

Comparative study between topical clindamycin solution (1%) versus combination of clindamycin (1%)/adapalene (0.1%) gel in the treatment of mild to moderate acne vulgaris

Received: 27/4/2013

Accepted: 1/12/2013

Tara F. Wali *

Intiha M. Almosuly **

Abstract

Background and objective: Acne vulgaris is a common skin disorder. Combination therapy with topical retinoid and antibiotic is recognized as an effective treatment of acne vulgaris. The aim of this study was to compare the efficacy and tolerability of topical clindamycin solution as a monotherapy with the combination gel of clindamycin/adapalene for the treatment of mild to moderate acne of the face.

Methods: This comparative therapeutic trial was conducted at the out patient department of Dermatology and Venereology at Rizgari Teaching Hospital in Erbil City from November 2008. Hundred patients with mild to moderate acne of the face were enrolled in the study and were divided in to two groups; group I (n=50); apply clindamycin phosphate solution 1%, and group II (n=50); apply a combination gel of clindamycin1% /adapalene 0.1%; once daily at night for 12 weeks.

Results: Of 100 patients, 89 patients completed their treatment as per protocol, 45 patients in group I, and 44 patients in group II. At the end of the 12 weeks; the mean percent reductions of noninflammatory, inflammatory, and total lesion count were greater in group II than in group I. A significantly greater reduction of total ($P = 0.008$), and noninflammatory lesions ($P = 0.002$) were seen in group II than in group I. Both treatments were well tolerated, and few side effects were reported.

Conclusion: This study demonstrates that the combination of topical clindamycin and adapalene is more effective than clindamycin solution alone, and provides faster benefit in treatment of mild to moderate acne.

Keywords: Acne vulgaris, clindamycin solution, clindamycin/adapalene gel.

Introduction

Acne is a chronic inflammatory disease of the pilosebaceous units.¹ The primary and pathognomonic lesion of acne is microcomedone (a microscopic lesion invisible to the eye). Some microcomedones evolve into either a noninflammatory lesion (open or closed comedone), or an inflammatory lesion such as papule, pustule, or nodule.² Acne is classified as mild, moderate, or severe. Mild acne; some non-inflammatory lesions (comedones) are present, with a few inflammatory (papulo-pustular) lesions, no nodulocystic lesions. Moderate acne; non-inflammatory lesions predominate, with multiple inflammatory lesions evident: several to many comedones and papules/

pustules, and there may or may not be one small nodulocystic lesion. Severe acne; inflammatory lesions are more apparent, many comedones and papules/pustules, there may or may not be a few nodulocystic lesions.³ The pathogenesis of acne is multifaceted, but four basic steps have been identified. These key elements are; follicular epidermal hyperproliferation, excess sebum production, inflammation, and the presence and activity of *Propionibacterium acne*.⁴ Topical retinoid derivatives of vitamin-A have been used to treat acne for almost three decades. They are the most effective comedolytic agents for the treatment of acne vulgaris by normalizing or even increasing the desquamation

* General directorate of health, Erbil, Iraq.

** Department of Medicine, College of Medicine, Hawler Medical University, Erbil, Iraq.

process, thereby decreasing the formation and the number of microcomedones. They also promote the clearing of preexisting comedones and decrease in papulopustular lesions. In addition, they have a marked anti-inflammatory effect by inhibiting the activity of leukocytes, the release of pro-inflammatory cytokines and other mediators, and the expression of transcription factors and toll-like receptors involved in immunomodulation. They also help penetration of other active agents. Tretinoin, which is the active form of a metabolic product of vitamin A, was the only available topical retinoid until recently. However, its use has been limited by local irritation after initiation of therapy. This side effect is a minimal problem with the third generation topical retinoid, such as adapalane.⁵ Propionibacterium acne, an anaerobic diphtheroid, is a normal skin resident and the principal component of the microbic flora of the pilosebaceous follicle.⁶ Topical antibiotics act predominantly antimicrobially, reducing follicular microbial colonization. They also demonstrate anti-inflammatory activity by suppressing chemotaxis. Although P. acne is sensitive to a range of antibiotic, the therapeutic value of individual antibiotics is dependent upon the degree to which these compounds are soluble in the lipid-rich environment within acne vulgaris lesions. Clindamycin is the more lipophilic of these antibiotics.⁷ Clindamycin phosphate applied topically penetrates to a very great extent into open comedones and thus produces a high percentage of sterile comedones.⁸ The combination of a topical antibiotic with a topical retinoid is a rational choice because of their distinct, complementary and additive mechanism of action.⁹ Acne is a common skin disease in the Department of Dermatology at Rizgari Teaching Hospital. However, no previous study has been conducted comparing the efficacy and tolerability of topical clindamycin with adapalene in the treatment of acne. Therefore, we conducted this study to compare the efficacy and tolerability of

topical clindamycin solution as a monotherapy with the combination gel of clindamycin/ adapalene for the treatment of mild to moderate acne of the face.

Methods

This comparative therapeutic trial was conducted at the outpatient Department of Dermatology and Venereology at Rizgari Teaching Hospital in Erbil City from November 2008. The study compared the efficacy and tolerability of topical clindamycin phosphate solution (1%) as a monotherapy with the combination gel of (clindamycin phosphate 1% / adapalene phosphate 0.1%) in the treatment of mild to moderate acne confined to the face. Hundred patients with mild to moderate acne of the face were enrolled in the study. All patients provided their informed consent prior to entering the study. The study was approved by the Ethics Committee of the College of Medicine of Hawler Medical University. The diagnosis in each case was based on the clinical ground. Both sexes and different ages (76 females and 24 males, aged 10 to 36 years) were included in the study. Pregnant and lactating females were excluded from the study as well as those with known hypersensitivity or previous allergic reaction to any of the active components of the study medication, females with hyperandrogenism states, patients who concurrently or concomitantly used photosensitizers and/or medications reported to cause or exacerbate acne (e.g. steroid acne), and patients taking systemic antibiotic or retinoid for the last two months or using topical treatments of acne for the last two weeks, were also excluded.

Examination;

Each patient was examined thoroughly for the types of acne lesions;

- Non-inflammatory lesions (NIL); comedones (closed and open).
- Inflammatory lesions (IL); papules, pustules, and nodules.

The lesions on the face were counted and

a grading for each patient was carried out according to the Evaluator's Global Severity Scale³ (Table 1).

Table 1: Evaluator's Global Severity Scale for counting and grading the lesions on the face

Grade	Description
Mild	Some comedones/few papules & pustules but no nodulocystic lesions
Moderate	Several to many comedones and papules/pustules, and there may or may not be one small nodulocystic lesion.
Severe	Many comedones and papules/pustules, there may or may not be a few nodulocystic lesions
Very Severe	Variable number comedones, many papules/pustules and many nodulo-cystic lesions.

Methods of treatment: Hundred patients with mild to moderate acne of the face were included in the study and divided into two groups;

Group I; Fifty patients were instructed to apply a thin layer of clindamycin phosphate solution 1% over the entire face once daily at night from baseline through week 12.

Group II; Fifty patients were instructed to apply a thin layer of a combination gel of clindamycin phosphate 1%/adapalene phosphate 0.1% over the entire face once daily at night from baseline through week 12. All the patients were instructed to wash their face before application of the treatment, using mild soap.

Medications used in this study;

1) Lindacin (Clindamycin Phosphate) solution. **API** (Amman Pharmaceutical Industries), **TF** 014, **Exp.** 07/2010

2) Adacin (Adapalene and Clindamycin Phosphate) gel. **Ajanta**, **AH** 246, **Exp.** 09/2010

The efficacy of the two drugs was evaluated at four weekly intervals by spot counting of the acne lesions. The criteria for effectiveness of the treatment were the reduction in the number of NIL, IL and total lesion count (TLC) at the end of the 12

weeks. The mean percent reduction of NIL, IL, and TLC were calculated for each of the two therapeutic groups.

The improvement was graded as follows,⁸

(1) Excellent, when there was more than 75% reduction in the lesion count.

(2) Good, when there was 50-75% reduction in the lesion count.

(3) Fair, when there was 25-50% reduction, and (4) Poor, when there was less than 25% reduction in the lesion count.

Any side effect (erythema, scaling, itching, burning) reported by the patient or observed by the investigator was noted in the case record form.

Statistical analysis; The response was statistically evaluated using Chi square test. P value of < 0.05 was considered statistically significant.

Results

A total of 100 patients with mild to moderate acne of the face, 76 females and 24 males, aged 10 to 36 years with mean age (\pm SD) of 19.45 \pm 4.78 years, were enrolled in this study and assigned to two groups. Group I (n=50); apply clindamycin phosphate solution (1%) as monotherapy. Group II (n=50); apply a combination gel of clindamycin phosphate (1%)/adapalene phosphate (0.1%). Eighty nine patients completed treatment as per protocol (12 weeks period), 45 patients in group I, and 44 patients in group II. Eleven patients failed to complete the study for various reasons like lost to follow-up and non-compliance. The skin at the baseline was oily in all patients, and the mean number of NIL, IL, and TLC of the face at the baseline for total number of patients were; 117.33, 29.42, and 146.75 lesions, respectively. The two treatment groups were balanced for these demographic and baseline characteristics. Patients in the two treatment groups showed a subjective satisfaction with the therapies. The mean percent reduction of NIL, IL and TLC at the end of the 12 weeks were greater in group II than in group I. The results in group II were 80.75%, 65.43%, and 79.07%,

respectively, while in group I the results were 65.24%, 61.51%, and 66.36%, respectively. The differences in the response of TLC to both treatments were observed as early as week 4 of the study (Figure 1). At the end of the 12 weeks; a significantly greater reduction of TLC ($P=0.008$), and NIL ($P=0.002$) were seen in group II than in group I. In the respect of TLC improvement, of the 44 patients in group II, excellent results reported in 34 patients, good in six, fair in one, and poor in three patients, while of the 45 patients in group I, excellent result reported only in 19 patients, good in 16, fair in five, and poor in another five patients. In the respect of

NIL improvement, of the 44 patients in group II; excellent results reported in 35 patients, good in five, fair in two, and poor in another two patients, while of the 45 patients in group I, excellent result reported only in 18 patients, good in 16, fair in six, and poor in five patients. Figure 2 and Figure 3 clarify the statistically significant difference between the two treatment groups in the respect of TLC and NIL reduction respectively. Both therapies were well tolerated. Although the worst scores for erythema ($P < 0.001$), and scaling ($P < 0.001$) were higher in the combination group than in the clindamycin group as shown in Figure 4.

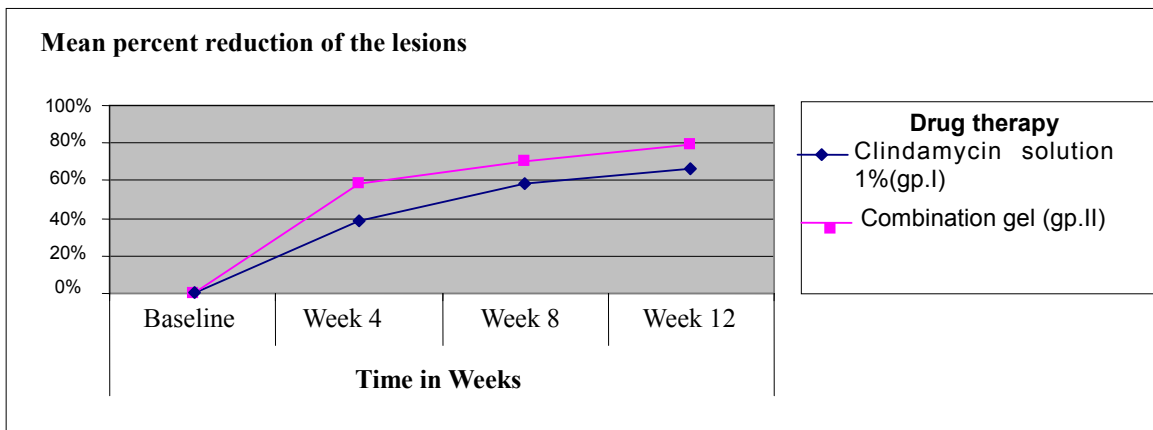


Figure 1: The Mean Percent Reduction of the Total Lesion Counts from the Baseline to the End of the 12 weeks.

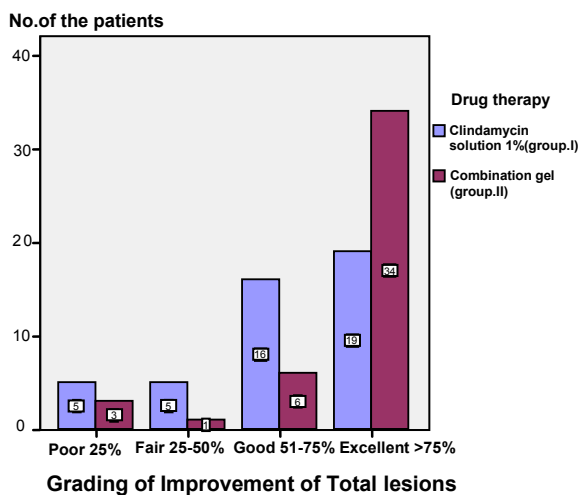


Figure 2: The response of the total lesions to the two treatment regimens at the end of the 12 weeks ($P=0.008$).

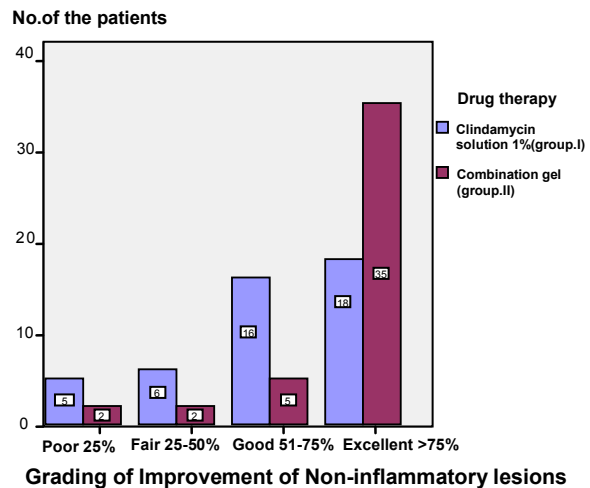


Figure 3: The response of the non-inflammatory lesions to the two treatment regimens at the end of the 12 weeks ($P=0.002$).

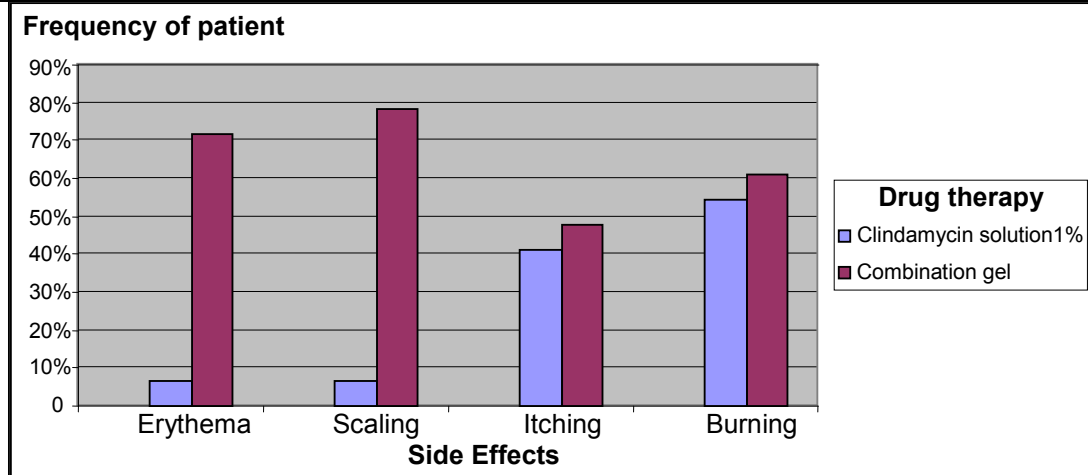


Figure 4: The frequency of development of side effects within the two treatment groups (more than one side effects may be observed in single patient).

Discussion

The results obtained from the present study demonstrated that the combination gel of clindamycin phosphate 1% /adapalene phosphate 0.1% is more effective than clindamycin phosphate 1% solution alone for the treatment of mild to moderate type of acne vulgaris. In the present study the mean percent reduction of NIL, IL, and TLC were greater in group II than in group I; the results were 80.75% versus 65.24% for NLL, 65.43% versus 61.51% for IL, and 79.07% versus 66.36% for TLC. These results were comparable with that obtained from a multicenter, randomized, investigator-blind study conducted by Wolf et al in 2003,¹⁰ who investigated the efficacy and tolerability of adapalene gel 0.1% plus clindamycin phosphate lotion 1%, compared with clindamycin plus vehicle for the treatment of mild to moderate acne vulgaris. The study revealed a greater mean percent reduction of NIL, IL, and TLC in clindamycin plus adapalene group than in the clindamycin plus vehicle group. The results were; 42.5% versus 16.3% for NIL, 55.0% versus 44.2% for IL, and 46.7% versus 25.5% for total lesion count (TLC). The present study revealed a statistically significant reduction of TLC ($P = 0.008$) and NIL ($P = 0.002$) from the baseline in group II than in group I (due to the comedolytic activity of adapalene in the combination

gel). These two findings were compatible with the findings obtained from a previous study,¹⁰ which revealed a significantly greater reduction of total ($P < 0.001$), and non-inflammatory lesions ($P < 0.001$) in clindamycin plus adapalene group than in the clindamycin plus vehicle group at week 12. The findings in the present study were also comparable with the findings obtained from a 2-phase, 24-week, multicenter, randomized, investigator-blind study performed by Zhang et al in 2004, which evaluated the efficacy and safety of adapalene 0.1% gel plus clindamycin topical 1% solution versus clindamycin topical 1% solution alone during the initial 12-week phase of treatment, and revealed a statistically significant greater reduction in total lesion counts from week four until week 12, and from week eight on for non-inflammatory lesion count ($P < 0.05$) for the combination therapy compared with monotherapy.¹¹ In respect of the TLC improvement, the present study revealed that the combination gel was 1.19 times more effective than clindamycin solution. It reduced TLC by as high as (79.07%), which was comparable with the results obtained from a single-blinded, randomized clinical trial done in Iran by Nilfroushzadeh et al in 2009.¹² The study compared the efficacy of clindamycin lotion 1% versus combination therapy of 1% clindamycin

Conclusion

This study demonstrates that the combination of topical clindamycin and adapalene is more effective than clindamycin solution alone, and provides faster benefit in treatment of mild to moderate acne.

Conflicts of interest

The authors report no conflicts of interest.

References

1. Simpson NB, Cunliffe WJ . Disorders of the Sebaceous glands. In: Burns T, Breathnach S, Cox N, Griffiths C editors. Rook's Textbook of Dermatology; 7th edition. Oxford: Black well scientific Publication; 2004. 43:15-42.
2. Kubba R, Bajaj AK, Thappa DM, Sharma R, Vedamurthy M, Dhar S, et al . Acne in india: Guidelines for management: Pathogenesis of acne. Indian J Dermatol Venereol Leprol 2009a; 75(1):S5-9.
3. The Evaluator's Global Severity Score (proposed at the Division of Dermatology Advisory Committee [DODAC] meeting of November 4 and 5, 2002).
4. Zaenglein AL, Graber EM, Thiboutot DM, Strauss JS.AcneVulgaris and Acneiform Eruptions. In: Wolff K, Goldsmith LA, Katz SI, Gilchrist BA, Paller AS, Leffell DJ editors. Fitzpatrick's Dermatology in General Medicine; 7th edition. New York: McGraw-Hill; 2008.P.690-703.
5. Piskin S, Uzunali E . A review of the use of adapalene for the treatment of acne vulgaris. PubMed Central: Ther Clin Risk Manag 2007; 3(4):621-4.
6. Habib T.P.Acne, Rosacea, and Related Disorder. In: Clinical Dermatology; 4th Edition. Philadelphia: Mosby; 2004. P.162-94.
7. Bowman S, Gold M, Nasir A, Vamvakias G .Comparison of clindamycin/benzoyl peroxide, tretinoin plus clindamycin, and the combination of clindamycin/benzoyl peroxide and tretinoin plus clindamycin in the treatment of acne vulgaris: a randomized, blinded study. J Drugs Dermatol 2005;4(5):611-8.
8. Dos SK, Barbhuiya JN, Jana S, Dey SK. Comparative evaluation of clindamycin phosphate 1% and clindamycin phosphate1% with nicotinamide gel 4% in the treatment of acne vulgaris. Indian J Dermatol Venereol Leprol 2003; 69: 8-9.
9. Jain GK, Ahmed FJ. Adapalene pretreatment increases follicular penetration of clindamycin: In vitro and in vivo studies. Indian J Dermatol Venereol Leprol 2007; 73: 326-9.
10. Wolf JE, Kaplan D, Kraus SJ, Loven KH, Rist T, Swinyer LJ, et al. Efficacy and tolerability of combined topical treatment of acne vulgaris with adapalene and clindamycin: a multicenter, randomized, investigator-blinded study. J Am Acad Dermatol 2003; 49:S211-7.
11. Zhang JZ, Li LF, Tu YT, Zheng J. A successful maintenance approach in inflammatory acne with adapalene gel 0.1% after an initial treatment in combination with clindamycin topical solution 1% or after mono-therapy with clindamycin topical solution 1%. J Dermatolog Treat 2004; 15(6): 372-8.
12. Nilfroushzadeh MA, Siadat AH, Baradaran EH, Moradi S. Clindamycin lotion alone versus combination lotion of clindamycin Phosphate plus tretinoin versus combination lotion of clindamycin phosphate plus salicylic acid in the topical treatment of mild to moderate acne vulgaris: A randomized control trial. Indian J DermatolVenereol Leprol 2009; 75: 279-82.
13. Caron D, Sorba V, Clucas A, Verschoore M . Skin tolerance of adapalene 0.1% gel in combination with other topical antiacne treatments. J Am Acad Dermatol 1997; 36(6 pt 2):S113-5.