

## Comparison of the efficacy of topical 0.05% Isotretinoin gel with 1% Clindamycin solution in the treatment of papulopustular acne vulgaris

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**Abstract: Background and Aim:** Acne vulgaris is a common disorder of adolescence which may lead to many cosmetically and psychological problems so various topical and systemic therapeutic modalities have been used. This study was designed to compare efficacy of topical Isotretinoin gel with 1% Clindamycin solution in the treatment of acne vulgaris. **Methods:** In this randomized clinical trial, 60 patients with mild to moderate papulopustular acne vulgaris were selected and randomly allocated into two (30 patients in each group). One group was treated with 0.05% Isotretinoin gel every night. The other group was treated with 1% Clindamycin solution twice daily. Both groups were followed every month for 3months. **Results:** The difference between TLC mean after treatment was meaningful in comparison with its mean before the treatment ( $P<0.001$ ). The variance analyze with multiple measurements showed significant difference in ASI after treatment in comparison with its number before treatment ( $P<0.001$ ). But satisfaction of patients in Clindamycin group was higher ( $P<0.001$ ). **Conclusion:** Decrease in TLC and ASI in both treatment groups had a significant difference but with considering the minimal complications and satisfaction of patients in Clindamycin group. We can recommend 1% solution of Clindamycin in papulopustular lesions of acne vulgaris.

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### 1. Introduction

There are several factors that contribute to acne, including Propionibacterium acnes activity, increased sebum production, androgenic stimulation, increased keratinization of follicular channel, inflammatory response (lymphocytic, macrophage and neutrophilic), and cytokinetic activity (Stathakis, 1997).

Acne Vulgaris is a disease of adolescence and youth era, and nearly 85 percent of 12 to 24 years old people are affected. In 12% of women and 3% of men, acne lesions remain until age of 44 years. The most common locations involved are face, back and chest. Despite popular belief, stress and diet do not worsen acne. On the contrary, hormones such as estrogen and progesterone are involved in acne (Bolognia, 2008).

The cause of acne inflammation before menstruation is the changes in hydration of pilosebaceous epithelium. Acne vulgaris lesions include inflammatory lesions (papules, pustules, nodules and cysts) and non-inflammatory lesions (open and closed comedones).

Rating the severity of acne is based on the number and type of lesions; so that the presence of open and closed comedones and a slight papule is considered as mild, more papules and pustules in addition to Comedones as moderate, and presence of

nodules and cysts besides the above lesions as severe acne (Johnson and Roberts, 1978).

The severity of acne is categorized into four groups: mild, moderate, severe and very severe. This categorization is based on the number of inflammatory lesions (papules + pustules), and not Comedones, in a half of the face; so acne is considered as mild if the number of lesions is between 1 to 5, moderate if between 6 to 20, severe if between 21 to 50, and very severe if more than 50 (Noakazu, 2008).

In addition to topical treatments, such as topical antibiotics, topical retinoids, Benzoyl Peroxide and Azelaic Acid, current popular treatments for acne also include the oral treatments such as antibiotics, Isotretinoin, Zinc and hormones (Meynadier and Alirezai, 1998).

Antibiotics act by decreasing neutrophil chemotaxis and regulating the complement pathway and inhibiting the production of lipase and Propionibacterium acnes (Jensen, 1991).

Since several studies have been conducted on the use of various topical antibiotics and other topical drugs for treatment of inflammatory acne lesions in the research centers around the world, and on the other hand, no such study has been conducted on the patients in our area, regarding the importance of the issue and in order to effectively cure papulopustular acne lesions in terms of their severity and

fragmentation, we intended to evaluate and study therapeutic effects of topical Tretinoin gel 0.05% and Clindamycin solution 1% in affected patients.

## 2. Material and Methods

In a randomized clinical trial at the Department of Dermatology, Tabriz University of Medical Sciences in 2012, therapeutic effects of Tretinoin gel 0.05% with Clindamycin topical solution 1% were studied in patients with mild to moderate acne vulgaris.

In a randomized clinical trial, 60 patients diagnosed with mild and moderate popular and pustular acne referred to specialized skin clinic of Sina hospital, Tabriz University of Medical Sciences and qualified with the inclusion criteria, were studied in two groups.

Patients in group A were treated with topical Isotretinoin gel 0.05%, and patients in group B were treated with Clindamycin solution 1%.

Both of the treatment methods were explained for the patients, and with their informed consent, they were randomly divided into the two groups and those dissatisfied with the treatment were excluded from the study.

Also in this study, no additional cost was imposed to the patients or their attendants, and no interference was taken place in the treatment or prevention of disease.

After selection, the patients underwent the intended treatment and were followed up for a period of 3 months. Study was single-blinded, and the initial examination of patients and the resulting changes after administration of the drugs were performed and recorded every 4 weeks by an assistant staff.

Response to treatment was compared by consecutive evaluation of the patients' treatment and their satisfaction, and improvement of the lesions. Application of topical Isotretinoin gel 0.05% was prescribed once a night and Clindamycin solution 1%, 2 times a day topically.

Both groups received treatment for 12 weeks. During the study, the patients were not allowed to use any cosmetics or other topical medications other than the prescribed drugs; and those violating this condition were excluded from the study and replaced by other patients.

Every 4 weeks, patients underwent a physical examination and the findings and if possible, the photographs of the skin lesions in patients were collected.

After 12 weeks of treatment and follow up, objective and functional signs, and possible complications were evaluated by the treating physician and the patients.

Number of inflammatory lesions (papules and pustules) and non-inflammatory lesions (Comedones) were recorded at the beginning of and during the study; so that the number of lesions (inflammatory and non-inflammatory) less than 5 was scored as mild, and the number between 5 and 20 as moderate type.

The effectiveness of medications was identified with the loss or reduction of inflammatory and non-inflammatory lesions during the study. Patients' satisfaction with each of the medications was also recorded.

During the treatment, side effects such as erythema, burning, itching, allergy to sunlight, patient's intolerance of the medication and other possible complications and reduction of the lesions were evaluated through the records and clinical examination.

Finally, the following formulas were used to determine the effectiveness of treatments on the severity of the acne, the total number of lesions and acne severity index:

Total acne Lesions Counting= TLC

TLC= Papules + pustules + nodules + Comedones

Acne Severity Index= ASI

ASI = (comedones/4) + 2 (pustules) + papules

In the first visit, the total number of lesions was considered as 100% and the ASI determined. At the end of the treatment, the reduction of the number was calculated in percentage and considered as recovery.

### Inclusion criteria:

Included patients with mild and moderate acne with age from 11 to 30 years.

### Exclusion criteria:

- 1 - Pregnant and lactating women
- 2 - Use of topical medications in the past one month
- 3 - Use of anti-acne oral medications in the past 2 months
- 4 - Infection by any skin disease other than acne
- 5 - Having severe nodulocystic acne
- 6 - Concomitant use of drugs that cause acne such as lithium - oral steroid - Vit B<sub>12</sub> - Medications containing iodine and bromine
- 7 - Presence of more than 20 inflammatory lesions or three nodules or cysts in one side of face.

### Statistical Analysis:

The results obtained are reported as Mean  $\pm$  SD and frequency and percentage as well. The statistical software used was SPSS™ ver.16.

To compare the effects of treatments, the mean difference test for the independent and the test

groups of RMA, and chi-square or Fisher's exact test were used. In all cases studied, the results with  $p < 0.05$  were considered statistically significant.

The mean total number of lesions and Acne Severity Index at the baseline and during the study is shown in Table 1.

Table 1. Evaluation prevalence of lesion types among the patients in both groups at the baseline and during the study

	Before treatment			4 Week late			8 Weeks late			12 Weeks Late		
	Isotretinoin gel 0.05%	Clindamycin solution 1%	P	Isotretinoin gel 0.05%	Clindamycin solution 1%	P	Isotretinoin gel 0.05%	Clindamycin solution 1%	P	Isotretinoin gel 0.05%	Clindamycin solution 1%	P
Blackhead Comedones	3.40 ± 2.19	4.97 ± 2.04	0.006	3.37 ± 2.16	3.53 ± 1.76	0.744	3.03 ± 2.03	2.07 ± 1.08	0.025	2.00 ± 1.64	0.83 ± 0.53	0.001
Whitehead Comedones	3.77 ± 2.33	5.47 ± 1.74	0.002	3.63 ± 2.34	3.33 ± 1.40	0.549	3.20 ± 2.43	1.73 ± 1.01	0.004	1.77 ± 1.45	0.47 ± 0.57	0.001
Papules	4.00 ± 2.30	4.23 ± 1.72	0.658	4.07 ± 1.62	1.93 ± 1.57	0.001	3.37 ± 1.54	1.03 ± .93	0.001	1.87 ± 1.33	0.30 ± 0.47	0.001
Pustules	1.43 ± 1.83	1.13 ± 1.48	0.488	1.23 ± 1.50	0.50 ± 0.73	0.021	1.17 ± 1.60	0.20 ± 0.41	0.003	0.53 ± 0.90	0.03 ± 0.18	0.005
TLC	12.83 ± 5.01	15.57 ± 3.82	0.021	12.30 ± 4.65	9.30 ± 3.36	0.006	10.77 ± 4.70	5.03 ± 2.43	0.001	6.17 ± 4.04	1.53 ± 1.04	0.001
ASI	6.74 ± 2.37	7.18 ± 2.47	0.490	6.43 ± 2.19	3.90 ± 1.85	0.001	5.51 ± 2.21	2.12 ± 1.23	0.001	3.08 ± 1.96	0.66 ± 0.53	0.001

Table 2. Satisfaction of patients in two groups

	Clindamycin solution 1%			Isotretinoin gel 0.05%			P
	4 Week	8 Weeks	12 Weeks	4 Week	8 Weeks	12 Weeks	
	late	late	Late	late	late	Late	
Complete Satisfied	2	6	13	-	-	-	0.001
Satisfied	23	24	17	1	5	19	
Dissatisfied	-	-	-	1	-	-	
Not changed	5	-	-	28	25	11	

Table 3. Side effects of treatment in both groups

	Clindamycin solution 1%			Isotretinoin gel 0.05%		
	4 Week late	8 Weeks late	12 Weeks Late	4 Week late	8 Weeks late	12 Weeks Late
Erythema	1(3.3%)	-	-	9(30%)	2(6.7%)	1(3.3%)
Scaling	-	-	-	1(3.3%)	-	-
purities	2(6.7%)	-	-	1(3.3%)	1(3.3%)	1(3.3%)
burn	1(3.3%)	-	-	-	-	-
xerosis	1(3.3%)	-	-	1(3.3%)	1(3.3%)	1(3.3%)

### 3. Results

In the Group A, 7 (23.3%) of the cases were male and 23 (76.7%) were female, while in Group B, 5 (16.7%) were male and 25 (83.3%) were female ( $P=0.51$ ).

The mean age of the patients was  $22.7 \pm 4.45$  years in the Isotretinoin group (Group A) and  $22.30 \pm 4.20$  in the Clindamycin group (Group B) ( $P=0.61$ ).

27 patients (90%) in the Clindamycin group and 24 patients (80%) in the Isotretinoin group were single ( $P=0.27$ ).

The prevalence of lesion types among the patients in both groups at the baseline and during the study is shown in Table 1.

The frequency of side effects between the two groups during the study is shown in Table 2.

Descriptive rating of patient satisfaction of the treatment provided between the two groups with respect to complications and effectiveness of the treatment during the study is presented in Table 3.

ANOVA results of RMA in the two groups indicate that Isotretinoin and Clindamycin significantly reduced the number of blackhead and whitehead Comedones, papules and pustules in the patients under study ( $P=0.001$ ).

There was no significant difference between the outcomes of the two treatment groups in reduction of the number of blackhead and whitehead Comedones and papules.

In general, comparison of the two groups shows that the effect of drugs on the pustules is not statistically significant ( $P=0.45$ ).

ANOVA results of RMA in the two groups indicate that Isotretinoin and Clindamycin significantly reduced the TLC and ASI in the patients under study ( $p<0.001$ ); and Clindamycin seems to be more effective in reduction of ASI.

#### 4. Discussions

In a single-blind randomized clinical trial, we studied the efficacy and side effects of 0.05 % Isotretinoin gel and 1% Clindamycin solution in the treatment of papulopustular acne lesions.

Antibiotics are commonly prescribed in either topical or systemic form for treatment of acne and the results are almost always excellent, but there is a risk of treatment failure. Antibiotics used in acne include: tetracycline (Tetracycline, Doxycycline, Minocycline and Lymecycline), erythromycin and Co-trimoxazole. Antibiotics acts through decreasing the neutrophil chemo taxis and regulation of the complement pathway and inhibition of *Propionibacterium acnes* lipase production (Jensen, 1991).

In a study by Dominguez and colleagues a similar improvement in the inflammatory lesions of acne patients with Isotretinoin gel and Tretinoin Cream was observed (Dominguez, 1998).

Unlike the study of Dominguez and colleagues in our study we evaluated the effect of the drugs only on inflammatory lesions. Similar to this study the intervals of patient assessment were monthly and the final assessment for efficacy of treatment and side effects was at the end of the 3<sup>rd</sup> month.

Khabnadideh and colleagues also investigated the effects of Clindamycin hydrochloride effects on and stated that this solution has describable anti-acne effects. Although Clindamycin gel is usually produced from phosphate ester hydrochloride, but also the use of hydrochloride salt is pharmacologically active and more economical than (Khabnadideh, 2009).

In our study, 1% Clindamycin solution can significantly decrease TLC and ASI in patients ( $P<0.001$ ).

With considering much less side effects and more patient satisfaction in Clindamycin group comparing to Tretinoin, Clindamycin is known to be the drug of choice, these findings is similar to the findings of Khabnadideh and his colleagues study.

In a study conducted by Ahmed and colleagues in 2009, it is stated that all of retinoid cause some degrees of irritation. Erythema and scaling was 2+ using topical Isotretinoin and 1+ using Adapalene (Ahmed and Sarwar, 2009).

In the present study, in the group receiving Clindamycin the drug side effects was seen in 4<sup>th</sup> week in 16.7% of patients but in the group receiving Clindamycin the side effects was seen in the weeks 4.8 and 12, in 36.7, 13.3 and 10 % of patients respectively.

This result was almost similar to the results of Ahmed and his colleagues.

In the Shiraz university of medical sciences Farokh Rad and his colleagues studied the effect of oral tetracycline and Azithromycin on acne vulgaris and stated that the Azithromycin is more effective that tetracycline in the treatment of the inflammatory lesions of face and the back and can used effectively in cases of resistance to the tetracycline (Rad, 2010).

In our study we did not use any oral treatments for acne inflammatory lesions.

In a study conducted in 2009 by Nilforosh Zadeh and colleagues, they investigated the effect of 1% Clindamycin lotion combination of Clindamycin phosphate Clindamycin phosphate 1% + 1% + Tretinoin combination 2% salicylic acid in the treatment of mild to moderate acne vulgaris and stated Clindamycin in combination with salicylic acid that ASI decreased significantly higher than the other two combination ( $P=0.03$ ) (Nilfroushzadeh, 2009).

Patient satisfaction rate was evaluated in the two group, this rate was significantly higher in the group under treatment with 1% Clindamycin comparing to the group under treatment with Isotretinoin ( $P=0.001$ ).

Ioannides and colleagues investigated the efficacy and tolerance of the Adapalene gel 0.1% and Isotretinoin gel 0.05% in the treatment of the acne and stated that the tolerance and satisfaction of patient receiving Isotretinoin was significantly higher in the group receiving Isotretinoin (Ioannides and Katsambas, 2002).

Similar to our study the side effects like erythema and scaling was higher in the group receiving Isotretinoin.

#### Conclusion:

In our study, a significant decrease in TLC and ASI was seen in the patients of the two groups but considering the less side effects and greater satisfaction with treatment in the Clindamycin group comparing to the Isotretinoin preferably Clindamycin 1% is recommended in the treatment of acne papulopustular lesions.

#### Suggestions:

There was some limitation in our study that with resolving them we can suggest the followings:

1- Conducting a similar study with more cases and to compare the effect of 1% Clindamycin and salicylic acid with 0.05 Isotretinoin.

2-conducting a similar study for comparing the effect of topical 1% Clindamycin with oral antibiotics like Azithromycin.

3-conducting a similar study with a long 6 month period.

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