

A double blind randomized study to compare efficacy of 5% Dapsone gel vs combination of Adapalene-clindamycin gel in the treatment of mild to moderate Acne vulgaris

Abstract

Background: Acne vulgaris is a disorder of the pilosebaceous glands affecting mainly the adolescent population and it is associated with significant morbidity.

Aim: To compare the efficacy of 5% Dapsone gel against a combination of 1% clindamycin-0.1% adapalene gel in the treatment of mild to moderate acne vulgaris.

Materials and methods: Clinically diagnosed cases of Acne vulgaris were evaluated using Global Acne Grading system (GAGS) and those classified as mild to moderate were included in the study. Dapsone 5% gel and combination of 1% clindamycin-0.1% adapalene gel were repacked in similar looking containers. Patients received the medication randomly such that 30 of them applied 5% dapsone gel and other 30 applied a combination of clindamycin-adapalene (AC) gel. They were reviewed at 4th week and their GAGS score were recorded.

Results: This study comprised of 60 subjects of which, 48(80%) were men and 12(20%) women. 24 subjects followed up after 4 weeks. Out of 24(40%), 14(58%) had improved as reflected by Wilcoxon signed rank test. Of these 14, 7 belonged to Dapsone and 7 others to clindamycin adapalene. The other 36(60%) subjects who couldn't follow-up in person were questioned telephonically. 6(35%) out of 17(47%) from the adapalene clindamycin (AC) group and 5(26%) out of 19(53%) from the dapsone group said their acne had improved. 2 out of 17 from AC group and 8 out of 19 from Dapsone group said they did not find any improvement with the medication and had thus not returned for follow up. 2 out of 17 from AC group and 1 out of 19 from dapsone group had skin irritation and or erythema due to which they dropped out of the study. 7 out of 17 from AC group and 5 out of 19 from Dapsone group, said they had not used the drugs regularly because of exams, travel and other reasons.

Conclusion: Adapalene-clindamycin group showed good efficacy and lesser side effects compared to the dapsone group. This study also highlights the fact that acne cases are poorly compliant with therapy. Larger studies are required to analyze the reasons for poor compliance in acne as well as efficacy and tolerability of various newer anti acne preparations.

Keywords: acne vulgaris, dapsone, clindamycin, adapalene, GAGS

Volume 2 Issue 4 - 2018

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Received: February 15, 2018 | **Published:** August 10, 2018

Introduction

Acne vulgaris is a common condition encountered in dermatology OPD. It affects approximately 85% of individuals in the age group of 11 and 24 years.¹ The pathogenesis of acne is comprises of 4 main steps which are as follows:

- i. Aberrant follicular keratinization,
- ii. Inflammation
- iii. Excess sebum and
- iv. Propionibacterium acnes.² The global consensus in treatment of mild to moderate acne is usage of fixed combination of topical retinoid and antibiotic.³⁻⁵ However, topical retinoids also have adverse effects such as irritation, erythema and photosensitivity which can

impact the compliance with therapy as well. Hence, the quest for newer safer and effective anti acne drugs has been going on.

Topical 5% dapsone gel contains sulfone and has an advanced solvent microparticulate delivery system that enables penetration of stratum corneum.⁶⁻⁷ Dapsone is known to have antibacterial as well as anti-inflammatory action which may help in reduction of acne. The role of topical retinoids in treating acne is well established. Adapalene is a topical retinoid used in the treatment of acne vulgaris. It acts through the retinoic acid receptors which modulate gene transactivation and gene expression in human keratinocytes inducing anti-comedogenic, anti-inflammatory and immunomodulatory effects.⁸ However, the use of topical retinoids is limited by their cutaneous side effects. But, adapalene is the least irritating retinoid of the lot.⁸ Clindamycin is a topical antibiotic which has been widely used in treatment of acne for many decades. The extensive use of antibiotics in acne has lead

to the development of resistance to antimicrobial therapy by many pathogens, including Propionibacterium acnes.⁹ Therefore, all the current guidelines strongly advocate limiting the use of monotherapy for prolonged duration in chronic diseases like acne.^{4,10} Combination of topical retinoids and antibiotic can reduce the development of resistance as well as improve therapeutic outcomes. Combination therapy is likely to have more significant effect because it targets almost all the steps in pathogenesis of acne.⁹

Aims of the study

- The aim of this study was to compare the efficacy of 5% Dapsone gel and combination of 1% clindamycin- 0.1% adapalene gel in the treatment of mild to moderate acne vulgaris.
- To study the possible adverse events due to these topical medications

Materials and methods

This study was conducted in the Dermatology OPD of Belagavi Institute of Medical Sciences Belagavi. Sixty patients who had mild to moderate acne as per Global Acne Grading Scale were enrolled in this study. Written informed consent was obtained from all the patients before being enrolled in the study. Patients who had used any topical/systemic anti acne preparations (including OTC/steroids) in the last 3weeks, those with severe grade (GAGS >30) acne, patients with known hypersensitivity to any of the study drug, pregnant and lactating women were excluded from the study.

Both gels were repacked in similar looking containers which were coded and randomized so as to blind the investigator and the patient. Patients randomly received the medication such that 30 of them received dapsone gel and other 30 got combination of clindamycin-adapalene gel. They were asked to follow up after 4weeks. Patients were asked to apply a pea sized quantity of drug over the face for 30min at night. They were advised sunscreen usage during the daytime (Table 1).

Table 1 Global Acne Grading Scale (GAGS)

Location	Factor
Forehead	2
Right cheek	2
Left Cheek	2
Nose	1
Chin	1
Chest and Upper back	3

Each type of lesion is graded depending on the severity as follows: no lesions=0, comedones=1, papules=2, pustules=3 and nodules=4. Score for each area is calculated = factor multiplied by grade. Global score is sum of local scores. 1-18 is mild, 19-30 is moderate, 31-38 is severe and >39 is very severe.

Results

Data was analyzed using Wilcoxon signed rank test (Table 2). In this study total 60 subjects are enrolled age 18-25 years. Males are 48(80%) and females are 12(20%). Each group contains 30 subjects (Table 3).

Table 2 Total study subjects

Total subjects	Adapalene-clindamycin(AC) group	Dapsone group
60	30	30

Table 3 At 4 weeks

Total subjects who followed up	AC group improved	AC group Not improved	Dapsone group improved	Dapsone group not improved
24	7	5	7	5

At the end of 4weeks of study only 24(40%) subjects followed-up, out of which 12 showed statistically significant improvement in their acne grading (Table 4).

Table 4 Subjects who did not follow up were questioned telephonically

Subjects who did not follow up	Total	Improved	Not improved	Side effects	Have not applied the medication
AC group	17	6	2	2	7 (Exams-3, Not used-4)
Dapsone group	19	5	8	1	5 (Exams-3 Not used-2)

Out of 60, 24 subjects followed-up after 4weeks and reported no adverse events with the medications. 36 subjects who did not follow-up were questioned telephonically. 3 subjects experienced side effects like dryness and erythema (AC group-2, Dapsone group-1) (Figures 1-4).



Figure 1 Adapalene-clindamycin group before treatment GAGS-21.

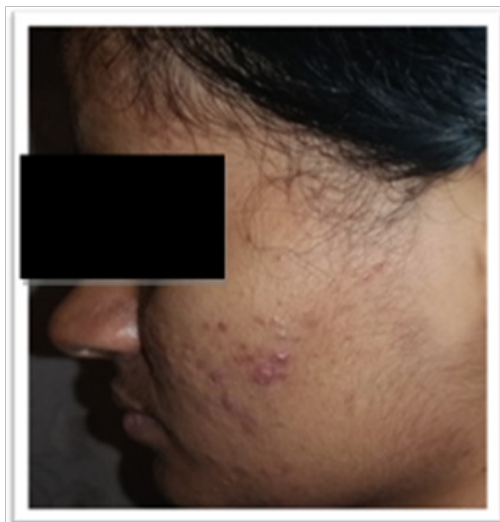


Figure 2 Adapalene-clindamycin groups after 4wks GAGS-14.



Figure 3 Dapsone gel group before treatment GAGS-18.



Figure 4 Dapsone gel group after 4wks GAGS-13.

Discussion

Acne vulgaris is one of the common skin disorders which dermatologists encounter in their daily practice. The clinical presentation varies from seborrhoea, comedones, erythematous papules, pustules and less frequently nodules, pseudocysts or scarring in few of them. The treatment options are also equally varied ranging from topical therapy (antibiotic creams, retinoids), systemic (antibiotics, retinoids, hormonal therapy), surgical therapy to peels and lasers.¹¹ The latest addition to the list is Dapsone gel. There are hardly any studies which have compared the efficacy of Dapsone gel with other topical medications and hence we decided to undertake this study. Dapsone gel is known to act on propionibacterium acne and also on the leucocytes, thereby reducing bacterial colonization as well as inflammation which are two key pathogenic factors in the development of acne.

30 patients were assigned to each group and treated for 4 weeks. This showed both drugs had similar efficacy. 36 subjects who did not follow-up, were telephonically interviewed, following which our statistics showed that adapalene-clindamycin group had a higher efficacy and less side effects compared to dapsone group.

Most of the studies done earlier with regard to Dapsone gel have evaluated the drug as a standalone therapy. But, we were comparing it to the most commonly recommended anti acne medication. A study done by Pickert et al.,¹² showed 5% Dapsone gel was clinically effective and well tolerated in mild to moderate acne vulgaris.¹² A study conducted by Lynde CW et al.,¹³ on 101 subjects showed that dapsone 5% is safe and effective in treatment of mild to moderate inflammatory facial acne.¹³ Another interesting study by Tanghetti et al.,¹⁴ concluded that dapsone gel had favorable outcome in females compared to the male counterparts.¹⁴ However, we did not see any such gender based bias in our study. Another study by Lucky et al.,¹⁵ concluded that Dapsone gel is safe and effective for long term treatment of acne vulgaris and has a rapid onset of action.¹⁵

As evident from all these studies, Dapsone gel is an effective and safe anti acne medication. The same was once again established by our study as well. However, in comparison to Adapalene-clindamycin gel it could not match the efficacy in terms of improvement in acne. Adapalene-clindamycin gel showed better results in terms of improvement in the acne and the side effects were slightly more than Dapsone group. But, a good number of patients in the Dapsone group were lost to follow up because their acne did not improve. This highlights the fact that quick response to therapy is a significant factor in deciding the compliance to therapy. If patients see good response, even with bare minimal adverse events they would be more compliant and not otherwise. There are large number of studies to support the fact that adapalene-clindamycin is an effective and safe therapeutic option in the treatment of acne. A study by Percy et al.,¹⁶ showed Adapalene gel is a safe and effective topical agent in the treatment of mild to moderate acne vulgaris in Indian patients. Adapalene may be combined with other topical and oral anti acne drugs.^{16,17} More than 50% cases in this study did not follow, which reflects the poor compliance to therapy in the Indian scenario.

This was taken up as a pilot study to compare the 2 drugs. Even though the number of cases was small, there was a significant dropout. The primary reason for recruiting a limited number of subjects was the cost of medications. This study did not receive any grants and the authors purchased the medications at their own cost. The possible

reasons for a large number of drop outs were adverse events to the study drug, the subjects were facing academic exams and in few other cases they lacked motivation because of poor response to therapy. Since this study was conducted at a tertiary government hospital, the long waiting queues could also have been a factor for the poor compliance. In order to overcome these pitfalls, we had to analyze some subjects telephonically. This study did not have a scale to analyze the severity of adverse effects. However, it was quite evident that the severity was not much, since only 3 subjects quoted adverse events as a factor for non compliance with the therapy.

Conclusion

Adapalene-clindamycin gel is more effective compared to Dapsone gel in the treatment of mild to moderate acne vulgaris. The common adverse effects seen were erythema and dryness which was slightly more with Adapalene clindamycin. Limitation of study:

- i. The study period was only for 4 weeks and hence, no long term adverse events could be elicited.
- ii. 50% study population did not follow up in person and hence, there could be certain errors.

Acknowledgments

Approved by Institutional Ethics Committee.

Conflict of interest

Author declares that there is no conflict of interest.

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