

Clindamycin lotion alone versus combination lotion of clindamycin phosphate plus tretinoin versus combination lotion of clindamycin phosphate plus salicylic acid in the topical treatment of mild to moderate acne vulgaris: A randomized control trial

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ABSTRACT

Background: Acne vulgaris is a common skin disease that affects 85% to 100% of people at some time during their lives. It is characterized by noninflammatory follicular papules or comedones and by inflammatory papules, pustules, and nodules in its more severe forms. **Aims:** To compare the efficacy of combination treatment of clindamycin+salicylic acid, versus clindamycin+tretinoin versus clindamycin alone in the treatment of the mild-to-moderate acne vulgaris. **Methods:** This was a single-blinded, randomized clinical trial. Forty-two female patients (age range: 15-25 years) with mild-to-moderate acne vulgaris were selected randomly and subsequently randomized to 3 groups. Group A patients were treated with 1% clindamycin lotion (C lotion) twice daily. Group B patients were treated with 1% clindamycin+0.025% tretinoin lotion once nightly (CT lotion). Group C patients were treated with 1% clindamycin+2% salicylic acid lotion twice daily (CS lotion) for 12 weeks. For comparison of efficacy of these treatments, and regarding the skewed distribution of the data, Kruskal-Wallis Test and Mann-Whitney U test were used. SPSS software was used for statistical analysis. **Results:** There was a significant difference between 3 types of treatment in the respect of the total lesion count (TLC) improvement ($P=0.039$). The efficacy of treatment on Acne Severity Index (ASI) was maximum for CS lotion (81.80% reduction in ASI). CT lotion reduced ASI by as much as 73.73% during 12 weeks of treatment. The efficacy of C lotion was calculated to be 37.87% in the reduction of ASI. **Conclusions:** Our data suggested that the efficacy of CS lotion was significantly more than C lotion with respect to the TLC and ASI, although there was no significant difference between CS and CT lotion.

Key words: Acne vulgaris, clindamycin, salicylic acid, treatment, tretinoin

INTRODUCTION

Acne vulgaris is a common skin disease that affects 85% to 100% of people at some time during their life time. It is characterized by noninflammatory follicular papules or comedones and by inflammatory papules, pustules and nodules in its more severe forms. Acne vulgaris affects the areas of skin with the highest population of sebaceous follicles; these areas include the face, upper part of the chest, and the back. The

pathogenesis of acne vulgaris is multifactorial. Four key factors are responsible for the development of an acne lesion. These factors are follicular epidermal hyperproliferation with subsequent plugging of the follicle, excess sebum, the presence and activity of *Propionibacterium acnes*, and inflammation.^[1]

Topical preparations constitute the sole treatment in many patients with acne vulgaris and are a part of therapeutic regimen in almost all patients. Topical

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treatment is enough for comedonal acne. In case of more severe acne, topical treatment can be combined with systemic treatment.^[2] Topical treatment of acne vulgaris has changed over the years. Agents containing sulphur or resorcinol were used in especially the first part of the 20th century. Salicylic acid, which is a keratolytic agent, was popular for some time. Nowadays, the most popular topical agents in use are retinoids, benzoyl peroxide, azelaic acid, and topical antibiotics.^[3,4]

As there is scarcity of data on efficacy of combination therapy of clindamycin + salicylic acid, we designed the following study to compare this combination therapy versus clindamycin + tretinoin and clindamycin alone in the treatment of the mild-to-moderate acne vulgaris.

METHODS

This was a single-blinded clinical trial. Forty-two female patients (age range: 15-25 years) with mild-to-moderate acne vulgaris were selected randomly from patients admitted to Skin Disease and Leishmaniasis Research Center and Isfahan University of Medical Sciences clinics from September 06 to August 07. Patients who were pregnant, lactating or who had acne caused by internal diseases or hyperandrogenism were excluded. Patients who had a history of drug use for treatment of acne vulgaris in the recent 1 month were also excluded. Informed consent was obtained from all patients.

Patients were randomized to 3 groups each including 14 patients. Group A patients were treated with 1% clindamycin lotion (C lotion) twice daily. Group B patients were treated with 1% clindamycin + 0.025% tretinoin lotion once nightly (CT lotion). Group C patients were treated with 1% clindamycin + 2% salicylic acid lotion twice daily (CS lotion). They were instructed to apply the medicine by slight rubbing of lotion on their face. The treatment was continued for 12 weeks. All patients were recommended to apply sufficient amount of oil-free sunscreen cream.

Patients were blinded to the type of treatment, and the type of treatment was revealed only at the end of the study.

The patients were visited at 15-day period for evaluation of the lesions and relevant side effects.

To determine the efficacy of treatments on acne severity, we used both total lesion counting (TLC) and acne severity index (ASI).

Acne severity index was calculated as:

$$\text{Acne severity index (ASI)} = \text{Papules} + (\text{pustules} \times 2) + (\text{comedones} \times 4).$$

Total acne lesions was calculated as:

$$\text{Total acne lesions counting (TLC)} = \text{Papules} + \text{pustules} + \text{comedones} + \text{nodules}$$

For comparison of efficacy of these treatments, and regarding the skewed distribution of the data, Kruskal-Wallis Test and Mann-Whitney U test and were used.

In the first visit, the total number of lesions counted was considered to be 100% and any decrease in number of lesions was calculated accordingly and regarded as improvement percentage. Means of these improvement percentage were calculated in each group of patients and were used for statistical analysis. At the end of study, the collected data were analyzed by using an SPSS program.

RESULTS

Efficacy on Total Lesions Counting (TLC)

All patients completed the study. Significant difference was seen between the 3 types of treatment with respect to the TLC, using Kruskal-Wallis Test ($P = 0.039$). The efficacy of treatment on TLC was maximum for CS lotion (77.91% reduction in TLC).

CT lotion reduced TLC by as high as 72.20% during the 12 weeks of treatment. The efficacy of C lotion was determined to be 55.95%.

In terms of TLC, CS lotion was 1.39 times more effective than C lotion. CT lotion was 1.29 times more effective than C lotion in this respect. There was no significant difference between CS and CT lotion in the TLC reduction ($P > 0.05$).

Efficacy on Acne Severity Index (ASI)

Significant difference was observed between the 3 types of treatment with respect to the TLC, using Kruskal-Wallis Test ($P = 0.02$).

The efficacy of treatment on ASI was maximum for CS lotion (81.80% reduction in ASI). CT lotion reduced

ASI to as much as 73.73% during the 12 weeks of treatment.

The efficacy of C lotion was calculated as 37.87% with regard to reduction in ASI.

In terms of ASI, CS lotion was 2.16 times more effective than C lotion. CT lotion was 1.94 times more effective than C lotion in this respect.

Efficacy on Closed Comedones Number (CCN)

There was a significant difference between the 3 types of treatment with respect to the CCN, as calculated using Kruskal-Wallis Test ($P = 0.011$).

CS lotion was shown to decrease CCN by as high as 87.05%. CT lotion reduced CCN by as much as 60.94% during 12 weeks of treatment. The efficacy of C lotion was calculated as 31.28% in the reduction of CCN.

Efficacy on Open Comedones Number (OCN)

No significant difference was found between the 3 types of treatment with respect to the OCN, using Kruskal-Wallis Test ($P > 0.05$).

CS lotion was shown to decrease the OCN by as high as 64.26%. CT lotion reduced OCN by as much as 67% during the 12 weeks of treatment. The efficacy of C lotion was calculated as 58.33% in the reduction of OCN.

Efficacy on Papule Numbers (PPN)

Significant difference was found between the 3 types of treatment with respect to the PPN, using Kruskal-Wallis Test ($P = 0.031$).

CS lotion was shown to decrease PPN by as high as 84.5%. CT lotion reduced PPN by as much as 71.67% during 6 weeks of follow-up. The efficacy of C lotion was calculated to be as low as 26.63% in the reduction of PPN.

Efficacy on Pustules Number (PUN)

No significant difference was found between the 3 types of treatment with respect to the PUN, using Kruskal-Wallis Test ($P > 0.05$).

CS lotion was shown to decrease PUN by as high as 90%. CT lotion reduced PUN by as much as 76.19% during 6 weeks of follow-up. The C lotion reduced PUN by as much as 80%. Except open comedone lesions, CS lotion twice daily was more effective than CT

lotions once daily on all components of acne vulgaris, although no significant difference was observed, using Mann-Whitney U test ($P > 0.05$).

Side Effects

Three patients (21.42%) in the CT lotion group complained of slight irritation that was tolerable for them. Seven patients (50%) in the CS group reported slight, transient burning sensation on application of CS lotion. No significant side effects were observed in the C lotion group.

DISCUSSION

Affecting 40 to 50 million people in the United States,^[5] acne vulgaris is one of the most frequently encountered condition in all dermatology and primary care practice. Even in its mild form, acne can have lingering impacts on mental health (eg, anxiety and depression), as well as on social interactions, self-confidence, self-esteem, and employment opportunities.^[6]

Although the use of successful drugs and adjunctive procedures have dramatically improved outcomes in many patients with severe acne, improvements in the much larger population of patients with mild or moderate acne remain more elusive. For this group, careful individualization of therapy and persistence by both patients and clinicians is the key.^[7]

In the current study, we compared the efficacy of combination therapy of clindamycin + salicylic acid versus clindamycin + tretinoin versus clindamycin alone in the treatment of the mild-moderate acne vulgaris.

Retinoids, which are derivatives of vitamin A, function by slowing the desquamation process, thereby decreasing the number of comedones and microcomedones. Retinoids have been suggested as the most effective comedolytic agents in use. They have been a mainstay of acne treatment for the past 25 years. Tretinoin was the only available topical retinoid until recently. This agent is effective as monotherapy in patients with noninflammatory or mild to moderate inflammatory acne.^[8] All tretinoin formulations can cause some skin irritation.^[8]

Salicylic acid is an ingredient of various over-the-counter preparations. It is available at a concentration of 0.5% or 2% in a number of creams and lotions. This agent inhibits comedogenesis by promoting the

desquamation of follicular epithelium. It has been shown to be as effective as benzoyl peroxide in the treatment of comedonal acne.^[9] Salicylic acid is well tolerated and should be applied once or twice daily.

Topical antibiotics work directly by killing *P. acnes*. Through their bactericidal activity, they also have a mild indirect effect on comedogenesis. These agents are available in a variety of forms and are applied once or twice daily. Topical erythromycin and clindamycin are the most commonly used agents and have similar efficacy in patients with acne.^[10] Clindamycin has been shown to be significantly more effective than topical tetracycline.^[10]

Our data suggested that the efficacy of CS lotion was significantly more than C lotion with respect to the TLC and ASI, although there was no significant difference between CS and CT lotion.

However, considering the better compliance of the patients for the CS lotion, usage of this treatment seems to be a good alternative treatment for CT lotion. This treatment was very well tolerated and some of the patients complained of only little burning sensation.

In addition, the CS lotion was significantly more effective than C lotion with respect to the closed comedones number. This observation is logical as this treatment is a keratolytic one and therefore is effective in the reduction of comedonal lesions.

The nonsignificant response with respect to the open comedonal lesions is possibly because of the manipulation of the open comedonal lesions by the patients, which caused a reduction in these lesions in all treated groups.

However, the CS and CT lotions were significantly more effective than C lotion alone in the reduction of the papular lesions. This difference is possibly related to the penetrance enhancer capabilities of salicylic acid and tretinoin. We did not find significant difference regarding pustules reduction in the 3 groups, which may be because of more bacterial nature of these lesions.

Hence, we suggest application of CS lotion twice daily and CT lotion once daily as the appropriate treatment against mild-moderate acne vulgaris.

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