The Efficacy of Tretinoin 0.025% Cream, Oral Minocycline, and a Skin Care Regimen in the Treatment of Acne

Zoe Diana Draelos, MD

Acne is one of the most common conditions treated in a general dermatology practice. Moderate to severe acne is typically treated with a topical agent for the comedonal component and an oral antibiotic for the inflammatory component. Topical retinoids, such as tretinoin, are well-established, effective agents that reduce existing comedones and prevent formation of microcomedones. Retinoids can also function to reduce inflammation by affecting IL-1α[1] Combining tretinoin with minocycline provides antibacterial and anti-inflammatory effects to complement the topical effect of retinoid.[2]

The treatment of acne with effective agents is only one part of the equation. The other important aspect for successful acne treatment is patient compliance. Without proper application or ingestion of the medications, no improvement can be expected. A novel approach to improved compliance is the combination of aesthetically pleasing topical skin care products and prescription acne therapy. Thus, the drying effects of tretinoin can be offset with well-formulated, complementary cleansers and moisturizers.[3] In addition, compliance with oral medication can be enhanced through skin care serums and face masks that can visibly improve acne quickly.

This study was conceived to evaluate the efficacy of tretinoin 0.025% cream in combination with 50 mg minocycline pellet-filled capsules and to also explore the compliance aspects of skin care products in acne therapy.

Method

This was a single-center, 40-subject, open-label study enrolling suitable male and female subjects 14 years and older who had signed an institutional review board–approved consent form. The subjects had moderate to severe acne defined as a minimum of 15 inflammatory lesions, 25 noninflammatory lesions, and less than 3 cysts. The subjects enrolled were nonlactating and took a pregnancy test to confirm they were not pregnant.

At the baseline visit, the dermatologist investigator performed a relevant medical history and dermatologic examination of the subjects. Subjects who were found to qualify for the study by the investigator returned for follow-up evaluations at weeks 4, 8, and 12. The investigator performed inflammatory and noninflammatory lesion counts and assessed subjects' acne improvement in terms of erythema, inflammation, dryness, stinging, and global impression on an ordinal 6-point scale (0=none; 1=minimal; 2=mild; 3=moderate; 4=moderately severe; and 5=severe). The subjects were also asked to assess their improvement on the same ordinal scale in terms of redness, peeling, roughness, stinging, itching, and acne severity. Clinical digital photography in combination with a 3-point head restraint assessed results at baseline and at weeks 4, 8, and 12.

All subjects were provided tretinoin 0.025% cream for nightly application and 50 mg oral minocycline pellet-filled capsules for twice-daily ingestion for the duration of the 12-week study. The prescription therapies were dispensed and packaged with complementary skin care products that replaced subjects' self-selected products. The tretinoin 0.025% cream was dispensed with a cleanser and moisturizer for twice-daily use. The 50 mg oral minocycline pellet-filled capsules were dispensed with a facial wipe and serum for use as needed, along with a once-weekly facial mask.

Results

Thirty-four of the 40 subjects completed the 12-week efficacy study. The 6 subjects who withdrew did not have any tolerability issues associated with the skin care products. Of those six, 4 withdrew due to an upset stomach associated with the oral minocycline. One subject

Dr. Draelos is Consultant and Researcher, Dermatology Consulting Services, High Point, North Carolina.

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Correspondence: Zoe Diana Draelos, MD (zdraelos@northstate.net).

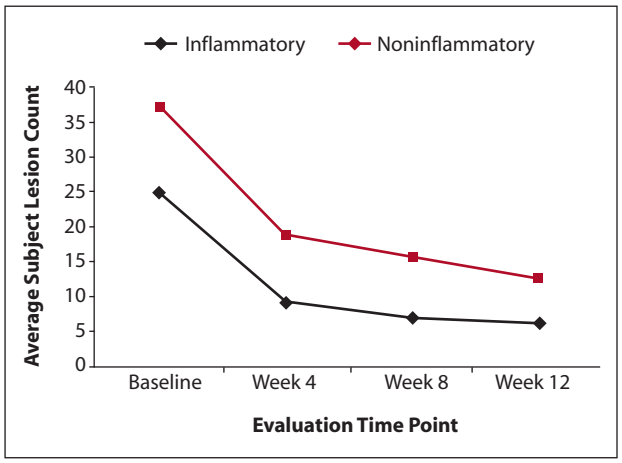

Figure 1. Improvement in inflammatory and noninflammatory lesion counts was statistically significant at all time points evaluated.

could not be contacted following enrollment in the study, and one subject became pregnant during the first 2 weeks of the study even though she had a negative pregnancy test at baseline. She was withdrawn by the dermatologist investigator.

There was statistically significant improvement ($P<.001$) assessed by the investigator in both inflammatory and noninflammatory lesion counts at weeks 4, 8, and 12 as compared with baseline (Figure 1). The average lesion count at baseline was 25 inflammatory papules and 37 noninflammatory lesions, which decreased after 12 weeks of treatment to an average of 6 inflammatory papules and 12 noninflammatory lesions (Figures 2 and 3). In addition, the investigator noted a statistically significant decrease ($P<.001$) in acne-induced erythema and inflammation beginning at week 4 and continuing into weeks 8 and 12. No change in dryness from baseline was observed, most likely due to use of the specially formulated ancillary skin care products. Stinging increased slightly at week 4 as compared with baseline ($P=.018$); however, the data were limited because only 5 of 36 subjects reported stinging. The increase in stinging was not noted at weeks 8 and 12. Overall, the investigator assessed acne improvement as statistically significant ($P<.001$) at weeks 4, 8, and 12.

There was no subject-assessed increase in redness, peeling, roughness, stinging, or itching at week 4. These side effects are sometimes associated with the use of topical tretinoin; however, they were not observed in this study due to the use of specially designed skin care products to decrease retinoid-induced dermatitis. Facial roughness improved at week 8 ($P=.031$) with continued improvement through week 12 ($P=.004$). Facial itching decreased at week 12 from baseline ($P=.008$) due to acne improvement. Finally, the subjects noted a statistically significant improvement ($P<.001$) in acne severity at weeks 4, 8, and 12.

Discussion

This research examined the effect of tretinoin 0.025% cream and 50 mg oral minocycline pellet-filled capsules in the treatment of moderate to severe acne. The beneficial combination of topical retinoids and oral antibiotics for enhanced acne therapy was previously established by Leyden et al.[4] A study comparing oral minocycline combined with retinoid tazarotene 0.1% gel with tazarotene 0.1% gel alone found both regimens effective in reducing moderately severe to severe acne.[5] After 12 weeks of therapy, there was a 54% decrease in inflammatory lesion counts with tazarotene 0.1% gel alone and a 66% decrease with use of minocycline and tazarotene 0.1% gel combined. The researchers recommended that oral antibiotics in combination with topical retinoids could be used to control acne, but once improvement occurred, topical retinoids could be used alone for maintenance therapy. This regimen reduced the chances of antibiotic resistance and side effects. These findings were further confirmed in a study evaluating the efficacy of doxycycline alone and in combination with adapalene 0.1% gel.[6] The combination was found to be statistically more effective than the adapalene 0.1% gel alone.

Figure Not Available Online

Figure 2. A male patient before (A) and 12 weeks posttreatment with topical tretinoin 0.025% cream, 50 mg oral minocycline pellet-filled capsules, and a skin care regimen (B).

Figure 3. A female patient before (A) and 12 weeks posttreatment with topical tretinoin 0.025% cream, 50 mg oral minocycline pellet-filled capsules, and a skin care regimen (B).

This study in this article examined the combination of 50 mg oral minocycline pellet-filled capsules and tretinoin 0.025% cream to determine if the combination of prescription therapy with a skin care regimen enhanced tolerability and compliance. The study was unique in that it demonstrated acne improvement not only in terms of inflammatory and noninflammatory lesion counts, but also improvement in skin attributes. The supplemental skin care regimen consisted of cleansers, moisturizers, and skin conditioning products designed to prevent retinoid-induced dermatitis, enhance compliance, and improve the efficacy of the prescription medications. The cleansers in the regimen were a liquid face wash and individually packaged facial wipes. The liquid face wash contained a syndet surfactant and was designed for morning and evening use at home. The facial wipe was designed to use as needed for quick cleansing during school or after sports activities. The facial wipe combined water-based cleansing with the humectants glycerin, sodium pyrrolidone carbonic acid, and panthenol to prevent the postcleansing dryness common in patients using topical retinoids.

The moisturizers included a twice-daily facial moisturizer and a calming serum for use as needed. The facial moisturizer contained the emollient cetearyl alcohol to smooth desquamating skin scales produced by retinoid use and dimethicone to function as an oil-free occlusive to trap water within the skin. In addition, the moisturizer contained glycerin to attract water to the dehydrated skin surface from the viable epidermis. Aloe juice, bisabolol, and green tea extract were added as botanical anti-inflammatories to minimize the redness associated with the use of topical retinoids and the erythema from the active acne lesions. For subjects with facial inflammation, use of the calming serum was recommended to decrease erythema. The calming serum contained minimal moisturizing properties appropriate for those with oily skin and focused on the use of bisabolol, silymarin, and green tea as anti-inflammatories. It contained a small amount of the humectant hyaluronic acid to draw water to the skin.

Finally, the skin care products included a once-weekly facial mask containing algae, the humectant glycerin, and the occlusive moisturizers dimethicone and cyclopentasiloxane. The facial mask was designed to moisturize dry skin when necessary.

The combination of the skin care products with 50 mg oral minocycline pellet-filled capsules and tretinoin 0.025% cream yielded excellent acne improvement in subjects with moderate to severe acne after 12 weeks of use, with statistically significant results observed after 4 weeks. The addition of the skin care regimen reduced side effects of redness, peeling, skin roughness, stinging, and burning. This study demonstrates the value of including complementary skin care products with prescription therapy.

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