



ORIGINAL ARTICLE

Effect of Dapsone Gel 7.5% Compared to Tazarotene Gel 0.1% for Treatment of Acne Vulgaris

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ABSTRACT

Background: Dapsone 7.5% gel was well tolerated, with a low incidence of treatment-related adverse events, with the majority of adverse events being related to topical application and mild or moderate in severity. Tazarotene helps to normalize the abnormal keratinization in the follicular infundibulum and changes the microenvironment of the follicle to reduce the proliferation of P. acnes. The aim of the study was to compare the efficacy and safety of dapsone gel 7.5% in relation to tazarotene gel 0.1% in the treatment of acne vulgaris. **Methods:** This study included 38 patients with different grades of AV, of different sexes and their ages ≥ 12 years, the patients were randomly selected from the outpatients clinics. Provided that the patients had not received any topical or systemic treatment for AV during the previous 2 weeks. A base line evaluation of the severity of acne was done by GAAS and lesional photography for each patient before the start of treatment with topical dapsone and tazarotene, then follow up at 2,4,8,12 weeks of treatment. **Results:** There is statistically significant difference between dapsone and tazarotene in side effects after treatment as 71.1% of the studied patients didn't complain of any side effects after dapsone while only 18.4 % of the studied patients had no side effects after tazarotene. The response to treatment with dapsone on the right side and tazarotene on the left side among the studied acne patients showed mild improvement occurred in 28.9% after dapsone and occurred in 15.8 % after tazarotene treatment, with no significant difference between both drugs. **Conclusions:** Dapsone 7.5% gel is a successful, effective and safe alternative in the treatment of acne vulgaris with insignificant side effects.

Keywords: Acne vulgaris; Tazarotene; Dapsone; Pathogenesis

INTRODUCTION

Acne vulgaris is chronic inflammatory disorder of pilosebaceous unit mainly characterized by comedones, papules and nodulocystic lesions affecting face and upper trunk [1]. The prevalence of acne vulgaris reported from various countries ranges to 87% of adolescents and up to 54% of adults. 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. There is a complex interrelationship between P. acnes, sebaceous

lipogenesis and inflammation [3]. *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 Ultra Violet light to convert into peroxidated squalene that has been demonstrated to induce production of inflammatory mediators in cultured keratinocytes. Then follicular occlusion and enhanced sebum retention leads to microcomedone formation [4].

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. Topical dapsone is an alternative and showed good safety profile even in Glucose 6Phosphate Deficiency patients [5]. In vitro, a wide range of anti-inflammatory effects have been associated with dapsone including inhibition of: Inter Leukin 8 release from cultured keratinocytes; leukocyte migration ; calcium-dependent neutrophil function; release of prostaglandins, leukotrienes, and lysosomal acid hydrolases; and formation of 5lipoxygenase metabolites. Antibacterial activities are similar to sulfones [6].

Dapsone 7.5% gel is indicated for the once-daily topical treatment of acne vulgaris in patients aged more than 12 years with moderate acne vulgaris, once-daily dapsone 7.5% gel reduced acne severity (as per the Global Acne Assessment Score) and lesion counts. The benefits of dapsone 7.5% gel were seen as early as week 2 for inflammatory lesion counts, and from week 4 or 8 for other outcomes [7]. Dapsone 7.5% gel was well tolerated, with a low incidence of treatment-related adverse events, with the majority of adverse events being administration-site related and mild or moderate in severity [8]. Tazarotene is a synthetic retinoid that has been approved by the United States Food and Drug Administration (FDA) for the treatment of acne vulgaris. Tazarotene is a prodrug that is converted to its active form, tazarotenic acid in the skin.

Tazarotene helps to normalize the abnormal keratinization in the follicular infundibulum and changes the microenvironment of the follicle to reduce the proliferation of *P. acnes* [9].

METHODS

This study was carried out at the Dermatology, Venereology and Andrology Department, Zagazig University Hospitals during the period from march 2017 to october 2018. It included 38 patients with different grades of acne vulgaris, of different sexes and their ages ≥ 12 years, the patients were randomly selected from the outpatients clinics . Provided that the patients had not received any topical or systemic treatment for AV during the previous 2 weeks. Written informed consents were taken from the patients. The study had the approval of the Institution Review Board (IRB) at Zagazig University.

This study included patients presenting with; Inflammatory and non-inflammatory acne vulgaris, both males and females are involved and the age of the patients more than 12 years. Exclusion criteria included patients having Pregnancy, breast feeding or planning a pregnancy, history of hypersensitivity or allergy to dapsone, tazarotene gel or any of the study medication ingredients, the use of isotretinoin within 3 months before the beginning of the study (Figure 1). The work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Patients were subjected to the following: Personal history including age , sex , and previous treatment, history of AV including onset ,course and duration, history of systemic disease, general examination, complete dermatological examination including type of acne (mild , moderate and severe), onset course and duration of acne. Base line evaluation of the severity of acne was done by GAAS and lesional photography for each patient before the start of treatment with topical dapsone and tazarotene.

Therapy of dapson: Dapsone 7.5% aqueous gel Prepared by Department of Pharmaceutics, Faculty of Pharmacy, Zagazig University.

Preparation of dapson gel 7.5%: Every gram of dapson gel 7.5% contains 75 mg of dapson in a fluid gel base of Carbomer 980, Diethylene glycol monoethylether (DGME), Methylparaben Sodium hydroxide and Purified water was added.

Each patient served as a control for himself. Each patient was instructed to use topical 7.5% dapson gel once daily at night for 12 weeks duration on right hemi-face. Left hemi-face of each patient was treated with topical tazarotene gel once daily at night for 12 weeks duration. The patients were re-assessed at 2,4,6,8 and 12 weeks of therapy(the end of treatment) ,using GAAS and lesional photography .

Global Acne Assessment Score GAAS include: Clear (0): normal clear skin. Almost clear(1): rare non inflammatory lesions. Mild(2): some non inflammatory lesions with few inflammatory lesions (papules,pustules). Moderate (3): many comedones,papules,pustules. Severe(4): inflammatory lesions more apparent,many papules ,pustules and may be few nodulocystic lesions.Very severe (5): highly inflammatory lesions and many nodulocystic lesions^[10].

Patient`s response to treatment was recorded as, good, moderate and mild.Good response if: there was clearance of the comedones, papules and pustules >75%. Moderate if: comedones, papules and pustules regressed in number or size by 50-75%.Mild if: there was 25-50% decrease in comedones, papules and pustules number or size [11].

Statistical analysis

The collected data were analyzed by computer using Statistical Package of Social Services version 24 (SPSS). Data were represented in tables and graphs. Continuous quantitative variables e.g. age were expressed as the mean \pm SD & median (range), and categorical qualitative variables were expressed as absolute frequencies (number) & relative frequencies

(percentage). Suitable statistical tests of significance were used after checked for normality. The results were considered statistically significant when the significant probability was less than 0.05 ($P < 0.05$). P-value < 0.001 was considered highly statistically significant (HS), and P-value ≥ 0.05 was considered statistically insignificant (NS).

RESULTS

The study included 38 patients (7 males and 31 females) as shown in table 1. Their ages ranged from 15 to 29 years old, with a mean of 20.34 ± 3.58 years. Table 2 showed that there is statistically significant difference between dapson and tazarotene in side effects after treatment as 71.1% of the studied patients didn't complain of any side effects after dapson while only 18.4 % of the studied patients had no side effects after tazarotene. Table 3 showed the response to treatment with Dapsone on the rt side and Tazarotene on the lt side among the studied acne patients where mild improvement occurred in 28.9% after Dapsone and occurred in 15.8 % after Tazarotene treatment, with no significant difference between both drugs. Table 4,5 showed that there is statistically significant change in Global Acne assessment score after treatment with Dapsone where clear and almost clear score is higher after treatment than before treatment (23.7% vs zero%) & (44.7% vs zero%) respectively. Table S1 showed that there is statistically significant change in Global Acne assessment score after treatment with Tazarotene where clear and almost clear score is higher after treatment than before treatment (26.3% vs zero%) & (52.6% vs zero%) respectively. Severe cases used combination of topical and systemic treatment. Table S2 showed Global Acne Assessment Score after treatment with dapson on the rt side and tazarotene on the lt side among the studied acne patients showed clear score in 23.7% after dapson and occurs in 26.3 % after tazarotene treatment, with no significant difference between both drugs.

Table 1. Demographic data of the acne patients (N=38).

Demographic data	Studied patients (N=38)	
	No.	%
Age (years)		
Mean \pm SD	20.34 \pm 3.58	
Median (Range)	19.5 (15-29)	
Sex		
Male	7	18.4
Female	31	81.6

Table 2. Side effects after treatment with Dapsone on the right side and Tazarotene on the left side among the studied acne patients (N=38).

Side effects	on right side Dapsone		on left side Tazarotene		p- value of fisher's
	No.	%	No.	%	
No side effects	27	71.1	7	18.4	0.000*
Irritation	11	28.9	20	52.6	0.035*
Erythema	0	0.0	14	36.8	0.000*
Burning sensation	0	0.0	9	23.7	0.002*
Desquamation	0	0.0	3	7.9	0.240

Table 3. Response to treatment with Dapsone on the rt side and Tazarotene on the lt side among the studied acne patients(N=38).

Improvement	on right side Dapsone		on left side Tazarotene		chi - square test	p- value
	No.	%	No.	%		
Mild improvement	11	28.9	6	15.8	1.914	0.384 (NS)
Moderate improvement	13	34.2	16	42.1		
Good improvement	14	36.8	16	42.1		

Table 4. Global Acne assessment score before treatment among the studied acne patients (N=38).

GAAS	studied acne patients (N=38)	
	No.	%
Mild	12	31.6
Moderate	24	63.2
Severe	2	5.3

Table 5. Global Acne assessment score after treatment with Dapsone on the rt side among the studied acne patients (N=38).

GAAS	Before Dapsone		After Dapsone		p-value of Friedman test
	No.	%	No.	%	
Clear	0	0.0	9	23.7	0.000* (HS)
Almost clear	0	0.0	17	44.7	
Mild	12	31.6	12	31.6	
Moderate	24	63.2	0	0.0	
Severe	2	5.3	0	0.0	

**Figure 1.** (A) Female patient (right side) before treatment (B) The same patient at the end of treatment by dapsonegel showing good response.**Figure 2.** (A) Female patient (left side) with moderate acne vulgaris before treatment by tazarotene gel.

(B) The same patient at the end of treatment showing good response.

DISCUSSION

Acne vulgaris (AV) is the most common cutaneous disorder seen in dermatology practice among adult populations [12]. Data from two identically designed pivotal studies of a new, once-daily formulation of topical

dapsone gel, 7.5% demonstrated safety and efficacy versus vehicle [13, 14]. The new formulation of dapsone gel, 7.5% recently gained approval from the United States Food and Drug Administration for the once-daily treatment of acne vulgaris [15]. Tazarotene is

approved for the treatment of psoriasis and acne. Only 0.1% strength is approved by the United States Food and Drug Administration (FDA) for the treatment of acne. Tazarotene cream 0.1% is indicated for acne vulgaris, and gel 0.1% is indicated for mild-to-moderate acne vulgaris, whereas foam 0.1% is indicated for moderate-to-severe acne. Comparison studies between tazarotene, adapalene, and tretinoin report mixed results, with some researchers suggesting comparable efficacy and tolerability, while others report greater efficacy and irritation with tazarotene [16].

Tazarotene is a synthetic retinoid that has been approved by the United States Food and Drug Administration FDA for the treatment of acne vulgaris. Tazarotene helps to normalize the abnormal keratinization in the follicular infundibulum and changes the microenvironment of the follicle to reduce the proliferation of *P. acnes* [17]. This study was established to compare the efficacy and safety of topical dapsone 7.5% gel for the treatment of AV on 38 patients of different sexes, ages and with different grades of acne. They were 7 males (18%) and 31 females (82%), patients act as control for themselves by applying dapsone gel 7.5% on their right side of the face and tazarotene gel 0.1% on the left side of the face. Duration of acne among the studied patients ranged from 1 month to 3 years, with a mean \pm SD of age was 20.34 ± 3.58 years, the mean \pm SD of the duration of acne was 12.26 ± 6.12 , and 57.9% of the studied patients suffered from acne for less than 9 months, while 42.1% of them have acne for 9 months and more.

Before treatment, 63.2% of the studied patients have moderate acne according to Global Acne assessment score while only 5.3% are severe. After treatment, there is statistically significant change in Global Acne Assessment Score after treatment with Dapsone where clear and almost clear score is higher after treatment than before treatment (23.7% vs zero%) & (44.7% vs zero%) respectively. Also there is statistically significant change in Global Acne assessment

score after treatment with Tazarotene where clear and almost clear score is higher after treatment than before treatment (26.3% vs zero%) & (52.6% vs zero%) respectively. Global Acne Assessment Score after treatment with Dapsone on the right side and Tazarotene on the left side among the studied acne patients where clear score in 23.7% after Dapsone and occurs in 26.3% after Tazarotene treatment, with no significant difference between both drugs. There is statistically significant difference between dapsone and tazarotene in side effects after treatment as 71.1% of the studied patients didn't complain of any side effects after dapsone while only 18.4% of the studied patients have no side effects after tazarotene, erythema and burning sensation are more statistically higher after tazarotene treatment than dapsone (26.3% vs zero%) and (23.7% Vs zero%) respectively.

Response to treatment with dapsone on the right side and tazarotene on the left side among the studied acne patients where mild improvement occurs in 28.9% after dapsone and occurs in 15.8% after tazarotene treatment, with no significant difference between both drugs. In agreement with this study, El-Tonsy et al. [18] studied the mean duration of acne in the study population was 29.27 months. In relation to response to treatment we found that the study shows that mild improvement, moderate improvement and good improvement occurs in 28.9%, 34.2% & 36.8% respectively after dapsone treatment, while after Tazarotene mild improvement, moderate improvement and good improvement occurs in 15.8%, 42.1% & 42.1% respectively. According to Del Rosso et al., [19] There were fifteen reports of erythema, dryness, oiliness, pruritus, or burning effects after Dapsone.

Similarly, adverse events were reported for 18.3 percent (396/2161) of patients who received dapsone gel, 7.5% and 18.8 percent (409/2175) of patients who received vehicle. Most adverse events were mild to moderate in severity. These events consisted of application site dryness,

application site pruritus, and application site pain. The incidence of these events for patients who received dapson gel 7.5% was similar to that for patients who received vehicle according to Thiboutot et al [20]. But according to Feldman et al. [21], Most adverse reactions after Tazarotene were mild to moderate in severity. Severe adverse reactions occurred in 3.0% of subjects; 2.6% of patients discontinued due to local skin reactions. There is no significant difference between response after dapson treatment and age or sex of the studied patients .As regard side effects there is statistically significant difference between dapson and tazarotene in side effects after treatment as 71.1% of the studied patients didn't complain of any side effects after dapson while only 18.4 % of the studied patients have no side effects after tazarotene, irritation, erythema and burning sensation are more statistically higher after tazarotene gel treatment than dapson(52.6% vs 28.9%) &(36.8% vs zero%) and (23.7% Vs zero %) respectively.

CONCLUSION

According to our results, we suggest that dapson 7.5% gel can be a successful, effective and safe alternative in the treatment of acne vulgaris with insignificant side effects.

We recommend trying dapson 7.5% gel on a greater number of patients for longer duration of treatment and to follow up cases after improvement to assess the recurrence of lesions after stoppage of the treatment. Further studies are required for standardization of dapson gel use in acne and the possibility of combining it with other medications for achieving better results.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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Tables S1, 2 are shown on the online supplement

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