

CASE REPORT

Comparative Evaluation of Topical Antibiotics in Treatment of Mild to Moderate Acne Vulgaris

Raniah OA AL-mosawi¹, Jubran K Hassan¹, Firas F AL-tameemi²

¹Department of Clinical Pharmacy, College of Pharmacy, University of Basrah, Basrah, Iraq

²Department of Dermatology and venerology, ALSader teaching hospital, Basrah, Iraq

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ABSTRACT

Acne vulgaris is the most common condition that brings the patient to the dermatology department in a hospital or clinic. It is a pleomorphic disease and can happen during any age in life most commonly present in teenagers between 14–25 years old with prevalence ranging from 50–95% in different populations worldwide. Acne vulgaris is considered a benign condition but can have an important psychological effect on the patient because it targets mostly the most important part of the human body which is the face of young patients.

Clindamycin topical gel and erythromycin topical gel is effective in the treatment of acne vulgaris by acting against gram-positive propionibacterium acnes. FDA has approved dapsone topical gel formulation in 2005. So, we compare the therapeutic efficacy of topical clindamycin, erythromycin, dapsone, and control group in our study by dividing 60 patients randomly into four groups of 15 for each group. Each group was subjected to twice daily application on clean skin for 12 weeks. Followed up every two weeks and the result was compared.

We found that the overall percentage of reduction of dapsone 5% gel is 13.3% has a good response after 12 weeks. While it is 6.7% with clindamycin and 0% with erythromycin, 2% have a good response. The side effect is slightly better in the dapsone 5% gel group when compared with clindamycin 1% gel group and erythromycin 2% gel. Dapsone can also be used as monotherapy without significant risk of developing resistance, while clindamycin and erythromycin being antibiotics don't have such privileges. So it is concluded that dapsone 5% gel is a slightly better topical option than clindamycin 1% gel and erythromycin 2% gel in mild to moderate acne vulgaris.

Keywords: Clindamycin 1% gel, Dapsone 5% gel, Erythromycin 2% gel, Moderate acne, Placebo.

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INTRODUCTION

Definition

Acne vulgaris is a common chronic skin disease of the pilosebaceous unit resulting from both ovarian and testicular androgens induced increased sebum production, alter in keratinization, inflammation, and bacterial colonization by *Cutibacterium acnes* (formerly known as *Propionibacterium acne*) that affect the hair follicles of the face, chest, neck, and back.¹ The majority of acne started in the pre-pubertal period and can continue into adulthood. Facial scarring effect up to 20% of acne patient.¹

Acne vulgaris are divided into two types:

Inflammatory papules or pustules.	Non-inflammatory lesions open or close comedones
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distribution of acne vulgaris depends on the density of the pilosebaceous unit in the face, neck, shoulder, chest, and back.²⁻⁸

Clindamycin

An antibacterial agent represents the preferred topical antibiotics for acne treatment. It is available in gel and solution. Few rare reports are showing a low risk of *clostridium difficile* infection-related colitis with topical clindamycin. It is pregnancy category B.⁹

Erythromycin

It is a macrolide antibiotic that is present in 2% concentration as lotion, cream, gel. Its efficacy is lower than clindamycin because of *C. acne* resistance.¹⁰

Dapsone Gel

It is a sulphone agent present as 5% gel and 7.5% uses twice daily for acne vulgaris treatment, it acts as an anti-inflammatory drug for mild to moderate acne. it has been proven safe and no hematological risk is present with oral dapsone also topical dapsone appears to be safe in G6PD deficiency. The mechanism of action is poorly understood and how it acts against C. acnes is unclear. In general, dapsone gels are pregnancy category C.¹¹⁻¹²

SUBJECTS, MATERIALS AND METHODS

Patients

In total, 78 young patients with acne previously and newly diagnosed. They met the inclusion criteria and were enrolled in this study after getting their verbal acceptance. Patients are randomly distributed into one of the study groups (Table 1 and Figure 1).

Clinical Outcome Assessment and Follow up

The primary endpoint of the trial was the comparison of the percentage of reduction of the total number of acne lesions at the end of the study as compared to baseline values. The patients were assessed at the baseline visit and during each subsequent treatment sessions using the following parameters:

- Numerical counting of the inflammatory and non-inflammatory acne lesions.
- Calculating and comparing to the baseline value the percentage of the total reduction of black and white

Table 1: Comparison differences in degree of declining in Comedones lesions, inflammatory lesions, and the total number of lesions after 12 weeks' treatment with topical antibiotics (Erythromycin, Clindamycin, and Dapsone). Data expressed as Mean ± Standard deviation . The total number of participants (N)=60

Topical treatment	Total N	Average decline	P-value
<i>The Effect on Comedones lesions</i>			
Placebo	15	-11.7 ± 11.11	<0.001
Erythromycin	15	-29.5 ± 12.77 ^a	
Clindamycin	15	-34.2 ± 11.07 ^a	
Dapsone	15	-39.3 ± 3.33 ^{ab}	
<i>The Effect on Inflammatory lesions</i>			
Placebo	15	-19.4 ± 5.24	<0.001
Erythromycin	15	-56.4 ± 1.43 ^a	
Clindamycin	15	-59.3 ± 8.04 ^a	
Dapsone	15	-62.7 ± 2.59 ^{ab}	
<i>The Effect on Total Lesions</i>			
Placebo	15	-18.4 ± 4.04	<0.001
Erythromycin	15	-50.6 ± 4.43 ^a	
Clindamycin	15	-54.5 ± 5.7 ^{ab}	
Dapsone	15	-57.1 ± 2.49 ^{ab}	

Kruskal Wallis test is used for data analysis
 p < 0.05 considered significant
a significant as compared with placebo values
b significant as compared with Erythromycin values

Comedones and inflammatory lesions .

- Grading the response according to the percentage of the total reduction of inflammatory and non-inflammatory acne lesions as using the following scale:¹³
 - A: ≥ 80% reduction excellent response
 - B: 60–79% reduction good response
 - C: 40–59%. Reduction moderate response
 - D: < 40% reduction poor response
- Monitoring for any side effects at each visit
- At the end of the study, patients' satisfaction and their attitude toward the treatment were assessed using 4 points scale:
 - Grading 1 unsatisfied (0–25%)
 - Grading 2 slightly satisfied (26–50%)
 - Grading 3 satisfied (51–75%)
 - Grading 4 very satisfied (76–100%)

Treatment

Topical treatment used in the study include the clindamycin gel 1%, erythromycin gel 2% and dapsone gel 5%.

RESULT

The results of a prospective placebo-controlled open-label clinical study revealed that the use of all three topical antibiotics give excellent response compared to placebo. Also we found that the topical dapsone gel is more effective than clindamycin and erythromycin gels in which 13.3% of patients achieved good response after 12 weeks of therapy in comparison to 93.3 of patients who achieved moderate response after 12 weeks of using both clindamycin and erythromycin gels (Figure 2-4).

We found that 93.3% of inflammatory lesions show a good response after using dapsone therapy in compare 26.7, 0% after using clindamycin and erythromycin respectively.

We found that 6(40%) of patients using dapsone gel are getting grade 3 in comparison to 12(80%) of patients using erythromycin gel are getting grade 2.

Regarding the adverse effects, we found erythromycin show more side effects than both clindamycin and dapsone in which 11(73.3%) of patients using erythromycin gel develop moderate



Figure 1: The number of patient in each group.

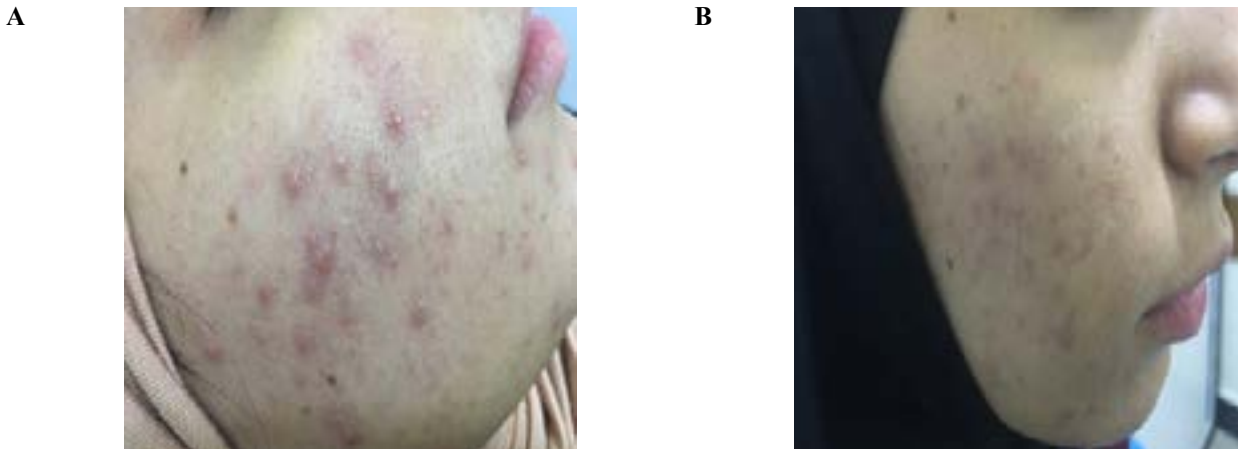


Figure 2: 17 years old patient before(A) and after 12 weeks of treatment with dapsone gel 5%

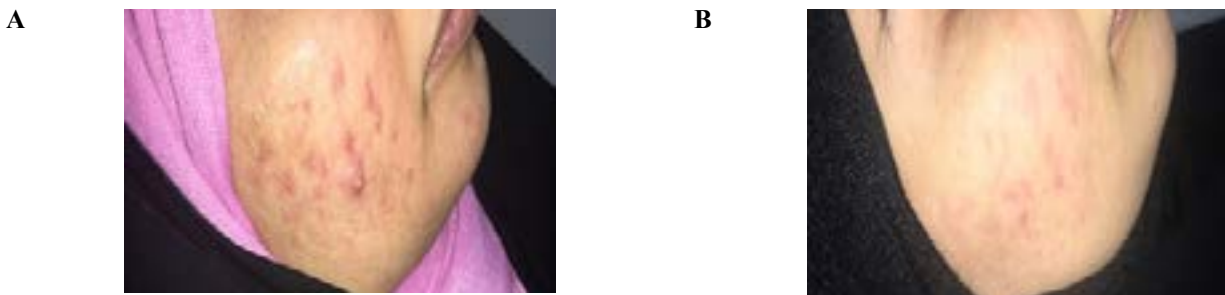


Figure 3: 18 years old female before(A) and after 12 weeks(B) of treatment with erythromycin gel 2%

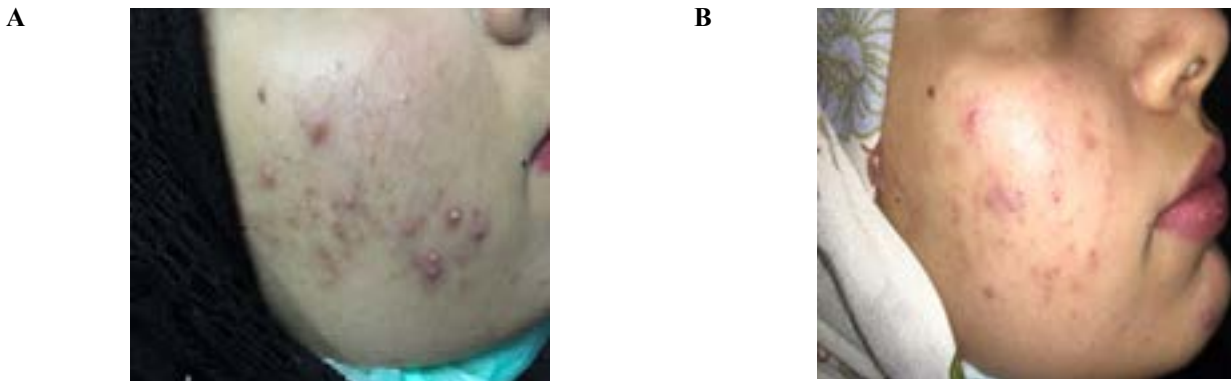


Figure 4: 19 years old female before(A) and after 12 weeks (B) of treatment with clindamycin gel 1%

itching and burning sensation while 12 Patients (80%) develop mild erythema.

DISCUSSION

Acne vulgaris is a disease of the pilosebaceous unit and is considered one of the common skin diseases that is affected mainly in adolescence. In Iraq, the prevalence rate of acne vulgaris is 73% in men and 62% in women. Scarring, post-inflammatory hyperpigmentation, as well as negative psychological impacts are considered as results in some patients with this disease.

The treatment of acne vulgaris may include topical, systemic, or light-based and laser therapy. Topical therapy may include antibiotics, keratolytic, and comedolytic. Systemic therapy may include antibiotics, retinoids, hormonal therapy.

Regarding light-based, it may include blue and red light, photodynamic therapy, and lasers.

Clindamycin, a topical antibiotic, is considered the preferred topical therapy for acne treatment. Erythromycin is also a macrolide antibiotic that acts on *C. acne* but has less efficacy and more risk of bacterial resistance. Dapsone is a sulphone antibiotic with an unclear mechanism on *C. acne* is FDA approved drug for acne vulgaris.

Topical antibiotics gel alone can be useful in the treatment of acne vulgaris. Clindamycin phosphate gel 1% and erythromycin gel 2% work by inhibiting *P. acnes* at the 50S ribosomal subunit where they bind irreversibly to inhibit protein synthesis. *P. acnes* can live in an environment that combines sebum and desquamated cells, where it change sebum to free fatty acids, which then stimulate the body's

immune system response. Topical antibiotics act against this bacterial organism and have anti-inflammatory properties, making these therapies useful in treating acne vulgaris.¹⁴⁻¹⁵

Dapsone gel 5% act by direct inhibition of leukocyte trafficking and the generation by leukocytes of chemical mediators of inflammation. However, it also have a structural similarities to trimethoprim sulfamethoxazole and other sulfonamides.

Topical dapsone may act indirectly in acne patient by altering the levels and/or activity of Clostridium bacteria that found in the upper third of the follicles.¹⁶

In the literature review, there are many studies about the efficacy of topical antibiotics in the treatment of acne vulgaris but most of the study only one antibiotic on comparing 2 antibiotics,

James J *et al.*, treated 102 patients with mild to moderate acne vulgaris by using topical clindamycin solution and erythromycin gel and he found that both of them are effective but no significant difference between them.¹⁷

Balvinder K *et al.*, compare dapsone gel 5% with clindamycin gel 1% in the treatment of acne vulgaris and they found that dapsone gel is most effective with fewer side effects.¹⁸

Zoe D. Draelos compare the depose gel 5% with a placebo gel in the treatment of acne vulgaris by twice daily application and they found that dapsone gel is more effective with the early result than placebo in both the inflammatory and non-inflammatory lesions with the mild side effect that not affected the compliance of the patients.¹⁹

While AMNDA Pickert and Sharron Raimer used topical dapsone gel 5% in the treatment of acne vulgaris of mild, moderate, and severe acne vulgaris, he found that the inflammatory lesions are the most and earliest response to the drug compared to non-inflammatory, which late and less responsive. Also, they conclude that topical dapsone has only mild topical side effects with any systemic hematological adverse effect.²⁰

William J. Cunliffe *et al.* compare the combination gel of clindamycin phosphate benzoyl peroxide with clindamycin gel only. They found that the combination is gel is the most effective in treatment for both the inflammatory and non-inflammatory lesions and also has an effect on the reduction of *P. acne* count while the increase in this resistance after using the clindamycin gel only.²¹

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