


RESEARCH PAPER/REPORT



## The effect on acne quality of life of topical azelaic acid 15% gel versus a combined oral contraceptive in adult female acne: A randomized trial

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### ABSTRACT

Acne vulgaris is a chronic inflammatory disease that affects the pilosebaceous unit. Recent studies have shown an increasing number of cases of acne in adult women. These cases are predominantly normoandrogenic and have show some clinical differences compared to adolescent acne. In addition to the physical aspects, acne has a strong psychosocial impact and can lead to the onset of signs and symptoms of depression, such as anger. Our objective was to evaluate the effect on acne-specific quality of life in adult women treated with topical azelaic acid versus a combined oral contraceptive. The study population consisted of 38 adult women with acne and without any features of hyperandrogenism recruited from the clinic of Dermatology Hospital Division of São Paulo, Federal University of São Paulo from January 2012 to September 2014. Patients were randomized into two different groups: one receiving containing 20 ug of ethinylestradiol and 3 mg drospirenone in a regimen of 24 days of medication, a combined oral contraceptive (COC), and the other group topical 15% azelaic acid (AA) gel, twice daily, both for six months. The quality of life was evaluated at baseline and end of treatment with an acne specific measure (Acne-QoL). Before treatment, our data revealed a significant impact of the presence of acne on quality of life. Both treatments resulted in improvement with significant statistical values in quality of life scores. Comparing the four domains of Acne-QoL, patients treated with an oral contraceptive showed greater improvement in two domains (self-perception and acne symptoms) than those treated with azelaic acid.

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### KEYWORDS

Acne; adult; female; quality of life

### Introduction

Researchers analyzing epidemiological data of acne in adult patients showed an increase from the age of 26 in the prevalence of acne in women, indicating a statistically significant difference when compared to men. The prevalence of acne in women ranges from 14–20% compared to 3–5% for men.<sup>1–5</sup> Furthermore, lesions in adult women are more severe Clinically; adult women have moderate acne severity with a characteristic involving the lower face and side of the neck (“U” type). In contrast, the typical presentation in adolescents involves the frontal area, nose, and cheekbones.<sup>6</sup> Not all adults have this “U” type pattern of distribution, and the presence of a large number of comedones was reported in smokers.<sup>7,8</sup> Previous studies consistently indicate a negative impact of acne on patient’s quality of life, with additional psychological

associations including depression, anxiety, anger, and low self-esteem.<sup>9–11</sup>

The impact of disease on quality of life can be measured by scales evaluating effect on general health, such as the DLQI or SF-36, or disease-specific measures, like Acne QoL.<sup>12</sup> The former may be more useful in comparing impact across diseases, while the latter may be more sensitive to the specific disease under study.<sup>13,14</sup>

### Objective

The objective of the study we conducted was to quantify the impact on quality of life in patients with acne in adult life and to analyze the evolution of psychometric tool (Acne-QoL) with two different treatment options.

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## Methods

A prospective randomized study of diagnosis and therapeutic intervention was developed to analyze the impact on quality of life in female patients. These patients were treated with different options and the impact of the presence of acne was measured with a psychometric tool. We assessed the eligibility of women between the ages of 26 and 44 admitted to the dermatology outpatient clinic of the Federal University of São Paulo, referring acne, between January 2012 and September 2014. We excluded patients with hyperandrogenic syndromes by evaluating the following: history, physical examination, laboratory tests (DHEA-S, total and free testosterone), and transvaginal ultrasound. We also excluded users of acne-inducing drugs; users of isotretinoin in the last six months or contraceptives in the last three months; and those with contraindications to the treatment options.

After inclusion, patients were randomized using an internet tool ([www.randon.org](http://www.randon.org)) into two groups for treatment. In one group, patients were treated with topical azelaic acid 15% gel twice a day; in the other group, they were treated with a combined oral contraceptive containing 20ug of ethinylestradiol and 3mg drospirenone in a regimen of 24 days of medication. At the first visit, patients answered the quality of life questionnaires (Acne-QoL), which were translated, adapted, and validated for the Portuguese language.<sup>15</sup> Afterwards, they were treated for 6 months with monthly visits; at the end of treatment, they answered the same questionnaire. The Research Ethics Committee – Federal University of São Paulo, approved the project / Hospital São Paulo, on November 4, 2011, under no. 1622/11 and was enrolled in Clinicaltrials.gov – Identifier: NCT01850095

Acne-QoL contains 19 questions organized into four domains that relate to facial acne: self-perception, social role, emotional role, and acne symptoms. For all domains, higher scores reflect better health-related quality of life (HRQOL). The total score of the questionnaire ranges from 0 to 114, and domain scores are distributed as follows: 0–30 (self-perception), 0–24 (social role), 0–30 (emotional role) and 0–30 (acne symptoms).<sup>12,16,17</sup>

For statistical analysis, the chi-square and Fisher's exact test were used for clinical categorical variables, and a Student's t-test was used for variable quantities. To compare, the questionnaire domains used the

**Table 1.** Clinical and demographic data according to the treatment subgroups.

	TREATMENT		p-value
	COC (n = 20)	AA (n = 18)	
Age <sup>a</sup> (years)	33,7 ± 5,5	33,1 ± 5,3	0,695 <sup>#</sup>
Smoking	1 (5,0%)	2 (11,8%)	0,584 <sup>##</sup>
"U type" lesion distribution	14 (70,0%)	13 (72,2%)	>0,999 <sup>##</sup>
Onset of acne			0,516 <sup>&amp;</sup>
adolescence	9 (45,0%)	10 (55,6%)	
adult	11 (55,0%)	8 (44,4%)	
Intensity			0,132 <sup>###</sup>
none	–	–	
comedones and rare papules	1 (5,0%)	1 (5,6%)	
predominance of papules and pustules	18 (90,0%)	12 (66,7)	
nodules	1 (5,0%)	5 (27,8%)	

<sup>a</sup>mean ± standard deviation.

<sup>#</sup>Student T test.

<sup>##</sup>Fisher's exact test.

<sup>###</sup>generalization of Fisher's exact test.

<sup>&</sup>chi-square.

analysis of variance model with repeated measures adjusted by the Proc-mixed module of SAS software 9.3. Results were considered significant when the p-value was less than 5% ( $p < 0.05$ ).

## Results and discussion

In total, 38 women between 26 and 44 years of age, with mild to moderate acne, were included in the study. Regarding the clinical variables described in Table 1, the statistical analysis found no differences between the groups, making the sample homogenous. The clinical data are in agreement with the majority of studies reported in the literature: The distribution of lesions at the jaw line and in the cervical region was equal or higher than 70%, and the intensity was moderate in over 65% of cases. In recent reviews,<sup>2,8</sup> most patients stated that their disease started in adolescence, but in our sample, there was an equivalence between these cases and those whose disease had a late onset.

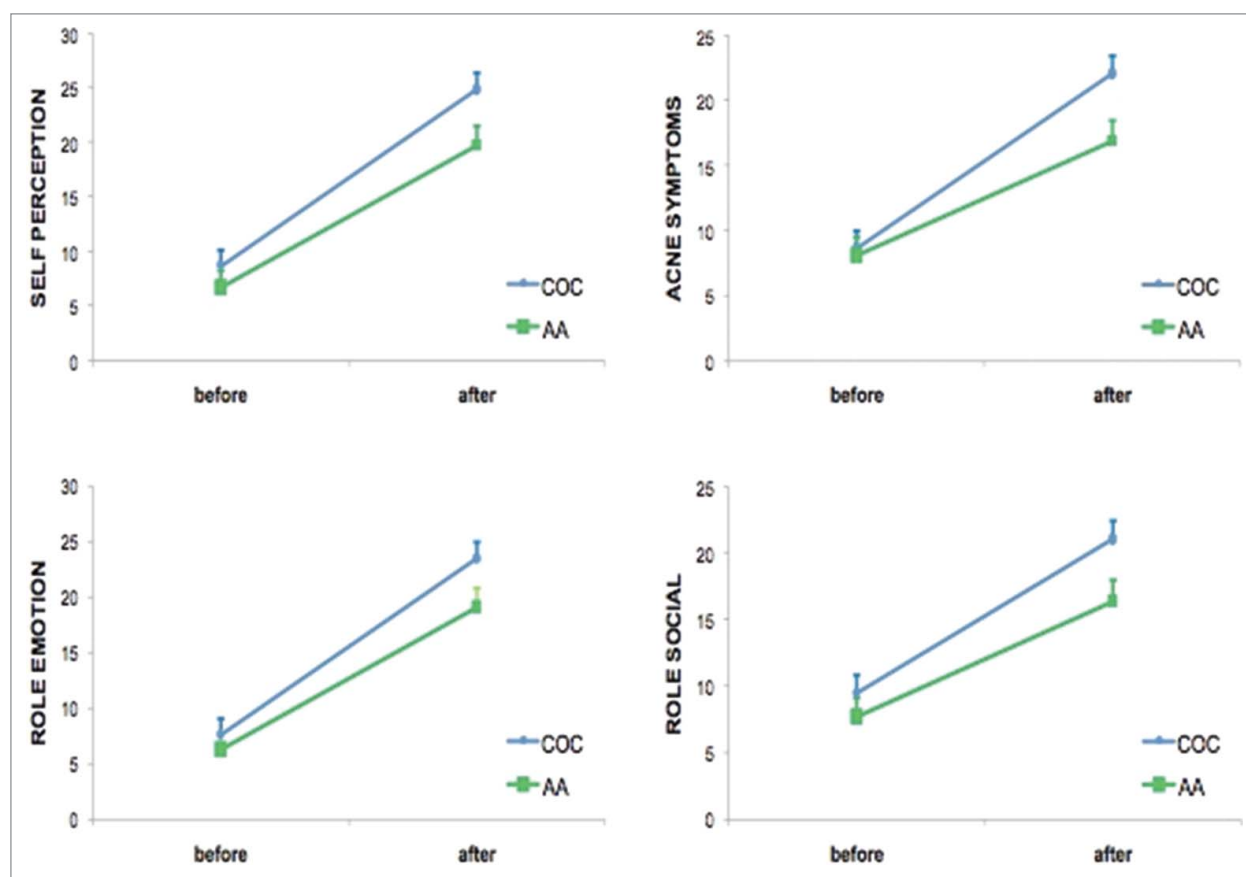
All subjects treated with oral contraceptives (N = 20) underwent six months of treatment; however, in the group treated with azelaic acid (N = 18), four patients terminated early. Probably the need for regular contraceptive use, thereby preventing pregnancy, ensured the absence of dropouts in the first group. In the azelaic acid group, none of the four dropouts decided to leave the study because of collateral effects, but rather justified their withdrawal for personal reasons.

The analysis of data on the quality-of-life pre-treatment questionnaires demonstrated low scores in all domains of Acne-QoL (**Fig. 1**). These results are in agreement with literature and demonstrate the high psychosocial impact of acne lesions in adult life, working as a useful tool to measure this impact. After treatment, regardless of the type (oral or topical), there was a statistically significant improvement in all domains; in two domains, self-perception and acne symptoms, the improvement of scores was significantly higher with the use of oral contraceptives in relation to the use of azelaic acid. Clinically, the two groups showed a significant improvement in lesion count but the result was superior with the contraceptive.

The use of disease-specific psychometric tools such as Acne-QoL quantifies the impact on quality of life in patients with acne. As the literature has shown, that impact does not always correlate with the degree of intensity of acne.<sup>11,12</sup> In this study, about 70% of patients had moderate acne, but their initial scores were low in all domains studied. Studying acne in

different age groups, Tan et al. have shown that total QoL scores worsens as the disease persists.<sup>18</sup> It has also been shown that the psychological impact of the presence of acne seems to be stronger on female than male patients.<sup>7</sup>

Another important analysis is present in the fact that all patients treated showed significant improvement in the scores of the four domains that constitute the Acne-QoL. This improvement has caught the attention of researchers because classic treatments for acne in adult life were compared but with quite different characteristics. Curiously, when the systemic treatment with a hormonal blockade conducted by ethinylestradiol, with an increase of sex hormone-binding globulin and a hypothalamic-pituitary-gonadal block plus a new generation of progesterone derived of spironolactone with anti-androgenic activity was compared to topical treatment with azelaic acid, it showed better statistical improvement only in two of the four domains analyzed (self-perception and acne symptoms). For the authors, adult acne patients need medical explanations and a long follow-up,



**Figure 1.** Evolution of the four domains (Acne-QoL) at baseline and after six months of treatment.

during the medical treatment to improve the psychological symptoms.

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