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A Study of the Efficacy of 5% Dapsone Gel as a Topical Therapy for Acne Vulgaris

Samia Ali Ibrahim, Soheir Ghonemy* and Howayda Sabry

Faculty of Human Medicine, Zagazig University, Zagazig, Egypt

***Corresponding author:** Soheir ghonemy, Faculty of Human Medicine, Zagazig University, Zagazig, Egypt, Tel: 00201007246548; E-mail: soheirghonemy@yahoo.com

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Abstract

Background: Effective treatment of Acne vulgaris (AV) is to reduce both severity and potential recurrence of the disease. Topical therapies remain the most common treatment option for mild-to-moderate AV.

Objective: To evaluate the efficacy of dapsone gel 5% in the treatment of AV. Methods: This cohort study included 80 patients with AV , their ages range between 13-27 years, Acne severity was graded using Investigator Global Acne Assessment Scale (IGAS). A pea-sized amount of dapsone gel 5% was applied to the affected area of the face twice daily for 12 weeks.

Results: The patients were 12 males and 68 females. There was a marked improvement in IGAS with marked reduction in the number of inflammatory and non-inflammatory lesions between the beginning of the study and through follow up visits. Clinical response to dapsone 5% gel was excellent in 12.5%, good in 67.5%, moderate in 17.5% and mild in 2.5% and satisfactions to treatment was 20% very satisfied, 60% satisfied and 20% somewhat satisfied. Side effects were low and only 5% of cases had mild irritation.

Conclusion: Dapsone 5% gel is effective and safe in the treatment of AV with minimal side effects.

Keywords: Acne vulgaris; Topical treatment; Dapsone gel

Introduction

Acne vulgaris (AV) is a common chronic skin disease involving blockage and/or inflammation of pilosebaceous units (hair follicles and their accompanying sebaceous glands). Acne can present as non-inflammatory lesions, inflammatory lesions, or a mixture of both, affecting mostly the face but also the back and chest [1].

Treatment options vary with each patient, depending on the severity of acne. Topical therapies may be used as a first-line approach for mild to moderate acne or in combination with orals for more severe disease. Some options include tretinoin, azelaic acid, benzoyl peroxide, sulfer, salicyclic acid, resorcinol, or routine face washing with mild soap [2,3]. Antibiotics that can be used for acne include tetracycline, doxycycline, erythromycin, trimethoprim, and clindamycin [4-8].

Dapsone, as an anti-inflammatory agent, introduced in 1950, the potential of oral dapsone to treat AV is well established. However, the risks of serious side effects hindered the widespread use of dapsone in the treatment of acne [9]. A topical formulation of dapsone 5% gel was approved for the treatment of acne [10,11].

Herein, the aim of this work was to evaluate the efficacy of topical dapsone 5% gel in the treatment of AV.

Materials and Methods

This cohort study was carried out at Dermatology, Venereology and Andrology Depratment, Zagazig University Hospitals during the period between April 2015 to January 2016. Eighty patients with AV of both sexes and different grades were included in the study. The patients were selected from the outpatient's clinics of dermatology and venereology department provided that the patients have not received any topical or systemic treatment for AV during the previous 2 weeks. All patients gave informed written consents, and the study was approved by the Institutional Review Board (IRB) at Zagazig University and local ethics committee. We excluded from our study pregnant and lactating women or women who are planning for pregnancy, patients with hypersensitivity or allergy to dapsone and patients on isotretinoin treatment within 3 months before the beginning of the study.

Patients were subjected to the following:

Careful history taking.

General examination.

Complete dermatological examination including type of acne and counting of inflammatory and non-inflammatory acne lesions.

The severity of acne was determined as five grades (clear, almost clear, mild, moderate and severe), depending upon the number of inflammatory and noninflammatory lesions, using Investigator Global Acne Assessment (IGAS) [12].

A base line evaluation of the severity of acne was done by IGAS assessment and lesional photography for each patient before the start of treatment with topical dapsone

Therapy:

Dapsone 5% aqueous gel Prepared by Al Kobtan compounding pharmacy, Ibrahymia Alexandria.

Each gram of dapsone gel 5% contains 50 mg of dapsone in an aqueous gel base of:

Carbomer 980.

Diethylene glycol monoethyl ether (DGME).

Methylparaben.

Sodium hydroxide.

Purified water.

To prepare the medicated gel, dapsone was incorporated at a 5% w/w concentration. This was achieved by grinding the drug and levigating the powder with part of the gel to form smooth paste. The rest of the gel was added gradually with continuous mixing until homogenicity. The treatment regimen consisted of application a pea-sized amount of dapsone gel 5% in a thin layer to the affected area of the face after the skin is gently washed and patted dry twice daily for 12 weeks.

The patients were re-evaluated at 2, 4, 6, 8 and 12 weeks of treatment (the end of therapy), using IGAS, lesional photography together with recording satisfaction of the patient by 4 points scale (as 1=not satisfied, 2=somewhat satisfied, 3=satisfied and 4=very satisfied) [13].

Patient's response to treatment was recorded and classified using 6 points scale into excellent, good, moderate, mild, unchanged and worse [14].

Safety and patient's compliance were recorded at each follow up visits.

Follow up visits in the next 3 months after the end of the study.

Statistical analysis

Data were checked, entered and analysed by using (SPSS version 15) software computer package. Data were expressed as mean ± standard deviation (SD) for quantitative variables, number and percentage for categorical variables. P value<0.05 indicated significant results.

Results

This study included 12 males (15%) and 68 females (85%), their ages ranged between 13-27 years (mean=18.23 ± 2.99). The duration of acne ranged from 1 month to 5 years with a mean ± SD (2.35 ± 1.2). The demographic and clinical data are presented in (Table 1).As regards IGAS at different follow up times in studied patients, at the beginning of treatment 7.5% of the cases were suffering from severe degree, 65% have moderate and 27.5% have mild acne. After 12 week no severe cases were found and only 5% were moderate, 55% were mild and 40% of the cases became almost free. There were statistically significant differences in IGAS between base line and all other follow up weeks in severity of disease among the studied patients (Table 2).

Variable	**(n=80)**
Age (years): Mean ± SD Range	18.23 ± 2.99 13-27
Duration (years): Mean ± SD	2.35 ± 1.2 1month - 5
Range	
Variable	**No**	**%**
Male Female	12 68	15 85

Table 1: Demographic data and duration of disease of the studied cases.

Variable	**(n=80)**	
	n	%
IGAS: Base line Mild Moderate Sever	22 52 6	27.5 65 7.5
IGAS: 2nd week Mild Moderate Sever	38 40 2	47.5 50 2.5
IGAS: 4th week Mild Moderate Sever	54 24 2	67.5 30 2.5
IGAS: 6th week Almost clear Mild Moderate	2 64 14	2.5 80 17.5
IGAS: 8th week Almost clear Mild Moderate	22 52 6	27.5 65 7.5
IGAS:12th week Almost clear Mild Moderate	32 44 4	40 55 5
#P	0.02*1 <0.001**2 <0.001**3 <0.001**4 <0.001**5	

Table 2: Investigator global assessment score (IGAS) at different follow up times in studied cases (#P: P value of Maccnemmar test, P1: Base line versus 2nd week, P2: Base line versus 4th week, P3: Base line versus 6th week, P4: Base line versus 8th week, P5: Base line versus 12th week, IGAS: Investigator Global Assessment Score).

At the beginning of treatment the number of inflammatory lesions among the studied patients ranged from 8 to 55 (mean 23.08 ± 11.88) lesions. After 12 weeks the number of inflammatory lesions among the studied patients ranged from 0 to 14) lesions with a mean ± SD (4.73 ±

3.75). There were statistically significant differences between base line and all other follow up weeks in the number of inflammatory lesions among the studied patients. A statistically significant differences were reported between base line and all other follow up weeks in the number of non-inflammatory lesions among patients as it ranged from 4 to 40 lesions with a mean ± SD (14.08 ± 9.68). After 12 week of treatment with topical dapsone gel, number of inflammatory lesions among the studied patients ranged from 0 to 25 lesions with a mean ± SD (4.55 ± 4.04) (Figure 1).

Variable	Satisfaction (n=80)						χ2	p
	Somewhat (n=16)		Satisfied (n=48)		Very Satisfied (n=16)			
IGAS: 12th week	N	%	N	%	N	%	36.36	<0.001**
Almost clear	0	0	16	33.3	16	100		
Mild	14	87.5	30	62.5	0	0		
Moderate	2	12.5	2	4.2	0	0		
Response:	2	12.5	0	0	0	0	124.4	<0.001**
Mild	14	87.5	0	0	0	0		
Moderate	0	0	48	100	6	37.5		
Good	0	0	0	0	10	62.5		
Excellent								

Table 3: Relation between IGA score, response and satisfaction of the studied cases. (n=number, χ2=qui-square, P=P-value, NS=non-significant).

As regards response to treatment 2.5% of the patients showed mild response to treatment, 17.5% showed moderate response, 67.5% showed good response and 12.5% showed excellent response (Table 3). Regarding satisfaction, 20% of the patients were somewhat satisfied, 60% were satisfied, and 20% were very satisfied (Table 4).

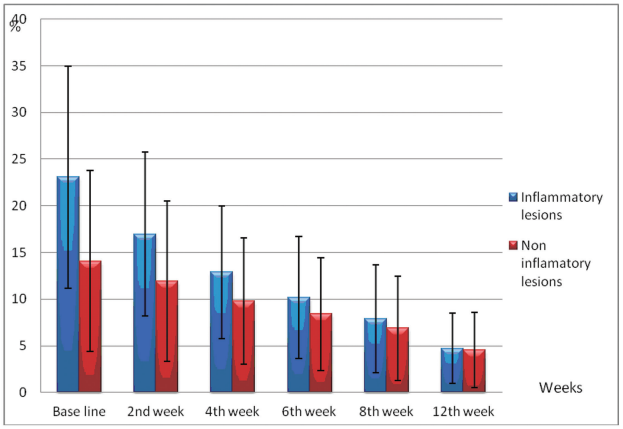

Figure 1: Number of inflammatory lesions and non-inflammatory lesions at different follow up times in studied cases.

There were statistical significant relations between satisfaction and final IGA score and between satisfaction and the response to treatment with an increase in the number of very satisfied patients among almost clear and excellent responded cases (Table 4). 95% of the patients had no side effect and only 5% showed mild irritation.

Variable	Duration (years)				X^2	p
	≤ 2 (n=48)		>2 (n=32)			
IGAS: 12th week	N	%	N	%	1.73	0.42
Almost clear	22	45.8	10	31.2		NS
Mild	24	50	20	62.5		
Moderate	2	4.2	2	6.2		
Response:					3.49	0.32
Mild	2	4.2	0	0		NS
Moderate	8	16.7	6	18.8		
Good	30	62.5	24	75		
Excellent	8	16.7	2	6.2		
Satisfaction:					0.14	0.93
Somewhat satisfied	10	20.8	6	18.8		NS
Satisfied	28	58.4	20	62.5		

Very satisfied	10	20.8	6	18.8		

Table 4: Relation between Duration & IGA at 12th week, response and satisfaction of the studied cases (n=number, χ2=qui-square, P=P-value, NS=non-significant).

Variable	Cases (N=80)	
	N	%
Satisfaction:	0	0
Not satisfied	16	20
Somewhat satisfied	48	60
Satisfied	16	20
Very satisfied		

Table5: Response to treatment among the studied cases (N=number).

There was no statistically significant relation between duration of acne and IGAS, response to treatment or satisfaction (Table 6). No statistically significant difference between males and females as regard response to treatment (P>0.05).

The photo micrographic documentations are presented in Figures 2-8.

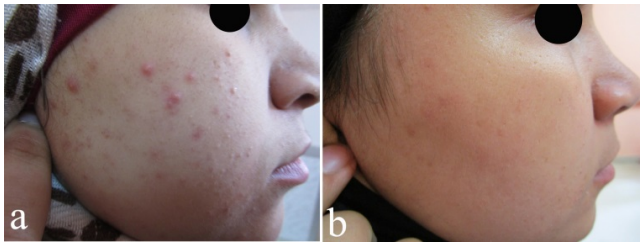

Figure 2: A female patient with moderate acne vulgaris.

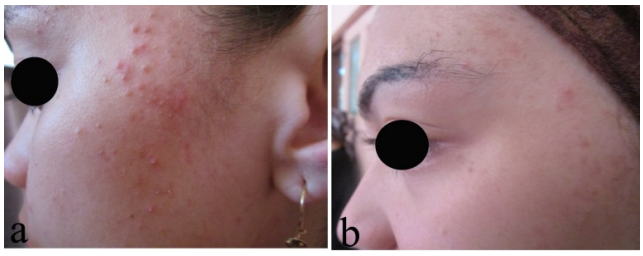

Figure 3: A female patient with moderate acne vulgaris.

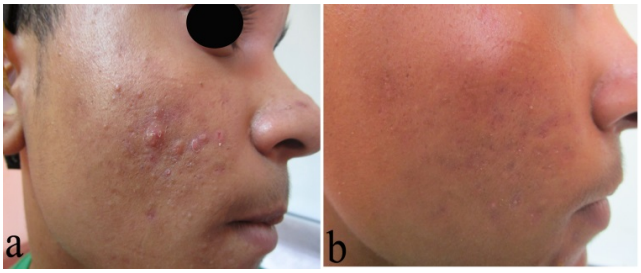

Figure 4: A male patient with moderate acne vulgaris.

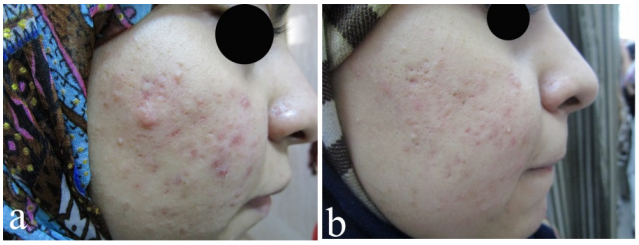

Figure 5: A female patient (right side) with moderate acne vulgaris.

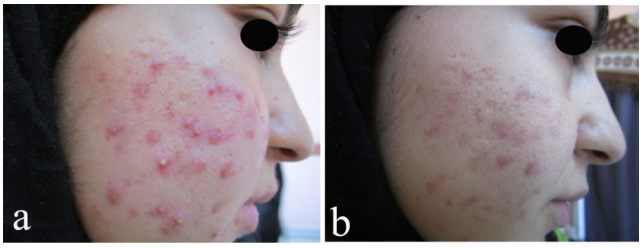

Figure 6a: Female patient (right side) severe acne vulgaris.

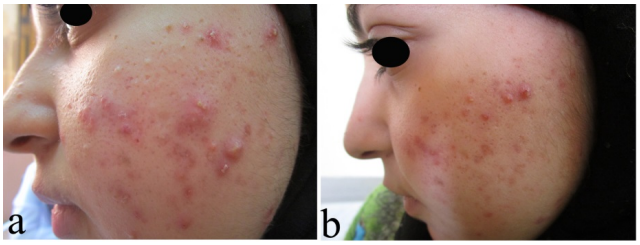

Figure 6b: Female patient (left side) severe acne vulgaris.

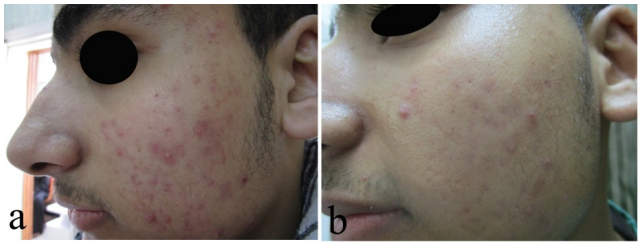

Figure 7: A male patient with moderate acne vulgaris.

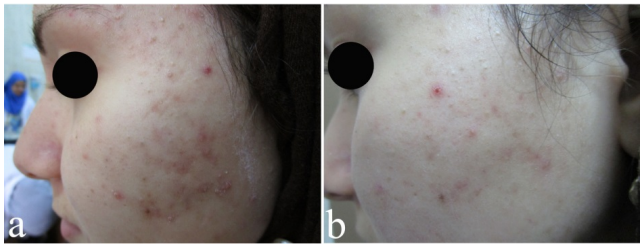

Figure 8: A female patient with moderate acne vulgaris.

Discussion:

Acne vulgaris is the commonest skin characterized by a prolonged course, a pattern of recurrence or relapse, manifesting as acute outbreaks or slow onset, and a psychological and social impact on the individual's quality of life [15]. The pathogenesis of acne is complex and multifactorial. Several factors such as abnormal keratinocyte function, excessive androgenic stimulation, sebum overproduction, hypercolonization by propionibacterium acnes and inflammation have been implicated [16].

Variable	Cases (N=80)	
	N	%
Satisfaction:		
Not satisfied	0	0
Somewhat satisfied	16	20
Satisfied	48	60
Very satisfied	16	20

Table 6: Satisfaction among the studied cases. (N= Number).

Treatment of acne will help to fight bacterial infections, reduce inflammation, and/or reduce oil production. Treatment options vary with each patient, depending on the severity of acne [17]. Most of the studies about treatment of AV in adult focus on the use of systemic therapies, with little emphasis on topical therapies. Overall, controlled trials evaluating the efficacy and safety of topical agents in the treatment of AV are lacking, with subgroup analyses completed with only a few therapeutic agents and formulations [18,19,20].

Dapsone is a sulfone administrated orally for the treatment of certain skin diseases, primarily dermatitis herpetiforms and leprosy. It has both antimicrobial and anti-inflammatory properties [21]. A gel formulation of dapsone was developed for the topical treatment of acne [22].

Topical dapsone 5% gel contains sulfone and has an advanced solvent micro particulate delivery system that enables penetration of the stratum corneum. The role of topical dapsone in the treatment of acne may be antibacterial, by inhibiting the bacterial synthesis of dihydrofolic acid, and anti-inflammatory, by blocking neutrophil myeloperoxidase and inhibiting neutrophil chemotaxis. It may also have a role in reducing the generation of oxygen free radicals. Its safety and efficacy has been demonstrated over a 12 month period in various randomized controlled studies [23-26].

This study was conducted to evaluate the efficacy of topical dapsone 5% gel for the treatment of AV .The mean age ± SD of patients was 18.23 ± 2.99 years, 85% of the patients were females and 15% were males and the mean duration of AV was 2.35 ± 1.2 years.

In relation to IGAS there were statistical significant differences in IGAS between base line and all other follow up weeks among patients (P value is<0.001) and IGAS success was (40%). These results are in accordance with that of Draelos et al. in 12 weeks double blind randomized study, reported a reduction in inflammatory lesions in dapsone treated group and vehicle control as 47.5% and 41.8% respectively in addition to superior results in terms of IGAS (P<0.001) [27].

Another study, reported that at week 12, dapsone 5% gel significantly reduced mean global acne assessment score (GAAS) (p<0.001); however, the proportion of subjects with clinical success (no or minimal acne based on global acne assessment score) at week 12 was greater in adult women (53.5%) versus adolescent females (45.3%, p=0.022) [28]. Also, Alexis et al found that 42.9% of subjects were responders to topical tratment with dapsone gel based on a GAAS of 0 or 1 at week 12 [29]. Lynde and Andriessen reported that treatment success (GAAS 0 or 1) at 12 weeks was achieved in 69.4% of women (t94=4.17, P=0.001) [11].

Another study of the effect of topical dapsone gel in the treatment of AV reported that the percentage of patients achieving treatment success in IGAS score of 0 (none) or 1 (minimal) was greater in dapsone plus tazarotene treated patients (42.2%) than in tazarotene-treated patients (21.8%; P=0.01) [23]. In another study patients treated with dapsone gel combined with adapalene gel had a significantly better response in the reduction of acne lesion count compared with patients who received the vehicle combination 3, [23]. These results indicate that the reduction of inflammatory lesions is the result of dapsone rather than the other components.

In relation to the mean number of inflammatory and non-inflammatory lesions there were marked reduction in the mean ± SD from (23.08 ± 11.88) to baseline (4.73 ± 3.75) at 12 weeks in inflammatory lesions and from (14.08 ± 9.68) to baseline (4.55 ± 4.04) at 12 weeks in non-inflammatory lesions. There were statistically significant differences between base line and all other follow up weeks in number of inflammatory and non-inflammatory lesions. These results are correlated with the studies [10,23,27,28,29] who reported that there were marked reductions in number of inflammatory and non-inflammatory lesions.

Although the clinical improvement in the results of this study was observed in both inflammatory and non-inflammatory lesions, dapsone gel was particularly effective in inflammatory acne lesions.

The reduction in inflammatory acne lesions was earlier than that of non-inflammatory lesions. These results coincide with those of [10,30,31] who reported greater and faster improvement in inflammatory lesions than non-inflammatory lesions .This explained by the mechanism of action of dapsone which exert an anti-inflammatory property on inflammatory lesions by suppressing neutrophils functions.

In relation to response to treatment we found that 12.5% showed excellent response, 67.5% showed good response, 17.5% showed moderate response and 2.5% of the cases showed mild response to treatment. Our results are superior to the result done by Shashikumar et al. who found that 60.6% of patients showed excellent to good response and 16.2% of patients showed Fair response, but only 7.2% had poor response [32].

As regard side effects only 5% had mild irritation and 95% had no side effects. These side effects were regressed after treatment by emollients. These results are in accordance with that of [11,31] who reported that topical dapsone is well tolerated with minimal side effects.

Despite there are several research articles that explain similar results to our study we decided to prepare this study as it is suitable for our locality regarding it is easily applied, available and cheap. The availability of dapsone gel delivers a clinically effective dose of dapsone with minimal systemic side effects [33]. Furthermore, this treatment modality could allow dermatologist to target the inflammation associated with acne by mechanisms that differ from other conventional antibiotics. Another with regard to topical therapy skin colour often reported as the Fitzpatrick skin phototype is frequently considered as an important clinical consideration because of the risk of post inflammatory hyperpigmentation that may be caused by resolved inflammatory AV lesions, dapsone gel is suitable for different skin phototypes [34]. In addition some topical medications may cause irritation which requires very cautious use especially in the face and neck [20], and dapsone gel was reported with mild irritation [31].

The results of this study showed that the treatment of AV with dapsone gel 5% is effective and safe. There are some limitations of this study; which is the short follow up period that should extend to one year after stoppage of treatment, also our study lack to compare combining dapsone gel with other medications for achieving better results thus more studies are required for standardization of dapsone gel use in AV.

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