

Comparison of topical 5% nicotinamid gel versus 2% clindamycin gel in the treatment of the mild-moderate acne vulgaris: A double-blinded randomized clinical trial

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Background: Acne vulgaris is considered one of the most common disorders for which patients seek dermatologic care. In the current study, we evaluated efficacy of the 5% nicotinamide gel versus 2% clindamycin gel in the treatment of the mild-moderate acne vulgaris. **Materials and Methods:** This was a randomized, controlled clinical trial that was performed in 2009-2010. Sixty female patients with mild or moderate acne vulgaris were recruited to be treated either with 5% nicotinamide or 2% clindamycin gel for 8 weeks. Acne severity index (ASI) was used to evaluate response to treatment and SPSS software was used to analyze the data. **Results:** The mean of ASI at the baseline was 16.85 ± 8.5 and 18.2 ± 12.27 in nicotinamide gel and clindamycin gel, respectively ($P > 0.05$). The mean of ASI was significantly decreased compared with baseline ASI during the time in both groups ($P < 0.0001$). However, there was not a significant difference regarding reduction of ASI between the nicotinamide and clindamycin gel ($P = 0.583$). **Conclusion:** Five percent nicotinamide gel is as effective as 2% clindamycin gel for treatment of mild to moderate acne vulgaris. No side effect was observed during the treatment.

Key words: Acne, clindamycin, nicotinamide, treatment

INTRODUCTION

Acne vulgaris is considered one of the most common disorders for which patients seek dermatologic care. Affecting the majority of the adolescent population, acne vulgaris remains prevalent in adults, with up to 40-50% of men and women in their 20s and 10-20% in their 40s reporting acne, accounting for at least 5-6 million visits to physicians a year.^[1]

Major factors contributing to the acne vulgaris include sebum secretion, abnormal desquamation of follicles, bacterial growth, and associated inflammation. New molecular and clinical studies have advanced knowledge in areas such as sebocyte biology, the role of androgens, nicotinamide, dietary factors, and the effect of cytokines, and toll-like receptors, helping identification of potential new targets for acne therapy.^[1]

For a long-time, topical and systemic antibiotic along with retinoid have been the mainstays of treatment for acne vulgaris. However, overuse of oral or topical antibiotics may contribute to the development of bacterial resistance, as well as side effects such as diarrhea, yeast infections, and photosensitivity. Therefore, alternative treatments, such as nicotinamide, have been suggested for treatment of the acne vulgaris.^[2]

Other medications that have been used for treatment of acne vulgaris include agents such as azelaic acid, salicylic acid, cyproterone actate, tea tree oil, and etc.^[3-6]

The previous studies had used 4% nicotinamide gel for treatment of the acne vulgaris. In the current study, we evaluated efficacy of the 5% nicotinamide gel versus 2% clindamycin gel in the treatment of the mild-moderate acne vulgaris as randomized clinical trial.

MATERIALS AND METHODS

This was a randomized, controlled clinical trial that was performed in 2009-2010 in St-Alzahra hospital, Isfahan University of Medical Sciences, Isfahan, Iran (Registration No. = 385171).

In this study, 60 female patients with mild or moderate acne vulgaris were recruited to be treated either with 5% nicotinamide or 2% clindamycin gel. Mild acne was defined as the presence of non-inflammatory lesions (including closed or open comedones), and the number of the papules, and pustules to be <10 without any nodules or cysts.^[3]

Moderate acne was defined as the presence of non-inflammatory lesions (including closed or open

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Received: 29-07-2012; **Revised:** 01-01-2013; **Accepted:** 28-01-2013

comedones) and the number of the papules and pustules to be <20 without any nodules or cysts.

Patients who had received any topical or oral medication for acne vulgaris in the last 1 month was excluded from the study. Patients with history of allergy to the clindamycin or nicotinamide or history of renal, hepatic or endocrine disorders were excluded from the study. Furthermore, pregnant and nursing patients or those who use oral contraceptive pill (OCP) were considered as the exclusion criteria for this study.

Informed consent was obtained from all the patients. At the baseline, demographic characteristic of the patients was obtained and recorded in especial questionnaires. For determination of acne severity, acne severity index (ASI) was calculated for each patient as following:

ASI: (2* pustules) + papules + (1/4* comedones).^[3]

Reduction of ASI less than 30% was considered as weak response, 30% to 60% reduction was considered as moderate response and more than 60% reduction was considered as excellent response.

Five percent nicotinamide gel and 2% clindamycin gel were provided by Isfahan Pharmacy School in the same containers, but with different labels of A and B. Both physicians and patients were blinded to the type of treatment and the patients had been allocated randomized and instructed to apply the drug twice daily for a period of 8 weeks. Patients were visited every 2 weeks in this period of time and the ASI score of the patients along with patient satisfaction and presence of side effects were recorded. At the end of study, the codes were revealed and the collected data was analyzed using SPSS (version 18) for Windows and statistical tests including, *t*-test and ANOVA and Fisher exact test.

RESULTS

Overall, 60 patients (30 patients in the nicotinamide gel and 30 patients in the clindamycin gel) were evaluated in this study. No one was excluded from the study and all of the patients completed the study. The mean of age in nicotinamide gel and clindamycin gel were 20.83 ± 3.34 years and 21.17 ± 3.53 years, respectively, and this difference was not statistically significant ($P > 0.05$).

The mean of ASI at the baseline was 16.85 ± 8.5 and 18.2 ± 12.27 in nicotinamide gel and clindamycin gel, respectively, and this difference was also not statistically significant ($P > 0.05$).

The mean of ASI was continuously decreased during the

visits in both groups and this reduction (final visit vs. baseline) was statistically significant as compared with baseline ASI in the both groups ($P < 0.0001$) [Table 1].

However, Fisher exact test showed that there was no significant difference regarding reduction of ASI between the nicotinamide and clindamycin gel ($P = 0.583$) [Table 2].

DISCUSSION

Nicotinic acid (niacin) and niacinamide (nicotinamide) are similarly effective as a vitamin because they can be converted into each other within the organism. It has been shown that topical application of niacinamide has a stabilizing effect on epidermal barrier function, seen as a reduction in transepidermal water loss and an improvement in the moisture content of the horny layer. Niacinamide can lead to increase in protein synthesis, have a stimulating effect on ceramide synthesis, speed up the differentiation of keratinocytes, and raise intracellular NADP levels. In addition, topical application of niacinamide improves the surface structure, smoothes out wrinkles and inhibits photocarcinogenesis and therefore, is effective in ageing skin. Its anti-inflammatory effects in acne, rosacea, and nitrogen mustard-induced irritation have also been suggested.^[7]

The use of nicotinic acid for treatment of the acne vulgaris goes back to 1955, when it was used for its effect as counteracting iodide aggravation in acne vulgaris.^[8] Treatment of acne vulgaris with nicotinic acid induced vasodilatation was described by Marchand in the same year.^[9]

However, the first study that used nicotinamide gel for treatment of acne vulgaris as a double-blind clinical trial was performed by Shalita *et al.* In their study, the safety and efficacy of topically applied 4% nicotinamide gel was compared against 1% clindamycin gel for the treatment of moderate inflammatory acne vulgaris. Seventy-six patients were randomly assigned to

Table 1: Comparison of acne severity index in the two groups during the treatment with nicotinamide and clindamycin gel

Group	Baseline	Week 2	Week 4	Week 6	Week 8	P value (t test)
Nicotinamid gel	16.85	13.275	9.708	6.375	5.150	<0.0001
Clindamycin gel	18.27	12.467	9.150	7.575	6.700	<0.0001

Table 2: Comparison of mean reduction of acne severity index by percent in the 2 groups during the treatment with nicotinamide and clindamycin gel

Group (%)	Week 2	Week 4	Week 6	Week 8	P value
Nicotinamid gel	72.31	70.1	52.5	87.72	0.583
Clindamycin gel	68.06	63.75	60.0	77.32	

Fisher exact test. No significant side effect was observed in the both groups

apply either 4% nicotinamide gel or 1% clindamycin gel twice daily for 8 weeks. After 8 weeks, both treatments produced comparable ($P=0.19$) beneficial results in the Physician's Global Evaluation of Inflammatory Acne; 82% of the patients treated with nicotinamide gel and 68% treated with clindamycin gel were improved. Both treatments produced statistically similar reductions in acne lesions, and acne severity. The authors concluded that 4% nicotinamide gel is of comparable efficacy to 1% clindamycin gel in the treatment of acne vulgaris.^[10]

In contrast, another research carried out by Sardesai and Kambli showed no benefit in combination of nicotinamide with clindamycin in the treatment of the acne. A total of 75 patients with inflammatory acne vulgaris were divided into three groups. Group A was treated with combination of 4% nicotinamide and 1% clindamycin combination, Group B was treated with plain 1% clindamycin and Group C, which was considered to have resistance to local antibiotics due to no response to treatment was treated with the combination. At the end of 8 weeks, it was concluded that in addition of nicotinamide was not as much value as in treating inflammatory acne and results were some as for plain clindamycin and also the combination did not offer much relief in treatment of resistant acne.^[11]

The effect of nicotinamide on facial sebum was demonstrated by Draelos *et al.* who showed that Topical 2% niacinamide may be effective in lowering the sebum excretion rate in Japanese individuals and casual sebum levels in Caucasian individuals.^[12]

It seems that nicotinamide along with the new suggested topical and systemic therapy can be effective for treatment of the acne vulgaris.^[13-15]

In the current study, we evaluated possibly more potent 5% nicotinamide gel instead of usual 4% concentration and in contrast to the previous studied we compared this compound with 2% clindamycin gel instead of 1% clindamycin gel. In addition, we used a blinded protocol to have a more reliable result.

Our results clearly showed that 5% nicotinamide gel is at least as effective as 2% clindamycin gel for treatment of mild to moderate acne vulgaris. Moreover, we observed no side effect during the treatment and the patients tolerated the treatment very well. Considering these results along with the anti-inflammatory effects of the nicotine amid that may help to reduce post acne erythema and its anti-pigmentary effect that may help to reduce the severity of post-inflammatory hyperpigmentation after acne may suggest 5% nicotinamide gel as an appropriate treatment for acne vulgaris.

To better evaluate the efficacy of 5% nicotinamide gel in the treatment of the acne vulgaris, more randomized clinical trial (RCT) with higher number of the patients and longer follow-up is recommended.

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How to cite this article: Shahmoradi Z, Iraj F, Siadat AH, Ghorbaini A. Comparison of topical 5% nicotinamide gel versus 2% clindamycin gel in the treatment of the mild-moderate acne vulgaris: A double-blinded randomized clinical trial. *J Res Med Sci* 2013;18:115-7.

Source of Support: Nil, **Conflict of Interest:** None declared.