# The Efficacy Of Topical Cyproterone Acetate Alcohol Lotion Versus Placebo In The Treatment Of The Mild To Moderate Acne Vulgaris: A Double Blind Study

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**Citation**

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**Abstract**

Background: Acne is an inflammatory condition of thye pilosebaceous unit. One of the essential factors for development of acne lesions is increased sebum excretion rate which is promoted by androgens. It is shown that oral cyproterone acetate significantly reduces the sebum excretion. In this study we evaluated the efficacy of cyproterone acetate alcohol lotion (CAAL) in the treatment of the mild to moderate acne vulgaris.

Methods: This was a randomized double-blind clinical trial study performed on eighty six female patients with mild to moderate acne. They were randomly divided into 3 groups and were treated with 0.5% CAAL (n=30), 1% CAAL (n=13) and placebo (n=43). They were followed every 15 days in a period of 45 days. Response to treatment was evaluated by the total acne lesions counting( TLC) and acne severity index (ASI) and was analyzed statistically by SPSS program.

Results: The efficacy of treatment on TLC was maximum for 1% CAAL (90% reduction in TLC)(P value=0.000). 0.5% CAAL was able to reduce TLC as high as 80.8% during 6 weeks of follow up. The efficacy of placebo was determined to be 38.5%. In term of TLC, 1% CAAL was 2.33 times more effective than placebo. 0.5% CAAL was 2.09 times more effective than placebo in this respect. The efficacy of treatment on ASI was maximum for 1% CAAL (88% reduction in ASI)(P value=0.000). 0.5% CAAL reduced ASI as much as 79.5% during 6 weeks of follow up. The efficacy of placebo was calculated to be 9.8% in reduction of ASI. In term of ASI, 1% CAAL was 8.97 times more effective than placebo. 0.5% CAAL was 8.06 times more effective than placebo in this respect

Conclusions: Regarding the results of this study, we suggest the use of cyproterone acetate alcohol lotion as one of the main treatments for mild-moderate acne in female patients and as an adjuvant treatment for moderate to severe acne vulgaris.

## BACKGROUND

Acne vulgaris remains one of the commonest diseases to afflict humanity. An analysis of the 1996 Census data in the United States of America indicated that the prevalence of acne in the age group 12-24 was 85% ([1]).Even in its mild form, acne can have lingering impacts on mental health (e.g., anxiety and depression), as well as on social interactions, self-confidence, self-esteem, and employment opportunities ([2]). On the other hand, antibiotics, which suppress Propionibacterium acnes, are the standard treatment for acne but are becoming less effective probably because of the emergence of antibiotic-resistant strains ([3,4,5,6]).

One of the suggested treatments for acne vulgaris is use of antiandrogens including oral cyproterone acetate that can decrease lipid secretion from the sebaceous glands. Unfortunately, oral cyproterone acetate has many side effects including fatigue, spontaneous milk secretion, development of the benign brest nodules, weight gain and rarely anemia ([7]).

Application of topical microsomal form of cyproterone acetate has been suggested for treatment of this condition ([8]). Regarding the price and difficulty in preparation of microsomal lotion of cyproterone acetate, we conducted a study to evaluate the efficacy of alcoholic lotion of cyprterone acetate for treatment of the mild to moderate acne

vulgaris in females.

## METHODS

This was a double - blind clinical trial. 86 female patients with mild to moderate were selected randomly from patients presenting to Skin Diseas and Leishmaniasis Research Center and Isfahan University of Medical Sciences clinics. Patients who were pregnant, breast feeding or who had acne due to internal diseases were excluded. Patients who had history of drug use for treatment of acne vulgaris in the recent 1 month, were also excluded. Informed causes were taken from all patients.

Patients were randomized t 3 groups. Group A included 30 patients and were treated with 0.5% cyprotrone acetate alcohol lotion (CAAL). Group B included 13 patients and were treated with 1% CAAL. Group C included 43 patients and were treated with placebo. Placebo included 70 ethylic included with 10% propylene glycol and talc powder (to mimic the appearance of the drug).

Patients were insulated to apply the drug twice daily for 45 days. The patients were visited of 15 days period for evaluation of the lesions and relevant side effects.

All the end of study, labels were unrevealed and the colleted date were analyzed by using SPSS program.

To determine the efficacy of treatments on acne severity we used absolute lesion count for each type of acne lesion end acne severity index. Acne severity was calcuted as:

Acne severity index= Papules + (2 x pustules )+ ((1/4) x comedones) ($_9$).

For comparison of efficacy of these treatments, statistical student - t test was used.

In the first visit, the total number of lesions was considered to be 100% and any decreasing of lesions was calculated accordingly and regarded as improvement percent. Mean of these improvement percents were calculated in each group of patients and were used for statistical analysis.

## RESULTS

### DEMOGRAPHIC RESULTS

The mean age of patients in the 0.5% cyproterone acetate treated group was 19.7 years. The mean age of patients was 17.9 for 1% CAAL and 19.6 for placebo. There was no significant difference regarding the age in these 3 groups.

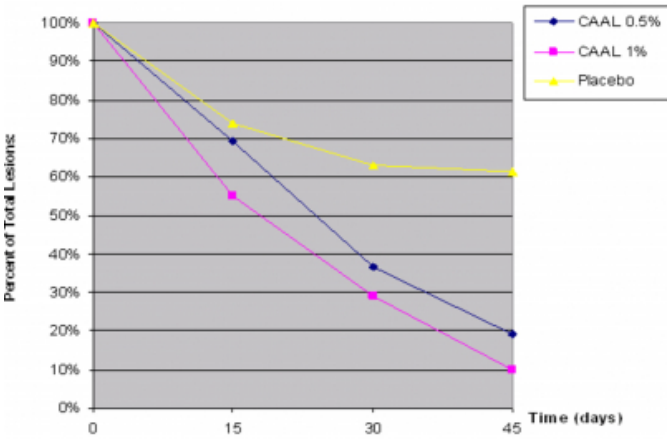
The efficacy of 0.5% CAAL and 1% CAAL was significantly more there placebo.

### EFFICACY ON TOTAL LESIONS COUNTING (TLC)

The efficacy of treatment on TLC was maximum for 1% CAAL (90% reduction in TLC)(P value=0.000). 0.5% CAAL was able to reduce TLC as high as 80.8% during 6 weeks of follow up. The efficacy of placebo was determined to be 38.5% (Graph 1).

**Figure 1**

Graph 1: Comparison between efficacy of Placebo, 0.5% CAAL and 1% CAAL in the total lesions counting.



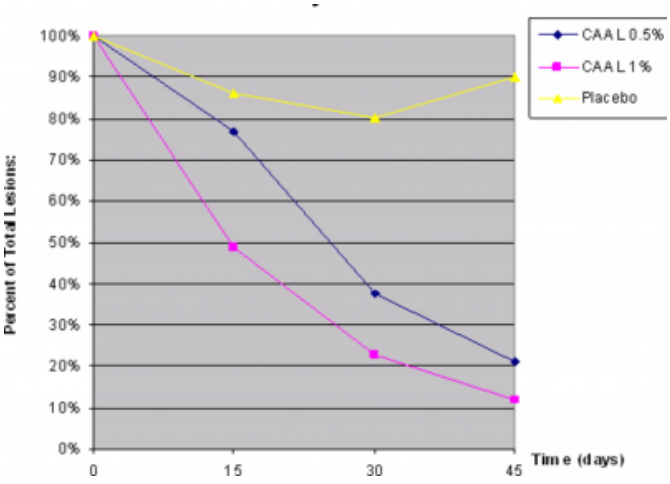

In term of TLC, 1% CAAL was 2.33 times more effective than placebo. 0.5% CAAL was 2.09 times more effective than placebo in this respect.

### EFFICACY ON ACNE SEVERITY INDEX (ASI)

The efficacy of treatment on ASI was maximum for 1% CAAL (88% reduction in ASI)(P value=0.000). 0.5% CAAL reduced ASI as much as 79.5% during 6 weeks of follow up. The efficacy of placebo was calculated to be 38.5% in reduction of ASI (Graph 2).

**Figure 2**

Graph 2: Comparison between efficacy of Placebo, 0.5% CAAL and 1% CAAL in the Acne Severity Index.




In term of ASI, 1% CAAL was 8.97 times more effective than placebo. 0.5% CAAL was 8.06 times more effective than placebo in this respect

## EFFICACY ON CLOSED COMEDONES NUMBER (CCN)

1% CAAL was shown to decrease CCN as high as 91% (P value=0.006). 0.5% CAAL reduced CCN as much as %82.5 during 6 weeks of follow up. The efficacy of placebo was calculated to be 51.9% in reduction of CCN).

## EFFICACY ON OPEN COMEDONES NUMBER (OCN)

1% CAAL was shown to decrease OCN as high as 92% (P value=0.002). 0.5% CAAL reduced OCN as much as %82.6 during 6 weeks of follow up. The efficacy of placebo was calculated to be 62% in reduction of OCN.

## EFFICACY ON PAPULES NUMBER (PPN)

1% CAAL was shown to decrease PPN as high as 91% (P value=0.000). 0.5% CAAL reduced PPN as much as %78 during 6 weeks of follow up. The efficacy of placebo was calculated to be as low as 9.4% in reduction of PPN.

## EFFICACY ON PUSTULES NUMBER (PUN)

1% CAAL was shown to decrease PUN as high as 92% (P value=0.000). 0.5% CAAL reduced PUN as much as %86.1 during 6 weeks of follow up. The placebo worsened PUN (74.5% increase in PUN).

## SAFETY OF TREATMENT

We did not measure serum level of cyproterone acetate but none of the patients complained of any local side effects related to drugs or placebo.

In comparison with placebo, CAAL was most effective on inflammatory lesions (papules & pustules) and least effective on non-inflammatory lesions (comedones).The effect of 1% CAAL was more than 0.5 CAAL in all courses of treatment and in all types of lesions (P<0.05) except on closed comedones. There was no significant difference between 0.5% and 1% CAAL in the treatment of the closed comedones (P> 0.05).

## DISCUSSION

The first use of anti androgens for treatment of acne vulgaris goes back to year 1969. In that study 12 patients were evaluated but there was no significant results regarding the efficacy of this treatment on acne vulgaris ([10]). 7 years later,this drug was used in the Cetomarogel Cream BPC but none of the patients showed significant results ([11]). Inocoterone acetate was used later but it also showed poor results ([12]).

In year 1998, 40 patients were evaluated for the efficacy of cyproterone acetate in the liposomal form. All of the patients were female and were allocated to receive liposomal cyproterone acetate, placebo or oral cyproterone acetate. They were treated and followed for 3 months. Doris and his colleagues concluded from this study that topical cyproterone acetate was equally effective as oral cyproterone acetate and was at least 40% more effective that placebo for treatment of acne vulgaris. The serum level of topical cyproterone acetate was 10% of oral cyproterone acetate ([8]).

It should be pointed out that preparation of the drug in the liposome form is expensive and difficult. Because of this fact, we used the alcoholic formulation of cyproterone acetate. Our results showed that in all patients 1% CAAL was more effective than 0.5% CAAL and both of these formulations were significantly more effective than placebo in the treatment of the acne vulgaris. Also in term of acne severity index, our results showed the results similar to Doris M et al. study ([8]). In Doris et al study, liposomal formulation of the drug was approximately 40% more effective than placebo in the treatment of acne vulgaris. Our study showed that CAAL was 40%-50% more effective than placebo for treatment of the mild to moderate acne vulgaris. The therapeutic effect became more prominent with continued use of the treatment.

In addition to regular lesion counting, we used acne severity index (ASI) to evaluate response to treatment. In this method, every type of lesion has different value and is calculated with different coefficient. By using this method, we can have better judgment about acne improvement during treatment ($_5$). Our results showed that CAAL was significantly more effective than placebo in improving acne severity index.

Black and white comedones are non-inflammatory acne lesions. CAAL was more effective in improvement of inflammatory lesions than non-inflammatory lesions. This finding may be due to the fact that non-inflammatory lesions are the results of the sebaceous gland duct obstruction and hyper cornification of the pilosebaceous ducts and these obstructions usually respond better to keratolytics. More studies are recommended in this respect.

## CONCLUSIONS

Regarding the results of this study, we suggest the use of cyproterone acetate alcohol lotion as one of the main treatments for mild-moderate acne in female patients and as an adjuvant treatment for moderate to severe acne vulgaris.

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