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Efficacy of 10% Azelaic Acid Gel with Hydro-alcoholic or Alcohol-free Bases in Mild to Moderate Acne Vulgaris; the First Clinical Trial

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Azelaic Acid is a very effective topical medication for treating acne vulgaris. This study aims to compare the efficacy of 10% azelaic acid gel with hydro-alcoholic and alcohol-free bases in mild-to-moderate acne vulgaris. This randomized, double blind, clinical trial, 40 patients with mild-to-moderate acne vulgaris were recruited from Sina Hospital from November 2009 through March 2011. They randomized in two equal age and sex-matched groups, receiving 10% azelaic acid gel with either hydro-alcoholic base or alcohol-free base once at night on their face for eight consecutive weeks. All the patients were revisited on weeks 1, 2, 4, 6 and 8 after treatment and facial acne lesions were counted on each session. Possible complications, as well as the effect of skin type were investigated. Total, inflammatory and noninflammatory acne lesion counts decreased significantly in both groups by the end of study period. However, there was no significant difference between the two groups in this regard ($p < 0.05$). There were minor, self-limited complications, including 3 cases of mild itching in both groups. For the count of inflammatory lesions, azelaic gel with alcoholic base was significantly more effective than azelaic gel with alcohol-free base in patients with oily facial skin ($p = 0.02$). All the patients (100%) were very satisfied with their treatments. In conclusion, both 10% azelaic gels with hydro-alcoholic and alcohol-free bases were comparably effective against mild-to-moderate acne vulgaris. In patients with oily skin, however, 10% azelaic acid with hydro-alcoholic base was superior to the medication with alcohol-free base in patients with oily skin.

Key words: Acne vulgaris, azelaic acid, alcoholic base

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INTRODUCTION

Acne vulgaris is a very common skin disease all over the world. Patients are usually adolescents and young adults. Although there are diverse options in treating acne vulgaris (Babaeinejad *et al.*, 2011; Fouladi, 2012; Khodaeiani *et al.*, 2012, 2013; Babaeinejad and Fouladi, 2013), the first-line in mild-to-moderate disease includes topical medications (Gollnick and Krauthaim, 2003; Krauthaim and Gollnick, 2004; Firooz and Fouladi, 2012). Azelaic acid is a natural dicarboxylic acid with known antibacterial, anti-inflammatory and anti-proliferative properties (Fleischer, 2006; Gupta and Gover, 2007). This is a safe medication with no prominent systemic complications or teratogenic effects. No photodynamic reaction has been ever observed in using azelaic acid. With high rate of tolerance among consumers, no significant induction of bacterial resistance has been reported with this medication (Graupe *et al.*, 1996). In acne vulgaris, in particular, azelaic acid prohibits growth of propionibacterium acne through inhibiting protein synthesis. In addition, this compound prevents follicular keratinization, which in turn inhibits comedone formation (Fluhr and Degitz, 2010). Antiproliferative effect of azelaic acid on hyperactive or abnormal but not normal melanocytes leads to prevention of skin hyperpigmentation (Healy and Simpson, 1994). It has been shown that azelaic acid prevents aggregation of propionibacterium acne, diminishes abnormal shedding of cells in the pilosebaceous ducts and ameliorates inflammation in acne patients (Thiboutot, 2000). Overall, azelaic acid is effective against both inflammatory and noninflammatory lesions of acne vulgaris (Graupe *et al.*, 1996). The present study aims to investigate the efficacy of 10% azelaic acid gel in patents with mild-to-moderate acne vulgaris, with emphasis of comparing compounds with hydro-alcoholic and alcohol-free bases for the first time in the literature.

MATERIALS AND METHODS

In this randomized, double blind, clinical trial, 123 patients with mild-to-moderate acne vulgaris (acne grade I-III) (Burke and Cunliffe, 1984) were studied in Tabriz Teaching Sina Hospital from November 2009 through March 2011. This study was approved by the ethics committee of Tabriz University of Medical Sciences. Informed written consents were obtained from the participants. The exclusion criteria were using medications such as contraceptives containing antiandrogens, systemic or topical steroids and systemic or topical antibiotics within 30 days before enrollment and

documented sensitivity to azelaic or similar compounds. Using Randlist software (ver. 1.2), the patients were randomized into two groups, receiving 10% azelaic acid gel with either hydro-alcoholic base or alcohol-free base once at night on their face for eight consecutive weeks. Azelaic gels were prepared by a pharmacist noninvolved in the study. The medication was filled in similar tubes, which were marked as "A" or "B". The contents were revealed only after data analysis. All the patients were revisited on weeks 1, 2, 4, 6 and 8 after topical treatment commencement and high-quality photographs were taken from their face in each session. Total number of inflammatory and noninflammatory facial acne lesions were counted and compared with the counts at baseline. Possible complications and final patients' satisfaction were documented, as well. The facial skin type (oily, non-oily) was determined by using a standard sebumeter (Sebumeter® SM 815, Courage and Khazaka, Cologne, Germany) according to available guidelines (Khodaeiani *et al.*, 2012). All the patients were instructed to avoid sun exposure, strenuous exercises and using particular foods/medications during the study period (Fouladi, 2012). Within the study period, 43 patients dropped out of the study due to noncompliance (16), using other medications (16), irregular visits (9) and miscellaneous causes (2); leaving 40 patients in each group.

Statistical analysis: The SPSS Software for Windows (ver.16.0, SPSS Inc., IL, USA) was used for analysis. Independent samples t test and the Chi-square (χ^2) or Fisher's exact tests were used. A p-value ≤ 0.05 was considered statistically significant.

RESULTS

Patient's characteristics and general data are summarized in Table 1. The two groups were comparable in terms of sex, age, skin type and family history of acne vulgaris. The total count of acne lesions decreased

Table 1: Demographic and other variables in the studied patients with mild-to-moderate acne vulgaris

Variables	Alcoholic base (n = 40)	Non-alcoholic base (n = 40)	p-value
Age (year)	22.82±4.50	22.02±3.70	0.39
Sex			
Male	5 (12.5)	11 (27.5)	0.09
Female	35 (87.5)	29 (72.5)	
Skin type			
Oily	24 (60)	23 (57.5)	0.55
Non-oily	16 (40)	17 (42.5)	
Family history of acne vulgaris	17 (42.5)	14 (35)	0.49

Data are presented as mean±standard deviation or frequency (%), p<0.05 is significant

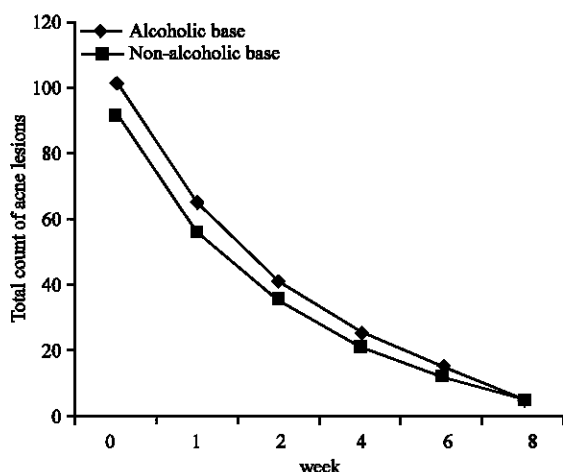


Fig. 1: Total count of facial acne lesions in the studied groups with acne vulgaris

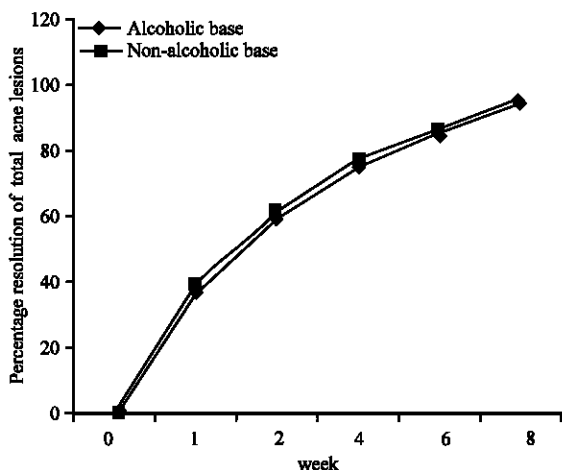


Fig. 2: Percentage resolution of total facial acne lesions in the studied groups with acne vulgaris

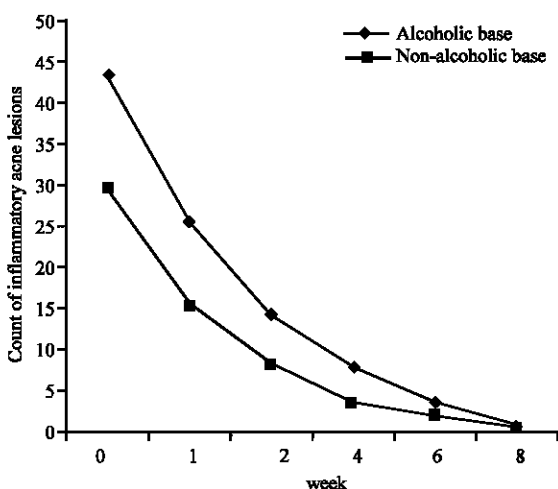


Fig. 3: Count of facial inflammatory acne lesions in the studied groups with acne vulgaris and oily skin

significantly in both groups within 8 weeks of treatment ($p < 0.001$) (Fig. 1). Percentage resolution of total acne lesions in both groups is shown in Fig. 2. There was no significant difference between the two groups in this regard ($p = 0.17$). The count of noninflammatory acne lesions decreased significantly in both groups by the end of study period ($p < 0.001$); however, there was no significant difference between the two groups in this regard ($p = 0.46$). Similar trend was also present for the count of inflammatory acne lesions, which decreased significantly in both groups ($p < 0.001$), with no significant inter-group difference ($p = 0.15$). Hyperpigmentation of previous acne lesions ameliorated significantly in both groups by the end of study ($p < 0.001$), with no significant difference between the two groups ($p = 0.64$). No effect was seen on old scars.

Regarding complications, there was only one case (2.5%) with mild itching in the patients who received azelaic gel with alcoholic base and 2 cases (5%) with mild itching in the other group ($p = 0.50$). All the patients in both groups (100%) were very satisfied with the results of their treatment.

Comparing overall outcome of treatment in patients with oily and non-oily facial skin, no significant difference was found ($p = 0.81$). Similarly, there was no significant difference between the patients with oily and non-oily facial skin in terms of the count of noninflammatory acne lesions ($p = 0.27$). For the count of inflammatory lesions, however, azelaic gel with alcoholic base was significantly more effective than azelaic gel with alcohol-free base in patients with oily facial skin ($p = 0.02$) (Fig. 3).

DISCUSSION

The first line in treating mild-to-moderate acne vulgaris is using topical medications. Antibiotics play a pivotal role in this regard. However, emerging bacterial resistance has dramatically limited their liberal use in acne vulgaris (Bojar *et al.*, 1993; Simpson, 2001; Bettoli *et al.*, 2006). In the present work, efficacy of 10% azelaic gel with hydro-alcoholic or alcohol-free base was examined in patients with mild-to-moderate acne vulgaris. Accordingly, both preparations were similarly effective against inflammatory and noninflammatory acne lesions (Fig. 1 and 2). This is line with results of previous studies that showed high efficacy of 20% azelaic gel in acne vulgaris (Fitton and Goa, 1991; Graupe *et al.*, 1996; Gollnick *et al.*, 2001; Iraj *et al.*, 2007). Gupta and Gover (2007) also reported effectiveness of 15% azelaic gel in treating facial inflammatory lesions. To the best of our knowledge, however, this is the first study that examined the efficacy of 10% azelaic gel in these patients. Pazoki-Toroudi *et al.* (2010) showed that combination of 5% azelaic and 2% erythromycin gels is as effective as a combination of 20% azelaic and

2% erythromycin gels in treating mild-to-moderate acne vulgaris. According to the results of the present study, however, 10% azelaic acid gel can be effectively used alone in such patients. Thiboutot (2008) showed that 10% azelaic acid is as effective as benzoyl peroxide in acne patients. They concluded that due to higher satisfactions of patients toward azelaic acid, it is superior to similar medications. All the patients in the present study were also completely satisfied with the results of their treatment. This is also in conformity with the results of another study by Gollnick and Krautheim (2003) that concluded many anti-acne medications can be replaced by azelaic acid. Lack of bacterial resistance against this medication was another suggested preference of azelaic acid over similar medications in this report. Furthermore, unlike many famous ant-acne medications, azelaic acid is safe in pregnant and lactating patients (Fluhr and Degitz, 2010). In the present work, there was not a significant difference between azelaic acid with hydro-alcoholic or alcohol-free base against acne lesions. However, the medication with hydro-alcoholic base was significantly more effective against inflammatory lesions in patients with oily skin. This difference may be attributed to pharmacodynamic specifications or the ability of medication in solving oily layer of the skin in patients with oily skin and hence, more facilitated access to inflammatory lesions, which are more frequent in such patients comparing with those with normal or dry skin type (Khodaeiani *et al.*, 2012). Finally, both medications were along with minor complications, i.e., mild itching in the site of application only in 2.5 and 5% of the patients in two groups. Significant complications have been reported as the major source of patient's non-adherence to any medication, particularly in young patients with acne vulgaris (Khodaeiani *et al.*, 2013).

CONCLUSION

Both 10% azelaic gels with hydro-alcoholic and alcohol-free bases are comparably effective against mild-to-moderate acne vulgaris. In patients with oily skin, however, 10% azelaic acid with hydro-alcoholic base is superior to the medication with alcohol-free base in patients with oily skin.

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