

Topical Adapalene 0.1% Gel versus Topical Combination of (Tretinoin 0.025% and Erythromycin 4%) Gel in Treatment of Acne Vulgaris (A Split Face Comparative Study)

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Abstract This study was conducted to compare the efficacy of topical adapalene 0.1% gel versus a combined formula of topical tretinoin 0.025% and erythromycin 4% gel in the treatment of mild to moderate inflammatory acne vulgaris. Thirty six patients with inflammatory acne vulgaris (papules and pustules) were enrolled in the study. A split face method was used in which each patient was instructed to use a combined gel formula (tretinoin 0.025% and erythromycin 4%) on the right side of the face and adapalene 0.1% gel on the left side. Each patient was instructed to use the same amount of both gels at night. The duration of therapy was 6 weeks. Only 30 patients completed the study, 23 females and 7 males, their ages ranged from 14-33 (20.66±4.79) years. After 3 weeks of treatment the mean percent of reduction of lesions of the right and left sides was 67.86% and 50.41% respectively. The difference was statistically significant p-value <0.0001. After 6 weeks it reduced to 91.69% and 87.36% respectively. The difference was not significant p-value = 0.065. Few patients had mild erythema and dryness at both sides. In conclusion, both formulae have comparable efficacy.

Key words Acne, Adapalene, Tretinoin, Topical Erythromycin

1. Introduction

Acne vulgaris is a chronic inflammatory disease of pilosebaceous units. *Propionibacterium acnes* proliferate in sebum and the follicular epithelium becomes altered and form plugs called comedons[1].

There are many therapies for acne. Adapalene, a naphthoic acid derivative with retinoid-like activity, it reduces the number of non inflammatory and inflammatory lesions in patients with mild to moderate acne[2]. Erythromycin acts both as antibacterial agent suppressing *Propionibacterium acnes* and as anti-inflammatory agents[3].

Topical tretinoin acts against comedones and microcomedones and have direct anti-inflammatory effects[4].

Many studies showed that adapalene gel 0.1% is as effective as 0.025% tretinoin gel[5, 6] and other study revealed that it has equivalent efficacy and was significantly better tolerated than tretinoin cream 0.05% in patients with mild to moderate acne vulgaris[7]. Also tretinoin enhances the penetration of topical antibiotics with synergistic

effect[1]. For the above conflicting results and to verify if a combined tretinoin - antibiotic has better effect than monotherapy; this study was conducted.

2. Patients and Methods

This was a single – blind comparative split face therapeutic study, conducted at the Department of Dermatology - Baghdad Teaching Hospital during October 2009 to October 2010.

A total of 36 patients with mild to moderate acne vulgaris were enrolled in the study. Their ages range from 14-33 years with a mean \pm SD, 20.58 \pm 4.81. Twenty five (69.4%) patients were females and eleven (30.6%) patients were males.

All patients were without any systemic and / or topical treatment for at least 2 months before starting the study.

Full history was taken from each patient regarding age, sex, duration of the disease and previous treatment.

Physical examination was done to evaluate the severity of acne.

Scoring the severity of acne was done according to the following method.[1].

1-Mild acne in which the count of pustules is less than 20

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and the count of papules is less than 10.

2-Moderate acne in which the count of pustules is ranging from (20 – 40) and the count of papules is ranging from (10-30).

3-Severe acne, in which the count of pustules is more than 40 pustules and the count of papules, is more than 30.

Patients excluded from the study were those with severe acne, nodulocystic acne, patients with systemic diseases, pregnant and lactating women.

A split face method for application of treatment was used in which each patient was instructed to use a combined gel formula of tretinoin 0.025% and erythromycin 4% on the right side of the face and adapalene 0.1% gel on the left side.

The drugs were bought from the market. The trade name of adapalene is sure cure made by Jamjoom pharmaceuticals, Jeddah, Saudi Arabia. The trade name of the combined gel (tretinoin and erythromycin) is retinomyacin made by Mediphar Laboratories Dbaya – Lebanon.

A formal consent was obtained from each patient. Ethical approval was granted from the ethical committee.

Each patient was instructed to use the same amount of both gels (finger tip method), ½ hour in the 1st night then wash and increase the time by ½ hour in the successive nights till reach 8 hours; thereafter to keep the applications till morning.

The duration of therapy was 6 weeks and follow up for another 6 weeks.

The clinical evaluation was done every 3 weeks by 2 dermatologists; the assessment was carried out by counting the inflammatory lesions (papules and pustules) and watching any local side effects.

The satisfaction of the patients to the treatment is classified into:

- 1- Full satisfaction.
- 2- Partial satisfaction.
- 3 - No satisfaction.

Statistical analysis was done by using EPI version 6. Both descriptive and analytic data used. *P*-value equal or less than 0.05 was considered significant.

Photographs were taken by Sony digital camera (dsc-w150), 8.1 mega pixels, with a fixed illumination and at the same place.

3. Results

Thirty patients completed the study, 23 females and 7 males, their ages ranged from 14-33 with a mean \pm SD, 20.66 \pm 4.79 years.

3.1. Right Side

The total number of papules before the treatment was 330. At 3rd and 6th weeks of treatment it was reduced to 110 and 25 respectively (Table 1). This reduction was statistically significant, *F* statistic = 141.7, *P*-value < 0.0001. The mean \pm SD number of papules per patient before the treatment was 11 \pm 4.59. At 3rd and 6th weeks of treatment it was reduced to

3.67 and 0.83 respectively (Table 2).

Table 1. The Total Number of Papules and Pustules for Patients Treated with Topical Combination (Tretinoin and Erythromycin) Versus Adapalene

	Tretinoin & Erythromycin (Right side)		Adapalene (Left side)	
	papules	pustules	papules	pustules
Before	330	82	325	86
3 rd week	110	21	172	32
6 th week	25	8	44	8
Follow up	34	23	54	26

Table 2. The Mean Number of Papules and Pustules Per Patient Treated with Topical Combination of (Tretinoin and Erythromycin) Versus Adapalene

	Tretinoin & Erythromycin (right side)		Adapalene (left side)	
	papules	pustules	papules	pustules
Before Treatment	11	2.73	10.83	2.87
3 rd week of treatment	3.67	0.7	5.73	1.06
6 th week of treatment	0.83	0.27	1.47	0.27
Follow up	1.13	0.77	1.8	0.87

The total number of pustules before treatment was 82. At 3rd and 6th weeks of treatment, it was reduced to 21 and 8 respectively (Table 1). This reduction was statistically significant, *F* statistic = 75.64, *P* value < 0.0001.

The mean \pm SD number of pustules per patient before the treatment was 2.73 \pm 1.48. It was reduced to 0.7 at 3rd week and 0.27 at 6th week of treatment (Table 2).

3.2. Left Side

The total number of papules before the treatment was 325. At 3rd and 6th weeks of treatment it was reduced to 172 and 44 respectively (Table 1). This reduction was statistically significant, *F* statistic = 142.8, *P* value < 0.0001.

The mean \pm SD number of papules per patient before the treatment was 10.83 \pm 17. At 3rd and 6th weeks of treatment it was reduced to 5.73 and 1.47 respectively (Table 2).

The total number of pustules before treatment was 86. At 3rd and 6th weeks of treatment it was reduced to 32 and 8 respectively (Table 1). This reduction was statistically significant, *F* statistic = 11.83, *P* value < 0.0001. The mean \pm SD number of pustules per patient before the treatment was 2.87 \pm 1.8. It was reduced to 1.06 at 3rd and 0.27 at 6th weeks of treatment (Table 2).

After 3 weeks of treatment, the mean percent reduction of inflammatory lesions (papules and pustules) at the right side was 67.86 %. It was higher than the mean percent of reduction at the left side which was 50.41%. This difference was statistically significant, *F* statistic = 35.24, *P* value < 0.0001

After 6th week of treatment, the mean percent reduction at the right side was 91.69 % (Figure 1), while at the left side it was 87.36% (Figure 2). This difference was not significant. *F* statistic = 3.57, *P* value = 0.065.

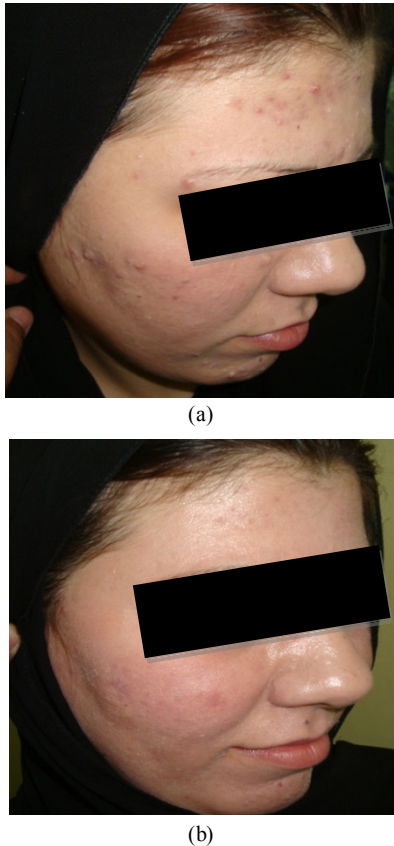


Figure 1. (a) A twenty two years old female with three years history of acne vulgaris treated with tretinoin and erythromycin gel (right side). (b) After 6 weeks of treatment

3.3. Side Effects

Mild erythema and dryness were observed in 25 (83.33%) patients in both sides, which were disappeared in few days and did not necessitate cessation of therapy.

3.4. Patients' Satisfaction

At the adapalene side 86% of patients were fully satisfied and 90% were fully satisfied at the combined formula side.

3.5. Follow up

Six weeks after stopping treatment, the recurrence rates for the adapalene and the combined formula were 5% and 4.5% respectively.

4. Discussion

Acne is a major problem in young people, which has both physical and psychological impacts on patients life. There are many therapies for acne ranging from topical agents such as retinoic acid, benzoyl peroxide, clindamycin solution, erythromycin and azelaic acid. Systemic agents such as antibiotics (doxycycline, erythromycin), retinoid and hormonal agents are also used. Both types of treatment are not free of side effects. Combination regimens that include an antibiotic and a retinoid to reduce follicular plugging are the mainstay of topical treatment[1].

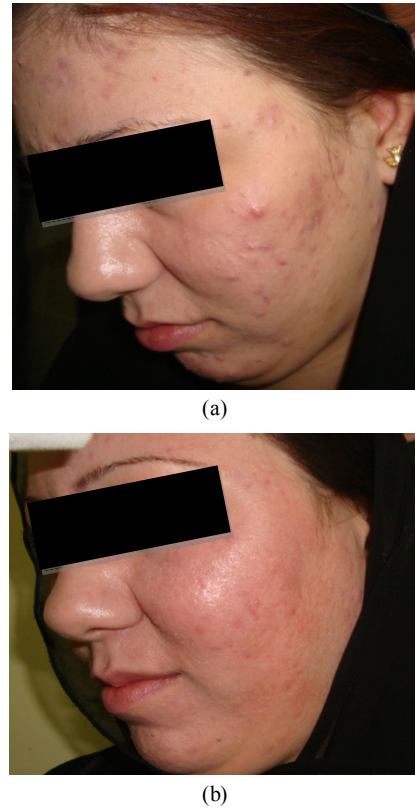


Figure 2. (a) The same patient treated with adapalene gel (left side). (b) After 6 weeks of treatment

The differences between the results on both sides of the face were statistically non significant at the end of 6th week. However at the end of 3rd week of treatment the results of the combination of (tretinoin and erythromycin) were superior to the result of adapalene, this means that the combination acts faster.

Comparing the present results with other studies which revealed that adapalene gel 0.1% is as effective as tretinoin gel 0.025%[5, 6] and as effective as tretinoin cream 0.05% showed that the results are comparable.

The combined formula at the left side has faster response, this can be explained by the fact that tretinoin enhances the penetration of other topical agents such as antibiotics[1].

In a study conducted by Mills et al on 26 patients with mild to moderate acne vulgaris treated with benzoyl peroxide 2.5%, the mean percent reduction of the inflammatory lesions was 54.3% and on 25 patients treated with benzoyl peroxide 5% was 47.2%[7].

The mean percent reduction of the inflammatory lesions in the present study was higher than of benzoyl peroxide, this may be related to that the anti-inflammatory effect of adapalene and (tretinoin and erythromycin) higher than that of benzoyl peroxide.

A study demonstrated that the combination of 5% w/w benzoyl peroxide and 3% w/w erythromycin has greater in vivo anti-propionibacterial activity than 3% w/w erythromycin alone, and brings about significant clinical improvement in acne patients with high numbers of erythromycin-resistant propionibacterial strains pretreatment[8]. These results go

with our findings that combined topical antibiotic and retinoid therapy has superior results.

A study conducted at the department of Dermatology and Venereology in Baghdad Teaching Hospital showed that topical tea lotion was effective in reducing papules and pustules in 8 weeks, these results were comparable to the results of present study[9].

Other study showed that topical 1% ciprofloxacin gel was effective in reducing papules and pustules in 8 weeks, these results were comparable to the results of present study[10].

5. Conclusions

1- Both topical adapalene 0.1% and a topical combination of (tretinoin 0.025% and erythromycin 4%) have comparable efficacy in treatment of mild to moderate inflammatory acne vulgaris.

2- If we consider that the combined formula has synergistic effect; then we can conclude that adapalene 0.1% has better efficacy than tretinoin 0.025 and erythromycin 4% alone.

3- A topical combination of (tretinoin 0.025% and erythromycin 4%) acts faster than adapalene 0.1%.

4- We recommend doing a similar study with a longer duration of treatment and following up in moderate to severe acne to show which has more efficacy and sustained effect.

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