Journal of the Turkish Academy of Dermatology

Research

The Interaction of Topically Applied 2% Erythromycin, 4% Erythromycin and Tetracycline with Narrow Band UVB

Cemal Bilaç*, MD, Mustafa Turhan Şahin, MD, Aylin Türel Ermertcan, MD, Serap Öztürkcan, MD

Address:
Department of Dermatology, Medical Faculty of Celal Bayar University, Manisa, Turkey.
E-mail: cemalbilac@yahoo.com
* *Corresponding author*: Cemal BİLAÇ, MD, Celal Bayar Üniversitesi Tıp Fakültesi, Dermatoloji Anabilim Dalı 45010 Manisa, Turkey

Published:
J Turk Acad Dermatol 2008;**2 (1)**:jtad82101a
This article is available from: http://www.jtad.org/2008/1/jtad82101a.pdf
Key Words: erythromycin, interaction, narrow band UVB, phototherapy, tetracycline, topical antibiotics

Abstract

Objective: Various topical agents block UVB penetration when applied before UVB therapy. The effects of topically used erythromycin and tetracycline on narrow band UVB has not been considered yet. We investigated the effects of topically used erythromycin 2%, erythromycin 4% and tetracycline on the penetration amount of narrow band UVB.
Methods: In this study 32 patients without any photodermatose were included. We determined MED values with phototest. We investigated the effects of thin (0.1 cc/25 cm²) and thick (0.3 cc/25 cm²) layers of erythromycin 2%, erythromycin 4% gel forms and tetracycline ointment on MEDs.
Results: In this study comparing MEDs of narrow band UVB alone and with topical application of each agent, it was determined that MED values of thin and thick layers tetracycline were statistically significant ($p<0.005$). However we found that there was no significant change in MEDs of topical erythromycin 2% and erythromycin 4%, both in thin and thick layers ($p>0.005$).
Conclusion: Thin and thick layers of topical erythromycin 2% and 4% could not change MEDs significantly, whereas thin and thick layers of tetracycline increased MEDs significantly decreasing the effect of the narrow band UVB.

Introduction

It is known that topical agents cause sensitivity to sunlight or prevent the effects of sunlight in several studies. Moreover, it is mentioned that if the same agents are applied before the UVB treatment, they block the UVB penetration. However the effect of topically applied erythromycin and tetracycline to the penetration of narrow band UVB is not known yet. Macrolide antibacterials continue to be important therapeutic class of drugs with established efficacy in a variety of skin infections. Numerous studies have demonstrated the efficacy and safety of erythromycin for various infectious diseases [1]. Erythromycin is generally used for the treatment of non-methicillin resistant *Staphylococcus aureus* infection, acne, rosacea, *Lyme* disease, perioral dermatitis, anthrax, erysipeloid, chancroid, and lymphogranuloma venereum [2].

Tetracyclines are broad-spectrum bacteriostatic antimicrobial drugs, traditionally used in dermatology for the treatment of acne. Owing to their beneficial antiinflammatory properties, and the low risk and modest side effects associated with them, tetracyclines are also useful in treating several other skin diseases-either alone, or in combination regimens to reduce the intensity of the immunsuppressive effect [3].

Narrow band UVB therapy has been used successfully for the treatment of inflammatory and pigmentary skin disorders including atopic dermatitis, psoriasis, mycosis fungoides, polymorphous light eruption, and vitiligo [4].

In this study we aimed to investigate the effects of topically applied erythromycin and tetracycline on the penetration amount of narrow band UVB by the help of MED test.

Materials and Methods

In this study, phototesting was performed on 32 volunteers (15 females, 17 males) to determine the minimal erythema dose (MED) for narrow band UVB. In this study, patients who do not have any disease such as solar urticaria, polymorphic light eruption, hydroa vacciniforme, lupus erythematosus, xeroderma pigmentosum, actinic prurigo, photoallergic dermatitis, metabolic photodermatoses, porphyria; patients who do not have any lesion on their back causing difficulty to apply the test; patients who do not use any phototoxic and photoallergic drug; and finally volunteers older than 15-years-old were included. All participants were informed and consent forms were obtained.

Waldmann 7001K (Waldmann Lichttecnik Gmbtt, Schwenningen, Germany) cabin was used for the light source of narrow band UVB.

In this single-blind, controlled study the beginning doses of narrow band UVB phototesting were determined according to *Fitzpatrick* skin types. The irradiated doses for narrow band UVB were up to 0.50 J/cm² for skin type I and II, 0.90 J/cm² for skin types III and IV. MED values were determined by irradiating 4 cm² of uninvolved skin on the back of each patient at gradually enhancing doses (0.05 J/cm², 0.10 mj/cm², 0.20 J/cm², 0.30 J/cm², 0.40 J/cm², 0.50 J/cm² for skin types I and II, 0.10 J/cm², 0.20 J/cm², 0.30 J/cm², 0.50 J/cm², 0.70 J/cm², 0.90 J/cm² for skin types III and IV). In addition, seven parallel rows of skin were tested after application of different topical agents. The first rows were only irradiated by narrow band UVB without application off any topical agent to determine the MED. A thin (0.1 cc/25 cm²) and a thick (0.3 cc/25 cm²) layers of 2% erythromycin gel, a thin (0.1 cc/25 cm²) and a thick (0.3 cc/25 cm²) layers of 4% erythromycin gel, thin (0.1 cc/25 cm²) and a thick (0.3 cc/25 cm²) layers of tetracycline ointment were applied respectively to the adjacent parallel rows.

The results were evaluated after 24 hours by a blinded investigator and MED values were determined (**Figure 1**).

Figure 1. A patient seen 24 hours after phototest

Paired-Samples t test was used for statistical analysis of obtained results were statistically significant with *Bonferroni* correction ($p<0.005$).

Results

The results of phototesting of all patients with pure narrow band UVB, with the application of thin and thick layers of 2% erythromycin gel, 4% erythromycin gel and tetracycline ointment are shown in **Table 1**. The MED values detected after the application of thin and thick layers of 2% erythromycin gel, thin and thick layers of 4% erythromycin gel have not been found significantly different from the MED values after pure narrow band UVB (Paired-Samples t test, $p>0.005$). The MED values detected after the application of thin and thick layers of tetracycline ointment have been found significantly different from the MED values after pure narrow band UVB (Paired-Samples t test, $p<0.005$).

There was no statistically significant difference between the MED values of thin and thick applications of 2% erythromycin gel, 4% erythromycin gel and tetracycline ointment (Paired-Samples t test, $p>0.005$).

Between the MED values detected after the application of thin layer tetracycline oint-

Table 1. Minimal Erythema Doses (n=32)

Topical Agents	MED (J / cm²)	
	Range	Mean ± SD
Narrow band UVB	0,30 - 0,90	0,587 ± 0,193
2% Erythromycin thin	0,30 - 0,90	0,587 ± 0,182
2% Erythromycin thick	0,30 - 0,90	0,571 ± 0,159
4% Erythromycin thin	0,30 - 0,90	0,556 ± 0,170
4% Erythromycin thick	0,30 - 0,90	0,565 ± 0,177
Tetracycline thin	0,30 - 0,90	0,681 ± 0,197
Tetracycline thick	0,40 - 0,90	0,734 ± 0,197

Table 2. Results of the Paired - Samples t Test

Compared Groups	Mean ± SD	t	Significance
UVB–2% ER	0,000 ± 0,110	0,000	1,000
UVB–2% ERT	0,016 ± 0,134	0,656	0,516
UVB–4% ER	0,031 ± 0,151	1,169	0,251
UVB–4% ERT	0,022 ± 0,158	0,783	0,440
UVB–TC	- 0,090 ± 0,143	- 3,695	0,001
UVB–TCT	- 0,146 ± 0,156	- 5,307	0,000
2% ER–2% ERT	- 0,016 ± 0,767	1,153	0,258
4% ER–4% ERT	- 0,009 ± 0,039	- 1,359	0,184
TC–TCT	- 0,050 ± 0,084	- 3,570	0,001
2% ER–4% ER	0,031 ± 0,123	1,438	0,161
2% ER–TC	- 0.090 ± 0,134	- 3,950	0,000
4% ER–TC	- 0,125 ± 0,080	- 8,803	0,000
2% ERT–4% ERT	0,006 ± 0,091	0,387	0,701
2% ERT–TCT	- 0,162 ± 0,090	-10,135	0,000
4% ERT–TCT	- 0,168 ± 0,114	- 8,313	0,000

UVB: Narrow band Ultraviolet B; **2% ER:** 2% Erythromycin thin layer; **2% ERT:** 2% Erythromycin thick layer; **4% ER:** 4% Erythromycin thin layer; **4% ERT:** 4% Erythromycin thick layer; **TC:** Tetracycline thin layer; **TCT:** Tetracycline thick layer; **SD:** Standart deviation

ment and thin layer 2% erythromycin gel, thin layer tetracycline ointment and thin layer 4% erythromycin gel, thick layer tetracycline ointment and thick layer 2% erythromycin gel, thick layer tetracycline ointment and thick layer 4% erythromycin gel, thin layer and thick layers tetracycline ointment have been found significantly different (Paired-Samples t test, $p<0.005$).

"Paired-Samples t test" results of the all compared groups are shown in **Table 2**.

Discussion

Retinoids including tretinoin, isotretinoin, adapalene, and tazarotene, azelaic acid, benzoyl peroxide, salicylic acid, and antibiotics such as erythromycin, clindamycin, and tetracycline are major topical agents in treatment of acne vulgaris. The lesions in acne vulgaris are frequently localized on sun exposed areas such as face. Thus, the effecs of these topical agents on UVB penetration can be important since they are used on sunlight exposed areas [**5**].

After a thorough medline search, we came across few studies which were evaluating the interaction of topical agents used for acne treatment like benzoyl peroxide, azelaic acid, adapalene, tretinoin and tazarotene with ultraviolet [**5, 6, 7, 8, 9**], but we could not find any study investigating the interaction of topically applied erythromycin or tetracycline with ultraviolet.

In the study of *Çetiner* et al, the phototoxic effects of topically applied azelaic acid, benzoyl peroxide and adapalene on to the normal skin before UVB application were investigated. It was found that the application of these agents had no effect on UVB penetration. They suggested that no topical application should be done before UVB treatment according to the results of other studies [**5**].

Jeanmougin and *Civatte* investigated benzoyl peroxide phototoxicity by photoepidermotests after repeated applications. They found 10% benzoyl peroxide gel to be phototoxic in eight out of 18 subjects tested [**6**].

Smit et al. 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, had not changed the MED [**8**].

Hecker et al. showed that while thin application of 0.1% tazarotene gel immediately before phototherapy had no significant effect on MED, thick application of the gel increased MED values slightly. They also reported that pretreatment with 0.1% tazarotene gel 3 times per week for 2 weeks before UVB had significantly reduced the MED [**9**].

Fetil et al. evaluated the effects of topically applied calcipotriol, clobetasole-17-propionate and tretinoin on broad band UVB penetration. They found that thin and thick applications of three topical agents were reducing UVB penetration and increasing the MED values, so that they should not be used before phototherapy [**10**].

In our study, we investigated the interaction of topically applied 2% erythromycin, 4% erythromycin and tetracycline with narrow band UVB. We determined that thin and thick layers of topical 2% erythromycin and 4% erythromycin application could not change the MEDs significantly. However, the application of thin and thick layers of

tetracycline had an increasing effect on MEDs and a decreasing effect on UVB penetration. Moreover, we recognised that titanium dioxide which was a component of topical tetracycline preparation had caused a decrease on MEDs because of its blocking effect on narrow band UVB penetration. Nevertheless, as a result of this study, we concluded that in phototherapy plus topical agent combination therapies, topical agents must not be applied before phototherapy.

References

1. Parsad D, Pandhi R, Dogra S. A Guide to Selection and Appropriate Use of Macrolides in Skin Infections. Am J Clin Dermatol 2003; 4: 389-397. PMID: 12762831
2. Scheinfeld NS, Tutrone WD, Torres O, Weinberg JM. Macrolides in dermatology. Clin Dermatol 2003; 21: 40-49. PMID: 12609587
3. Autio P, Keski-Oja J. Tetracyclines as anti-inflammatory treatment in skin diseases. Nord Med 1996; 111: 348-351. PMID: 8992467
4. Samson Yashar S, Gielczyk R, Scherschun L, Lim HW. Narrow-band ultraviolet B treatment for vitiligo, pruritus, and inflammatory dermatoses. Photodermatol Photoimmunol Photomed 2003; 19: 164-168. PMID: 12925186
5. Cetiner S, Ilknur T, Ozkan S. Phototoxic effects of topical azelaic acid, benzoyl peroxide and adapalene were not detected when applied immediately before UVB to normal skin. Eur J Dermatol 2004; 14: 235-237. PMID: 15319156
6. Jeanmougin M, Civatte J. Prediction of benzoyl peroxide phototoxicity by photoepidermotests after repeated applications. Preventive value of a UVB filter. Arch Dermatol Res 1988; 280 (Suppl.): S90-93. PMID: 3408262
7. Kornreich C, Zheng ZS, Xue GZ, Prystowsky JH. A simple method to predict whether topical agents will interfere with phototherapy. Cutis 1996; 57: 113-118. PMID: 8646856
8. Smit JV, de Jong EM, de Jongh GJ, van de Kerkhof PC. Topical all-trans retinoic acid does not influence minimal erythema doses for UVB light in normal skin. Acta Derm Venereol 2000; 80: 66-67. PMID: 10721847
9. Hecker D, Worsley J, Yueh G, Kuroda K, Lebwohl M. Interactions between tazarotene and ultraviolet light. J Am Acad Dermatol 1999; 41: 927-930. PMID: 10570375
10. Fetil E, İlknur T, Altiner D, Ozkan S, Gunes AT. Effects of calcipotriol cream and ointment, clobetasol cream and ointment and tretinoin cream on the erythemogenicity of UVB. J Dermatol 2005; 32: 868-874. PMID: 16361746