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THERAPEUTICAL ACTIVITY OF CLINDAMYCIN/ZINC GEL ALONE OR COMBINED WITH A COSMETIC CREAM CONTAINING BOVINE COLOSTRUM IN PATIENTS WITH MILD TO MODERATE INFLAMMATORY ACNE: RESULTS FROM THE ZETA PROJECT

N. CASSANO, D. FAI, C. CALVI, P. LIGORI, C. MALVINDI, S. PELLÈ, A. PUGLIESE, I. ROMANO, S. MANCO, A. MANCINO, G. MAZZARELLA, G. A. VENA

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Therapeutical activity of clindamycin/zinc gel alone or combined with a cosmetic cream containing bovine colostrum in patients with mild to moderate inflammatory acne: results from the ZETA project

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Aim. **The aims of this study were 1) to determine the efficacy and tolerability of treatment with clindamycin/zinc gel in patients with mild to moderate acne and 2) to evaluate the activity of a cosmetic cream containing bovine colostrum in such patients.**

Methods. **This open parallel-group study was carried out in patients with mild to moderate inflammatory acne of the face. Patients were allocated to the following two treatment groups: 1) monotherapy with 1% clindamycin phosphate/0.5% zinc acetate gel, applied once daily; 2) once-daily application of the same clindamycin/zinc gel combined with the regular once-daily use of a cosmetic cream, containing bovine Colostrum H1. The scheduled treatment period was 12 weeks.**

Results. **A total of 193 patients were included in the final analysis. In both treatment groups, there was a relevant reduction of both inflammatory and non-inflammatory lesions and a significant improvement of erythema, dryness and local symptoms throughout the study period. A trend in favour of the combined regimen with clindamycin/zinc gel plus colostrum-based cream was noted for the reduction of non-inflammatory lesions at week 4, and for the improvement of skin dryness at week 12. Treatment was very well tolerated in both groups.**

Conclusion. **This experience confirms the effectiveness and safety of clindamycin/zinc gel for the treatment of acne, and highlights that the combination with a cosmetic cream containing bovine colostrum is well tolerated and may cause additional benefits.**

KEY WORDS: Acne vulgaris - Photochemotherapy - Clindamycin-2-phosphate.

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Acne vulgaris is a very common skin disorder of the pilosebaceous unit that has a multifactorial pathogenesis.[1,2] Treatment strategies are balanced against the nature and severity of acne, and array several types of topical and systemic approaches, which act as modulators of one or more of the pathogenic events implicated in the development of acne lesions:[3] seborrhoea, abnormal cornification of pilosebaceous ducts, *Propionibacterium acnes* colonization and inflammation.

Topical antimicrobials are well-established and effective agents in the management of mild to moderate inflammatory acne, and their activity is mediated by the reduction of microbial colonization and by direct or indirect anti-inflammatory effects.[4]

The objectives of this study were 1) to determine the efficacy and tolerability of a 12-week treatment with clindamycin/zinc gel in patients with mild to moderate inflammatory acne and 2) to evaluate the adjuvant role of a cosmetic cream containing bovine colostrum in such patients.

Materials and methods

Male and female patients aged 12 years or older with mild to moderate acne vulgaris of the face with at

least 15 inflammatory and/or non-inflammatory acne lesions were evaluated in this open-label multicenter study. The study followed the principles of the declaration of Helsinki and was consistent with good clinical practice guidelines.

Patients who were receiving anti-acne treatments were required to stop such treatments for an adequate period of time prior to the inclusion in the study: two weeks for topical therapies, four weeks for oral antimicrobials, six months for oral contraceptives and systemic retinoids. Female patients who took contraceptive pills for at least six months and planned to continue their use could be included in the study population. Any treatments potentially capable of interfering with acne severity and study evaluations, including intense exposure to natural or artificial sources of ultraviolet radiations or photodynamic therapy, were considered prohibited.

Patients with comedonic acne, secondary acne, acne conglobata or *fulminans*, severe nodulocystic lesions or gram-negative folliculitis were excluded from the study, as well as patients with more than 75 acne lesions of either inflammatory or non-inflammatory type. Males with beards or moustaches were not included in the trial. The following conditions were also considered exclusion criteria: known resistance of acne to the study medications, hypersensitivity to any ingredients of the study products, presence of other facial dermatoses, pregnancy and lactation.

The study was performed through autumn, winter and spring, thus minimizing the possible influence of sunshine.

After informed consent had been obtained by patients and/or their parents, eligible subjects were sequentially assigned to the following arms in a 1:1 ratio:

— treatment with a gel containing 1% clindamycin phosphate and zinc acetate dihydrate (Zindaclin® gel, Difa Cooper S.p.A., Caronno P.lla, Varese, Italy), applied once daily, at bedtime, to the affected areas of the face;

— the same treatment above mentioned with Zindaclin® gel, combined with the regular use of a cosmetic cream, whose main ingredient was bovine Colostrum H1 (Eutrosis® forte, Difa Cooper S.p.A), once daily in the morning over the whole face.

The scheduled treatment period was 12 weeks.

Patients were visited at the baseline, week 4, and week 12. Additional visits could carried out at any time for variable reasons, including complete remission, worsening of acne, patient's request and adverse events.

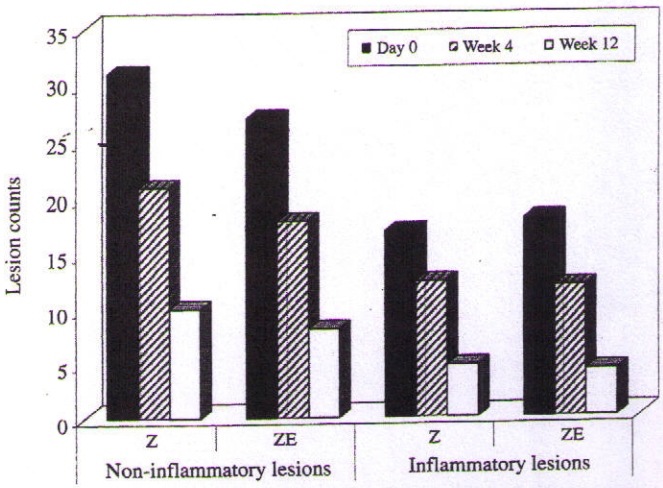

Figure 1. —Change of lesion counts throughout the study period in patients treated with clindamycin/zinc gel alone (Z) and in those treated with clindamycin/zinc gel combined to colostrum-based cream (ZE).

Treatment efficacy was determined by non-inflammatory and inflammatory lesion counts made on the entire face. At each visit the severity of facial erythema, skin dryness and local symptoms was assessed using a four-score rating scale (0=absent; 1=mild; 2=moderate; 3=notable).

Local adverse events were recorded and monitored. At the final assessment, patients and dermatologists gave their independent opinion about the efficacy of treatment, and patients also rated treatment acceptability and tolerability.

Statistical analysis

Statistical analysis was performed using the non-parametric Wilcoxon test to evaluate change of signs and symptoms from baseline in each treatment group, whereas these parameters were compared between groups at any visit using the Mann-Whitney test (significance for P values <0.05 in both analyses).

Results

A total of 198 patients entered the study, and five of them prematurely interrupted the participation because of consent withdrawal (N.=2), use of prohibited treat-

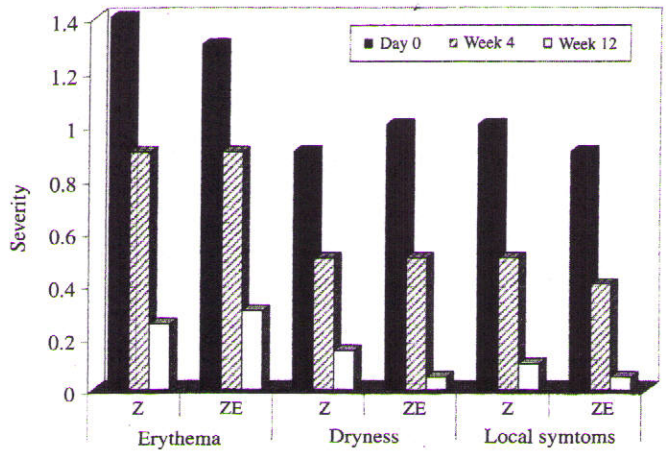

Figure 2.—Change in the severity of erythema, skin dryness and local symptoms throughout the study period in patients treated with clindamycin/zinc gel alone (Z) and in those treated with clindamycin/zinc gel combined to colostrum-based cream (ZE).

ments (N.=2) or non-compliance (N.=1). Therefore, a total of 193 patients were included in the final analysis: 97 patients, 48 males and 49 females, aged 12 to 40 years (mean age, 20.5), in the group treated with clindamycin/zinc gel alone, and 96 patients, 38 males and 58 females, with a mean age of 19.9 years (range, 12 to 37 years), in the other arm consisting of clindamycin/zinc gel combined with the colostrum-based cream.

In both treatment groups, there was a relevant reduction of both inflammatory and non-inflammatory lesions at each post-baseline assessment as compared to baseline ($P \leq 0.001$) (Figure 1), and a significant improvement of erythema, dryness and local symptoms was concomitantly observed throughout the study period (Figure 2) ($P<0.01$).

The magnitude of response between the two treatment groups was quite similar, although a trend in favour of the combined regimen with clindamycin/zinc gel plus colostrum-based cream was noted for the reduction of non-inflammatory lesions at week 4 ($P=0.032$). As concerns the other clinical parameters, the comparison between the two treatment arms did not disclose any relevant differences, with the exception of skin dryness which was found to be significantly less severe at week 12 in the group treated with the combined therapy than in patients who received topical clindamycin/zinc alone ($P=0.02$).

Treatment was very well-tolerated with only an adverse reaction, represented by a transient erythema, reported by a patient treated with clindamycin/zinc monotherapy.

TABLE I.—*Patient's and dermatologist's assessment of the efficacy of treatment.*

	Clindamycin/ zinc gel alone (%)	Clindamycin/zinc gel + colostrum-based cream (%)
Patient's assessment		
— Poor	3%	4%
— Sufficient	9%	9%
— Good	68%	56%
— Excellent	20%	31%
Dermatologist"s assessment		
— Poor	3%	4%
— Sufficient	12%	5%
— Good	70%	65%
— Excellent	15%	26%

TABLE II.—*Patient's assessment of the acceptability and tolerability of treatment.*

	Clindamycin/ zinc gel alone (%)	Clindamycin/zinc gel + colostrum-based cream (%)
Acceptability		
— Poor	3%	1%
— Sufficient	9%	9%
— Good	62%	66%
— Excellent	26%	24%
Tolerability		
— Poor	0%	0%
— Sufficient	11%	3%
— Good	63%	55%
— Excellent	26%	42%

The patient's and dermatologist's assessment of efficacy was almost similarly rated as good or excellent in the majority of cases (Table I). Moreover, acceptability and tolerability of treatment were considered positively by patients on most occasions (Table II).

Discussion

Topical antimicrobials are well-established and effective agents in the management of mild to moderate inflammatory acne. Clindamycin is one of the most widely used topical antibacterial drugs for the treatment of acne thanks to its activity against *Propionibacterium acnes* and its anti-inflammatory effects.[4, 5] Randomized controlled studies in acne

patients consistently demonstrated the superiority of topical clindamycin in reducing not only inflammatory lesions but also open comedones as compared to placebo.[4]

Clindamycin/zinc gel contains zinc acetate dihydrate in a gel formulation that minimizes the extent of systemic absorption of clindamycin in comparison with the older formulation of clindamycin lotion as shown by the results of a pharmacokinetic study.[6] Therefore, the low systemic exposure with clindamycin/zinc gel creates the premises for a favourable safety profile and reduced risk of systemic effects. Moreover, a randomized trial in patients with mild/moderate acne demonstrated the equivalent efficacy of clindamycin/zinc gel either once or twice daily to clindamycin lotion twice daily, in terms of both clinical and microbiological responses.[7] The simple dosing regimen, consisting in once-daily application, offers great advantages on patient's compliance, thus improving chances of treatment success.

Our results confirm the effectiveness and tolerability of treatment of mild-moderate acne with topical clindamycin/zinc acetate gel. Moreover, we also evaluated the potential clinical activity of a cosmetic cream containing bovine colostrum, which is a well known source of antimicrobial proteins and peptides, and several immunomodulatory and antioxidant substances.[8-11]

In this pilot experience, such a cosmetic cream was well-tolerated in our series of acne patients and its use was associated to a greater improvement of non-inflamed lesions at week 4 and also to a better control of skin xerosis at week 12 as compared to patients treated with topical clindamycin alone. Interestingly, at the end of the treatment period, more patients among those treated with the combined regimen rated as excellent both the efficacy (31% compared to 20% of patients treated with clindamycin monotherapy) (Table I) and tolerability (42% compared to 26% of patients treated with clindamycin alone) (Table II).

Riassunto

Attività terapeutica di un gel a base di clindamicina e zinco, da solo o in associazione ad una crema cosmetica a base di colostro bovino, in pazienti con acne infiammatoria lieve-moderata: risultati del progetto ZETA

Obiettivo. Le finalità di questo studio sono state 1) determinare l'efficacia e la tollerabilità del trattamento con un gel a base di clindamicina/zinco in pazienti con acne infiammatoria lieve-moderata e 2) valutare il ruolo addizionale di una crema cosmetica contenente colostro bovino negli stessi pazienti.

Metodi. Questo studio in aperto è stato condotto in pazienti affetti da acne infiammatoria lieve-moderata del volto. I pazienti hanno ricevuto uno dei seguenti trattamenti: monoterapia con un gel a base di clindamicina fosfato 1%/zinco acetato 0,5%, applicato una volta al dì, oppure la stessa terapia con il suddetto gel associata all'uso regolare, per una volta al giorno, di una crema cosmetica contenente colostro bovino H1. Il periodo programmato di trattamento era di 12 settimane.

Risultati. In totale, 193 pazienti sono stati inclusi nell'analisi finale. In entrambi i gruppi, si è osservata nell'arco del periodo di studio una riduzione rilevante delle lesioni acneiche infiammatorie e non infiammatorie, così come un significativo miglioramento di eritema, secchezza e sintomi locali. Il confronto tra i due gruppi ha evidenziato un miglioramento significativamente maggiore delle lesioni acneiche non infiammatorie alla settimana 4 e della secchezza cutanea alla settimana 12 nei pazienti trattati con la terapia combinata con clindamicina/zinco gel e crema a base di colostro rispetto all'altro gruppo. La tollerabilità è risultata particolarmente buona in entrambi i gruppi.

Conclusione. Questa esperienza conferma efficacia e tollerabilità del gel contenente clindamicina/zinco nel trattamento dell'acne, mostrando inoltre che la combinazione con una crema cosmetica a base di colostro bovino è ben tollerata ed in grado di apportare benefici aggiuntivi.

PAROLE CHIAVE: Acne vulgaris - Terapia topica - Clindamicina/zinco gel.

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