

Treatment of Acne Vulgaris with 5-Alpha Avocuta Cream 2% in Comparison with Tretinoin Cream 0.025% (Single Blind Comparative Study)*

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ABSTRACT

Background: Acne vulgaris is a common skin disease. Its pathogenesis is multifactorial, and therapy can now be directed at many of these factors. Among these factors are androgen hormones which play an important role in the pathogenesis of acne. Accordingly, many antiandrogens have been developed to treat acne by systemic and topical ways. Five-Alpha Avocuta 2% cream is a new topical 5-Alpha reductase inhibitor extracted from the tropical fruit “avocado”.

Objectives: To evaluate the effectiveness and safety of 5-Alpha Avocuta cream and compare it to tretinoin 0.025% cream, in the treatment of acne vulgaris. **Patients & Methods:** This single blinded comparative study was done in Department of Dermatology—Baghdad Teaching Hospital, from July 2009 through October 2010. All demographic points related to the disease were obtained from each patient to evaluate severity of acne. Sixty-eight patients with acne were divided into two groups and instructed to apply the drugs for three months. **Group A** uses 5-Alpha Avocuta 2% (Teen-derm K) cream and **Group B** uses tretinoin (Acretin) 0.025% cream. Severe acne was excluded from the study. The clinical improvement was evaluated by counting the number of inflammatory lesions before and after treatment and compare between them by paired t-test. **Results:** Fifty-eight patients completed the study, their age ranged from 12 - 30 years with a mean of 18.21 ± 4.64 years. In **Group A** there was a significant reduction of the mean number of papules from 29.7 before treatment to 15.5 after treatment ($p < 0.0001$), while the mean number of pustules decreased from 4.9 to 0.6 ($p = 0.019$). In **Group B** the mean number of papules was reduced from 28.5 to 14.9 ($p < 0.0001$), while the mean number of pustules dropped from 5.3 before treatment to 0.7 after treatment ($p = 0.009$). The mean difference of papules after 14 weeks in **Group A** was 15.55 ± 6.95 while in **Group B**, the mean difference was 14.86 ± 6.99 . This result was statistically not significant ($p = 0.708$, t-test). The difference in the mean percentage of reduction of inflammatory lesions at week 14 between the two groups was not statistically significant (p -value = 0.999). The side effect was negligible in **Group A** and not required stopping the drug while in **Group B** treatment stopped in 2 patients. **Conclusions:** 5-Alpha Avocuta was an effective mode of therapy in treatment of acne vulgaris, and it was comparable to tretinoin, with little side effects.

Keywords: Acne; 5-Alpha Avocuta; Tretinoin; Treatment; Iraq

1. Introduction

Acne vulgaris is an extremely common skin disorder whose incidence peaks at 18 years of age, but substantial numbers of men and women aged 20 - 40 years are also affected by the disorder [1]. Although most patients improve with time acne is a cause of suffering for many young people; in addition it may lead to a life-long scarring. Many therapies had been introduced to control acne

vulgaris which are based on etiological factors, these drugs are either topical such as (erythromycin, clindamycin, azaleic acid, benzyl peroxide and retinoic acid) or systemic which include: Antibiotic such as tetracycline, erythromycin, co-trimoxazole and others, oral retinoid and hormonal therapy [2]. However many have side effects. Topical treatments were sometimes associated with irritation and systemic are not without unwanted effects and precautions.

Acne patients, males and females secrete an average more sebum than normal subjects; sebaceous activity is

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predominantly dependent on androgen sex hormones of gonadal or adrenal glands [3]. Since 5-Alpha Avocuta reduces sebum secretion [4] it was tested in the present study for the treatment of acne in comparison with topical tretinoin.

So, this study was carried out to evaluate the effectiveness and safety of 5-Alpha Avocuta cream and compare it to tretinoin 0.025% cream, in the treatment of acne vulgaris.

2. Patients and Methods

The single-blinded comparative clinical trial was conducted at the Department of Dermatology in Baghdad Teaching Hospital during the period from July 2009 through October 2010. Sixty-six patients participated in the study however 8 patients defaulted for unknown reasons and 58 completed the study.

Full history was taken from each patient including age, duration of the disease, previous treatment and ensured that every patient had stopped any systemic and topical treatment at least 3 months before starting the present therapy. Close physical examination was done to evaluate the severity of acne. Scoring the severity of acne was chosen according to P. Habif *et al.* [5].

1) Mild acne in which the count of papules is less than 10 and the count of pustules is less than 20;

2) Moderate acne in which the count of papules ranges from 10 - 30 and the count of pustules ranged from 20 - 40;

3) Severe acne in which the count papules are more than 30 and/or the count of pustules is more than 40.

Ethical approval was taken from the Scientific Council of Dermatology and Venereology-Baghdad/Iraq before the beginning with the study.

Formal consent was taken from each patient after full explanation about the nature, course, treatment complication and prognosis of the disease.

Severe acne and nodulo-cystic types were excluded from the study.

Digital photography was done for all patients (one front and two side photos: **Figures 1 and 2**) at the first visit and at each visit after, using Sony H50 nine mega pixel digital cameras in a good illumination and same place.

Patients were divided into two groups:

1) Group A:

In this group 29 patients were treated with topical 5-Alpha Avocuta 2% creams (Teen Derm K@ Manufactured by Modern cosmetic Co./Syria/ISIS Pharmaceuticals/France) twice daily application for 14 weeks.

2) Group B:

In this group 29 patients were treated with topical tretinoin 0.025% cream (Acretin@ Manufactured by Jam-

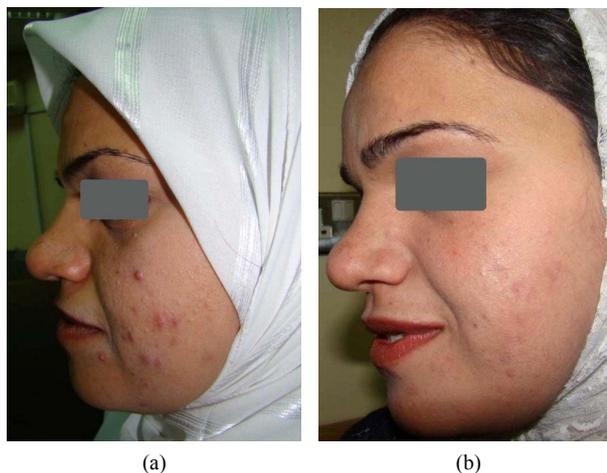


Figure 1. Twenty-eight years old female with 1 year history of acne vulgaris on 5-Alpha Avocado for 14 weeks before (a) and after (b) treatment.



Figure 2. Seventeen years old female with 4 years history of acne vulgaris on 5-Alpha Avocado for 14 weeks before and after treatment.

jom Pharmaceuticals, Jeddah, Saudi Arabia), patient instructed to apply the cream at night for 2 hours, every another day at the first 2 weeks and then daily overnight thereafter.

Clinical evaluation of response to treatment was done at week 2, 6, 10, 14. The assessment was carried out by counting the inflammatory lesions (papules and pustules) and recording any side effects. Follow up was carried out for 2 months after stopping treatment.

Comparison of the mean difference in outcome after 14 weeks between two the groups was calculated in the following:

The mean number of papules after treatment was deduced from the mean number before treatment for both groups. The same was done for the number of pustules for the 2 groups. These differences were then compared in both groups.

Satisfaction of Patients to treatment was assessed as such:

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

All adverse events experienced during the trial were recorded. Patients experiencing significant adverse events were withdrawn from the study at the discretion of the investigator. If severe irritation occurred, the dosing frequency of study medication could be reduced to every other night. If irritation was not alleviated by reduced dosing frequency, a facial moisturizer chosen by the investigator was used.

All data were coded and entered to the computer by using Microsoft Excel 2010 and Epi-info version 6. Comparison between all groups was done by using analysis of variance. The number of lesions before and after treatment in each group was compared using t-test and p-value < 0.05 was considered to be significant.

3. Results

Fifty-eight patients completed the course of treatment (29 patients in each group). 5-Alpha Avocuta group included 22 females and 7 males, their age ranged between 13 - 30 years with a mean of 20.24 ± 5.03 years, while tretinoin group included 21 females and 8 males, their age ranged between 12 - 28 years with a mean of 19.03 ± 4.24 years.

In 5-Alpha Avocuta group there was a significant reduction of the mean number of papules from 29.7 before treatment to 15.5 after treatment ($p < 0.0001$). While the mean number of pustules decreased from 4.9 to 0.6 ($p = 0.019$). See **Table 1**. In tretinoin group the mean number of papules was reduced from 28.5 to 14.9 ($p < 0.0001$), while the mean number of pustules dropped from 5.3 before treatment to 0.7 after treatment ($p = 0.009$). See **Table 2**. The mean percentage of reduction of inflammatory lesions over the treatment period was 33.8%, 44.3%, and 51.529% at week 6, 10 and 14 respectively. Regarding tretinoin group the mean percentage of reduction of

Table 1. Mean and SD of number of papules and pustules before and after treatment with 5-Alpha Avocuta.

Papules		Pustules		
Before	After	Before	After	
29.72	15.55	4.93	0.62	Mean
9.66	6.95	2.85	1.44	SD
93.49	48.32	8.13	2.10	Variance
<0.0001		0.019		p-value
0.240968604		6.701		t-test

Table 2. Mean and SD of number of papules and pustules before and after treatment with Tretinoin.

Papules		Pustules		
Before	After	Before	After	
28.51	14.86	5.344	0.72	Mean
8.06	6.99	3.02	1.19	SD
65.11	48.90	9.16	1.42	variance
<0.0001		0.008		p-value
5.84099E-09		4.32432E-09		t-test

inflammatory lesions was 38.7%, 47.1%, and 51.522% at week 6, 10 and 14 respectively. The mean difference of papules after 14 weeks in group A was 15.55 ± 6.95 while in tretinoin group; the mean difference was 14.86 ± 6.99 . This result was statistically not significant ($p = 0.708$, t-test) **Table 1**. The mean difference of pustules after 14 weeks in 5-Alpha Avocuta was 0.62 ± 1.44 while in group B the mean difference was 0.724 ± 1.19 . This result was statistically not significant ($p = 0.766$, t-test) **Table 2**.

The difference in the mean percentage of reduction of inflammatory lesions at week 14 between the two groups was not statistically significant (p -value = 0.999).

Twenty (68.9%) patients in 5-Alpha Avocuta group were fully satisfied and six (20.7%) patient showed partial satisfaction and three (10.3%) patients were not satisfied. In tretinoin group nineteen (65.5%) patients were fully satisfied and six (20.6%) patients showed partial satisfaction and four (13.7%) patients were not satisfied.

Regarding side effects in 5-Alpha Avocuta group one patient (3.4%) had mild facial erythema and one patient (3.4%) had burning sensation which both didn't required stop the treatment. While in tretinoin group three patients (10.3%) had mild-moderate facial erythema, one patient (3.4%) had dryness, one patient (3.4%) had mild peeling, two patients (6.8%) had burning sensation, and three patients (10.3%) had itching, treatment stopped in two patients because of erythema and itching and then it was re-introduced after two weeks.

4. Discussion

Five-Alpha Avocuta is an original patented active ingredient derived from avocado pears, it inhibits 5-Alpha-reductase type I activity with proven efficiency on human scalp and skin disorders related to hyper-seborrhoea [4]. Avocado used as: anti-inflammatory (in the treatment of psoriasis combined with vitamin B12 in a cream) [6], management of cutaneous disorders associated with itchy and dry skin (anti-itching) [7], reduce

UVB-induced damage and inflammation in skin. [8], and as Effective inducer of cutaneous defensive functions in atopic dermatitis [9].

However the only study about the efficacy of 5-Alpha Avocuta a multi-centric clinical evaluation, under dermatologist control, was conducted on 27 volunteers by Piccardi N. *et al.* who concluded that after 3 weeks of twice daily application it was able to reduce the sebum production of the face and to reduce the number of open comedons [4].

In the present study 5-Alpha Avocuta was investigated in the treatment of 58 patients with inflammatory acne in comparison with a well-known topical anti-acne medication (tretinoin). Good response to treatment with avocuta was evident in 58% of our patients after 14 weeks of treatment; this was comparable to patients treated with tretinoin. There was no statistically significant difference regarding the reduction in the number of papules and pustules between patients treated with avocuta and those treated with tretinoin. However 5-Alpha Avocuta was better tolerated, it was not necessary to stop the therapy in any patient. Two patients showed mild side effects; one patient had mild facial erythema and one patient had burning sensation, while in the tretinoin group ten patient showed side effects in the form of erythema, dryness, burning sensation and itching. Patients applied avocuta cream overnight on a daily base from the start while with tretinoin cream patients were asked to apply it every other day in the evening and for 2 hours and then to increase the duration and frequency of application later to avoid irritation.

On comparing our results with other studies Shalita *et al.* compared adapalene gel 0.1% and tretinoin gel 0.025% in the treatment of acne vulgaris in a multi-center trial. After 12 weeks of treatment there was a 48% reduction in the number of inflammatory lesions with adapalene and 38% with tretinoin. Side effects in the form of erythema and burning were also noted in their patients [10]. While in the present study there was 51.229% reduction of the mean percentage of inflammatory lesions in those treated with 5-Alpha Avocuta and 51.522% reduction of the mean percentage of inflammatory lesions in those treated with tretinoin at week 14.

Burke *et al.* conducted a double-blind clinical study in 94 subjects comparing benzoyl peroxide 5% cream and erythromycin 1.5% lotion. There was a significant reduction in the inflammatory lesions starting at the 4th week of treatment and more pronounced at the 8th week. Both benzoyl peroxide and erythromycin produced a reduction in total inflammatory lesions at the 4th and 8th weeks (the benzoyl peroxide by 33% and 37% and the erythromycin by 42% and 39% subsequently) [11]. However side effects in the form of erythema and itching

were noticed in both groups. One patient on benzoyl peroxide developed dermatitis [11]. While in our work both 5-Alpha Avocuta and tretinoin produced a reduction in total inflammatory lesions at the 6th and 10th week (the 5-AA by 33.88% and 44.83%, and the tretinoin by 38.75% and 47.14%). These changes were significant at the 6th and the 10th weeks for both preparations.

Finestrone 0.01% solution was compared to clindamycin 1.5% solution by Matloob *et al.* [12]. Both formulations were found to be effective in reducing the number of acne lesions. Side effects were few. However finestrone is contraindicated in women in the child bearing age.

The mode of action of 5-Alpha Avocuta is not well known, however, it could be attributed to its effects on hyper-seborrhea. The drug was shown to reduce sebum production in a controlled trial [4]. Also it can inhibit 5-Alpha reductase enzyme (type-1) thus inhibiting peripheral testosterone conversion [4].

The present work, showed that 5-Alpha Avocuta is an effective drug in the treatment of acne vulgaris especially in mild and moderate acne and was comparable to topical tretinoin with few side effects.

To the best of our knowledge and as revealed from our search of the medical literature, this is the first study which investigated the use of 5-Alpha Avocuta in the treatment of acne vulgaris.

In conclusion, 5-Alpha Avocuta approved as an effective safe easily applied remedy for treatment of mild and moderate acne vulgaris with negligible side effects.

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