

Original Research Article

Efficacy of Dapsone 5% gel in treatment of Acne vulgaris

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ABSTRACT

Background: Acne vulgaris is chronic inflammatory disorder of pilosebaceous unit mainly characterized by comedones, papules and nodulocystic lesions affecting face and upper trunk. Topical dapsone 5% gel is approved to treat acne vulgaris because of its anti-inflammatory and anti-bacterial activities.

Methods: A single center, open label interventional study was conducted during 1 year period in dermatology OPD of Jawaharlal Nehru Medical College, Sawangi (Meghe), Wardha, Maharashtra. Patients were enrolled in the study considering inclusion criteria. Patients were asked to apply dapsone 5% gel twice daily on face for 12 week. Efficacy was evaluated by mean percent reduction in total, inflammatory and non-inflammatory lesions and success rate on change in investigator global acne severity assessment scale while tolerability was assessed by evaluating skin dryness, erythema, stinging or burning sensation and scaling at baseline, 1, 2, 4, 8 and 12 week.

Results: At end of 12 week, success rate reached to 31.54%. Dapsone 5% gel was effective in reduction of total, non-inflammatory and inflammatory lesions by 57.75%, 52% and 63.1% respectively. Side effects with dapsone gel were tolerable, mild and transient.

Conclusions: Dapsone 5% gel was efficacious and well tolerated in non-inflammatory as well as inflammatory acne lesions.

Keywords: Acne vulgaris, Dapsone 5% gel

INTRODUCTION

The prevalence of acne vulgaris reported from various countries ranges to 87% of adolescents and up to 54% of adults.¹ Though acne is self limiting disease, the presence of active acne lesions impacts the physical appearance and creates negative effects on psycho-social function for individual.²

Acne vulgaris pathogenesis is characterized by excess sebum production, colonization of the follicular infundibula with *Propionibacterium acnes*, hyperkeratinization and production of inflammatory mediators.³ Various studies carried out in acne-prone patients and early acne lesions suggest that inflammation may precede microcomedone formation and may serve as a trigger for

the hyperkeratinization that leads to follicular occlusion.⁴ There is a complex interrelationship between *P. acnes*, sebaceous lipogenesis and inflammation.⁸

P. acnes, a gram positive anaerobe that resides in the follicular infundibulum, enhance sebaceous lipogenesis. Squalene, a major component of sebum, can be oxidized in the presence of UV light to convert into peroxidated squalene that has been demonstrated to induce production of inflammatory mediators in cultured keratinocytes.⁹ Inflammatory mediators like IL-1 and IL-8 induce keratinocyte proliferation, which may contribute to follicular occlusion and enhanced sebum retention that leads to microcomedone formation.¹⁰ VCAM and E-selectin expression are important ligands for tethering and migration of inflammatory cells from the circulation

to the dermis and are important in regulating lymphocyte trafficking in the skin.¹⁰

In vitro, a wide range of anti-inflammatory effects have been associated with dapsone including inhibition of: IL-8 release from cultured keratinocytes; leukocyte migration via inhibition of integrins; signal transduction after G-protein activation; calcium-dependent neutrophil function; release of prostaglandins, leukotrienes, and lysosomal acid hydrolases; and formation of 5-lipoxygenase metabolites.¹¹ Antibacterial activities are similar to sulfones.

Oral dapsone is effective in the treatment of severe, nodulocystic inflamed acne but haematological and other complications limits its use on routinely healthy acne patients.^{12,13} Topical dapsone is an alternative and showed good safety profile even in G6PD deficiency patients.^{14,15} The aim of our study was to evaluate efficacy and safety of topical dapsone 5% gel on acne patients.

METHODS

A single center, open label interventional study was conducted to evaluate the efficacy and safety of dapsone 5% gel in treatment of acne vulgaris.

Study was held in outpatient dermatology department, Jawaharlal Nehru Medical College, DMIMS, Sawangi (Meghe), Wardha, Maharashtra during 1 period from October 2015 to September 2016. Male and female patients of acne vulgaris between 12 to 35 years of age with grading 2, 3 and 4 on the investigator global assessment scale for acne vulgaris were enrolled into the study.⁸ Patients who had not been taking topical treatment for 2 week and systemic treatment for 4 weeks for acne were also included into the study.

Patients with grade 5 on investigator global assessment scale for acne, acne conglobata, acne fulminant, secondary acne, patients with known hypersensitivity to sulphone drugs, pregnant female, female with sign of PCOS and on any systemic medications that interfere with outcome of study (hormonal therapy, antidiuretics, steroids) were excluded from study.

This study was reviewed and approved by institutional ethical committee. After taking written informed consent and patients who fulfill inclusion criteria were enrolled into the study. Patients were instructed to apply dapsone 5% gel twice daily on face for 12 week. Routine blood investigation like CBC, G6PD, LFT were done on each visit. Each patient was followed up at week 1, 2, 4, 8 and 12 to assess efficacy and side effects.

Efficacy of the study group was assessed by mean percent change in total number of lesions, non-inflammatory lesions, and inflammatory lesions. Success rate i.e. percentage of patients rated clear (0) or almost clear (1) on investigator global assessment scale for acne

vulgaris and patients assessment of therapeutic efficiency (completely resolved, marked improvement, moderate improvement, poor) were also evaluated in the study group.

Safety and tolerability were assessed by evaluation of clinical signs and symptoms like stinging and burning sensation, erythema, dryness and scaling on four point scale (0- absent, 1- mild, 2- moderate, 3- severe).

RESULTS

Among 86 enrolled patients, 78 completed the study. Six patients were excluded because of non-compliance with treatment regimen or the follow up schedule. 78 patients were analyzed for the results. Of total 78 patients, 35 were males and 43 were female patients with average age of 21 as presented in Table 1. At end of 12 week, success rate reached to 31.54% with dapsone 5% gel as shown in Figure 1. From baseline to week 12, patients treated with dapsone 5% gel showed mean percent reduction of total lesions by 57.75%. There was mean reduction of 63.1% in inflammatory lesions and 52.4% in non-inflammatory lesions after 12 week of treatment with dapsone 5% gel. Mean percent reduction of inflammatory lesions were more as compared to non-inflammatory lesions as seen in Figure 2.

Table 1: Patients demographics characteristic at baseline.

IGA grading of acne	Male	Female	Total
2	13	14	27
3	17	21	38
4	5	8	13

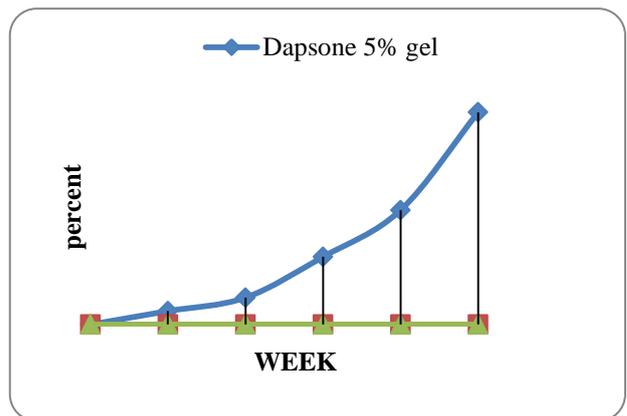


Figure 1: success rate i.e. percentage of patients rated clear (0) or almost clear (1) on investigator global assessment scale for acne vulgaris.

Patients assessment of therapeutic efficacy showed that dapsone 5% gel is showed promising response. At end of 12 week grade II (IGA) acne vulgaris; complete resolution, marked improvement and moderate improvement were assessed by 18.51%, 48.14% and 29.62% of

patients respectively. In grade 3 (IGA) acne vulgaris; complete resolution, marked improvement and moderate improvement were assessed by 21.05%, 55% and 13.15% of patients. In grade 4 (IGA) acne vulgaris 23% showed

marked and moderate improvement. Overall dapsone gel showed complete resolution by 17.94% of patients, marked improvement by 47% and moderate improvement by 20.51% of patients as given in Table 2.

Table 2: patients self evaluation of dapsone gel treatment after 12 week of treatment.

IGA grading of acne	Grade 2	Grade 3	Grade 4	Total
Completely resolved	5 (18.51%)	8 (21.05%)	1 (7.69%)	14 (17.94)
Marked improvement	13 (48.14)	21 (55%)	3 (23.07)	37 (47.43%)
Moderate improvement	8 (29.62)	5 (13.15%)	3 (23.07)	16 (20.51%)
Poor	2 (7.40)	4 (10.52%)	6 (46.15)	12 (15.38%)

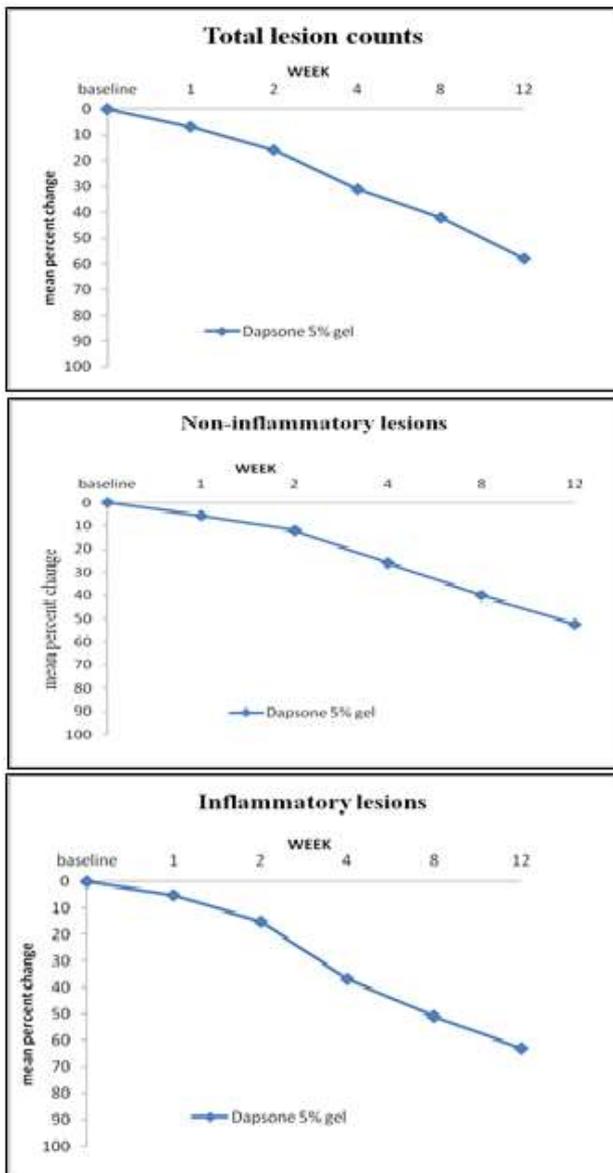


Figure 2: Mean percent change in total lesions count, non-inflammatory lesions and inflammatory lesions.

Dapsone gel was very well tolerated by patients and only six patients experienced side effects like itching, burning and dryness. Side effects were mild, transient and

subsided in due period of time. No haematological changes were seen on investigation in any patients.



Figure 3: Pre-treatment photo of acne vulgaris patient.



Figure 4: 4 weeks after treatment with topical dapsone 5% gel.



Figure 5: 12 weeks after treatment with topical dapsone 5% gel.

DISCUSSION

Acne vulgaris is a challenge to treat because of its chronicity and sequel which makes adolescent and young adult psychologically disturbed. Various systemic and topical drugs are available which targets the different stages of pathogenesis of acne. Inflammation is also considered to be major factor in pathogenesis of acne vulgaris. Systemic antibiotic and other anti-inflammatory drugs are being used for treatment of acne vulgaris. In present scenario we are facing resistance to available topical antiinflammatory and antimicrobial drugs and we are in search of new options to overcome above problem. Dapsone is used in many dermatological conditions like leprosy and dermatitis herpetiformis. Oral dapsone has been promising in treatment of acne vulgaris due to its antimicrobial and anti-inflammatory effects but the risk of serious side effects restricts its use in relatively healthy acne patients. Dapsone known to cause dose dependant haemolysis due to oxidative damage to red blood cells from its hydroxylamine metabolite specially in G6PD deficient individuals.¹⁶⁻¹⁸

Topical formulation of dapsone 5% gel is available and FDA approved for use in treatment of acne vulgaris.¹⁹ Topical dapsone has not been associated with haemolysis risk and no regular laboratory test is needed. In clinical trials, twice-daily topical application of dapsone as directed for the treatment of acne did not induce significant changes in haemoglobin or other hematologic indicators, even in G6PD-deficient patients.^{15,17,18,20} Continuous use of dapsone 5% gel is not associated with an increase in plasma concentrations of the drug.¹⁵

In this study, reduction in total lesion, inflammatory lesions and non-inflammatory were 57.75%, 63.1% and 52.4% respectively. Similar results were seen in two 12 week, double-blind, randomized, parallel group, phase III studies conducted by Draelos et al in which inflammatory lesion was reduced by 47.5% and non-inflammatory lesion by 41.8%.¹⁵

At the end of 12 weeks with mean acne reduction of 58.2%, 19.5%, and 49.0% for inflammatory, non-inflammatory, and total lesion counts respectably was seen in Lucky et al study which was similar to the present study.¹⁸

In present study excellent to marked response were seen in 51% of patients using topical dapsone gel which correlate with the findings seen in Raimer with 40.1% excellent to good response.²¹

Success rate in present study was 31% that was similar to the findings in other studies.^{18,21} Topical dapsone has shown similar efficacy and tolerability in long term treatment.

In one year open label non-comparative trial of topical dapsone showed steady decrease in lesions counts over 6

months which were maintained through 12 months and there was more reduction in inflammatory counts as compared to non-inflammatory counts.¹⁸ It was well tolerated over a period of 12 month with few treatable side effects.¹⁸

Greater mean percent reduction in inflammatory and non-inflammatory lesions were seen when topical dapsone was combined with topical adapalene and benzoyl peroxide than topical dapsone monotherapy.²¹

Only 6 (7.79%) out total 78 patients experienced side effects on application site which conforms to the 2-8.2% in other studies that were mild and no one have discontinued treatment because of side effects.^{15,18,21} None of the patient in this study had non-application site adverse events though headache and nasopharyngitis has been experienced by patients in many studies.^{15,18} Also no changes occur in haematological or blood chemistry parameters.

Present study clearly demonstrate that novel action of dapsone which targets the major stage of pathogenesis of acne i.e. inflammation and antimicrobial action against *P. acne* makes it an alternative topical choice in treatment of acne vulgaris.

CONCLUSION

Antimicrobial and anti-inflammatory properties of dapsone gel formulation can be used in treatment of acne vulgaris without risk of serious haematological side effects. Topical dapsone is effective and tolerable option for acne vulgaris patients.

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Conflict of interest: None declared

Ethical approval: The study was approved by the institutional ethics committee

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