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Combination therapy with hydrogen peroxide (4%), salicylic acid (0.5%) and D-panthenol (4%): efficacy and skyn tolerability in common *acne vulgaris* during sun exposure period

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Abstract. – OBJECTIVE: ***Acne vulgaris*** **is a disease of the sebaceous follicle which affects up to 90% of adolescent patients. Topical retinoids, benzoyl peroxide and antibiotics are the main treatments for mild to moderate acne vulgaris. The use of such topical treatments is often associated with local irritation and dryness making the skin more sensitive to the sun. The aim of our study was to assess the efficacy and skin tolerability of a fixed-dose combination therapy with hydrogen peroxide (4%), Salicylic acid (0.5%) and D-panthenol (4%) (HSD) gel, in mild-moderate acne vulgaris, during the period of sun exposure.**

PATIENTS AND METHODS: We retrospectively observed 30 patients of Central Italy with mild to moderate acne between April and September 2012. All the patients selected underwent only therapy with HSD gel once a day in the evening for 60 days, while in the morning they just applied SPF 50 sunscreen. We evaluate the efficacy at 30 and 60 days with the "Global Evaluation Scale" (GES) and the tolerability with a 0-3 qualitative scale.

RESULTS: The mean GES value showed a statistically significant reduction: 2.03 (SD 0.81) at baseline, 1.63 (SD 0.81) and 0.90 (SD 0.71) respectively at 30 and 60 days ($p < 0.01$). 21 (70%) and 27 patients (90%) did show good or very good tolerability at 30 and 60 days respectively.

CONCLUSIONS: Topical treatments with retinoids, antibiotics and antiseptics may increase skin irritation reducing patient adherence to the treatment. HSD gel has shown a good skin tolerability and efficacy in reducing acne lesions, even during the sun exposure period in which traditional treatments should be cautiously used.

Key Words:
Acne vulgaris, Photosensitivity, Hydrogen peroxide, Salicylic acid, D-Panthenol.

Introduction

Acne vulgaris is a common disease of the sebaceous follicle that manifests as non inflammatory and inflammatory lesions typically located on the face, the chest and the upper back. *Acne vulgaris* affects up to 90% of all teenagers and half of them continue to experience symptoms as adults[1]. It usually improves at the end of puberty with either no sequelae or sequelae such as postinflammatory hypo/hyperpigmentation and scars which may result in psychological and emotional distress[2]. The pathogenesis of acne is multifactorial: sebaceous hyperplasia, follicular hyperkeratinization, proliferation of *Propionibacterium acnes* and inflammation play a key role in both inflammatory and non inflammatory lesion formation. In fact evidences has emerged supporting the role of inflammation at all stages of acne development, even sub-clinically before comedone formation[3]. The inflammatory pathways underlying the initiation and sthe pread of acne lesions are still being under investigation, but involve *Propionibacterium acnes* as well as several inflammatory mediators (cytokines, defensins, peptidases, sebum lipids, and neuropeptides) and their target receptors[3]. Since the pathogenesis is multifactorial, the European evidence-based guidelines for treatment of acne suggest combination therapy as the most effective[4].

Background

Topical retinoids such as tretinoin, adapalene and tazarotene may cause cutaneous dryness, irritation and make the skin more sensitive to the sun. Even topical treatments with antiseptics as

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well as some antibiotics, although effective on acne lesions, may increasing skin sensitivity[5]. Furthermore many excipients may modify the characteristics of the skin and deliver both parent drug and vehicle to the skin[6]. Therefore, during sun exposure it is important to choose products that should be effective and at the same time minimize irritancy in sensitive skin[7-8].

The aim of our study was to assess the efficacy and skin tolerability of a fixed-dose combination therapy with Hydrogen peroxide (4%), Salicylic acid (0.5%) and D-Panthenol (4%) (HSD) gel, in mild or moderate *acne vulgaris*, during sun exposure.

Patients and Methods

In our retrospective cohort epidemiological study we selected 30 patients with mild to moderate *acne vulgaris* among the patients followed in our acne outpatient between April 2012 and November 2012. We evaluated the tolerability and the efficacy of hydrogen peroxide (4%), salicylic acid (0.5%) and D-panthenol (4%) gel. Main inclusion criteria were: male or female, aged between 10 and 30 years, mild to moderate *acne vulgaris* according to Lehmann et al[9] and defined as: at least 10 but less than 50 inflammatory lesions, at least 10 but less than 100 non-inflammatory lesions and no more than two nodulocystic lesions. Patients with severe acne, such as acne conglobata, requiring systemic treatment and patients applying another topical drug were excluded. All patients underwent only therapy with HSD gel once a day in the evening for 60 consecutive days, while in the morning they just applied SPF 50 sunscreen. The clinical examination allowed a description of the type of lesions, localization and grading by using the "Global Evaluation Scale" (GES) proposed by the Food and Drug Administration (Table I) in order to objectively evaluate the severity of the acne in therapeutic trials[10-11]. Efficacy in reducing acne lesions was assessed at 30 and 60 days using the GES which involves the assignment of a 0-5 score depending on the type and number of acne lesions. The tolerability was assessed at 30 days and 60 days on a 0-3 qualitative scale (0, poor tolerability; 3 very good tolerability) and side effects such as erythema, dryness, desquamation, pruritus, burning were each evaluated using a 0-3 qualitative score (0 = None; 1 = Mild; 2 = Moderate; 3 = Severe).

Table I. The "Global Evaluation Scale" (GES) grading system.

0	Healthy clear skin with no evidence of acne vulgaris.
1	Almost clear, rare non-inflammatory lesions present; rare non-inflamed resolving papules.
2	Some non-inflammatory lesions present; few inflammatory lesions (papules/pustules only, no nodulocystic lesions).
3	Non-inflammatory lesions predominate; multiple inflammatory lesions present; several to many comedones and papules/pustules; one small nodulocystic lesion .
4	Inflammatory lesions predominate; many comedones and papules/pustules; may or may not be a few nodulocystic lesions.
5	Highly inflammatory lesions predominate; variable number of comedones; many papules/pustules and nodulocystic lesions.

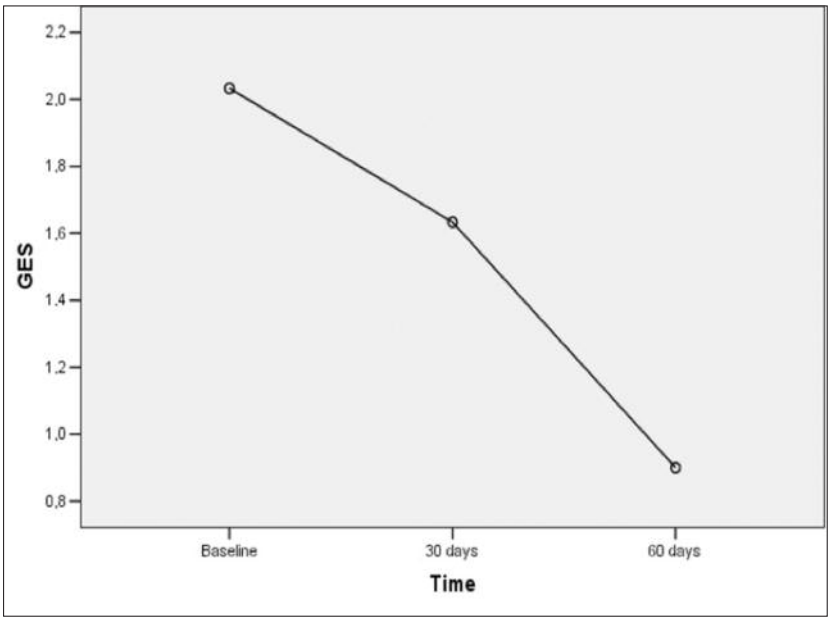

Figure 1. GES score from baseline to 60 days.

Statistical Analysis

A descriptive analysis of the sample was carried out by means of absolute and relative frequencies and means and standard deviation (SD) for qualitative and quantitative variables respectively. In order to analyze treatment efficacy, a General Linear Model for repeated measurement was used to assess GES changes in time and a post-hoc analysis with Bonferroni correction was conducted. Furthermore a description of safety and tolerability results was performed by means of absolute and relative frequencies. $p < 0.05$ was considered statistically significant.

Results

A total of 30 patients, 15 males (50%) and 15 females (50%) aged between 10 and 30 years (average 17.23 years) (SD 5.89) were enrolled in the study. The mean baseline GES score was 2.03 (SD 0.81). The analysis of repeated measures showed a statistically significant reduction of GES compared to baseline ($p < 0.01$). Particularly, the mean GES value was 2.03 (SD 0.81) at baseline, 1.63 (SD 0.72) and 0.90 (SD 0.71) at 30 and 60 days respectively. The post-hoc analysis demonstrated a significant difference between values at baseline and at 30 and 60 days ($p < 0.01$) and between values at 30 and 60 days ($p < 0.01$) (Figure 1). As far as tolerability was concerned, 21 (70%) and 27 patients (90%) did show good or very good tolerability at 30 and 60 days respectively. Side effects such as erythema, dryness, desquamation, pruritus and burning were infrequent and more frequently low grade both at 30 and 60 days as shown in Table II.

Discussion

Our study showed that topical therapy with hydrogen peroxide (4%), Salicylic acid (0.5%) and D-panthenol (4%) gel during sun exposure

Table II. Side effects at 30 and 60 days.

		30 days	60 days
Erythema	None	18 (60%)	21 (70%)
	Mild	9 (30%)	9 (30%)
	Moderate	3 (10%)	0 (0%)
	Severe	0 (0%)	0 (0%)
Dryness	None	24 (80%)	29 (96.7%)
	Mild	3 (10%)	1 (3.3%)
	Moderate	3 (10%)	0 (0%)
	Severe	0 (0%)	0 (0%)
Desquamation	None	22 (73.3%)	30 (100%)
	Mild	8 (26.7%)	0 (0%)
	Moderate	0 (0%)	0 (0%)
	Severe	0 (0%)	0 (0%)
Pruritus	None	19 (63.3%)	24 (80%)
	Mild	9 (30%)	5 (16.7%)
	Moderate	0 (0%)	0 (0%)
	Severe	2 (6.7%)	1 (3.3%)
Burning	None	7 (23.3%)	16 (53.3%)
	Mild	13 (43.3%)	9 (30%)
	Moderate	6 (20%)	3 (10%)
	Severe	4 (13.3%)	2 (6.7%)

period (from April until November, period of maximum solar exposure in the center of Italy) is well tolerated and effective in reducing acne lesions. Patients also applied SPF 50 sunscreen and at the end of the therapy none of these showed hyperpigmentations or dark spots on the skin. Benzoyl peroxide in monotherapy is quickly effective as topical treatment in *acne vulgaris*, in concentrations ranging from 2.5% to 10%, but sometimes may cause mild skin irritation and dryness[12,13]. The benzoyl peroxide, after application, decomposes into hydrogen peroxide and benzoic acid, the latter seems to be the responsible of the irritation[14]. Furthermore the study of Milani et al[15] showed that hydrogen peroxide 1% is an antimicrobial agent which may be effective in the treatment of mild and moderate acne as well as benzoyl peroxide. Salicylic acid is a beta-hydroxy acid with comedolytic and keratolytic properties, which is absorbed into the follicles and dissolve when dead skin cell is built up, encouraging the shedding of the top layer and preventing the pores from becoming congested[16,17]. D-panthenol or Pro Vitamin B5 is a water-soluble derivative of vitamin B5, which is activated and converted into panthotenic acid in the skin. Due to its restructuring, anti-inflammatory and moisturizing properties, D-panthenol may be effective in several disease such as: mild skin irritations, radiodermatitis and atopic dermatitis[18,19]. A previous study on 10 patients with acne the HSD gel showed a reduction of comedones and pustules, respectively 90% and 60%, after 60 days[20]. In our study, HSD gel has shown a significant improvement in reducing acne lesions in patients with mild and moderate acne. Furthermore this combination has dimonstrated a good tolerability during sun exposure period, in which both topical retinoids or antibiotics/antiseptic treatments should be cautiously used.

Conclusions

We suggest the use of HSD gel in patients with mild to moderate acne even in case of sun exposure or as maintenance therapy when other more effective treatments are not suitable due to incompatibility with solar exposures.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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