Effects of Topical Salicylic Acid and Erythromycin on the Erythema Induced by UVB

TOPiKAL SALiSiLiK ASiT VE ERiTROMiSiNiN UVB TARAFINDAN OLUŞTURULAN ERiTEME ETKiLERi

Şenel YURTSEVER, MD,[a] Turna İLKNUR, MD,[a] Şebnem ÖZKAN, MD[a]

[a]Department of Dermatology, University of Dokuz Eylül, Faculty of Medicine, İZMİR

Abstract

Objective: Various studies have shown blocking or enhancing effects of topical agents on UVB penetration. Since the lesions in acne vulgaris are frequently localized on sun exposed areas, the interaction between topical agents used in acne treatment and UVB is important. In this study, our purpose was to examine interactions between UVB and salicylic acid gel, erytromycin gel which are frequently used in the topical treatment of acne vulgaris.

Material and Methods: In thirty-three volunteers, a phototest was performed to determine the minimal erythema dose (MED) and the test was repeated with gel forms of 2% salicylic acid, 2% and 4% erythromycin applied as a thin (0.1 cc/25 cm^2) and a thick (0.3 cc/25 cm^2) layer. After 24 hrs, the effects of each agent on MED was investigated.

Results: The topical application of thin and thick 2% salicylic acid gel significantly increased the MEDs. On the other hand, thin application of 2% and 4% erythromycin gel, and thick application of 4% erythromycin gel significantly decreased the MEDs.

Conclusion: It can be advised to use erythromycin gel carefully for acne lesions in day time due to its possible enhancing effects of erythema of UVB.

Key Words: UVB, erythromycin, salicylic acid

Özet

Amaç: Farklı çalışmalar UVB penetrasyonu üzerine topikal ajanların bloklayıcı yada artırıcı etkilerini göstermiştir. Akne vulgariste lezyonlar sıklıkla güneş gören alanlara lokalize olduğundan akne tedavisinde kullanılan ajanlar ve UVB arasındaki etkileşim önemlidir. Bu çalışmada, amacımız akne vulgarisin topikal tedavisinde sıklıkla kullanılan salisilik asit jel ve eritromisin jel ile UVB arasındaki etkileşimi incelemekti.

Gereç ve Yöntemler: Otuz üç gönüllüde minimal eritem dozu (MED) saptamak için fototest yapıldı ve test hepsi jel formunda olan ince (0.1 cc/25 cm^2) ve kalın (0.3 cc/25 cm^2) %2 salisilik asit, %2 ve %4 eritromisin ile tekrarlandı. 24 saat sonra, her bir ajanın MED'u üzerine etkileri araştırıldı.

Bulgular: İnce ve kalın %2 salisilik asit jel uygulanımı MED'unu önemli derecede arttırdı. Diğer taraftan, %2 ve %4 eritromisin jelin ince uygulanımı, ve %4 eritromisin jelin kalın uygulanımı MED'unu önemli derecede azalttı.

Sonuç: Sonuç olarak, UVB eritemi üzerine olası arttırıcı etkisinden dolayı eritromisin jelin gün içinde akne lezyonları için kullanımında dikkatli olunması önerilebilir.

Anahtar Kelimeler: UVB, eritromisin, salisilik asit

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Acne vulgaris is one of the most common skin diseases, seen primarily on the face, involving the sebaceous follicles. Various topical agents are used for the treatment of acne vulgaris, including salicylic acid and erythromycin.[1,2] UVB is primarily responsible for sunburn.[3] Some studies have shown blocking effects of topical agents on UVB penetration.[4-10] However, the use of some lubricants applied prior to UVB treatment enhances the penetration of UVB.[4,5,11]

The interaction between topical agents used in acne treatment and UVB can be important since the lesions in acne vulgaris are frequently localized on sun exposed areas. So, the blocking effects of topical agents on UVB penetration can be ignored, but the enhancing effects of topical agents on UVB penetration are important due to their increased sunburn risk. In this study, the effects of 2% sali-

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Yazışma Adresi/*Correspondence:* Şebnem ÖZKAN, MD
University of Dokuz Eylül, Faculty of Medicine
Department of Dermatology, İZMİR
sebnem.ozkan@deu.edu.tr

cylic acid, 2% and 4% erythromycin on UVB penetration was investigated in an in-vivo research.

Material and Methods

In this single-blind study, phototesting was performed on 33 volunteers to determine the minimal erythema dose (MED) for UVB. The study protocol and consent form was approved by the local ethics committee of Dokuz Eylül University Faculty of Medicine. Informed written consent has been obtained from all of the patients before the study. The patients were untanned and not taking any medication. Waldmann 8001 K (Waldmann Lichttecnik Gmbtt, Schwenningen, Germany) cabin was used for the light source of UVB.

The beginning doses of UVB phototesting were determined according to the skin types of the volunteers. The irradiated doses for UVB were up to 120 mJ/cm^2 for skin types I and II, 140 mJ/cm^2 for skin types III and IV and 200 mJ/cm^2 for skin type V.[12] MED values were determined by irradiating 4 cm^2 of uninvolved skin on the back of each patient at increments of 20 mJ/cm^2 in one row. In addition, seven parallel rows of skin were tested after application of different topical agents. The first rows were only irradiated by UVB without application of any topical agent to determine the MED. A thin (0.1 cc/25 cm^2) and a thick (0.3 cc/25 cm^2) layer of 2% salicylic acid (Salsil-2 gel®), a thin (0.1 cc/25 cm^2) and a thick (0.3 cc/25 cm^2) layer of 2% erythromycin (2% Aknilox gel®), a thin (0.1 cc/25 cm^2) and a thick (0.3 cc/25 cm^2) layer of 4% erythromycin (4% Aknilox gel®) all in gel forms were applied respectively to the adjacent parallel rows. In each patient, the rows of topical agent applications were exchanged. Then all the rows were irradiated with UVB at increments of 20 mJ/cm^2 immediately after the application of the agents without waiting. The results were evaluated after 24 hrs by a blinded investigator and MED values were determined (Figure 1). Wilcoxon signed ranks test was used for statistical analysis. Bonferroni-corrected significance level of $p<0.0033$ was considered to be statistically significant.

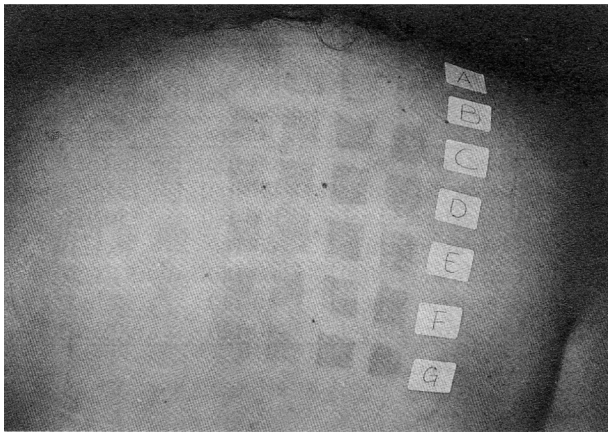

Figure 1. A patient seen 24 hrs. after photothest. (A: thin layer of 2% salicylic acid, B: thick layer of 2% salicylic acid, C: Pure UVB, D: Thin layer of 2% erythromycin, E: Thick layer of 2% erythromycin, F: Thin layer of 4% erythromycin, G: Thick layer of 4% erythromycin).

Results

The results of phototesting of all patients are shown in Table 1. The MED values detected after the application of thin and thick layers of 2% salicylic acid gel, thin layers of 2% and 4% erythromycin gel, thick layer of 4% erythromycin gel have been found significantly different from the MED values with pure UVB (Wilcoxon signed ranks test, $p<0.0033$). On the other hand, although the MED value after the application of thick layer of 2% erythromycin gel was found to be lower than that with pure UVB, the difference was not statistically significant (Wilcoxon signed ranks test, $p>0.0033$). These results indicated that MED values were increased by thin or thick application of 2% salicylic acid gel and decreased by thin and thick layers of 4% erythromycin gel and thin layer of 2% erythromycin gel. The highest MED values were detected with thick 2% salicylic acid gel and were followed by thin 2% salicylic acid gel. The lowest MED values were detected with thin 4% erythromycin gel and were followed by thick 4% erythromycin gel, thin 2% erythromycin gel and thick 2% erythromycin gel.

The differences between the MED values, statistically significant and not significant ones, are all shown in Table 2.

Table 1. MEDs of volunteers (n=33).

	MED (mJ/cm^2)	
Preparation	**Range**	**Mean±SD**
UVB without any agent	60-160	100.6±22.6
Thick 2% salicylic acid gel	100-180	155.8±24.4
Thin 2% salicylic acid gel	100-180	150.9±26.5
Thick 2% erythromycin gel	60-140	96.4±19.7
Thin 2% erythromycin gel	60-140	94.5±20.8
Thick 4% erythromycin gel	40-140	92.1±22.3
Thin 4% erythromycin gel	40-140	90.3±21.3

SD: Standard deviation

Table 2. Wilcoxon signed ranks test ($p<0.0033$ was considered to be significant).

Paired groups	Mean±SD	T	Significance
UVB-S2G	-50.3±25.1	-11.531	.000
UVB-TS2G	-55.2±26.0	-12.188	.000
UVB-E2G	6.1±9.3	3.730	.001
UVB-TE2G	4.2±8.3	2.935	.006
UVB-E4G	10.3±12.4	4.784	.000
UVB-TE4G	8.5±11.2	4.346	.000
S2G-TS2G	-4.8±12.3	-2.268	.030
E2G-TE2G	-1.8±5.3	-1.789	.083
E4G-TE4G	-1.8±7.7	-1.359	.184
S2G-E2G	56.4±23.7	13.666	.000
S2G-E4G	60.6±25.7	13.530	.000
E4G-E2G	-4.2±9.7	-2.514	.017
TS2G-TE2G	59.4±23.7	14.391	.000
TS2G-TE4G	63.6±25.2	14.491	.000
TE4G-TE2G	-4.2±8.3	-2.935	.006

SD: Standard deviation, **t:** value of 't', UVB: UVB without any agent, **S2G:** Thin 2% salicylic acid gel, **TS2G:** Thick 2% salicylic acid gel, **E2G:** Thin 2% erythromycin gel, **TE2G:** Thick 2% erythromycin gel, **E4G:** Thin 4% erythromycin gel, **TE4G:** Thick 4% erythromycin gel.

Discussion

Few investigations have been undertaken to determine the interaction between topical agents and UVB penetration. In these studies, topical agents used for psoriasis treatment have been usually chosen since they could be used in conjunction with UVB therapy. These studies showed the blocking effects of some topical agents such as calcipotriol, tar and anthralin when they were used prior to UVB.[6-9,13] Also some clinical and experimental studies have suggested that the use of some lubricants applied prior to UVB treatment may enhance the penetration of UVB to psoriatic plaques.[4,5,11]

Various topical agents can be used for the treatment of acne vulgaris which is frequently localized on sun exposed areas.[1,2] Sunlight involves ultraviolet irradiation that causes sunburn. UVB comprises radiation between the wavelengths 290 and 320 nm, primarily responsible for sunburn.[3] At this point, the blocking or enhancing effects of topical agents on UVB penetration which are used before exposure to sunlight should be considered.

The potential effects of salicylic acid on UVB penetration have been investigated in several in-vitro and in-vivo studies. In an in-vitro study, Kristensen et al.[4] found that 2% salicylic acid in non-light-absorbing cream showed some absorption in the UVB range 300-320 nm. Kornreich et al.[13] measured the absorption spectrum of 3% salicylic acid in petrolatum between the wavelengths of 260 to 400 nm with an ex-vivo technique. They found that 3% salicylic acid in petrolatum had substantial absorption in the UVB range 280-320 nm. Lebwohl et al.[5] studied transmission of UVB light through a clear filter coated with 6% salicylic acid ointment and they reported that salicylic acid ointment completely blocked transmission of UVB light.

Väänänen et al.[14] investigated the effects of topical 5% acetylsalicylic acid on UVB erythema using a standardized chamber application test technique before and after UVB irradiation in an in-vivo test. They showed that while topical 5% acetylsalicylic acid significantly inhibited UVB erythema when applied before irradiation, it had no effect when applied after irradiation. In an in-vivo test, Kristensen et al.[4] have studied the effect of the salicylic acid in non-UVB-absorbing cream on UVB transmission in two different test series. Salicylic acid was evaluated and compared in different concentrations (0.5, 1, 2, 5, 10%) before and after UVB. In the second series, the duration of the photoprotection afforded by salicylic acid was studied by applying different concentrations (2, 5, 10%) at different times prior to UVB. They found that sali-

cylic acid had a dose-dependent inhibiting influence on UVB when applied prior to irradiation, while it had no effect on UVB erythema when applied after UVB. Furthermore, they determined that salicylic acid inhibited erythema at all concentrations (2, 5, 10%), and the duration of photoprotection was found to be for at least 12 hrs and sometimes more than 24 hrs. Lebwohl et al.[5] reported that 6% salicylic acid ointment application prior to exposure to UVB can block UVB radiation and reduce its erythemogenicity in an in-vivo study. In another in-vivo study based on determining MED, Fetil et al.[10] showed blocking effects of 20% salicylic acid in petrolatum on UVB. Likewise, in our study the blocking effects of 2% salicylic acid in gel form on UVB penetration was determined when applied immediately before UVB.

In the literature, we could not find any study investigating the interaction between topical erythromycin and UVB. However, there were few studies dealing with topical tretinoin, azelaic acid, benzoyl peroxide, and adaphalene which can be used for acne vulgaris treatment. Kornreich et al.[13] measured the absorbance of tretinoin cream in different concentrations (0.025, 0.05, 0.1%) and 0.01% tretinoin gel between the wavelengths 260 to 400 nm, with an ex-vivo technique. They found that tretinoin had substantial absorption in the UVA range. In addition they determined that the absorbance of tretinoin preparations was concentration-dependent, with higher values for more concentrated formulations. Smit et al.[15] evaluated the MED for UVB on 0.05% tretinoin cream in an in-vivo study. They showed that topical treatment with 0.05% tretinoin cream for several days before UVB, did not change the MED. In another study, which was performed with similar protocol, showed that azelaic acid cream, benzoyl peroxide gel and adaphalene gel do not have enhancing effects on UVB erythema.[16]

In this study, we observed blocking effects of salicylic acid gel on UVB penetration when applied immediately before UVB, which increased with the application thickness. In addition, we observed statistically significant UVB penetration enhancing effects of thin layer of 2% erythromycin gel and thin and thick layer of 4% erythromycin gel when applied immediately before UVB. On the other hand, although the MED value after the application of thick layer of 2% erythromycin gel was lower than the MED of pure UVB, the difference between them was not statistically significant. This result may be both due to the higher absorbance capacity of the thick layer and to the lower UVB penetration in relation with the low concentration of effective ingredient in 2% erythromycin gel. Likewise, lower MED values were detected in thin erythromycin gel applications when compared with thick applications both in 2% and 4% concentrations. Present study has shown that erythromycin gel has enhancing effects on UVB when applied immediately before UVB. On the other hand, this study has not investigated the duration of this enhancing effect. In conclusion, 2% salicylic acid gel can be used on sun exposed areas in day time. However we suggest that one must be careful if erythromycin gel will be used on sun exposed areas immediately before sunlight in day time because of its possible enhancing effect on UVB erythema.

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