

Adapalene 0.1% gel has low skin irritation potential even when applied immediately after washing

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Summary

The purpose of this study was to evaluate the difference, if any, in facial skin tolerance of adapalene 0.1% gel applied immediately after washing, compared to delayed application as recommended for the other topical retinoids: tretinoin and isotretinoin. Twenty-five acne patients with mild to moderate acne vulgaris were included in this intra individual randomized comparison study where adapalene 0.1% gel was applied immediately after washing on one half of the face and 20–30 min after washing on the contralateral half-face, for 22 consecutive days.

No difference between the two regimens was detected by the investigator or by 21 of the 22 patients who completed the study. It was concluded that application of adapalene gel 0.1% is well tolerated even when applied immediately after washing.

Adapalene is a recently introduced, naphthoic acid der-ivative, retinoid agonist proved safe and effective in the topical treatment of acne vulgaris. Previous studies^{1–5} demonstrated good skin tolerance to adapalene 0.1% gel compared to various tretinoin formulations using a standardized protocol of 21-day semi occlusive patch assay and intraindividual, bilateral, paired comparison studies in acne patients. Additional clinical information⁶ confirmed the effectiveness and good tolerance of adapalene 0.1% gel during routine usage by acne patients. One of the complications of first generation retinoid therapies (tretinoin and isotretinoin) is the thinning of the stratum corneum leading to tretinoin-induced irritant dermatitis. This side-effect has caused physicians to impose unusual dosage regimens on their patients in an attempt to alleviate this irritation.^{1,7,8}

Dermatologists commonly recommend patients not to apply topical tretinoin or isotretinoin immediately after washing to help minimize the risk of skin irritation. Adapalene, although possessing a retinoid pharmacological profile, does not commonly induce 'tretinoin dermatitis' and therefore does not require complicated dosage regimens to improve its skin tolerance. In this study, our objective was to confirm that adapalene 0.1% gel can be applied immediately after washing without compromising skin tolerability.

Subjects and methods

Before initiating the study, the protocol was approved by an independent ethics committee and written informed consent was obtained from each subject. Subjects were not to have used interfering systemic therapy that could affect the results (e.g. anti-inflammatory drugs or retinoids). Twenty-five subjects, 18 women and 7 men, diagnosed with mild to moderate acne vulgaris and having skin phototypes I through III, were enrolled in the study. Twenty-two completed the study. Their age ranged from 13 to 39 (mean \pm SD = 19.4 \pm 6.93). The tested product, adapalene 0.1% gel (Differin[®] Gel, Galderma Laboratories Inc.) was randomly applied in the quantity of 0.5 mg immediately after washing to one side of the face, and to the opposite side of the face 20–30 min after washing. The test material was applied by the patients themselves using the tip of one finger. Washing was effected in a standardized manner with Cetaphil[®] Gentle Cleansing Bar and warm tap water and the face then rinsed and patted dry with a towel. In order to maintain consistency throughout the study, each patient was also to use Cetaphil[®] Gentle Cleansing Bar for other washings of the face. No other topical medication, moisturizers, toners, perfumes or astringent products were allowed to be used on the face during the study. The patients were treated and evaluated daily at the investigation site for up to 15 days.

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Clinical assessment of dryness and erythema were made by the same investigator on both sides of the face prior to washing and application of adapalene 0.1% gel. Erythema and dryness scores were rated on a scale of 0–9. Patients were asked at every visit, following treatment applications, which side was less irritated, taking into account any or all of the following: stinging/burning, itching, dryness and erythema.

At the final visit, patients were also asked which application method they preferred.

Data Analysis

Erythema and dryness scores and preferences responses by patients were entered into a computer through a double-entry procedure with an edit and consistency check. Statistical analysis was performed using the Wilcoxon sign rank test for significant treatment differences between the two washing methods for erythema, dryness and irritation. The sign test was used to test subjects' preferences. All tests were two sided with $\alpha = 0.05$.

Results

Twenty-two patients completed the study. No subject discontinued the study due to dermatologically-related adverse events. The mean erythema score for both sides at baseline was 0.4.

The investigator assessment of erythema after 15 days of use resulted in a mean of 1.0 on the side where adapalene 0.1% gel was applied immediately after washing, and a mean of 0.86 on the delayed application post washing side (scale from 1 to 9, 9 being the most severe).

The mean dryness scores at baseline were 0.36 on the immediate application side and 0.28 on the delayed application side. The mean dryness scores at day 15 were 1.41 on the immediate application side and 1.32 on the delayed application side. Both sides exhibited a very slight increase in erythema and dryness at day 15; however, all of these scores can be categorized as 'mild' on the scale from 0 to 9.

There were no significant differences between sides in either erythema ($P = 0.375$) or dryness ($P = 0.180$). When the subjects were asked to differentiate between sides for overall irritation, there were 21 of the 22 who could not differentiate at day 15. There was no statistical difference in preference between the dosing regimens ($P = 0.84$).

Discussion

The irritation potential of tretinoin and isotretinoin^{7,8} is a limiting factor to its wide use and obliges the patient to follow unusual dosing regimens to avoid symptoms of 'tretinoin dermatitis.' Adapalene is a new type of retinoid which exhibits efficacy in acne similar to other topical retinoids, but which does not induce

Table 1 Self assessment of irritation with adapalene 0.1% gel: immediate vs. delayed application after washing (day 15) $n = 22$

Moderately less	0
Mildly less	0
Slightly less	0
Both sides equal	95.5%
Slightly more	4.5%
Mildly more	0
Moderately more	0
Dramatically more	0

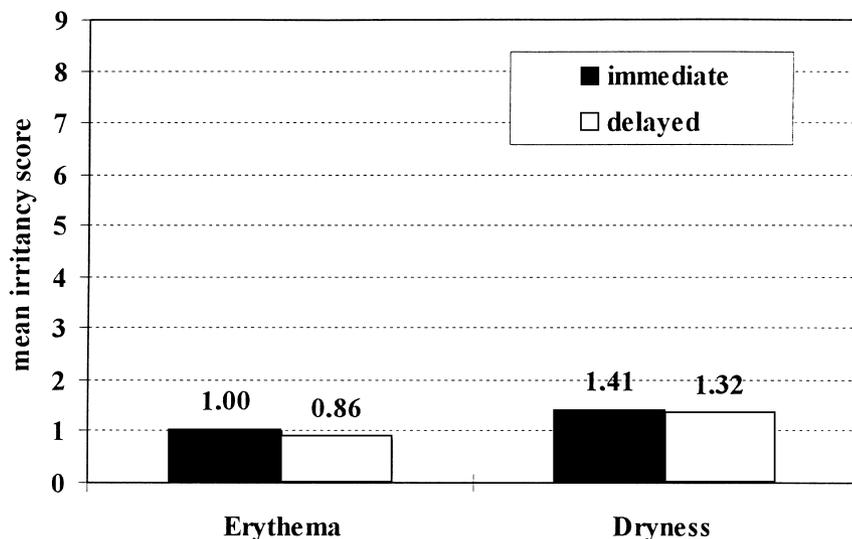


Figure 1. Mean irritancy scores of erythema and dryness for immediate and delayed application of adapalene 0.1% after washing.

tretinoin dermatitis. This study confirmed that the good skin tolerability of adapalene is not affected when applications are performed immediately after washing or delayed 20–30 min after washing. The good tolerability with either regimen was confirmed by the patients themselves who could not detect differences in irritation between the two sides of their face.

In conclusion, special treatment/washing regimens are not needed for adapalene 0.1% gel. The patient is free to apply the product as their lifestyle permits. Freedom from complicated treatment regimens may result in better patient compliance and greater treatment success.

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