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Original Research Article

Assessment of efficacy and safety of clindamycin with nicotinamide in mild to moderate acne vulgaris: a prospective study

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ABSTRACT

Background: Acne vulgaris is a very common skin disease that is usually treated with topical products, systemic medications, or a combination of both. Acne vulgaris affects approximately 9% of the population worldwide causing permanent physical scarring, negatively affects the quality of life and self-image, and has been associated with increased rates of anxiety, depression, and suicidal ideation.
Methods: This was a prospective study conducted at BMCRI including thirty-five subjects who were diagnosed with mild to moderate acne vulgaris. Patients were treated with topical clindamycin 1% with nicotinamide 4%. Efficacy was assessed by mean change in acne severity index (ASI) and total lesion count (TLC) from baseline and at the end of 4, 8 and 12 weeks. Safety was assessed by adverse events reported.
Results: There was statistically significant improvement noted at the end of each visit. Baseline ASI was 88.05±4.02 and end of 12 weeks was 14.17±2.7. Baseline TLC was 30.17±1.33 and at the end of 12 weeks was 4.25±0.99. Both the ASI and TLC results were statistically significant at the end of fourth, eighth and twelfth-week p value <0.0001.
Conclusions: Combination topical formulations are the most broadly used treatment regimen for Acne vulgaris to target one or more steps in the pathogenesis of acne. From the results of the present study the participants on combination of clindamycin with nicotinamide had a significant improvement in acne lesions at end of 12th week of topical application and were satisfied with the therapy with no major adverse effects.

Keywords: Acne vulgaris, Clindamycin, Nicotinamide, Prospective study

INTRODUCTION

Acne vulgaris is a very common skin disease that is usually treated with topical products, systemic medications, or a combination of both. Choosing an appropriate agent from various options available for the management of acne vulgaris has always been considered a great challenge.[1] This selection is presumably influenced by various factors, such as the severity of acne, predominant lesions, type of skin, lifestyle and even the age of patients. Acne vulgaris affects approximately 9% of the population worldwide (approximately 85% of individuals aged 12-24 years, and approximately 50% of patients aged 20-29 years) causing permanent physical scarring, negatively affects the quality of life and self-image, and has been associated with increased rates of anxiety, depression, and suicidal ideation.[2]

The Global Alliance to Improve Outcomes in Acne recommends combination treatment as the cornerstone and as the first line treatment for mild to moderate acne.[3] Combination therapy, which targets *P. acnes* proliferation, inflammation, and hyper keratinization- three major areas of acne pathophysiology- has a greater impact than conventional therapies due to its multifactorial pathogenesis and limitations. This reduces both inflammatory and non-inflammatory lesions.[4] Many studies have effectively used both topical and systemic

antibiotics, as it is believed that inflammation generated by *Propionibacterium acnes* is the fundamental cause of this illness.[5] Clindamycin, chlorinated lincosamide antibiotic being more lipophilic targets *P. acnes* and has anti-inflammatory and anti-comedogenic effect.[6]

Reduction of inflammation plays a vital role in the management of acne. Nicotinamide a newly approved alternative therapy for acne, possesses a potent anti-inflammatory effect.[7] It also has a beneficial effect due to its sebo-suppressive, healing property and it is extremely well tolerated by facial skin. Studies of clindamycin with nicotinamide have not been extensively evaluated, hence this present study was conducted to assess of efficacy and safety of clindamycin with nicotinamide in mild to moderate acne vulgaris.

METHODS

It was a prospective study done at patients diagnosed with mild to moderate acne vulgaris on the face who attended dermatology outpatient department in Victoria Hospital attached to Bangalore Medical College and Research Institute conducted from November 2017 to June 2019.

After obtaining approval and clearance from the institutional ethics committee, patients fulfilling the inclusion criteria were subjects of either of sex, aged 18 to 35 years, subjects with mild to moderate acne vulgaris on face [grade 2 and 3 of investigator's global assessment scale (IGAS)] and subjects willing to give written informed consent. The exclusion criteria were subjects who have used topical antibiotics or topical steroids on the face, facial procedures, or any investigational therapy within the past 4 weeks or systemic retinoids within the past 6 months, drug induced acne, pregnant and lactating mothers, and history of hypersensitivity to any of the study medication were enrolled in the study after obtaining informed consent. Ethical committee approval was from the institutional ethics committee attached to Bangalore Medical College and Research Institute and the approval number is BMC/PGs/289/2017-18. Thirty-five patients received topical clindamycin 1% with nicotinamide 4% and were advised to apply pea-sized amount of medication into a thin layer on the face once daily in the evening/night after facial cleansing, avoiding the eyes, lips and mucous membrane. Treatment was continued up to 12 weeks and follow up was done at the end of 4 weeks, at the end of 8 weeks, at the end of 12 weeks for evaluation of efficacy and safety of the study drug.

On visit 1, each patient was given a unique identity number. Demographic data, medical history, concomitant medications, physical examination, clinical examination including recording of vital signs and details of drug prescription by the treating doctor was recorded in the study proforma and relevant clinical assessment was done.

Follow-up visits was done at the end of 4 weeks (visit 2), at the end of 8 weeks (visit 3) and at the end of 12 weeks (visit 4) after administering the study medication. A deviation of ±2 days for first follow-up and ±1 week for subsequent follow-ups was accepted. At follow-up visits clinical assessment was recorded. Concomitant medications that are necessary was given at the discretion of the doctor and was recorded. Adverse events were recorded using CDSCO-ADR form and graded according to severity.

Efficacy was assessed by using acne severity index (ASI), total lesion counts (Inflammatory lesions and non-inflammatory lesions) and patients satisfaction score by Turkish academy of dermatology. Safety was assessed by erythema, scaling, pruritus, and burning sensation. Each being assessed using a five-point scale.

RESULTS

Demographic and clinical characteristics of the patients at baseline as shown in Table 1.

Table 1: Demographic data of the patients with acne vulgaris at baseline.

Parameters	Category	Number
Age	Age in years (mean)	25.57
Sex	Male	16
	Female	19
Residence	Urban	20
	Rural	15

The mean age of the participants was 25.57, with female preponderance and mostly seen in urban population.

Efficacy parameters

Efficacy parameters are shown in the tables and figures given below.

Table 2: Comparing the mean difference of acne severity index (ASI) at the end of 4th, 8th and 12th weeks.

Visits	Mean±SD	Mean difference	P value
Baseline	88.05±4.02	From baseline	From baseline
At the end of four weeks	48.51±3.06	39.54±0.96	<0.0001*
At the end of eight weeks	26.65±2.56	61.4±1.46	<0.0001*
At the end of twelve weeks	14.17±2.7	73.88±1.32	<0.0001*

ASI- Acne Severity Index = papules + (pustules x 2) + (comedones x 4)

Wilcoxon signed rank test- *p value where p<0.05 is significant. The ASI score at the end of fourth, eighth and twelfth week was statistically significant.

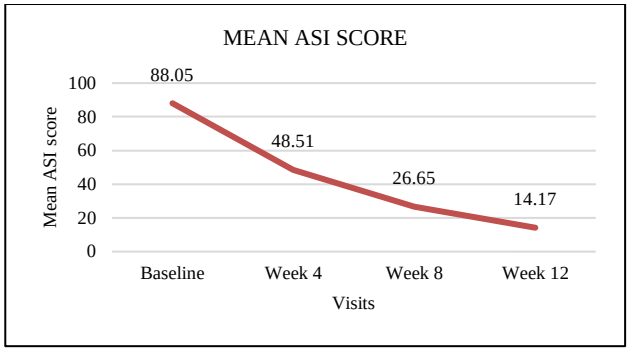

Figure 1: Mean acne severity index score at the end of 4th, 8th and 12th week.

The mean ASI score showed a reduction from the baseline (88.05) to 48.51 at the end of fourth week, which was further reduced 26.65 at the end of eighth week, and the final reduction was 14.17 at the end of twelfth week and it was statistically significant.

Table 3: Comparing the mean difference of total lesion count (TLC) at the end of 4th, 8th, and 12th weeks.

Visits	Mean±SD	Mean difference	P value
Baseline	30.17±1.33	From baseline	From baseline
At the end of four weeks	16.54±0.92	13.63±0.41	<0.0001*
At the end of eight weeks	8.71±0.81	21.46±0.52	<0.0001*
At the end of twelve weeks	4.25±0.99	25.92±0.34	<0.0001*

Total lesion counts= Inflammatory lesions + Non inflammatory lesions

Wilcoxon signed rank test- *p value where p<0.05 is significant. The TLC score at the end of fourth, eighth and twelfth week was statistically significant.

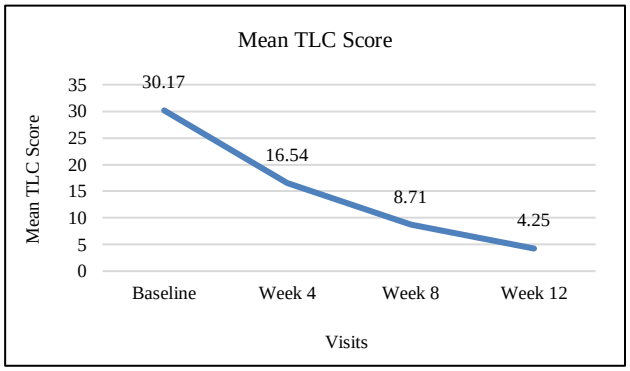

Figure 2: Total lesion count score (TLC) at the end of 4th, 8th and 12th weeks.

The mean TLC score showed a reduction from the baseline (30.17) to 16.54 at the end of fourth week, which was further reduced to 8.71 at the end of eighth week, and the final reduction was 4.25 at the end of twelfth week and it was statistically significant.

Safety parameters

Adverse effects

During the study period, mild adverse drug reactions were recorded. and showed mild itching followed by burning, scaling, and redness. None of the participants discontinued the application in the study period.

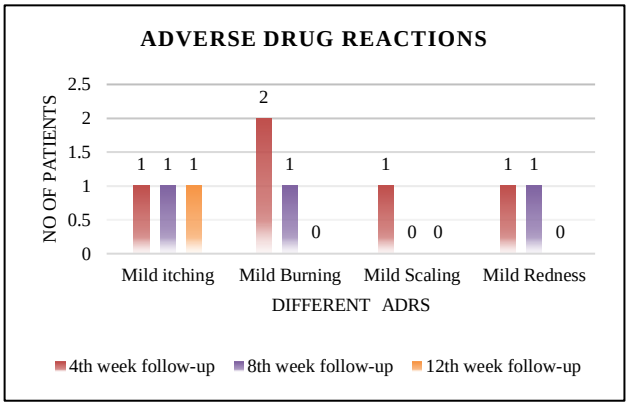

Figure 3: Adverse drug reactions at the end of each week follow up.

DISCUSSION

Topical therapy is the first-line treatment for all types of acne.[8] The selection of drugs to be applied is made according to the degree of acne lesions, the preferred route of administration, and the patient's medical condition. The main goal for drug treatment is achieving the topical penetration and retention of the drug at the desired skin layers as they constitute the sole treatment in many patients and are a part of therapeutic regimen in almost all patients with acne vulgaris.

The efficacy of topical combination therapy of clindamycin with nicotinamide in the treatment of the mild-moderate acne vulgaris was studied. Tetracycline, clindamycin, and erythromycin are antibiotics available in a variety of forms, commonly used either topically or systemically in acne therapy.[9] Clindamycin is more effective than tetracycline and is comparable to erythromycin. In addition to its antibacterial activity, clindamycin possesses anti-inflammatory and a mild indirect effect on comedogenesis.[10] Nicotinamide, also known as niacinamide, is a form of vitamin B_3, which is an essential water-soluble nutrient present in a variety of foods. Nicotinamide possesses potent anti-inflammatory action and represents a potential treatment modality for acne vulgaris.[7]

In the present study as shown in Table 1 the demographic data at baseline depicts the mean age of the participants to be 25.57 years and is in accordance with the study done by

Rao et al.[11] The gender distribution of the participants showed female: male ratio was 54:46 seemed to be a slight increase in female preponderance, which is in contrast to the study done by Cunliffe et al, demonstrated that acne incidence was higher among adolescent men than adolescent women.[12] However, Cunliffe and colleagues found that, in adults 18 years of age and older, this prevalence decreases for both sexes, but becomes more prevalent in adult women than adult men.[12] Adult female acne is caused by a combination of abnormal follicular keratinization, *Propionibacterium acnes* bacterial colonization of the pilosebaceous duct, and excessive sebum production. Furthermore, hormones, the use of medications and/or cosmetics, and prolonged stress have all been suggested as possible causative causes. The urban participants (20) of our study were slightly higher than the rural (15) which was similar to the study done by Pandey et al reported increased chances of exposure to the pollutants of industrialization may the factor contributing to a higher prevalence among urbanites. He also states that acne the disease due to civilization meaning urbanization and blamed "pop, chocolate and candies" for the increased incidence.[13]

The efficacy of the study drugs was evaluated by acne severity index (ASI) and total lesion count (TLC). The acne severity index at the baseline was 88.05±4.02, at the end of fourth week it was reduced to 48.51±3.06, at the end of eighth week it was further decreased to 26.65±2.56 finally at the end of twelfth week showed a reduction to 14.17±2.7 which was significant statistically (p value <0.0001). The total lesion count at the baseline was 30.17±1.33, at the end of fourth week it was reduced to 16.54±0.92, at the end of eighth week TLC further decreased to 8.71±0.81 finally at the end of twelfth week TLC reduced to 4.25±0.99 with statistically significant results (p value <0.0001). Draelos et al demonstrated that 2% topical nicotinamide resulted in a significant reduction in sebum excretion rate in a Japanese study group, and decreased sebum levels (sebum on the skin surface) in a Caucasian study group over four weeks.[14] In addition, topical nicotinamide helps protect the natural barrier of the skin against infection and may have a bacteriostatic effect on *P. acnes.*[15] Lastly, nicotinamide decreases the in vitro secretion of interleukin 8, a cytokine secreted by keratinocytes in response to pathogens (including *P. acnes*), thereby exerting an anti-inflammatory effect through inhibition of leukocyte chemotaxis.[16] Additional anti-inflammatory action may occur via inhibition of lysosomal enzyme release and mast cell degranulation.[17] A study done by Shalita et al demonstrated that 4% nicotinamide as monotherapy has a comparable efficacy to 1% clindamycin in the treatment of acne vulgaris.[18] Studies done by Sardesai et al in evaluation of clindamycin phosphate monotherapy versus combination therapy of clindamycin phosphate with nicotinamide in the treatment of acne vulgaris, showed that both treatments produced a statistically similar reduction in the number of acne lesions and their severity.[19] In the current study the treatment regimens were tolerated, although patients did experience mild local side effects such as mild itching, mild burning, mild scaling and mild redness.

The strength of the study was a prospective study evaluating the efficacy of the combination therapy of clindamycin with nicotinamide in mild to moderate acne vulgaris among south Indian patients.

The limitation of our study was that the study was conducted only at one tertiary care centre and the results of the study cannot be generalized.

CONCLUSION

Combination topical formulations are the most broadly used treatment regimen for acne vulgaris to target one or more steps in the pathogenesis of acne. From the results of the present study the participants on combination of clindamycin with nicotinamide had a significant improvement in acne lesions at end of 12th week of topical application and were satisfied with the therapy with no major adverse effects. Hence, topical clindamycin with nicotinamide represents a potential first line combination therapy in mild to moderate acne vulgaris which requires further large-scale studies.

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Ethical approval: The study was approved by the Institutional Ethics Committee of Bangalore Medical College and Research Institute and the approval number is BMC/PGs/289/2017-18

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