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Cutaneous and Ocular Toxicology

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/icot20

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To cite this article: Güllü Gencebay, Özge Aşkın & Server Serdaroğlu (2021): Evaluation of the changes in sebum, moisturization and elasticity in acne vulgaris patients receiving systemic isotretinoin treatment, Cutaneous and Ocular Toxicology, DOI: 10.1080/15569527.2021.1922434

To link to this article: https://doi.org/10.1080/15569527.2021.1922434

Published online: 12 May 2021.

CUTANEOUS AND OCULAR TOXICOLOGY
https://doi.org/10.1080/15569527.2021.1922434

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ORIGINAL ARTICLE

Evaluation of the changes in sebum, moisturization and elasticity in acne vulgaris patients receiving systemic isotretinoin treatment

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ABSTRACT

Aim: The aim of this study was to determine the change in facial skin sebum, hydration and elasticity of acne vulgaris patients after being treated with systemic isotretinoin.

Method: Patients who were diagnosed with acne vulgaris and who received systemic isotretinoin treatment for 6 months in Cerrahpaşa Medical Faculty Department of Dermatology between June 2012 and May 2017 were included in this study. The sebum, hydration and elasticity of the skin were measured non-invasively with a device called *"Soft Plus Skin Analyses System"* before treatment and 6 months after treatment. The relationship between the pre-treatment and post-treatment values were evaluated statistically. 35 adult patients (20 female, 15 male) who were diagnosed with acne vulgaris and who received systemic isotretinoin treatment for 6 months.

Results: The pre-treatment sebum value for both sexes ranged between 5 and 100 and the mean value was calculated as 75.8 ± 28.0. The post-treatment sebum values ranged between 1 and 98 and the mean value was calculated as 48.4 ± 31.8. The difference between the pre-treatment and post-treatment values was statistically significant, $p < 0.001$. The decline in sebum value after treatment was 36%. The pre-treatment hydration values ranged between 9 and 77.5 and the mean was 34.6 ± 14.6. The post treatment hydration values ranged between 4.8 and 100 and the mean was calculated as 62.4 ± 28.6. The difference between the pre-treatment and post-treatment hydration values were statistically significant, $p < 0.001$. The post-treatment increase in hydration was 79%. The pre-treatment skin elasticity ranged between 28 and 50; the mean was 40.4 ± 5.5. The post-treatment elasticity values ranged between 20 and 50; and the mean was 37.5 ± 8.2. However, the difference was not statistically significant ($p = 0.1$).

Conclusion: With this study, it was concluded that, systemic isotretion leads to a 36% decline in skin sebum values and a 79% increase in the skin hydration. However, the change in skin elasticity was not statistically significant. Furthermore, the changes in sebum and skin hydration did not lead to a change in skin elasticity.

ARTICLE HISTORY
Received 16 February 2021
Revised 29 March 2021
Accepted 21 April 2021

KEYWORDS
Acne; elasticity; hydration; isotretinoin; sebum

1. Introduction

Acne vulgaris is a chronic inflammatory disease of the pilosebaceous unit. It is characterized by the inflammatory lesions (e.g. comedones, papules, pustules and nodules) in the seborrehic areas of the body such as the face, the chest and the back. It is a disease that can affect all age groups; however, it has an increased prevelance in the adolescents[1]. There are four important components in the pathogenesis of acne vulgaris. These are the increased production of sebum, follicular hyperkeratinization, colonisation of propniobacterium acnes and inflammation[2,3].

As sebum production is one of the components of acne pathogenesis, the changes in the sebum levels can affect the disease course. Sebum is composed of sebaceous and extracellular lipids. The sebaceous lipids moisturise the skin, decrease transepidermal water loss and add on to the antimicrobial barrier of the skin[4,5]. The moisturization level of the skin is determined by the hydration level of the upper epidermis which in turn is determined by the transepidermal water loss of the skin[6–8]. The mechanical properties of the skin is determined by its composition of collagen and elastin fibres. The elasticity of the skin is decreased with aging and ultraviolet exposure[9–11].

Acne vulgaris is a frequent challenge in the outpatient clinics because not only patients are using off-the counter products but also have a propensity of being unsatisfied due to their increased anxiety caused by the disease. Providing effective treatment for acne requires a good history and detailed dermatologic examination[12]. The treatment modalities can be divided into two groups: topical and systemic. Systemic treatment modalities include systemic antibiotics (e.g. macrolides and tetracyclines), hormonal therapies and oral isotretinoin[12,13]. Oral isotretinoin is an FDA approved treatment modality that has been used for nodulocystic acne lesions since 1982[14]. Isotretinoin is a pre-drug that is transformed into its metabolites which have high affinities towards the retinoic acid nuclear receptors (RAR and RXR) and retinol binding protein. This way isotretinoin decreases follicular hyperkeratinization and thus decreases comedone formation. Isotretinoin also

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decreases the colonisation of propniobacterium acnes indirectly and has anti-inflammatory properties. Six weeks of isotretinoin therapy is known to reduce the sebum production up to 90%[15]. The therapy should be initiated at 0.5–1 mg/kg/day and if the patient tolerates the drug, the dose may be increased up to 1 mg/kg/day. The frequently encountered side effects of the drug are mucocutaneous, ophtalmic and skeletal symptoms resembling hypervitaminosis A, which subside when the therapy is stopped[16].

The aim of this study was to determine the changes in facial skin sebum, hydration and elasticity of acne vulgaris patients after being treated with systemic isotretinoin.

2 Method

2.1 Patient selection

Thirty-five adult patients (20 female, 15 male) who were diagnosed with acne vulgaris and who received systemic isotretinoin treatment for 6 months in Cerrahpaşa Medical Faculty Department of Dermatology between June 2012 and May 2017 were included in this study. The ages of the patients ranged from 16 to 32 years. Patients under the ages of 16 years were excluded. The other exclusion criteria were pregnancy, lactation, use of other systemic drugs for comorbid diseases, use of other topical or systemic drugs for acne vulgaris and hormonal irregularities. Patients with other dermatological diseases on the face (such as herpes infection, impetigo, perioral dermatitis, seborrhoeic dermatitis, lupus erythematosus) were excluded in the study because they may affect the parametres.

2.2 Evaluation of skin sebum, moisture and elasticity

The sebum, hydration and elasticity of the skin were measured non-invasively with a device called "Soft Plus Skin Analyses System" before treatment and 6 months after treatment. The parameters were recorded before measuring each patient: age, gender and temperature of the environment. The sebum, hydration and elasticity of the skin were measured with three different probes of the device. The measurement was taken by touching the suitable probe to the skin of patients. Four different points were measured for sebum and moisture levels. The forehead and cheeks were measured for sebum; and the cheeks and the chin were measured for moisture. Elasticty was measured from the peri-orbital skin. An average reference value could not be determined since sebum, moisture and elasticity change according to age and gender of each patient.

2.3 Statistical analysis

The relationship between the pre-treatment and post-treatment values were evaluated statistically with SPSS20. Mean and standard deviation was used for measurable parameters. Numbers and percentages were used for categoric parameters. Unparied t-test and Mann–Whitney U-test were used to compare groups. $p < 0.05$ was evaluated as statistically significant.

3 Results

3.1 Patient characteristics

A total of 35 patients (20 female and 15 male) were included in this study. All of the patients were diagnosed with acne vulgaris and were receiving oral isotretinoin therapy. The therapy were initiated at 0.5–1 mg/kg/day and if the patient tolerated the drug the dose increased up to 1 mg/kg/day. Overall, the ages of the patients ranged from 16 to 32 years and the average was 21.2 ± 3.6 years. Female patients' ages ranged from 18–32 years and the average was 22.5 ± 3.8 years. Male patients' ages ranged from 16–25 years and the average was 19.4 ± 2.4 years.

The skin types of the patients according to sebum, moisture and elasticity are categorized in Table 1.

3.2 Pre-treatment and post-treatment sebum levels

Overall, the pre-treatment sebum levels varied from 5 to 100; the average was 75.8 ± 28.0. The post treatment sebum levels varied from 1 to 98 and the average was 48.4 ± 31.8. This difference was statistically significant ($p < 0.001$).

The female patients' pre-treatment sebum levels ranged from 5 to 100 and the average was 69.3 ± 31.7. The post-treatment sebum levels ranged from 1 to 98 and the average was 50.9 ± 33.3. This difference was statistically significant ($p = 0.048$).

The male patients' pre-treatment sebum levels ranged from 27 to 100; and the average was 84.6 ± 20.1. The post-treatment sebum levels ranged from 1 to 98 and the average was 45.1 ± 30.6. The difference was statistically significant ($p = 0.002$).

The pre-treatment and post-treatment sebum levels and their differences overall and for each gender are summarized in Table 2. Overall, a 36% decline in the sebum levels was observed after treatment; as shown in Table 3.

Table 1. Skin types of the patients according to sebum, moisture and elasticity.

Sebum	*n* (%)
Oily	23 (66)
Mix	4 (11)
Normal	3 (9)
Dry	5 (14)
Moisture	
Severely dehydrated	28 (80)
Dehydrated	6 (17)
Normal	1 (3)
Elasticity	
Normal	22 (63)
Decreased	12 (34)
Severely decreased	1 (3)

Table 2. Pre-treatment and post-treatment sebum levels of acne vulgaris patients.

	Pre-treatment	Post-treatment	*p* value
Female	69.3 ± 31.7	50.9 ± 33.3	$p = 0.048$
Male	84.6 ± 20.1	45.1 ± 30.6	$p = 0.002$
Overall	75.8 ± 28.0	48.4 ± 31.8	$p < 0.001$

3.3 Pre-treatment and post-treatment moisture levels

Overall, for both genders, the pre-treatment moisture levels ranged from 9 to 77.5 and the average was 34.6 ± 14.6. The post-treatment levels ranged from 4.8 to 100 and the average was 62.4 ± 28.6. The difference was statistically significant. ($p < 0.001$).

Female patients' pre-treatment moisture levels ranged from 9 to 51.5 and the average was 30.2 ± 10.8. The post-treatment moisture levels ranged from 4.8 to 100 and the average was 63.7 ± 30.6. The difference was statistically significant ($p = 0.002$).

The male patients' pre-treatment moisture levels ranged from 15.2 to 77.5 and the average was 40.4 ± 17.2. The post-treatment moisture levels ranged from 27.8 to 100 and the average was 60.7 ± 26.7. The difference was statistically significant ($p = 0.023$).

The pre-treatment and post-treatment moisture levels and their differences overall and for each gender are summarised in Table 4. An overall 79% increase in the moisture level was observed after treatment; as shown in Table 5.

3.4 Pre-treatment and post-treatment elasticity levels

Overall, the pre-treatment elasticity levels ranged from 28 to 50 and the average was 40.4 ± 5.5.The post-treatment elasticity levels ranged from 20 to 50 and the average was 37.5 ± 8.2. This difference statistically insignificant ($p = 0.1$).

Female patients' pre-treatment elasticity levels ranged from 34 to 50 and the average was 41.4 ± 4.0. The post-treatment elasticity levels ranged from 20 to 49 and the average was 37.1 ± 9.0. This difference statistically insignificant ($p = 0.067$).

Male patients' pre-treatment elasticity levels ranged from 28 to 49 and the average was 39.2 ± 6.9. The post-treatment elasticity levels ranged from 26 to 50 and the average was 38.0 ± 7.3. This difference statistically insignificant ($p = 0.63$).

The pre-treatment and post-treatment elasticity levels and their differences overall and for each gender are summarized in Table 6.

Table 3. The average pre-treatment and post-treatment sebum levels of acne vulgaris patients.

	Pre-treatment	Post-treatment	Decline
Average Sebum Level	75.8	48.4	%36

Table 4. Pre-treatment and post-treatment moisture levels of acne vulgaris patients.

	Pre-treatment	Post-treatment	*p* Value
Female	30.2 ± 10.8	63.7 ± 30.6	$p = 0.002$
Male	40.4 ± 17.2	40.4 ± 17.2	$p = 0.023$
Overall	34.6 ± 14.6	62.4 ± 28.6	$p < 0.001$

Table 5. The average pre-treatment and post-treatment moisture levels of acne vulgaris patients.

	Pre-treatment	Post-treatment	Increase percentage
Average Moisture Level	34.6	62.4	%79

4 Discussion

The aim of this study was to determine the changes in sebum, moisture and elasticity in acne vulgaris patients receiving oral isotretinoin therapy. The given skin parameters were evaluated in 35 acne vulgaris patients who have received a cumulative dose of isotretinoin for 6 months. Regarding the pre-treatment sebum levels, 23 (66%) of the 35 patients had oily skin type. A previous study compared the skin sebum levels of adolescent male patients with acne vulgaris to a healthy male adolescent control group and has found that the sebum levels were statistically significantly higher in the patient group[17]. Another study, again with an adolescent patient population, demonstrated that the sebum levels were statistically significantly higher, especially on the cheeks, in patients with acne vulgaris compared to the healthy control group[18]. Our study has demonstrated that the sebum level decreases 36% in acne vulgaris patients receiving oral isotretinoin treatment achieving the cumulative dose for 6 months. The sebum reducing effect of isotretinoin was first demonstrated by Orfonos and Zouboulis[19]. Isotretinoin decreases the size of sebaceous glands and inhibits the proliferation of basal lipocytes and thus decreases the sebum production; besides it inhibits the in vivo differentiation of lipocytes[20]. Geissler et al. histopathologically demonstrated that low-dose oral isotretinoin treatment for 6 months in treatment resistant acne vulgaris patients decreased the sice of sebaceous glands 51% and decreased the sebum production 64%[21]. Another study showed that the sebum secretion declined statistically significantly in 20 patients receiving oral isotretinoin therapy for 6 months[22]. Kmiec et al. have also performed a study regarding the effect of oral isotretinoin on sebum levels. The biophysical parameters of the skin of thirty patients receiving oral isotretinoin therapy for four to seven months were evaluated and a decline in the sebum levels was observed[23]. Furthermore, systemic isotretinoin treatment is used in the treatment of other acneiform and inflammatory disorders[24]. A study compared the changes in sebum production in patients with severe seborrhoea and seborrhoeic dermatitis. The decline in sebum production was statistically significant in the patients receiving low dose oral isotretinoin compared to the group receiving topical treatment modalities[25]. Uslu et al. evaluated the sebum levels of patients receiving low-dose oral isotretinoin treatment for acne rosacea and demonstrated that the decline in skin sebum levels were statistically significant after completing 6 months of treatment[26]. One of the properties of skin sebum is to increase the epidermal permeability due to the anti-oxidant and anti-microbial lipids in its composition. In patients with acne vulgaris, increased sebum leads to increased lipids which disturbs the hydrolipid barrier of the epidermis and thus increases the transepidermal water loss. Melo et al.

Table 6. Pre-treatment and post-treatment elasticity levels of acne vulgaris patients.

	Pre-treatment	Post-treatment	*p* Value
Female	41.4 ± 4.1	37.1 ± 9.0	$p = 0.067$
Male	39.2 ± 6.9	38.0 ± 7.3	$p = 0.63$
Overal	40.4 ± 5.5	37.5 ± 8.2	$p = 0.1$

showed that the transepidermal water loss is increased in the oily skin type[27].

Stratum corneum serves as a physical barrier that decreases the transepidermal water loss. The moisture level of stratum corneum depends on its composition of amino-acids, ammonia, urea and piridolin carboxylic-acid which is known as the natural moisturising factor. An intact epidermal barrier is of utmost importance for skin hydration. The skin sebum levels, skin moisture levels, the skin pH and the epidermal permability are the most important factors for the skin homoeostasis[27–31]. A study has compared the skin physiology of 300 healthy individuals and showed that the transepidermal water loss was lower in young males compared to young females. Furthermore, the same study showed that the skin hydration was higher in young males compared to young females[32]. Our study demonstrated that the average moisture level of the skin increased 79% after the cumulative oral isotretinoin therapy. This result is in parallel with previous literature showing that increased lipids leading to disturbed epidermal barrier and declined skin hydration[27–31]. On the other hand, Kmiec et al. demonstrated that transepidermal water loss increased and hydration decreased with systemic isotretinoin therapy[23].

The skin elasticity is determined by its composition of collagen and elastic fibres and these proteins may be destroyed with aging, leading to decreased elasticity[33]. Numerous studies showed that the skin elasticity is reduced with aging[34–37]. Some of the previous studies demonstrated that there was no difference between the genders in terms of skin elasticity[38], however Firoos et al. showed that the skin elasticity was higher in females compared the males, yet this difference was statistically insignificant[39]. Bailey et al. demonstrated that the trunk skin elasticity was increased in female patients compared to male patients[40]. Although there are many studies evaluating the change in skin elasticity with ageing, there are only a few studies evaluating the skin elasticity in patients with acne vulgaris. Kim et al. evaluated 30 male and 30 female patients and have showed that there was a negative correlation between the number of pores and the skin elasticity in the facial region of male patients: as the number of pores increased, the skin elasticity decreased[41]. Another study investigating the skin sebum and elasticity demonstrated that the skin elasticity decreased and the number and size of the pores increased with aging. Again, this study demonstrated a statistically significant relationship between skin sebum levels and skin elasticity. Furthermore, the same study showed that the use of topical antiageing products could lead to a decline in the number and sizes of pores and an increase in the skin elasticity[11].

There is no study comparing the elasticity levels of the skin before and after systemic isotretinoin treatment in the literature. Our study failed to demonstrate a statistically significant change in the skin elasticity with systemic isotretinoin treatment. Since our patient population was young and the ages ranged from 16 to 32 years, a comparison of skin elasticity in terms of age could not be performed.

In conclusion, systemic isotretinoin treatment has led to a 36% decline in the skin sebum levels and this decline was statistically significant. The therapy has led to a 79% increase in the skin hydration, which again was statistically significant. However, the difference between the pre-treatment and post-trearment skin elasticity levels was statistically insignificant. Regarding this results, one can conclude that oral isotretinoin therapy leads to a significant decline in the skin sebum levels and a significant increase in the skin hydration. However, its effect on skin elasticity is insignificant.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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