# Efficacy and safety of oral dapsone in acne vulgaris – experience of a tertiary care teaching hospital in central Lahore

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## ABSTRACT

**Background:** Acne is the eighth most prevalent disease affecting 9.4% of the population worldwide and its prevalence in our country is estimated to be around 5%. Severe inflammatory acne is most likely to leave scars and in order to prevent facial disfigurement due to acne scarring, early treatment is desirable. Various treatment options have been formulated for acne, and are tailored according to the severity of the disease. Numerous clinical trials have been conducted till now, to determine the usefulness and side effect profile of such therapies, making acne treatment a highly studied area in dermatology. Objective of this study is to highlight the fact that oral Dapsone could be used as a cheaper alternate to isotretinoin in recalcitrant severe acne, especially in females where retinoids are sometimes contraindicated.

**Patients and methods:** 51 patients, suffering from severe nodulocystic acne, fulfilling the criteria, were enrolled from the Department of Dermatology, Sir Ganga Ram Hospital, Lahore. All the study patients were given oral Dapsone 50mg for initial two weeks and then 100mg daily for the next 10 weeks along with oral cimetidine and topical clindamycin application twice daily. Investigator Global Assessment Scale (IGAS) was employed to measure effectiveness. The treatment was considered 'effective' if the patient achieves 2 or more than 2-grade improvement or almost clear or clear skin at the end of 12 weeks according to IGAS scale. The lesion counts were also done before the start of therapy (day 1) and at every two weeks follow up for 12 weeks. The change in lesion count observed between the baseline number and that seen at follow up visits was also used to evaluate the effectiveness of oral Dapsone. Safety was analyzed by fortnightly visits of the patients to look for any undesirable side effects and monitoring of the hematologic profile of the patients. Final follow up was done at the end of 16 weeks.

**Results:** The study was conducted on 51 patients, with a ratio of 1:3 for males and females and a mean age of 25.2 years (SD ±5.81). At 12th week, patients had significant reduction in their acne lesions; with 7 patients (13.7%) showing completely clear skin, 17 patients (33.3%) had almost clear skin, 5 patients (9.8%) had 3-grade improvement. Twelve patients (23.5%) had 2-grade improvement from baseline score and only 2 patients (3.9%) had 1-grade improvement from baseline. Based on percentage reduction of lesions, excellent response was seen in 32 patients (62.7%), good response in 9 patients (17.6%), moderate response in 2 patients (3.9%), while no patient showed poor response. Dapsone was discontinued in 8 patients due to derangement of hematologic profile.

**Conclusion:** Oral Dapsone, when given carefully, is a very effective therapeutic option in severe recalcitrant acne, with limited side effects.

**Keywords:**
Dapsone, Investigator Global Assessment Scale, effectiveness, acne vulgaris

## INTRODUCTION

The psychosocial impacts of acne vulgaris are a major concern, especially because it affects teens at a crucial period when they are developing their personalities.[1] Studies show that the longer the facial acne vulgaris lasts, the more likely it is to affect one's emotional stability and personality, thereby an individual has to face many challenges.[2] The available most commonly advised treatment options include topical and systemic antimicrobials (doxycycline, azithromycin, clindamycin and erythromycin, etc), topical and systemic retinoids, and oral hormonal therapy.[2,3] Oral retinoids are the best potent treatment option in severe and resistant acne vulgaris, although there are numerous case studies and articles which have explained a considerable number of their untoward effects on the patients. Moreover, they are highly teratogenic and they can also result in worsening of disease in initial few weeks. Oral Dapsone can be an efficacious and relatively safer option in severe acne vulgaris patients especially in females of child bearing age.[3] Dapsone has both anti-inflammatory

and anti-bacterial action, as it inhibits bacterial synthesis of dihydrofolic acid, thereby inhibiting synthesis of nucleic acid.[3] Dapsone has well known systemic adverse effects like methemoglobinemia and hemolytic anemia.[3] These adverse effects can be avoided if G6PD levels are done at the baseline and the patients are closely monitored by doing serial examination at follow ups and laboratory tests like liver function tests and reticulocyte counts.[3] When given under careful monitoring and observation, it might also prove to be a good alternative therapeutic option for severe nodulo-cystic acne if oral retinoids fail.[3] The objective of this study was to find out the efficacy and side effect profile of oral Dapsone in acne vulgaris, in the local population presenting at the Department of Dermatology, Sir Ganga Ram Hospital, Lahore.

## PATIENTS AND METHODS

A single center, interventional longitudinal study was carried out in the Dermatology Department, Sir Ganga Ram Hospital, Lahore, to find out the efficacy and safety of oral Dapsone 100mg daily in the management of nodulo-cystic acne. Nodulocystic acne is characterized by multiple inflamed and uninflamed papules, pustules, nodules and cysts. Both male and female patients of acne, between 12 to 35 years of age, with grading 3, 4 and 5 on the Investigator Global Assessment Scale (IGAS) for acne vulgaris, were enrolled into the study. 51 cases were selected for this study, out of which 38 were females (74.5%) and 13 males (25.5%). Patients who were pregnant or feeding their babies or women who wanted to conceive, patients with known allergy to Dapsone or other sulpha drugs and patients who have been taking isotretinoin during the last 3 months, were excluded. A detailed history was taken from all the patients, with a thorough clinical examination including the cutaneous examination (type of acne and lesion counts mentioning inflammatory and non-inflammatory lesions separately). G6PD test and baseline laboratory investigations including liver function tests, complete blood picture and reticulocytes count, were carried out in all the patients before starting the treatment. IGAS was employed to calculate a baseline severity of acne (Table 1) and photographs of each patient were taken before the start of treatment and on each follow up at two weekly intervals for a period of 12 weeks. Patients were given oral Dapsone 50mg for initial two weeks and then 100mg daily for the next 10 weeks along with oral cimetidine twice daily and topical clindamycin application twice daily. IGAS scoring was used for measuring effectiveness. Score 0

was a clear skin with no inflammatory or non-inflammatory lesions, score 1 for almost clear skin with rare non-inflammatory lesions and no more than one small inflammatory lesion, score 2 for mild severity with some non-inflammatory lesions and no more than a few inflammatory lesions (papules/pustules only, no nodular lesions), score 3 for moderate severity with some-to-many non-inflammatory lesions and possibly some inflammatory lesions, but no more than one small nodular lesion, score 4 for severe disease greater than Grade 3 with some-to-many non-inflammatory and inflammatory lesions, but no more than a few nodular lesions and score 5 for very severe disease greater than Grade 4 with many non-inflammatory and/ or inflammatory lesions with some or many nodular lesions.[4] The treatment was considered 'effective' if the patient achieved 2 or more than 2 grade improvement or almost clear or clear skin at the end of 12 weeks according to IGAS scale. The treatment was considered ineffective or failure in those patients who failed to achieve 2-grade improvement, or had achieved 1-grade or nil improvement from baseline grade. The number of lesions was also recorded at baseline before the start of therapy and at 12th week. The difference between these two counts was also used to determine the beneficial effect of Dapsone. A difference greater than 75 percent reduction was considered "excellent", 50-75 percent as "good", between 20 and 50 percent as "moderate," and less than 20 percent as "poor". Safety was assessed by monitoring reticulocyte count and LFTs at baseline, after two weeks of commencing treatment and at 4th week. Final follow up was done at the end of 16 weeks to look for any recurrences. Data was analyzed by computer software S.P.S.S version 20 and test applied was chi-square. Age was presented as mean± standard deviation. Gender and outcome (excellent to good response) was presented as frequency and percentage.

## RESULTS

Out of the total 51 patients, 13 (25.5%) were males and 38 (74.5%) females with a ratio of 1:3, having a mean age of 25.2 years (SD ±5.81). At baseline, 22 (43.1%) patients had very severe form of acne (Grade 5 on IGA scale), 24 (47.1%) patients had severe acne (Grade 4) and only 5 (9.8%) patients had moderate acne. At 12th week, 7 patients (13.7%) showed completely clear skin (score 0 according to IGA scale), 17 patients (33.3%) had almost clear skin (score 1 according to IGA scale), 5 patients (9.8%) revealed a Grade 3 progress, 12 patients (23.5%) had Grade 2 and only 2 patients (3.9%) showed

| Characteristics | Baseline n (%) | After 12 weeks n (%) |
|---|---|---|
| Acne IGA score | | |
| Clear | 0 | 7 (13.7%) |
| Almost clear skin | 0 | 17 (33.3%) |
| Mild | 0 | 14 (27.4%) |
| Moderate | 5 (9.8%) | 4 (7.8%) |
| Severe | 24 (47.1%) | 1 (1.9%) |
| Very severe | 22 (43.1%) | 0 |
| Grade 1 improvement | 0 | 2 (3.9%) |
| Grade 2 or 3 improvement | 0 | 17 (33.3%) |
| Almost clear skin | 0 | 17 (33.3%) |
| Clear skin | 0 | 7 (13.7%) |
| Discontinuation of treatment | 8 (15.6%) | |
| Relapse at 16th week | 5 (9.8%) | |

a Grade 1 improvement from baseline (Table 1). In 8 patients (15.6%), Dapsone had to be discontinued due to side effects (6 patients had deranged reticulocyte count, 4 patients had deranged liver function tests and 2 patients had derangement in both reticulocyte count and liver function studies). Maximum deranged reticulocytes counts observed was 9%. The mean period of derangement of hematologic profile was 3.1± weeks at which the patients were taking oral Dapsone at dosage of 100mg per day. These patients were given only oral Cimetidine and were kept in follow up till their hematologic profile returned to normal, and were shifted to other acne therapies afterwards. Based on percentage reduction of lesions, excellent response (>75% reduction of lesions) was seen in 32 patients (62.7%), good response (50-75% reduction) in 9 patients (17.6%), moderate response (20-50% reduction of lesions) in 2 patients (3.9%), while no patient showed poor response. At 16th week follow up, only 5 patients (9.8%) had relapse. Five patients (9.8%) who had relapse at 16th week were those who presented with Grade 5 acne. Of these 5 patients, 4 had Grade 2 improvement and one had only Grade 1 improvement from baseline.

## DISCUSSION

Acne is the most commonly seen chronic inflammatory pilo-sebaceous dermatological disorder, affecting about 85% of teens.[5] Treatment of severe acne which is characterized by nodules and cysts is always cumbersome and needs systemic intervention. Various available treatment options include oral drugs like tetracyclines, azithromycin, clindamycin, hormonal anti-androgens for females, isotretinoin and combination of different therapeutic modalities.[2,3,5] Oral isotretinoin is a very effective treatment modality for recalcitrant nodulocystic acne, while some of its side effects like liver damage, anxiety, depression, suicidal ideation and teratogenic potential in females of child bearing age have hindered its use.[3,4] Oral Dapsone is being used in various dermatologic conditions for over 60 years.[6] In 1945, it was discovered to be effective in leprosy in inhibiting its progression.[6] A lot of research has been done on Dapsone due to its anti-inflammatory and anti-bacterial effects, especially its use in certain resistant and unusual cutaneous disorders like leprosy and bullous diseases. Some untoward hematological problems occurring even at low doses have curtailed its use in diseases. Up till now, Oral Dapsone is approved by FDA for the treatment of dermatitis herpetiformis and leprosy.[6] Few case studies have been published where Dapsone has been used for severe acne.[3] At the same time, very few studies have been conducted[7] where a comparison of Dapsone with other acne therapies has been done, most probably due to its already known systemic side effects like hemolysis and methemoglobinemia. This study evaluated the efficacy and safety of oral Dapsone in the local population presenting at a tertiary care hospital in Central Lahore. This drug could become a viable alternative, if proven efficacious, especially in severe acne vulgaris patients in whom oral isotretinoin cannot be prescribed, either due to dyslipidemias or teratogenicity issues. It may also be a useful treatment option in patients who had shown resistance to isotretinoin therapy or had a relapse. Female patients outnumbered males probably because of the increasing trend among female population of using whitening creams, which lead to eruption of acne due to steroids in these creams. Dapsone had to be discontinued in this study in 8 patients because of hematological and hepatic side effects. In spite of prior investigations of Hb and G6PD, and close monitoring of patients, still patients developed these side effects. Therefore while prescribing Dapsone one has to be vigilant and conscious about any untoward happening with the patient.

An uncontrolled study conducted by Kaminsky and coworkers on 484 patients suffering from acne of various grades given 300 mg of Dapsone per week, reported an excellent response in Grade IV acne, with disappearance of 80% of lesions at the end of study period i.e. 3 months.[8] However, the authors did not mention how did they evaluated their patients and they haven't given statistical details, due to which their results are difficult to analyze. Another study conducted by Geniaux and colleagues reported a beneficial effect of 75% in 9 patients (total 11 patients enrolled) within 8 weeks of giving oral Dapsone at 300 mg weekly dose.[9]

In the present study, efficacy was determined by two different parameters, i.e. by percentage reduction in lesion count and upgradation in acne scale according to Investigator Global Assessment Scale. This study was carried out on 51 patients and it showed more than 75% reduction of lesions in 33 patients (64.7%) and 50-75% reduction in 9 patients (17.6%). An interesting fact is that in both the above mentioned studies a very high dose of Dapsone 300mg was employed, while we used a comparatively smaller dosage that is 100mg daily and we achieved almost comparable results.[8,9] As both the studies have not mentioned any details about side effects in their patients, therefore this aspect is difficult to be compared with their studies.

## CONCLUSIONS

Oral Dapsone may be used as safe and effective alternative in patients of acne vulgaris, in both genders. It can also be used as an effective alternative in patients where isotretinoin cannot be prescribed especially married females, or patients who fail to respond to other regimens.

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