

Effects of Isotretinoin on the Thyroid Gland Volume and Serum Thyroid Stimulating Hormone in Patients of Acne Vulgaris

Rohal Chandrakar ¹, Raghav Gupta ²

¹Assistant Professor, Department of Dermatology, Chandulal Chandrakar Memorial Government Medical College, Samarpan Bhawan, Durg

²Assistant Professor, Department of Dermatology, Bundelkhand Medical College, Sagar, Madhya Pradesh

Received: 19-07-2022 / Revised: 23-08-2022 / Accepted: 20-09-2022

Corresponding author: Dr Raghav Gupta

Conflict of interest: Nil

Abstract

Background: With an estimated 85% frequency, AV is a dermatological disorder that primarily affects adolescents. It affects women more than men; among women. Acne causes severe morbidity, including psychological problems including low self-esteem, sadness, and anxiety, as well as persistent scarring, which has a detrimental impact on one's quality of life. A pharmacologically important derivative of vitamin A called isotretinoin chemically represented as 13-cis retinoic acid has been prescribed to treat moderate to severe nodulocystic acne, problems with the sebaceous glands of skin, and to avoid skin cancer.

Aim: To evaluate effects of isotretinoin on the thyroid gland volume and serum thyroid stimulating hormone in patients of acne vulgaris.

Methods and Materials: After 12 hours of fasting, a fasting blood specimen was taken through venipuncture of the big antecubital vein, and the sample was shipped to a biochemical lab to be tested for serum TSH. The linear volusons 6 pro high resolution ultrasound probe with an 8–12MHz is used to measure the thyroid. The patient was examined while lying flat on his back with his neck extended. Each lobe as well as isthmus had a transverse and longitudinal scan to determine its length, width, and depth in centimetres, from which the volume was determined.

Results: Majority of the patients in present study belong to age group of ≤ 20 years (41%) followed by 21-25 years (40%). Majority of the patients were female (64%) followed by males (36%). Comparing FTSH level after 4 months of therapy with the baseline levels we found that mean FTSH level was significantly higher after 4 months (3.41 ± 0.88 mIU/ml) of treatment as compared to initial levels (2.15 ± 0.79 mIU/ml). Comparing thyroid volume after 4 months of therapy with the baseline levels we found that mean thyroid volume was significantly lower after 4 months (8.05 ± 1.33 ml) of treatment as compared to initial levels (8.42 ± 1.40 ml).

Conclusion: Acne Vulgaris is more common among the young age group female. Mean FTSH level was significantly higher and thyroid volume was significantly lower after 4 months of treatment.

Keywords: Isotretinoin, thyroid gland, acne vulgaris

This is an Open Access article that uses a fund-ing model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Background

Acne vulgaris (AV) is usually a chronic inflammatory condition of the sebaceous glands that manifests as nodules, pustules and papules that can produce scar as well as non-inflammatory abnormalities including both open as well as closed comedones. With an estimated 85% frequency, AV is a dermatological disorder that primarily affects adolescents. It can continue throughout adulthood, with a prevalence estimates of 50.9 percent in people aged 20 years to 29 years compared to 26.3% in persons aged 40 years to 49 years.

It affects women more than men; among women over 25 years old, it accounts for one-third of the total dermatology clinics visits and two-thirds of total dermatologist appointments [1,2]. Acne causes severe morbidity, including psychological problems including low self-esteem, sadness, and anxiety, as well as persistent scarring, which has a detrimental impact on one's quality of life. In an analysis of the research by Yentzer *et al.*, 8.8 percent of acne affected patients also experienced depression, with women experiencing it twice as frequently as males and it being unrelated to the severity of the acne.

A pharmacologically important derivative of vitamin A called isotretinoin chemically represented as 13-cis retinoic acid has been prescribed to treat intermediate to extreme nodulocystic acne, problems with the sebaceous glands of skin and keratinization, and to avoid skin cancer. The effects of isotretinoin on other organs and the metabolic system have garnered a lot of attention as its use, particularly for the treatment of acne vulgaris and other illnesses, has increased [3,4].

It has long been known that vitamin A affects the production of thyroid hormone. Simkins illustrated the effective application of a high amount of vitamin A in treating patients suffering

from hyperthyroidism in 1947. For many years, there has been curiosity in the impact of vitamin A analogues on thyroid function. Although it has been suggested that isotretinoin can disrupt thyroid function and lead to reversible hypo- and hyperthyroidism, this notion is not solid. An isotretinoin-related substance called bexarotene increases the peripheral breakdown of thyroid hormones through a non-deiodinase-mediated route, in addition to acting centrally to produce hypothyroidism.

Seven individuals with extensive rosacea were managed for 12 weeks with one mg/kg each day of isotretinoin in the trial by Marsden *et al.* The generation of hormones secreted by thyroid gland has been discovered to be impacted by vitamin A [5,6]. After therapy, their serum concentration of T3 and T4 levels were much lower, but they still had the same sensitivity to TRH stimulation.

These results were in part ascribed to isotretinoin's stimulation of microsomal enzymes of the liver. Another research by Lyons *et al.* revealed that therapy using 0.8 mg/kg of 13-cis retinoic acid for three months resulted in a slight decline in the parameters of thyroid function. After the therapy was stopped, it was seen that these modifications returned to normal after a month. Three publications about the consequences of isotretinoin upon thyroid function were found in our literature search [7].

To our experience, there is little information available on clinical studies looking into how isotretinoin affects thyroid growth and function. In the current study, we looked at how isotretinoin affected thyroid volume and thyroid function tests in acne patients.

This information will enable us adjust the amount of isotretinoin without affecting thyroid hormone levels.

Methods and Materials

Design of study: It was a prospective study.

Centre of study: Department of Dermatology, Venereology and Leprosy, Peoples College of Medical Sciences, Bhopal.

Sample Size of research: 100 study subjects.

Study Population: Patients with AV grade III and IV of presenting as OPD patients in the Dept. of Dermatology and Venereology and Leprosy, Peoples College of Medical Sciences, Bhopal.

Inclusion criteria

- Study participants having AV of grade III and IV.
- Patients who agreed to participate in the study.

Exclusion Criteria

- Those patients who are unwilling to take part in the study.
- Patient has a history of pituitary and thyroid disorders.
- History of Pregnancy.
- History of diabetes mellitus, chronic renal failure, abnormalities of blood pressure, rheumatic disorder.
- Oral retinoid therapy or other hormone therapy has been used in the past three months for any reason.

Data collection procedure

1. All patients who met the inclusion requirements were chosen and enrolled in the trial.
2. After explaining the study's nature and goal to each patient, we got their written informed permission. They received a guarantee that privacy would be rigorously upheld. There was always the choice to stop the study.
3. Pre-designed proforma were used for data collection, and the results were recorded.

4. The data were gathered, examined, and subjected to the proper statistical tests. A USG was performed to measure the volume of thyroid and fasting blood TSH before as well as after receiving accutane 20 mg per day for four months.

Biochemical Parameter

After 12 hours of fasting, a fasting blood specimen was taken through venipuncture of the big antecubital vein, and the sample was shipped to a biochemical lab to be tested for serum TSH.

Assessment of Thyroid Volume

The Linear Voluson S6 Pro High Resolution Ultrasound Probe with an 8–12MHz is used to measure the thyroid.

The patient was examined while lying flat on his back with his neck extended.

Each lobe as well as isthmus had a transverse and longitudinal scan to determine its length, width, and depth in centimetres, from which the volume was determined.

Statistical Analysis

The IBM SPSS version 20 software was used for all data analysis. Tables were created using cross tabulation and frequency distribution. The graphs were created using Microsoft Office 2010. Quantitative information was expressed as mean SD, and student t test as well as paired t test was employed to compare the means whilst categorical variables were expressed as % and analysed using Chi square test. A 5% significance level was determined.

Results

Majority of the patients in present study belong to age group of ≤ 20 years (41%) followed by 21-25 years (40%). (Table 1). Majority of the patients were female (64%) followed by males (36%).

(Table 2). Comparing FTSH level after 4 months of therapy with the baseline levels

we found that mean FTSH level was significantly higher after 4 months (3.41 ± 0.88 mIU/ml) of treatment as compared to initial levels (2.15 ± 0.79 mIU/ml). (Table 3). Comparing thyroid volume after 4 months of therapy with the baseline levels we found that mean thyroid volume was significantly lower after 4 months (8.05 ± 1.33 ml) of treatment as

compared to initial levels (8.42 ± 1.40 ml). (Table 4).

Mean age was 21.92 ± 4.21 years. Mean weight was 55.68 ± 5.80 kgs. (Table 5). Comparison FTSH and thyroid volume between genders revealed that mean FTSH and thyroid volume was similar between genders ($p > 0.05$). (Table 6).

Table 1: Age distribution

Age group	No of patients	Percentage
≤20	41	41.0
21-25	40	40.0
26-30	16	16.0
31-35	2	2.0
36-40	1	1.0
Total	100	100.0

Table 2: Sex distribution

Gender	No of patients	Percentage
Female	64	64.0
Male	36	36.0
Total	100	100.0

Table 3: Comparing FTSH after 4 months of follow up with baseline

FTSH level (mIU/ml)	Mean	No. of Patients	Std.Deviation	Std. Error Mean	P value
Baseline	2.15	80	0.79	0.089	<0.001
After 4 month	3.41	80	0.88	0.099	

Table 4: Comparing thyroid volume after 4 months of follow up with baseline

Thyroid volume (ml)	Mean	No. of Patients	Std. Deviation	Std. Error Mean	P value
Baseline	8.42	80	1.40	0.16	<0.001
After 4 month	8.05	80	1.33	0.15	

Table 5: Descriptive Statistics

Variables	No. of Patients	Minimum	Maximum	Mean	Std. Deviation
Age	100	18	40	21.92	4.21
Weight(kg)	100	42.0	68.0	55.68	5.80

Table 6: Comparing FTSH and thyroid volume between genders

	Female	Male	Total	P value
FTSH after 4 month (mIU/ml)	3.38 ± 0.86	3.47 ± 0.96	3.41 ± 0.88	0.703
USG thyroid volume (ml) after 4 months	8.04 ± 1.22	8.04 ± 1.60	8.04 ± 1.33	0.955

Discussion

Although well known, the impact of vitamin A along with retinoids upon this hypothalamic-pituitary-thyroid axis is not fully understood. Retinoids affect cellular

proliferation, differentiation, activity, and metabolism through two pairs of nuclear hormone binding sites called retinoic acid binding sites and retinoid X receptors.

Additionally, steroid as well as thyroid hormone activity is mediated by these receptors [8]. Patients under the age of 20 are more likely to develop AV (41%) than those between the ages of 21 and 25 (40%). This shows that the younger age group is where AV is more prevalent.

Our study's median age of 21.92 ± 4.21 years confirms that adolescents are most affected by AV. According to Saxena *et al* study which was conducted in accordance with the current study, the mean age of an AV patient was $20.66 (\pm 4.05)$ years. According to Uyar *et al*, the average age of the group receiving isotretinoin was 22.68 ± 4.51 years (age range of 18–36 years). Females made up the majority of the patients (64%) while men made up 36%. This demonstrates that AV has a greater impact on the female population. These findings support the findings of Al-Ameer *et al*. and Tallab. However, Adityan *et al*. stated that there were more male participants in their research than female ones.

Similar findings were made by Kane *et al*, demonstrating that female patients who were younger and marriageable had a larger concern about facial attractiveness. In a related study, Saxena *et al*. found that the ratio of female patients to male patients was 1.44:1, with a mean age of $21.68 (\pm 4.29)$ years, which falls within the range of marriageable age. According to Uyar *et al*., the isotretinoin-treated group consisted of 14 (21.2%) males and 52 (78.8%) females, whereas the control group received no isotretinoin treatment and consisted of 8 (21.1%) males and 30 (78.9%) females [9-12]. AV is a dermatological condition that primarily affects adolescents, with an estimated 85% prevalence. It can persist throughout adulthood, with prevalence estimates ranging from 50.9% in those between the ages of 20 and 29 to 26.3% in those between the ages of 40 and 49. More women than men are affected by it; among females over 25 it accounts for one-third

of all visits to dermatological clinics and two-thirds of all dermatologist appointments [13].

A person's quality of life is negatively impacted by acne's significant morbidity, which includes psychological issues like low self-esteem, unhappiness, and anxiety as well as permanent scarring. According to a review of the research by Yentzer *et al*., 8.8% of acne sufferers also had depression, with women being more likely than men to do so and the level of their sadness having no bearing on the severity of their acne. Isotretinoin, a chemically known as 13-cis retinoic acid, is a significant vitamin A derivative that has been given to treat moderate to severe nodulocystic acne, issues with the skin's sebaceous glands and keratinization, and to prevent skin cancer.

Isotretinoin's use, particularly for the treatment of acne vulgaris and other disorders, has expanded, drawing attention to its effects on other organs and the metabolic system [14]. In this study comparing FTSH level after 4 months of therapy with the baseline levels we found that mean FTSH level was significantly higher after 4 months (3.41 ± 0.88 mIU/ml) of treatment as compared to initial levels (2.15 ± 0.79 mIU/ml). Comparing thyroid volume after 4 months of therapy with the baseline levels we found that mean thyroid volume was significantly lower after 4 months (8.05 ± 1.33 ml) of treatment as compared to initial levels (8.42 ± 1.40 ml). Majority of the patients in present study belong to age group of ≤ 20 years (41%) followed by 21-25 years (40%). Majority of the patients were female (64%) followed by males (36%). Mean age was 21.92 ± 4.21 years. Mean weight was 55.68 ± 5.80 kgs. Comparison FTSH and thyroid volume between genders revealed that mean FTSH and thyroid volume was similar between genders ($p > 0.05$). It has long been understood that vitamin A has an impact on how thyroid hormone is made. Simkins

demonstrated in 1947 how a significant amount of vitamin A could be used to effectively treat people with hyperthyroidism. The effect of vitamin A mimics on thyroid function has long piqued interest.

The idea that isotretinoin can interfere with thyroid function and cause reversible hypo- and hyperthyroidism is unfounded. In addition to working centrally to cause hypothyroidism, an isotretinoin-related chemical known as bexarotene stimulates the peripheral breakdown of thyroid hormones through a non-deiodinase mediated pathway. In the experiment by Marsden *et al.*, seven patients with severe rosacea were treated for 12 weeks with one mg/kg of isotretinoin daily [11-13]. It has been found that vitamin A has an effect on the thyroid gland's ability to produce hormones.

After treatment, their serum T3 and T4 concentrations were significantly lower, but their sensitivity to TRH stimulation remained the same. The activation of liver microsomal enzymes by isotretinoin was partly responsible for these outcomes. Another study by Lyons *et al.* found that a three-month course of therapy involving 0.8 mg/kg of 13-cis retinoic acid caused a small reduction in the markers of thyroid function. It was observed that these alterations restored to normal after the therapy was halted after a month [15].

Conclusion

Acne Vulgaris is more common among the young age group female. Mean FTSH level was significantly higher and thyroid volume was significantly lower after 4 months of treatment. The increasing number of studies assessing the effects of isotretinoin on the thyroid gland will help clinicians to predict its side effects and to plan treatment accordingly.

References

1. Bhate K, Williams HC. Epidemiology of acne vulgaris. *Br J Dermatol* 2013; 168(3):474–85.
2. Collier CN, Harper JC, Cafardi JA, Cantrell WC, Wang W, Foster KW, *et al.* The prevalence of acne in adults 20 years and older. *J Am Acad Dermatol* 2008;58(1):56–9.
3. Yentzer BA, Hick J, Reese EL, Uhas A, Feldman SR, Balkrishnan R. Acne vulgaris in the United States: a descriptive epidemiology. *Cutis* 2010; 86(2):94–9.
4. Ramos-e-Silva M, Ramos-e-Silva S, Carneiro S. Acne in women. *Br J Dermatol* 2015; 172:20–6.
5. Uyar B., Solak A., Saklamaz A., Akyildiz M., Genc B., Gökdoğan A. Effects of isotretinoin on the thyroid gland and thyroid function tests in acne patients: A preliminary study. *Indian Journal of Dermatology, Venereology and Leprology* 2016;82(5): 587-588
6. Kraft J, Freiman A. Management of acne. *CMAJ* 2011;183: E430-5.
7. Simkins S. Use of massive doses of vitamin A in the treatment of hyperthyroidism: A preliminary report. *J Clin Endocrinol. J Clin Endocrinol Metab.* 1947 Aug;7(8):574-85.
8. Smit JW, Stokkel MP, Pereira AM, Romijn JA, Visser TJ. Bexarotene induced hypothyroidism: bexarotene stimulates the peripheral metabolism of thyroid hormones. *J Clin Endocrinol Metab* 2007; 92:2496–2499.
9. Marsden JR, Trinick TR, Laker MF, Shuster S. Effects of isotretinoin on serum lipids and lipoproteins, liver and thyroid function. *Clin Chim Acta* 1984; 143:243–251.
10. Lyons F, Laker MF, Marsden JR, Manuel R, Shuster S. Effect of oral 13-cisretinoic acid on serum lipids. *Br J Dermatol* 1982; 107:591–595.
11. Karadag AS, Ertugrul DT, Tural E, Akin KO. Isotretinoin influences pituitary hormone levels in acne patients. *Acta Derm Venereol* 2011; 91:31-4.

12. Tabasum H, Tanzeel Ahmad, Farzana Anjum, Hina Rehman. The historical panorama of acne vulgaris. *Journal of Pakistan Association of Dermatologists* 2013;23 (3):315-319.
13. Cunliffe W.J., & Simpson N. Disorders of the sebaceous glands. In R.H. Champion J.L. Burton, D.A. Burns, & S.M. Breathnach (Eds.), *Rook/Wilkinson/Ebling textbook of dermatology*. Oxford: Blackwell Science. 1998;1927-2002.
14. Odom, R.B., James, W.D., & Berger, T.G. Acne. In *Andrew's diseases of the skin: Clinical dermatology*. Philadelphia: W.B. Saunders. 9th ed. 2000; 284-306.
15. Strauss, J.S., & Thiboutot, D.M. Diseases of the sebaceous glands. In I. M. Freedberg, A.X.Z. Eisen, K. Wolff, K.F. Austen, L.A. Goldsmith, & S.I. Katz (Eds.), *Fitzpatrick's dermatology in general medicine*. New York: Mc Graw-Hill. 1999- 769-784.