure beyond daily routine exposure during the trial. Sunscreen consists of titanium dioxide, natural melanin, vitamin E and silicone.

STATISTICAL ANALYSIS

For all study parameters, investigators examined statistical significance for both [9]5% confidence ($p < 0.050$) and 90% confidence ($p < 0.[10]0$). For parameters involving facial lesion counts (papules, pustules and nodules), testing for differences between time periods was done using a one-way repeated measures analysis of variance (ANOVA) depending on whether normality and homogeneity of data variances were maintained.

For the remaining scoring parameters (erythema, edema, dryness, telangiectasias, subjective stinging, burning, flushing and dryness), researchers assessed differences between time periods by using a nonparametric Friedman test (ANOVA on ranks). For patient ratings of the condition and symptoms of their rosacea and its susceptibility to environmental factors, investigators used a Wilcoxon signed-rank test to calculate statistically significant differences from baseline.

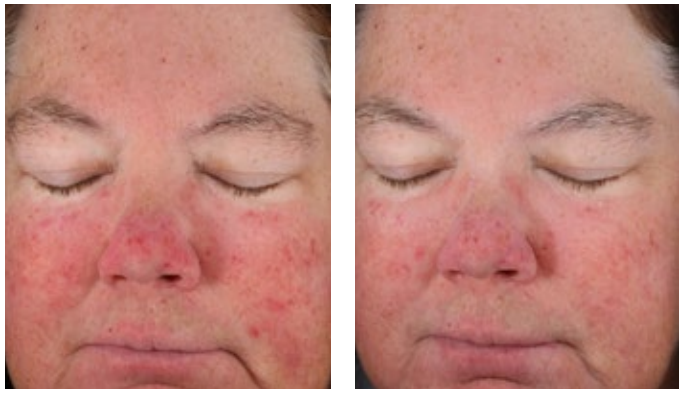
Regarding image analysis, investigators sent all patient photos to Canfield Scientific for "red area" analysis of the cheek, portions of the nose and portions of the periorbital regions. At each evaluation point, Canfield calculated scores for redness severity and fractional areas impacted by rosacea.

OBJECTIVE RESULTS

Ultimately, 22 patients (including 2 men) between the ages of 32 and 66 years completed the study, during which no adverse events occurred. The following objective parameters achieved significant improvements (at 95% and 90% confidence):

- Telangiectasias of the left medial cheek at 2 weeks, and the right medial cheek at 2 and 6 weeks
- Erythema of the right lateral cheek at 6 weeks, of the left medial forehead and left lateral cheek at 2 and 6 weeks, and of the right and left chin at 4 and 6 weeks
- Total lesion counts and inflammatory papule counts (mean: –4.1 for both) at Week 6

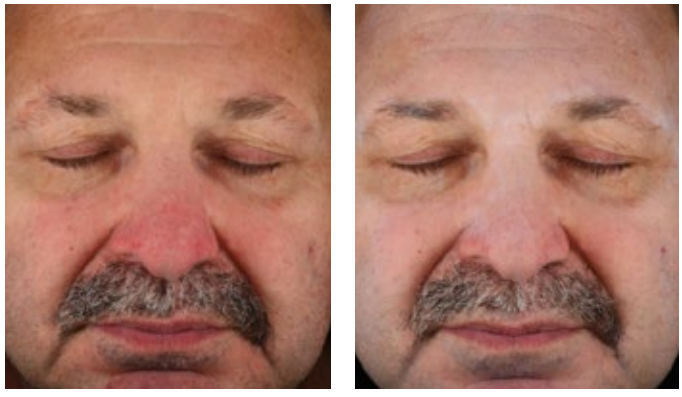
PATIENT 1



BASELINE 6 WEEKS

Female subject 007 baseline & 6 weeks after: Female subject at baseline and 6 weeks after treatment with the 3-step rosacea regimen.

PATIENT 2



BASELINE 6 WEEKS

Male subject 008 baseline & 6 weeks after: Male subject at baseline and 6 weeks after treatment with the 3-step rosacea regimen.

3-STEP Topical Regimen for Rosacea

Zein Obagi, MD
Rachael Eckel, MD

Statistically significant improvements at 90% confidence occurred in the following parameters:

- Erythema of the right medial forehead at 2 and 6 weeks, of the left medial cheeks and left chin at 2 weeks, the left lateral cheeks at 4 weeks, and the right medial forehead at 2 and 6 weeks
- Telangiectasias of the left medial cheek at 6 weeks

Among subjective measures, the test regimen achieved statistically significant improvements (at 95% and 90% confidence) in these parameters:

- Flushing at 2, 4 and 6 weeks
- Rosacea severity, redness and susceptibility to environmental factors at 6 weeks.

ANALYSIS OF SUBJECTIVE RESPONSES

Patient ratings revealed a statistically significant reduction in overall rosacea severity – on a scale of 0 to 4, average patient rating fell from 1.82 at baseline to 1.50 at Week 6 ($p = 0.016$).

Additionally, significantly more patients agreed than disagreed that treatment had created visible improvement in skin texture, smoothness and dryness, and the appearance of redness and inflammation. Other outcome statements with which significantly more patients agreed included noticeable reductions in hypersensitivity (stinging, burning, flushing), the size/number of visible blood vessels, susceptibility to environmental or other triggers, and evenness of skin color.

Significantly more patients also agreed that their skin appeared and felt healthier, that its red and sensitive areas felt soothed and comforted, and that regular use of the treatment regimen improved their rosacea. Two-thirds of patients said they would likely continue using the treatment outside the study.

STUDY LIMITATIONS

Perhaps the study's most serious shortcoming was that its population included no patients with severe rosacea. Of the 22 who completed the study, 16 had mild rosacea, and 6 had moderate rosacea. Additionally, researchers relied largely on patient self-reporting of adherence behavior. However, investigators attempted to verify subjects' reporting by collecting all product containers at the study's conclusion. The 3-step regimen ultimately resulted in objective and subjective improvements in areas including redness, telangiectasias, lesion counts, dryness and susceptibility to environmental triggers.

REFERENCES

1. Steinhoff M, Schmelz M, Schauber J. Facial erythema of rosacea – aetiology, different pathophysiologies and treatment options. *Acta Derm Venereol.* 2016;96:579-586.
2. Tan J, Berg M. Rosacea: current state of epidemiology. J Am Acad Dermatol. 2013;69(6 Suppl 1):S27-S35.
3. National Rosacea Society. Where is rosacea worst? New map shows geographic prevalence. https://www.rosacea.org/press/where-rosacea-worst-new-map-shows-geographic-prevalence. Published September 4, 2013. Accessed March 31, 2017.
4. Del Rosso JQ, Thiboutot D, Gallo R, et al. Consensus recommendations from the *American Acne & Rosacea Society* on the management of rosacea, part 1: a status report on the disease state, general measures, and adjunctive skincare. Cutis. 2013;92:234-240.
5. Wilkin J, Dahl M, Detmar M, et al. Standard classification of rosacea: report of the National Rosacea Society Expert Committee on the classification and staging of rosacea. J Am Acad Dermatol. 2002;46:584-587.
6. Cardwell LA, Alinia H, Moradi Tuchayi S, Feldman SR. New developments in the treatment of rosacea – role of once-daily ivermectin cream. Clin Cosmet Investig Dermatol. 2016;9:71-7.
7. Del Rosso JQ, Thiboutot D, Gallo R, et al. Consensus recommendations from the American Acne & Rosacea Society on the management of rosacea, part 5: a guide on the management of rosacea. Cutis. 2014;93:134-138.
8. Hwang JH, Lim SB. Antioxidant and anti-inflammatory activities of broccoli florets in LPS-stimulated RAW 264.7 cells. Prev Nutr Food Sci. 2014;19(2):89-97.
9. Bouterfas K, Mehdadi Z, Elaoufi MM, Latreche A, Benchiha W. Antioxidant activity and total phenolic and flavonoids content variations of leaves extracts of white Horehound (Marrubium vulgare Linné) from three geographical origins. Ann Pharm Fr. 2016;74(6):453-462.
10. Dobner MJ, Sosa S, Schwaiger S, et al. Anti-inflammatory activity of Leontopodium alpinum and its constituents. Planta Med. 2004;70(6):502-8.