Topical lincomycin gel in acne vulgaris: A multicentric placebo controlled study

A. D. Sharma, P. D. Gupte,* M. Sundaram, V. R. Janaki,*** V. L. Rege,**** F. E. Bilimoria,***** J. Arora******

Wallace Pharmaceutical Ltd., Mumbai, India;*Department of Skin & VD, KEM Hospital, Mumbai, India; **Department of Dermatology, Govt. General Hospital, Chennai, India; ***Department of Dermatology, Govt. General Hospital, Chennai, India; ****Department of Skin & VD, Medical College, Goa, India; *****Department of Dermatology, B. J. Medical College & Civil Hospital, Ahmedabad, India; *****Govt. Medical College & Associated Hospitals, Jammu, India.

Address for correspondence: A. D. Sharma, Medical Advisor, Wallace Pharmaceutical Pvt. Ltd., A-101/102, Floral Deck Plaza, Off Central MIDC Road, Andheri (E), Mumbai - 400073, India. E-mail: anildadsouza@wallacepharma.net

ABSTRACT

Introduction: Acne vulgaris is commonly treated with topical antibacterials. We evaluated lincomycin gel, a new topical formulation for mild to moderate acne. **Material and Methods:** A multicentric, randomized, double blind, placebo controlled, clinical trial was conducted with lincomycin hydrochloride in 2% gel form in 200 patients with grade II and grade III acne. The severity of acne lesions was noted at baseline and after 4 weeks. **Results:** About 70% cases in the study group showed a good to excellent response, which was significantly more as compared to 23% in the placebo group. The frequency and severity of adverse reactions in the two groups were similar. **Conclusion:** Lincomycin hydrochloride gel is an effective and safe treatment option for mild to moderate acne vulgaris.

Key Words: *Propionibacterium acnes,* Acne vulgaris, Lincomycin

INTRODUCTION

Topical antibacterials used in acne vulgaris act against *Propionibacterium acnes*. They also have a mild indirect effect on comedogenesis and anti-inflammatory activity by impeding neutrophil chemotaxis. Erythromycin and clindamycin are currently the two most commonly used antibiotics. Many cases reported to be resistant to erythromycin have surfaced[1] and hence lincosamides like clindamycin have gained acceptance. Lincomycin is another antibacterial from this group that has potent activity against *Propionibacterium acnes*.[2]

MATERIAL AND METHODS

After the initial clearance through toxicological studies like acute and chronic dermal toxicity studies using different animal models,[3] a multicentric clinical trial on lincomycin hydrochloride 2% gel (Lynx; Wallace Pharma Pvt. Ltd., India) was initiated to study its efficacy and safety in acne vulgaris. This trial was conducted at five different centres approved by the Drug Controller General of India.

Two hundred and sixteen patients of either sex over 12 years of age with clinically confirmed and graded acne vulgaris lesions were included. These patients were enrolled from the dermatological OPD of the above centers after taking a valid consent. Patients with a known history of hypersensitivity to lincosamides were excluded from the study. Ambulatory patients with Grade II and Grade III acne vulgaris were included in the study. The grading was done using the Pillsbury grading scale.[4] Photographs of the acne lesions were taken on day 1, 7, 14, 21 and 28 to assess the efficacy of the drug.

Of the patients enrolled at each centre about half of

them were assigned randomly to the drug treatment group and the other half to the placebo group. As per their group, patients were told to apply either 2% lincomycin gel or the placebo gel (the same gel formulation without lincomycin) over acne lesions twice daily after washing the face with soap and water. No other concomitant anti-acne therapy was allowed. The number, size and the severity of inflammation of the lesions were noted separately for each body region at the initial visit and every week thereafter for 4 weeks. Double blinding was carried out by the study monitor.

The response to the treatment was assessed as follows:

Excellent response: Complete healing of acne lesions clinically.

Good response : 50% or more reduction in number of acne lesions.

Fair response : 25%-50% reduction in number of acne lesions

Poor response : No response, flare-up of lesions, or less than 25% reduction in the number of acne lesions.

Patients were monitored for adverse drug reactions during the study period. The data was statistically analyzed using t-test and chi-square statistical tests. The proportion of patients with a reduction in the number of lesions, i.e. improvement or cure of acne, and with flare up of disease depending on the baseline lesions, evaluated on clinical basis are presented as percentages.

OBSERVATIONS AND RESULTS

All in all 200 patients completed the study, 100 belonging to the placebo group and 100 to the lincomycin group. The two groups were comparable in terms of the age and sex distribution of patients, duration of disease and total number of acne lesions at baseline (Table 1).

Table 1: Comparison of the two groups before therapy

Parameters	Placebo (n = 100)	Lincomycin (n = 100)
Mean age (years)	20.16*	19.50
Mean duration (Months)	20.61*	20.93
Sex (%) Male	61.0	53.0
Female	39.0	47.0
Total number of lesions	46.86*	42.84

* *p > 0.05* (differences not significant)

After the treatment was initiated, the number of lesions started reducing from the first week onwards in both the groups, but the reduction was 57.04% in the lincomycin treated group, which was significantly more as compared to 31.28% in the placebo group (Table 2).

Upon global assessment, in the lincomycin group 70% of the cases showed more than 50% reduction in acne lesions, which was significantly more than the corresponding figure of 23% in the placebo treated group (Table 3).

The adverse reactions were mostly mild and self limiting; common ones were itching, burning, dryness, erythema, scaling and pigmentation. Itching, erythema and pigmentation were slightly more common in the placebo group than in the lincomycin group (Table 4). The drop out rate in the lincomycin in group was 6% wheras that in the placebo group was 10%. No patient dropped out on account of severe adverse event.

DISCUSSION

Acne is a multifactorial disorder. Suppression of *P. acnes*

Table 2: Comparison of the two groups after therapy

	Mean no. of lesions (SD)	
	Placebo group	Lincomycin group
Week 0	42.04 (26.21)	46.86 (27.54)
Week 1	37.46 (23.81)	38.87 (26.14)
Week 2	33.47 (21.18)	31.43 (25.20)
Week 3	30.59 (22.10)	26.78 (20.81)
Week 4	28.99 (20.80)	21.31 (19.70)
Change from week 0	13.15* (17.20)	26.73† (19.50)

* *p > 0.05* (not significant), † *p < 0.05* (significant)

Table 3: Global assessment of efficacy

Response	Placebo (No. of pts.)	Lincomycin (No. of pts.)
Excellent	6	32
Good	17	38
Fair	21	17
Poor	56	13
Total	100	100

Table 4: Adverse reactions

Adverse reactions	Placebo		Lincomycin	
	No.	(%)	No.	(%)
Itching	5	(5)	2	(2)
Burning	5	(5)	5	(5)
Dryness	1	(1)	1	(1)
Erythema	2	(2)	1	(1)
Scaling	1	(1)	1	(1)
Pigmentation	2	(2)	–	

with antibiotic therapy correlates with clinical improvement.[5,6] Antibiotics like erythromycin and clindamycin, and more recently azithromycin, are most frequently used to treat acne vulgaris.[7] Topical preparations for acne are available in various formulations, the gel formulation being most commonly preferred since it is cosmetically acceptable and best suited for oily skin. Topically applied lincomycin has good tissue penetration with potent activity against *P. acnes* (MIC < 0.1-1.6 mcg/ml).[14] By its action on *P. acnes*, lincomycin eliminates the production of free fatty acids and other local irritating enzymes produced by bacteria. Further, it may have some immunomodulating effect in reducing inflammation.[15] These attributes of lincomycin prompted the development of its topical formulation, lincomycin hydrochloride as a 2% gel (Lynx ®), for acne.

In the present study, the resolution of acne lesions was quite satisfactory; good response (reduction in severity of acne by 50% or more at the end of 4 weeks) was seen in 70% of patients as compared to only 23% of the placebo treated group. Such a response in 70% of patients with grade II and grade III acne is suggestive of noteworthy anti-acne properties of 2% lincomycin gel.

The adverse effects observed were localized skin reactions like itching, erythema, scaling and pigmentation. They were mild in intensity and self limiting. They occurred more commonly in the placebo group, one possible explanation being a flaring up of the disease. No case of contact sensitization or severe allergic skin reaction was noted. Almost all topical antibiotics are associated with some minor skin irritation. This adverse effect may be influenced by the vehicle used.[8]

The emergence of erythromycin resistance in cutaneous propionibacteria was first reported in USA in the late 1970's in patients treated with topical erythromycin or clindamycin.[9] The good response to topical lincomycin in this study could be due to the fact that *P. acnes* has developed resistance against commonly used antibiotics such as erythromycin, whereas lincomycin still remains effective against these strains of *P. acnes.* However, this needs to be established by in vitro and in vivo comparision of lincomycin with erthromycin. Moreover, cross resistance between lincomycin and erythromycin is not observed,[10] and for lincomycin it develops in a stepwise manner.[11] In a clinical study by Eady et al, one in every four acne patients attending the clinic carried erythromycin-resistant propionibacteria on the facial skin.[9,12] The development of resistance in acne can be limited by the rational use of topical antibiotics and restricting oral antibiotic therapy.[9,13]

SOURCE(S) OF SUPPORT

Initiated and financed by Wallace Pharma Pvt. Ltd., India.

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