

Efficacy of Adapalene 0.1% Versus Tretinoin 0.025% Cream For The Treatment of Mild Acne Vulgaris

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Abstract

Background

Acne vulgaris (AV) is a chronic inflammatory of the pilosebaceous unit. Topical retinoid is a mainstay of mild AV first-line treatment.

Methods

The randomized double-blind clinical trial was conducted from June to September 2019 at Dr. Mohammad Hoesin General Hospital Palembang. A total of 70 mild AV patients who fulfilled inclusion criteria were enrolled consecutively. Patients randomly treated with adapalene 0.1% cream or tretinoin 0.025% cream and evaluated every 2 weeks for 8 weeks to examine the number of AV lesion (inflammation, non-inflammation and total lesion).

Results

There were reduction in number of inflammatory and non-inflammatory lesions at both groups but only inflammatory lesion was statistically significant ($p < 0.05$). Total lesions also decreased in adapalene and tretinoin group (21.66 vs 5.75, 22.21 vs 7.96, respectively) and statistically significant ($p < 0.05$).

Conclusion

Adapalene 0.1% cream showed non-inferiority to tretinoin 0.025% cream in efficacy, especially in the reduction of non-inflammatory and total lesions.

Keywords: adapalene, tretinoin, topical retinoid, efficacy, mild acne vulgaris

Introduction

Acne vulgaris (AV) is a chronic inflammatory of the pilosebaceous unit, characterized by open and closed comedones and inflammatory lesions such as papules, pustules, or nodules.^{1,2} Acne vulgaris is the most commonly occurring skin disease, especially in the face and back area.¹ Acne vulgaris affects approximately 20-90% adolescence and commonly found in 14-17 years old female or 16-29 years old male.³ This disease can persist until adulthood and more often affected females compared to males.¹ The prevalence of AV was estimated about 9.4%.⁴

Topical retinoids, derivatives of vitamin A have been recommended for AV for almost three decades. Adapalene, the third-generation of retinoid, is a derivative of naphthoic acid. The mechanism of action of adapalene is similar to tretinoin, selectively binds with RAR γ , which leads to keratinocyte normalization. Adapalene is stable and lipophilic which leads to higher concentration achieved in stratum corneum and pilosebaceous unit. Additionally, there is a unique anti-inflammatory effect of adapalene by inhibiting oxidative metabolism of arachidonic acid through lipoxygenase 5 and 15.^{5,6}

Efficacy of adapalene has been evaluated over decades. Ellis, *et al.* compared adapalene 0.1% vs tretinoin 0.025% in 297 patients for 3 months showing there was no difference in efficacy of both adapalene and tretinoin.⁷ A 12-week double-blind study which compared tretinoin gel microsphere 0.1% with adapalene gel 0.1% showed similar efficacy in the resolution of acne lesions, with the significantly greater reduction of comedones seen at week 4 in the tretinoin group ($p=0.047$).⁸ A meta-analysis evaluated 900 patients from five studies which compared between adapalene 0.1% gel and tretinoin 0.025% gel demonstrating equivalent efficacy in terms of reducing total lesion count. Adapalene demonstrated more rapid efficacy significantly, that indicated by reduction of inflammatory lesions and total lesions at week 1.⁹ Thus, we will compare the efficacy of adapalene 0.1% versus tretinoin 0.025% cream in terms of reduction of inflammation, non-inflammation and total lesion in mild AV in our setting.

Methods

This was a double-blinded clinical trial to compare the efficacy of two drugs for treatment of mild AV in Department of Dermatology and Venereology, Cosmetic-dermatology Division, dr. Mohammad Hoesin General Hospital Palembang from June to September 2019. The sample of this study were 70 mild AV patients who fulfilled inclusion criteria, were consecutively enrolled. Diagnosis of acne vulgaris was established clinically by dermatologist (researcher). The AV was classified as mild AV based on Lehmann (2002), which is comedones <20, papules or pustules <15, no nodules, and total lesions < 30. We included mild AV patients aged 18 years or older. Verbal and written informed consent was obtained from all patients. We excluded patients with other topical or systemic therapies for AV, on contraception,

hypersensitivity to topical retinoid, other skin disease, outdoor daily activities and sun-exposed more than 2.5 hours/day, pregnant and breastfeeding. This study was approved by Health Research Review Committee of Mohammad Hoesin Central Hospital and Faculty of Medicine Sriwijaya University Palembang, Indonesia.

Patients were given randomly either adapalene 0.1% cream (PT. Ferron Pharmaceuticals, Indonesia) or tretinoin 0.025% cream (PT. Genero Pharmaceuticals, Indonesia) and were followed-up on week 2, 4, 6, and 8 to assess the efficacy. Patient applied the cream once daily at night, without any other medication or skin care product except mild facial wash that provided by researcher. Efficacy was measured by number of lesion. Lesion was classified into inflammatory (papule and pustule) and non-inflammatory (comedones) lesions. Total lesions is the total number of inflammatory and non-inflammatory lesions.

Data was processed using Statistical Package for Social Sciences (SPSS) version 24.0 software. We performed repeated ANOVA to compare inflammatory and non-inflammatory lesions and paired t-test to compare total lesions at baseline and after treatment. All data were analyzed and considered significant if p value < 0.05 .

Results

About 70 patients were assigned randomly into two groups, 35 patients in group A (adapalene 0.1% cream), and 35 patients in group B (tretinoin 0.025% cream). Five patients were dropped out because they did not fulfilled all research protocols. Sociodemographic characteristic of patients is presented in **Table 1**.

Efficacy of both groups in reduction of total lesions can be seen in **Table 2 and 3**. In every follow-up there is a reduction of mean total lesions from baseline in both groups. Reduction of mean total lesions in adapalene group at *baseline* and week 8 was 22.21 and 7.96 whereas there is a statistically significant difference between total lesion before and after treatment ($p = 0.00$). Similar to adapalene group, reduction of mean total lesion in tretinoin group before and after treatment was 21.56 and 5.57 ($p = 0.00$).

Tabel 1. Distribution of patient based on age and gender

Distribution of sample		Group A	Group B	Total
		n (%)	n (%)	n (%)
Age	18 – 20	11 (33.3)	8 (25)	19 (29.2)
	21 – 23	11 (33.3)	14 (43.8)	25 (38.5)
	24 – 26	3 (9.1)	3 (9.4)	6 (9.2)
	27 – 29	4 (12.1)	4 (12.5)	8 (12.3)
	30 – 32	2 (6.1)	2 (6.3)	4 (6.2)
	33 – 35	2 (6.1)	1 (3.1)	3 (4.6)
Gender	Male	11 (33.3)	10 (31.3)	21(32.3)
	Female	22 (66.7)	22 (68.8)	44 (67.6)
	Total	33 (100)	32 (100)	65 (100)

The inflammatory and non-inflammatory lesions in both groups (**Figure 1 and 2**) decreased in number in every follow-up period. Non-inflammatory lesions in adapalene group shown rapidly decreasing mean lesion from baseline to week 4 than tretinoin group. In contrary, the inflammatory lesion both group shown decreasing gradually from baseline to week 8. The reduction of non-inflammatory lesions were statistically significant ($p= 0.00$) in both group. Whereas, the reduction of the inflammatory lesions before and after treatment is not statistically significant ($p=0.1$).

Tabel 2. Total lesions on both groups

Week	Group A	Group B
Baseline	21.66	22.21
2	15.12	17.21
4	11.36	13.871
6	8.12	11.06
8	5.75	7.96

Tabel 3. Mean of non-inflammation, inflammation and total lesions at baseline and after treatment

	Group A	Group B	<i>p</i> value
Inflammatory lesions			
Baseline	8.57	8.86	0.1
After treatment	3.67	3.65	0.1
Non-inflammatory lesions			
Baseline	13.27	8.46	0.00
After treatment	3.84	2.68	0.00
Total lesions			
Baseline	21.66	22.21	0.00
After treatment	5.75	7.96	0.00

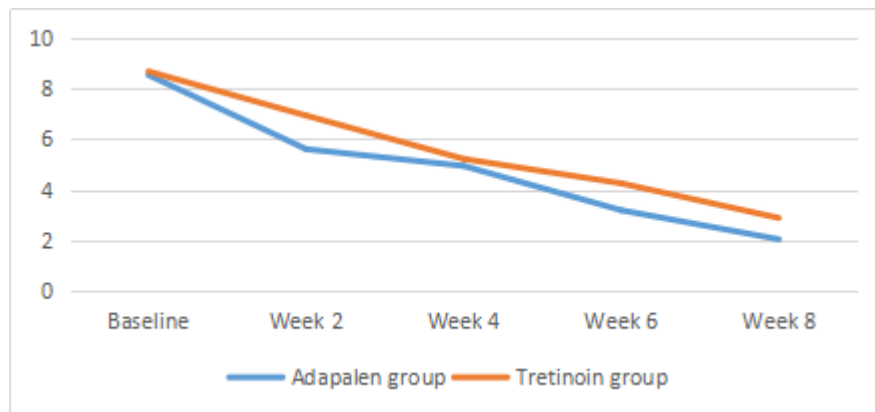


Figure 1. Reduction of inflammatory lesions in both groups

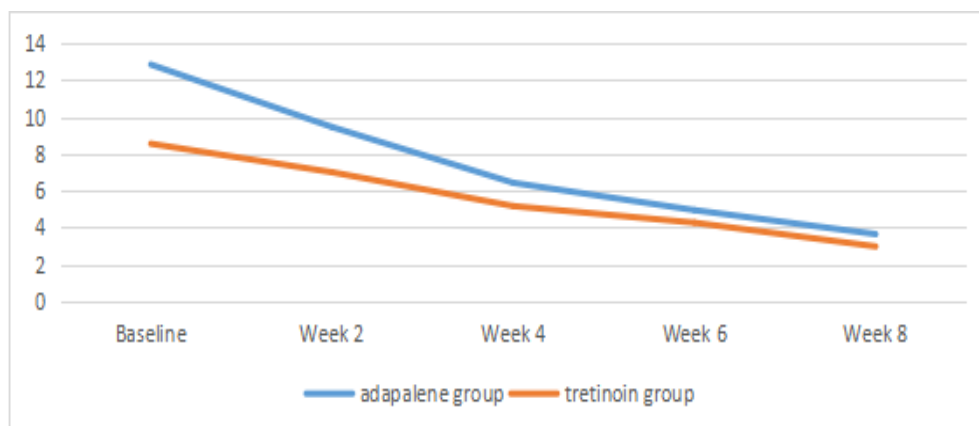


Figure 2. Reduction of non-inflammatory lesions in both groups

Discussion

Topical retinoid is mainstay recommended therapy for AV. Topical retinoid play important role in management of AV by acting against comedones and microcomedones, and exerting anti-inflammation effects.¹⁰ There are several types of topical retinoid, including tretinoin, adapalene, and tazarotene. This double-blinded clinical trial compared the efficacy of adapalene 0.1% cream and tretinoin 0.025% cream on 70 mild AV patients.

Adapalene have similiar biologic activity as tretinoin. Adapalene has restricted receptor specificity, possessing poor affinity for retinoid acid receptors (RAR)- α , higher affinity for RAR β dan γ , and no interaction with retinoid X receptors (RXR)- α . Predominant retinoid receptor in human skin are RAR- γ and RXR- α . When RAR-adapalene complex binds retinoid X receptors (RXR), this regulate gene transcription by binding specific DNA that caused keratinocyte differentiation.¹¹

Reduction of total lesion in adapalene group and tretinoin group was statistically significant. In Tu *et al*, 150 patients AV grade II-III treated with 0.025% tretinoin and 0.1% adapalene found reduction in total, inflammatory and non-inflammatory lesion with range 69-74%.¹² Optimal efficacy of topical acne treatment depends on the achievement of a high concentration of drug at the target site, the pilosebaceous unit. Adapalene has unique physicochemical properties, because the unstable double ring of tretinoin replace to aromatic ring of naphthoic acid. This structure makes adapalene more stable and lipophilic, so that, adapalene is able to penetrate better into sebaceous gland follicles. Adapalene also has very low percutaneous absorption once the drug has penetrate the stratum corneum.^{11,13}

This study found that there are reduction in the number of inflammatory and non-inflammatory lesions both in adapalene and tretinoin group, but only significant in non-inflammatory lesions. Leyden *et a*, compare topical retinoid in reduction of inflammatory lesion in 577 AV patients with high resolution digital photographs found significant clinical improvement in all retinoid (adapalene, tretinoin and tazarotene).¹³ Shalita *et al* found that adapalene 0.1% was significantly more effective in reduction acne lesions (total, non-inflammatory and inflammatory lesions) than tretinoin 0.025% (49% vs 37% ($p < 0.01$), 46% vs 33% ($p = 0.02$), 48% vs 38% ($p = 0.06$), respectively).¹⁴ An animal model showed the changes of expression of the sebum-rich keratin plug to the surface of the skin, reduced

keratinocyte proliferation, and a normalization of the follicle.¹⁵ A post-marketing surveillance study showed that 96.3% of patients improve in their acne from baseline.¹⁶

This study has several limitations. Firstly, the number of sample is limited and hospital-based so the results of the study cannot be generalized to general population. Secondly, the assessment of efficacy is only based on visible evaluation. The objective tool such as computation imaging techniques can give more accurate results.

Conclusion

Adapalene 0.1% cream showed non-inferiority to tretinoin 0.025% cream in efficacy, especially in the reduction of non-inflammatory and total lesions.

Conflict of Interest

There are no conflict of interest.

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