

Facial hypertrichosis in the course of isotretinoin treatment: Four-year retrospective observation

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Abstract. *Background:* isotretinoin is a synthetic retinoid used in the treatment of acne. There are limited and inconsistent data about the effects of isotretinoin on hormones and hair growth. *Aim:* to investigate a probable connection, a single center four-year retrospective data of female acne patients who were treated with oral isotretinoin and developed facial hypertrichosis was reported. *Methods:* in the years 2019-2023, 327 female patients between 16-33 years of age (Mean \pm Standard Deviation: 23.4 ± 4.7) were treated with 0.5-0.8 mg/kg/day isotretinoin, approximately for 6 months (6.2 ± 0.8). The patients who developed facial hypertrichosis were additionally analysed for dehydroepiandrosterone sulfate, prolactin and thyroid stimulating hormone values. *Results:* thirty one patients (9.5%) in all ages (22.9 ± 4.3) declared excessive hair growth on cheeks and/or chin during treatment. All declarations were between the 2nd and 4th months (2.6 ± 0.8). The mean values of analysed hormones were in normal ranges. Twenty seven of the thirty one patients (87%) stated that the excessive hair growth terminated completely at the end of 4th month (3.1 ± 0.7) after the cessation of the treatment, and the others declared it was diminished to a great extent. *Conclusions:* mainly due to normal mean values of the analysed hormones, it is hard to consider that the cause of hypertrichosis is hormonal irregularity. However, 9.5% is a considerable ratio. A more extensive prospective study should be performed to reveal the cause of this phenomenon.

Key words: isotretinoin, facial hypertrichosis, hirsutism

Introduction

Isotretinoin is a synthetic retinoid derivative which is being used in the treatment of acne. It inhibits the proliferation of sebocytes, reduces sebum secretion, normalizes the desquamation of the epithelium and diminishes the formation of acneiform lesions. There is growing evidence that the major mode of action of isotretinoin in acne is sebocyte apoptosis, which causes sebum suppression. Its teratogenicity is also regarded as an apoptotic effect on neural crest cells^{1,2}. There is limited and inconsistent data about the effects of isotretinoin on hormones and hair growth. This brief report compiles single center four-year retrospective

data of female acne patients who were treated with oral isotretinoin and developed facial hypertrichosis.

Materials and Methods

In the years 2019-2023, 327 female acne patients between 16-33 years of age (Mean \pm Standard Deviation: 23.4 ± 4.7) with 0.5-0.8 mg/kg/day isotretinoin were treated, for approximately 6 months (6.2 ± 0.8). All of the patients were evaluated monthly and ordered the standard serum tests as aspartate aminotransferase, alanine aminotransferase, triglyceride and low density lipoprotein-cholesterol. For

a general screening, the patients who declared facial hypertrichosis during the course of treatment, were also analysed for their dehydroepiandrosterone sulfate (DHEAS), prolactin and thyroid stimulating hormone (TSH) serum values. After completing the therapy, the patients with hypertrichosis were evaluated monthly for an additional four-month period. All of the procedures were performed in accordance with the ethical principles established for medical research (Helsinki Declaration of World Medical Association 1975, and amendments as revised in 1983).

Results

Thirty one of these patients (9.5%) in all ages (22.9 ± 4.3) declared excessive growth of hair on cheeks and/or chin during the treatment period. All declarations were between the 2nd and 4th months (2.6 ± 0.8). There was no increase in hair growth in any other region of the skin. In Figure 1, hypertrichosis of various severity in six different patients at the end of the 4th month of therapy are depicted. The mean values of DHEAS, prolactin and TSH were found in normal ranges. Only four of thirty one patients (12.9%) had some values outside the normal ranges, and they had up to $\pm 10\%$

divergence in one or more parameters (Table 1). In general the patients declared a complete resolution of hypertrichosis between the 2nd and 4th month after the cessation of treatment. Twenty seven out of thirty one patients (87%) stated that the excessive hair growth ceased completely at the end of the 4th month (3.1 ± 0.7), and the others declared it diminished greatly.

Discussion and Conclusions

There are contradicting reports about the effects of isotretinoin on serum hormone levels and the growth of body hair. In a study performed on forty female patients with additional polycystic ovary syndrome, it was reported that the treatment of isotretinoin significantly decreased free testosterone (fT) levels and Ferriman-Gallwey (FG) score³. In another study performed on seventy six female patients, there were significant increases in fT, total testosterone (tT) and DHEAS levels at the end of third month, and approximately 20% of the patients had an increase in FG score⁴. Furthermore, in a recent study performed on thirty female patients, while there were no changes in tT and DHEAS levels, approximately 17% of patients had a significant increase in their FG score at the end



Figure 1. Hypertrichosis with various severity in six different patients at the end of the 4th month of therapy.

Table 1. Hormonal depiction of four patients who had some values outside the normal ranges.

Patient	DHEAS	Prolactin	TSH
1	N	N	↓
2	↑	↑	↓
3	N	↑	N
4	↑	↑	N

Abbreviations: N: Normal; ↑: Higher than normal; ↓: Lower than normal.

of the third month⁵. Although the abovementioned studies suggest the changes in whole body hair, there are also isotretinoin reports indicating the increases in facial hair only, without a notable cause^{6,7}. In the hormonal analyses performed in our patients, due to normal mean values, a relatively low ratio of patients with abnormal values and low divergence ratios, it is hard to consider that the cause of hypertrichosis is hormonal irregularity. Nevertheless, the ratio of 9,5% in the development of facial hypertrichosis is quite substantial. More extensive prospective studies should be performed, to reveal the cause of isotretinoin induced facial hypertrichosis, whether it is due to interactions of multiple hormones, increased steroid effects related with isotretinoin dependent emotional stress, or some other mechanism due to genetic susceptibility.

Conflict of Interest Statement: there is no conflict of interest to declare.

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