ORIGINAL ARTICLE

Comparative evaluation of Dapsone 5% gel vs Clindamycin 1% gel in mild to moderate acne vulgaris

Balvinder Kaur Brar, MD, Sumir Kumar, MD, Naveen Sethi, MD

Department of dermatology, G.G.S. Medical College & Hospital, Faridkot, India

ABSTRACT

Acne vulgaris is a most common condition bringing patients to dermatology clinic. It is a pleomorphic disorder most commonly present between 12-25 years of age with prevalence ranging from 50-95% in different countries. Though it is considered as a benign disorder, but can have profound psychological impact on the patients, because of face being its main target in mostly young population.

Clindamycin is effective in the treatment of acne acting on *Propionibacterium acnes*. Oral dapsone is occasionally used for the treatment of nodulocystic acne, it has both anti-inflammatory as well as antimicrobial effect. FDA has approved topical formulation of Dapsone in 2005.

So, we compared therapeutic efficacy of topical clindamycin with topical dapsone in our study by dividing 60 patients from our out patient department randomly into two groups of 30 each. Each group was subjected to once daily application of Dapsone 5% gel and Clindamycin 1% gel respectively for 12 weeks. Patients were followed up four weekly till 12 weeks and results were compared. We found that overall efficacy of Dapsone 5% gel is 53.19% with 50% patients being completely free of acne after 12 weeks. While, it is 50% with clindamycin with 46.67% patients being completely free of acne.

Side effects in both groups were comparable. Results are statistically not significant, but patients on DLQI basis fared slightly better in dapsone 5% gel group when compared with clindamycin 1% gel group. Dapsone can also be used as monotherapy without significant risk of development of resistance, while clindamycin being antibiotic doesn't has such privilege.

So it is concluded that Dapsone 5% gel is slightly better topical option than Clindamycin 1% gel in mild to moderate acne.

KEY WORDS: Dapsone 5% gel, clindamycin 1% gel, moderate acne

INTRODUCTION

The term acne is derived from Greek word "acme" meaning "prime of life". Though considered as a benign disorder, it can have profound psychological impact on the patients, especially with those having disfiguring scars, which can persist for life.[1] It is a chronic inflammatory disorder of pilosebaceous unit resulting from increased sebum production, altered keratinization, inflammation and bacterial colonization of hair follicles by *P. acnes*.[2] It is the most common condition bringing patients to dermatology clinic. It is a pleomorphic disorder, and most commonly presents between 12-25 years of age, but can manifest at any age. Even if mild manifestations are not included, frequency of moderate to severe acne is still 20-35%. Clinical features include seborrhea, non-inflammatory lesions like open & closed comedones, and inflammatory lesions like papules, pustules and scarring in severe cases. As the pathogenesis of acne is becoming clear in recent years, newer treatment modalities are coming up.[3] There are a number of treatment modalities

Correspondence: *Dr. Naveen Sethi, Opposite Guru Nagar, Zira road, Ferozepur City, India - E-mail: drnaveensethi@gmail.com*

available for the treatment of acne, varying from topical to systemic therapies. Clindamycin is effective in the treatment of infections produced by streptococci and staphylococci. It is also effective for acne vulgaris acting on *Propionibacterium acnes*. These days topical clindamycin is an established treatment modality effective in mild to moderate acne either alone or along with other systemic therapies. Dapsone is a sulfone that has been used mainly as an oral medication for leprosy and less commonly as a treatment for nodulo cystic acne. Although dapsone is classified as an antibiotic due to its inhibition of bacterial DNA synthesis, it is also an effective anti-inflammatory agent. Nevertheless, due to the concerning side effects that come along with ingestion of the drug (hematologic and hepatic issues), a topical formulation has been produced. In 2005, the FDA approved dapsone for acne patients under the condition that they test negative for G6PD deficiency; however, following a phase IV trial, the FDA removed this restriction, improving feasibility. Dapsone's dual anti-inflammatory and anti-microbial effects may offer physicians a novel multimodal monotherapy for targeting acne. As there is a known resistant to antibiotics like macrolides and quinolones, used in acne and quiet a few side effects are associated with other systemic therapies like retinoids, and many people prefer topical treatments over systemic, so best possible topical treatment is sought for. Hence, we thought of comparing the efficacy of 5% dapsone gel with well-established treatment modality like 1% clindamycin gel.

Aim of the study

To compare the therapeutic efficacy of 5% Dapsone gel with 1% Clindamycin gel in mild to moderate acne.

MATERIAL & METHODS

This study was conducted in department of dermatology, Guru Gobind Singh Medical College & Hospital, Faridkot, India. A total of 60 patients attending out patient of dermatology department, presenting with mild to moderate acne were selected for the study. Patients selected were of age between 14-30 years. Both males as well as female patients were enrolled for the study. Only patients with history of less than 3 months of duration were enrolled in the study. Patients excluded from the study were patients having history of previous treatments with some systemic agents, having un realistic expectations, with history of more than 3 months disease duration, having some secondary infection of skin and adnexa, pregnant and lactating women, and patients having severe hematological abnormalities. Patients were divided randomly into two groups of 30 each. After taking informed consent from each patient, group 1 was subjected to 5% Dapsone gel topically at bedtime on the lesions daily for 12 weeks. While, group two was given clindamycin 1% gel treatment once daily for 12 weeks. All the inflammatory as well as non-inflammatory lesions were counted and graded before starting treatment. All the patients were followed up 4 weekly for 12 weeks, reduction in lesions was noted on each follow-up. At the end of the 12 weeks treatment, improvement was compared statistically and results were noted. Comparison of DLQI score of all the patients was also done with DLQI questionnaire at baseline and at 12 weeks of therapy in both groups.

RESULTS

Age & sex distribution

Randomly distributed 30 patients in the dapsone group included 13 males & 17 females. Age distribution showed 24 out of 30 patients were of age group 14 to 24 years. While, 6 were above 24 years of age (Table 1). Whereas, those treated with clindamycin 1% included 14 males and 16 females. Age group distribution showed 22 patient were between 14-24 years of age, while rest 8 were above 24 years of age (Table 2).

Grading of acne

In dapsone group 13 patients were of mild grade acne, 17 were that of moderate severity, at start of treatment (Table 3). While, in clindamycin group 16 patients had mild, 14 had moderate acne before starting treatment (Table 4).

Response of treatment in dapsone monotherapy (Table 3):

Response to treatment was noted at every 4 weeks starting from first follow-up at 4 weeks, then on 8 weeks, and on 12 weeks. Improvement in grading was noted in tabulated form on the basis of reduction in inflammatory as well as non-inflammatory lesions. After 4 weeks of therapy, 1 patient cleared from acne, while 17 had mild & 12 had moderate acne. After 8 weeks 11, 9 & 10 patients were cured, had mild and moderate acne respectively. After total 12 weeks, moderate results were noticed with 15 patients being cleared from acne while 8 & 7 patients had mild and moderate acne respectively. So 50% patient were clear from acne and overall success rate of the therapy was 53.19%.

Response of treatment in Clindamycin monotherapy (Table 4):

Almost similar improvement pattern was noticed with clindamycin 1% monotherapy. Results were noted in tabulated form after 4 week, 8 weeks and 12 weeks. After 12 weeks of therapy 14 out of total patients were clear from acne, giving overall clearance of 46.7% and overall success of 50%.

Table 1 Age group distribution Dapsone 5% group

Sex	14-24 Years	>24 Years
Male	11	2
Female	13	4
Total	24	6

Table 2 Age group distribution Clindamycin 1% group

Sex	14-24 Years	>24 Years
Male	10	4
Female	12	4
Total	22	8

Table 3 Initial and follow-up grading of lesions in Dapsone 5% group

Grade	Week 0	Week 4	Week 8	Week 12
Cured	0	1	11	15
Mild	13	16	9	8
Moderate	17	13	10	7
Total	30	30	30	30

Table 4 Initial and follow-up grading of lesions in Clindamycin 1% group

Grade	Week 0	Week 4	Week 8	Week 12
Cured	0	1	6	14
Mild	16	17	16	10
Moderate	14	12	08	06
Total	30	30	30	30

Comparison of success rate

Results from both groups were recorded in tabulated form and statistically analyzed with p value of <0.05 kept as significant. When compared after 4, 8 and 12 weeks, difference in both groups was not significant. After 4 weeks p value calculated was 0.9787, which was not significant. Similar patterns were noticed at 8 weeks and 12 weeks with p value of 0.6195 and

0.8574 respectively, which was not significant at any given time . So, moderate success was noticed with both Dapsone 5% gel and clindamycin 1% gel after 12 weeks of therapy with no significant statistical difference. But patients with Dapsone 5% gel therapy fared slightly better in DLQI assessment after 12 weeks of therapy when compared with patients who were on clindamycin 1% gel therapy.

DISCUSSION

According to the combined acne severity classification, acne is divided into three levels; mild, moderate and severe on the basis of number & type of lesions.

Severity	Number	Lesions
Mild	<30	Mainly comedones
Moderate	30-125	Comedones, papules & pustules
Severe	>125	Above + cysts or nodules.

There are mainly four pathogenic factors, which play a major role in formation of acne lesions, though exact sequence of events remains unclear: There is androgen dependent increased and altered sebum production, altered keratinization which leads to formation of comedones due to obstruction of pilosebaceous canal. Then there is follicular canalization of *P. acnes*, which hydrolyses sebum triglycerides, producing free fatty acids further leading to microcomedo formation. Finally, there is release of inflammatory mediators by *P. acnes* enzymes and other factors like keratin, sebum & others leading to accumulation of T-helper lymphocytes, neutrophils and foreign body giant cells, further leading to formation of inflammatory papules, pustules and nodulocystic lesions.

There are several treatment options available for the management of acne, which are based on skin type, clinical classification, pre-existing scarring and most important patient's personal preference. The various options include proper skin care, which is the most important thing in the management of acne, topical & systemic antibiotics, topical and systemic retinoid, benzoyl peroxide, and oral contraceptives for female patients. Treatments can be combined to have the desirous effects.

Systemic therapies are indicated in moderate to severe inflammatory acne,[4] but topical agents are preferred in mild to moderate acne. Acne is essentially a disease of young generation, so side effects of systemic agents are the most important limiting factors for their use.

Various antibiotics used in acne include: Tetracyclins, macrolides, clindamycin, Co-trimoxazole & quinolones. Major problem in antibiotic use is resistant, which is more common with macrolides and quinolones. Tetracyclins form the cornerstone of the oral antibiotic therapy in acne. Clindamycin though is very effective, but is rarely used as oral therapy due to potential serious side effects like pseudomembranous colitis. Topical clindamycin being active against *staphylococcus, Streptococcus* & *P. acnes* is an established treatment modality for acne.

Other well established topical treatments are:

Benzoyl peroxide: It has been used in acne for many years. It is used in different vehicles and different concentrations (2.5-10%).[5,6] It acts as a bactericidal agent through its oxidizing action,[7] it also has anti inflammatory, keratolytic and comedolytic properties. But it can lead to cutaneous irritation or dryness and bleaching of clothes, hair, and bed linen.[8] It can cause burning, erythema, peeling, and dryness.[9]

Retinoids: Retinoids are being used in acne for many years, and are preferred as first line topical therapy by many. It acts by targeting the abnormal follicular epithelial hyper proliferation, reduces follicular plugging and reduces microcomedones and both noninflammatory and inflammatory acne lesions.[10-12] The most commonly used topical retinoids for acne treatment are tretinoin and adapalene.[13] Primary irritant dermatitis, presenting as erythema, scaling, burning sensation is the most common adverse effect.

Topical antibiotics: These are used alone or in combination. Topical antibiotics act by inhibiting the growth of *P. acnes* and reducing inflammation. Erythromycin and clindamycin are the most popular topical antibiotics used in the management of acne and available in a variety of vehicles and packaging.[14] Both are available as a topical form in combination of 1-4% with or without the addition of zinc.[15-17]

Clinical trials for the efficacy and safety of other topical antibiotics available in India like topical clarithromycin, azithromycin, and nadifloxacin are lacking.

Side effects are minor, but pseudomembranous colitis has been rarely reported with clindamycin.[18] Bacterial resistance and cross-resistance are most important limitations of topical antibiotics, so these should not be used as monotherapy.

Other topical treatments available like salicylic acid (less potent than topical retinoids),[19] azelaic acid, lactic acid/lactate lotion, tea tree oil 5% & picolinic acid gel 10% are not as effective and have their own limitations.

Dapsone gel 5%: It is a sulfone with anti-inflammatory and antimicrobial properties. Dapsone has both anti-inflammatory and antimicrobial properties. A combination of these activities may account for its efficacy in acne. It has got good activity against Propionibacterium species, including *Propionibacterium acnes*.

The trials have confirmed that topical dapsone gel 5% is effective and safe as monotherapy and in combination with other topical agents in mild-to moderate acne vulgaris.[20] Safety of topical dapsone has also been established in those patients who are G6PD deficient. So we decided to compare the efficacy of topical dapsone with topical clindamycin.

Comparison of efficacy of Dapsone 5% gel vs clindamycin 1% gel.

As seen in results that after 12 weeks of therapy with both treatment modalities there was moderate improvement. With dapsone 5% gel, 50% patients were completely clear of the lesions. Whereas, the number was 46.6% with clindamycin. After analyzing the data statistically it was found that overall improvement was 53.19% with dapsone 5% gel as compared to 50% with clindamycin. Side effect profile was almost similar with nothing special to mention. But p-value was not statistically significant.

CONCLUSION

Hence it is being concluded from this study that dapsone 5% gel monotherapy and clindamycin 1% gel monotherapy have almost equal efficacy when compared after 12 weeks of therapy with p value of 0.8574, which is not significant. But dapsone 5% gel therapy is slightly better than clindamycin 1% gel therapy in DLQI assessment and due to the fact that it can

be used as monotherapy without any risk of developing resistance. But, we should not use clindamycin therapy as monotherapy due to risk of development of resistance in antibiotic therapies. So, dapsone 5% gel being both anti inflammatory and anti bacterial is considered slightly better than clindamycin 1% gel alone but long-term therapeutic trials are needed with larger pool of patients before commenting about long-term side effects of topical dapsone.

REFERENCES

1. Leung AK, Robson WL. Acne. J R Soc Health 1991: 111:57-60.
2. Golnick H, Cunliffe W, Berson D, et al. Management of acne: a report from a Global Alliance to Improve Outcomes in Acne. J Am Acad Dermatol. 2003; 49:S1-S38.
3. Leyden JJ. New understanding of the pathogenesis of acne. J Am Acad Dermatol. 1995; 32:515-25.
4. Cunliffe WJ, Gollnick HP. Acne: Diagnosis and management. 1st ed. London: Martin Dunitz Ltd; 2001.
5. Plewig G, Kligman AM. Acne and Rosacea. 3rd ed. New York: SpringerVerlag; 2000.
6. Packman AM, Brown RH, Dunlap FE, Kraus SJ, Webster GF. Treatment of acne vulgaris: Combination of 3% erythromycin and 5% benzoyl peroxide in a gel compared to clindamycin phosphate lotion. Int J Dermatol. 1996; 35:209-11.
7. Yang DJ, Quan LT, Hsu S. Topical antibacterial agents. In: Wolverton SE, editor. comprehensive dermatologic drug therapy. 2nd ed. Philadelphia: Saunders Elsevier; 2007. pp. 525-46.
8. Bojor RA, Cunliffe WJ, Holland KT. The short term treatment of acne vulgaris with benzoyl peroxide: Effects on the surface and follicular cutaneous microflora. Br J Dermatol. 1995;132:204-8.
9. Eady EA, Cove JH, Joanes DN, Cunliffe WJ. Topical antibiotics for the treatment of acne vulgaris: A critical evaluation of the literature on their clinical benefit and comparative efficacy. J Dermatol Treat. 1990; 1:215-26.
10. Krishnan G. Comparison of two concentrations of tretinoin solution in the topical treatment of acne vulgaris. Practitioner. 1976; 216:106-09. [PubMed: 131310].
11. Shalita A, Weiss JS, Chalker DK, Ellis CN, Greenspan A, Katz HI, et al. A comparison of the efficacy and safety of adapalene gel 0.1% and tretinoin gel 0.025% in the treatment of acne vulgaris: A multicentric trial. J Am Acad Dermatol. 1996; 34:482-85. [PubMed: 8609263].
12. Leyden JJ, Shalita A, Thiboutot D, Washenik K, Webster G. Topical tretinoin in inflammatory acne: A retrospective, investigatorblinded, vehiclecontrolled, photographic assessment. Clin Ther. 2005; 27:216-24. [PubMed: 15811485].
13. Jain S. Topical tretinoin or adapalene in acne vulgaris: An overview. J Dermatol Treat. 2004; 15:200-07.
14. Johnson BA, Nunley JR. Topical therapy for acne vulgaris. How do you choose the best drug for each patient? Postgrad Med. 2000; 107:73.
15. Dobson RL, Belknap BS. Topical erythromycin solution in acne.Results of multicentric trial. J Am Acad Dermatol. 1980; 3:478-82. [PubMed: 6452463] .
16. Shalita AR, Smith EB, Bauer E. topical erythromycin vs clindamycin therapy for acneA multicenter, double blind comparison. Arch Dermatol. 1984; 120:351-55. [PubMed: 6230999].
17. Kurokawa I, Nishijima S, Kawabata S. Antimicrobial susceptibility of Propionibacterium acne isolated from acne vulgaris. Eur J Dermatol. 1999; 9:2528. [PubMed: 9920982].
18. Parry MF, Rha CK. Pseudomembranous colitis caused by topical clindamycin phosphate. Arch Dermatol. 1986; 122:583-84. [PubMed: 2939805].
19. Shalita AR. Treatment of mild and moderate acne vulgaris with salicylic acid in an alcoholdetergent vehicle. Cutis. 1981; 28:556-58, 561. [PubMed: 6458457].
20. DelRosso JQ. New topical therapies for the treatment of acne vulgaris. Cutis. 2007; 80:400-10. [PubMed: 18189027].