Research Article

Dapsone Niosome: A Novel Formulation for Treatment of Mild to Moderate Acne Vulgaris

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Abstract
Background: Acne vulgaris is a common multifactorial inflammatory skin disorders. Topical drugs have been used successfully to treat acne for decades. Dapsone is a sulfone antibacterial with anti-inflammatory actions, which are thought to be largely responsible for its efficacy in treating acne vulgaris. **Objectives:** The present study aims to evaluate the efficacy of dapsone noisome as a novel formulation for treatment of mild to moderate acne vulgaris. **Patients/Methods:** Fifteen patients with mild to moderate acne vulgaris were selected and received dapsoneniosome as a single topical treatment for their acne lesions. Photography and clinical assessment were done before and after 2 and 8 weeks of treatment. **Results:** The clinical improvement was noticeable after 2 weeks of treatment with highly significant improvement decrease of the score of acne lesions after 8 weeks of treatment (P <0.001). Dapsone noisome topical application was tolerable was minimal side effects apart of mild erythema and post-inflammatory hyperpigmentation. **Conclusions:** Dapsoneniosome is a promising topical formulation for safe, tolerable and effective drug delivery system with noticeable improvement in mild to moderate acne vulgaris.
Keywords: Dapsone, Acne vulgaris, antibacterial, inflammatory

Introduction
Acne vulgaris is a multifactorial inflammatory skin disease commonly affect in gadolescents and young adults; however, it can persist intoadulthood with significant physical, psychological, and psychosocial burden on those affected (Zaenglein et al., 2016).

Dapsone, a synthetic sulfone antibacterial with anti-inflammatory properties, has been available in an oral dosage form since the 1950s (Stotland et al., 2009), although it was poorly adopted for the treatment of acnedue to the potential of systemic toxicities. Topical dapsone5% gel was developed to reduce the systemic absorption and hence improve the tolerability of the drug; however, itrequires twice-daily application, which some patients mayfind inconvenient(Al-Salama and Deek, 2017).

The present study aims to evaluate the efficacy of dapsone noisome as a novel formulation for treatment of mild to moderate acne vulgaris.

Patients and Methods
The present study was conducted on 15 patients suffering from mild to moderate acne vulgaris according to the global acne grading system (Doshi et al., 1997). Patients were recruited from attendants of the Dermatology outpatient clinic, Minia University Hospital. The duration of scars ranged from 1 to 14 years with a mean of 6.63±4.03. Patients enrolled in the study did not receive any treatment for their acne lesions at least 3 months prior to the study.

An informed consent was taken from each volunteer for treatment, photography and clinical follow up. This study was approved by the Committee for Postgraduate Studies and Research of Faculty of Medicine, Minia University.

All volunteers have been subjected to full history taking, general and local examination and photographing of the lesions.

Exclusion Criteria included pregnancy, lactation, Presence of any skin condition that would interfere with the diagnosis or assessment of acne vulgaris, history of hypersensitivity or allergy to dapsone, or methemoglobinemia or subjects with known G6PD (Glucose 6-Phosphate Dehydrogenase) deficiency or congenital or idiopathic methemoglobinemia.

Dapsone noisome was applied as a topical treatment for acne lesions every night for 8 weeks as thin film over the acne lesions. Clinical evaluation according to the global acne grading system (Doshi et al., 1997) as well as any side effects were reported before, 2 and 8 weeks after treatment.

Statistical Evaluation

The collected data had been analyzed and figured using a computer based program, SPSS software package for statistical analysis (SPSS for Windows, Version 16.0, copyright ©; SPSS Inc., Chicago, IL, USA). The data had been summarized in the form of mean ± SD. The significance of clinical improvement in the same group was assessed using Dependent (paired) t test. This was interpreted in the form of P value. The value of $P \leq 0.05$ was regarded statistically significant.

Results

The study included 15 patients with acne vulgaris. Nine patients had mild acne lesions (60%), while the remaining 6 patients had moderate acne (40%). Twelve patients were females (80%) and 3 were males (20%), their age ranged from 15 to 25 years with a mean age ± SD of 19.53 ± 3.04 years. The duration of acne ranged from half to 4 years with a mean duration of 1.53 ± 0.92. Inflammatory lesions (papules and pustules) were present in 8 patients (53%), meanwhile non-inflammatory lesions (comedones) were the main lesions in 7(47%) of patients.

Before treatment, clinical evaluation revealed a score ranged from 6 to 28 with a mean score of 15.53 ± 6.8. Clinical improvement was noticeable after 2 weeks of treatment with highly significant decrease of the score to 9.13 ± 3.99 (P <0.001). With continuing treatment up to 8 weeks, the clinical improvement still showed the highly significant decrease of the score with a mean of 7 ± 3.49 when compared to before treatment (P <0.001). Also, a highly significant improvement was observed when comparing mean scores of lesions after 2 and 8 weeks of treatment (P =0.001) **(Fig. 1)**.

The effect of dapsone noisome topical application was clear on both non-inflammatory and inflammatory acne vulgaris during the whole duration of the study. In non-inflammatory, there was a highly significant decrease in the severity of lesions from 9.57 ± 2.15 before treatment to 5.86 ± 2.67 (P =0.001) and 4.29 ± 2.63 (P =0.001) after 2 and 8 weeks of treatment respectively. There was non-significant difference when compared lesion after 2 and 8 weeks (P =0.06) **(Fig. 2)**.

Meanwhile, inflammatory acne lesions showed a highly significant decrease in the severity of lesions from 20.75±4.68 before treatment to 12± 2.39 (P <0.001) and 9.38± 2.13 (P =0.001) after 2 and 8 weeks of treatment respectively. There was a significant difference when compared lesion after 2 and 8 weeks (P =0.009) **(Fig. 3)**.

Side effects were minimal apart from mild erythema in 2 patients (13%), which resolved after one week of treatment. Post-inflammatory hyperpigmentation was reported in one case (6.5%). **(Fig. 4).**

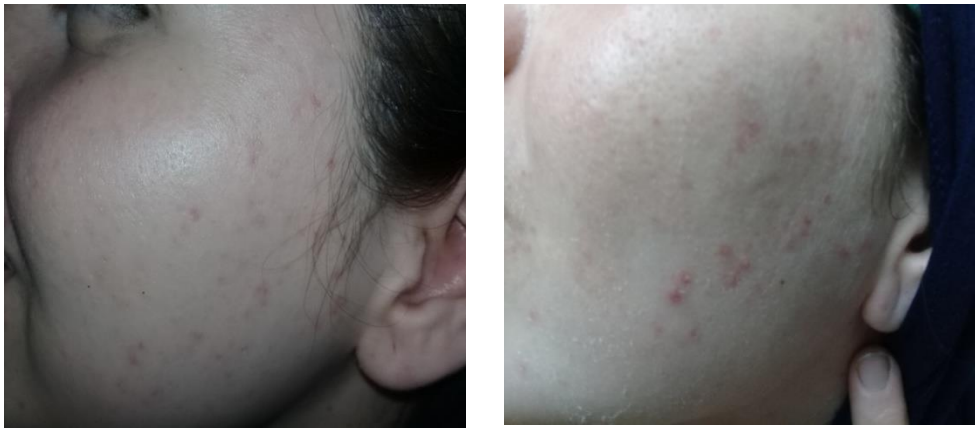

Fig. 1: Significant improvement of patient with mild acne vulgaris in the right cheek of 15 years-old female after 8 weeks of treatment with dapsone noisome.

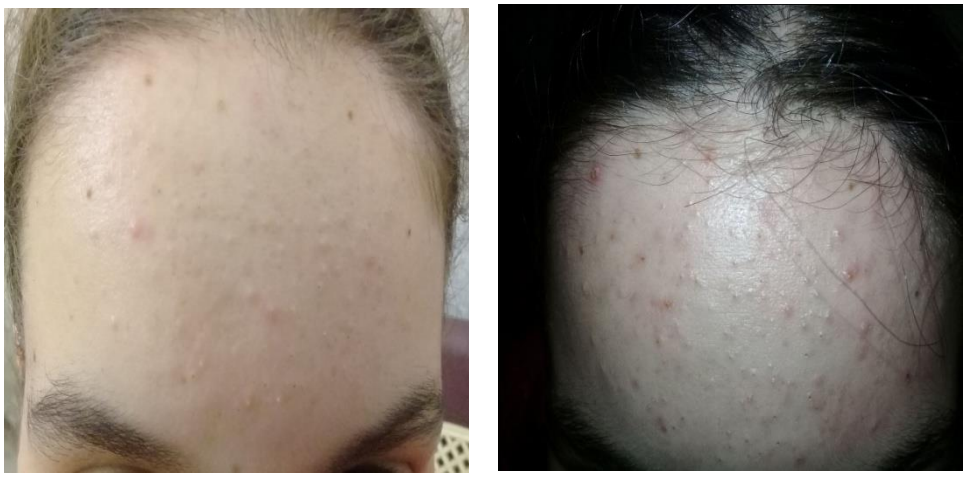

Fig. 2: Non-inflammatory (comedonal) acne vulgaris on in the forehead of 20 years-old female showed significant improvement with marked reduction in the number of lesions after 8 weeks of treatment with dapsone noisome.

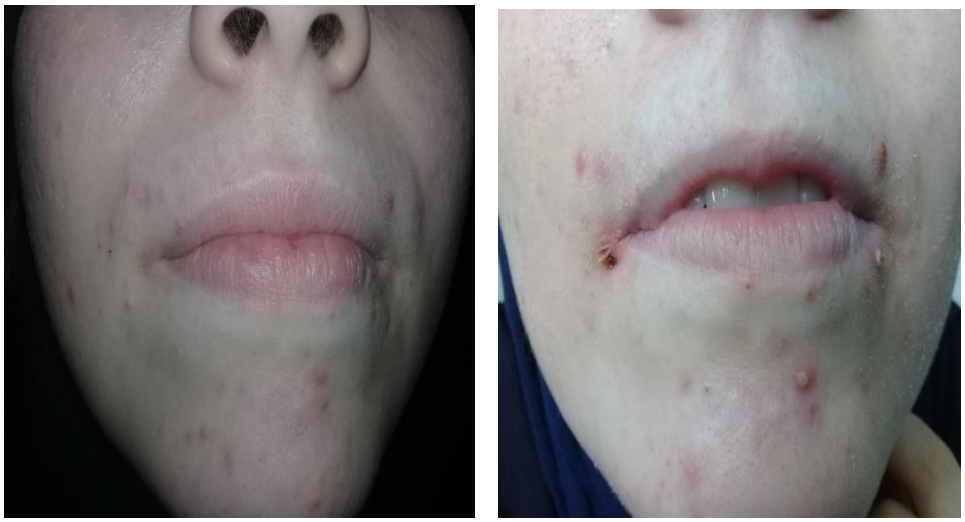

Fig. 3: Inflammatory (papulo-pustular) lesions of acne vulgaris affecting the lower face of 23 years-old female with significant reduction in severity of inflammation after 8 weeks of treatment with dapsone noisome.

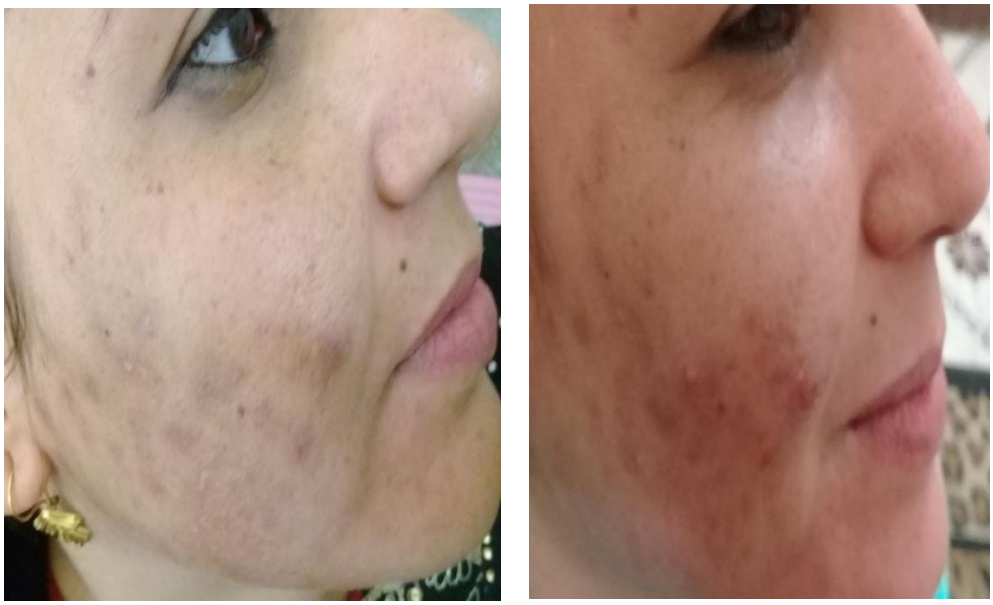

Fig. 4: Significant improvement of 24 years-old female patient with inflammatory acne vulgaris after 8 weeks of treatment with dapsone noisome with residual post-inflammatory hyperpigmentation.

Discussion

Acne is a chronic inflammatory disease of the pilosebaceous unit resulting from androgen-induced increased sebum production, altered keratinisation, inflammation, and bacterial colonisation of hair follicles on the face, neck, chest, and back by Propionibacterium acnes(Williams et al., 2012).

There is no ideal treatment for acne, although a suitable regimen for reducing lesions can be found for most patients. Good quality evidence on comparative effectiveness of common topical and systemic acne therapies is scarce. Topical therapies including benzoyl peroxide, retinoids, and antibiotics when used in combination usually improve control of mild to moderate acne(Williams et al., 2012). The potential of oral dapsone to treat acne vulgaris is well established, but the risks of serious side effects have made it an undesirable drug for use in the relatively healthy acne population (Pickert and Raimer, 2009).

Topical dapsone 5% gel offers documented efficacy for the reduction of both inflammatory and non-inflammatory acne lesions. It has been proven safe, presenting none of the hematologic risks associated with oral dapsone. Data suggest the vehicle formulation enhances healing and contributes to tolerability, making topical dapsone 5% gel a worthwhile anti-inflammatory treatment for many patients with mild-to-moderate acne vulgaris (Kircik, 2010).

A topical formulation of dapsonehas been approved by the FDA for the treatment of acne vulgaris. Data suggests that dapsone gel 5% has the potential to become an established topical drug for the treatment of acne vulgaris. However, studies comparing the clinical effectiveness of the dapsone gel 5% to other available topical antiacne drugs are needed as are studies accessing its usefulness and safety when combined with other acne pharmaceuticals (Pickert and Raimer, 2009).

In the present study, we introduced a novel formulation for dapsone as a noisome which allowed maximal penetration and absorption of active material with minimal risk of either local irritation or systemic absorption. The once daily topical application of dapsone demonstrated a very promising results with obvious clinical improvement as early as 2 weeks of initiation of treatment, which is maintained with better response up to 8 weeks ($P < 0.001$). Also, a highly

significant improvement was observed when comparing mean scores of lesions after 2 and 8 weeks of treatment (P =0.001).

Data continue to establish the role of inflammation, not only in the pathogenesis of acne but also in the development of its most devastating sequelum, scarring. Although topical therapy is preferred by most acne patients and the physicians who treat them, historically no topical intervention has provided primarily anti-inflammatory effects (Kircik, 2010).

Both inflammatory and non-inflammtory lesions of acne vulgaris responds well to dapsone noisome topical application with more pronounced effect on the mean score of inflammatory lesions (P<0.001).

The obtained results were in agreement with the study of Al-Salama and Deek (2017) which reported a reduction in acne severity (as per the Global Acne Assessment Score) and lesion counts with once-dailydapsone 7.5% versus vehicle. The benefits of dapsone 7.5% gel over vehicle were seen as early as week 2 for inflammatory lesion counts, and from week 4 or 8 for other outcomes.

In the present study, side effects were minimal apart from mild erythema in 2 patients (13%), which resolved after one week of treatment. Post-inflammatory hyperpigmentation was reported in one case (6.5%). These results reflects the safety and tolerability of the dapsone noisome when compared with dapsone gel 7.5% which showed adverse effects of mild to moderate severityas stinging/burning, dryness, scaling, and erythema (Thiboutot et al., 2016).

The present study highlights the effect of a dapsone noisome as a topical once-daily treatment of mild to moderate acne vulgariswith early and maintained clinical improvement with minimal side effects. To the best of our knowledge,there are no reports in the literature on the effect of dapsone noisome on acne vulgaris.

The authors are aware that one of the limitations of the present study is the relatively small number of patients and the cost of noisome preparation. Hence, furtherstudies on a larger group of patients are needed to confirm and clarifysuch findings.

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