Isotretinoin's Effect on Fasting Lipid Profile in Acne Patients

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ABSTRACT

Objective: To determine the isotretinoin's effect on fasting lipid profile in patients with acne.

Study Design: Observational study.

Place and Duration of the Study: Outpatient Department of Dermatology, Dow International Medical College, Dow University of Health Sciences, Karachi, Pakistan, from 22nd June to 21st December 2022.

Methodology: Patients of clinically moderate and severe acne were selected and prescribed a dose of 0.5mg /kg cap isotretinoin for 6 months. They were advised to get a fasting lipid profile at the baseline and then after two months of isotretinoin therapy. National Cancer Institute Common Terminology Criteria for Adverse Events v5.0 grading system and Adult Treatment Panel III were used for the grading of abnormalities. McNemar Bowker test was used to assess the difference in variables [serum triglycerides (TGs), cholesterol, high-density lipoproteins (HDL), and low-density lipoproteins (LDL)] at the baseline and after 2 months follow-up.

Results: A total of 214 patients were evaluated. After 2 months of isotretinoin therapy, TGs and cholesterol levels were elevated to higher grade in 2% of the patients. Likewise in 1% of patients, LDL levels rised to higher grade. Moreover, HDL levels declined to lower grade in 2% of the patients taking isotretinoin.

Conclusion: Insignificant alterations in the various serum lipid parameters were observed in acne patients during isotretinoin therapy. It is advisable to obtain a baseline fasting lipid profile in all acne patients on isotretinoin and repeated in those with baseline abnormal levels and in patients with a clinical sign of metabolic syndrome and a family history of dyslipidemias.

Key Words: *Acne, Hyperlipidemias, Isotretinoin, Laboratory monitoring.*

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INTRODUCTION

Acne vulgaris is a common inflammatory dermatological problem involving the sebaceous follicles. Clinically patients have comedones, red papules, pustules, and in severe cases, nodules and cysts. They are mainly present on the face, chest, upper back, and shoulders.[1] It affects 85% of the adolescent population.[2,3] Globally, and in Pakistan, prevalence of acne vulgaris is approximately 9.4% and 5%, respectively.[4] Excessive production of sebum, abnormal differentiation of follicles with increased keratinisation, and propionibacterium acnes hypercolonisation in the follicles play role in its pathophysiology.[5] Acne vulgaris is managed with topical benzoyl peroxide, clindamycin, erythromycin with and without topical retinoids and systemic doxycycline, minocycline, azithromycin, isotretinoin, and oral contraceptive pills.

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Oral isotretinoin has been approved by US Food and drug administration (FDA) since 1982 and is a drug of choice for severe nodulocystic acne. It works by binding to intranuclear-retinoic acid A receptors (RARs) and retinoic acid X receptors (RXRs). It regulates growth along with differentiation of epidermal cells. It also affects the pathways of inflammation, apoptosis of cells, and modulate the immune system. Frequent side effects of retinoids are dryness, chelitis, photosensitivity, headache, arthralgia, myalgia, and lipid profile abnormalities. Teratogenicity, hepatotoxicity, and pancreatitis are serious side effects.[6] In view of the laboratory abnormalities, clinicians use different monitoring intervals of CBC, LFTS, and FLPS for the patients on isotretinoin and most of the work demonstrated that lab abnormalities usually show up after a month or two of starting isotretinoin.[7] As notable changes are not observed in CBCs and LFTs of the patients taking retinoids, routine testing is not performed.[8] International studies have warranted lipid testing as this has been the commonest of the lab abnormality seen in patients while on isotretinoin.

The aim of this study was to see the effects of systemic isotretinoin on various lipid parameters. As there is a paucity of data in the local population regarding the drug's impact on patient's serum lipids, observations from this study may guide and aid in assessing its safety profile.

METHODOLOGY

This prospective study was conducted in the Outpatient Department, Department of Dermatology, from 22nd June to 21st December 2022, after approval from the Review Board of University of Health Sciences. A total of 214 patients, both male and female, aged between 16 and 40 years, who were diagnosed clinically with moderate and severe acne by the presence of non-inflammatory comedones and/or erythematous papules, pustules, nodules and cysts, graded by using the Global Acne Grading System (GAGS),[9,10] and not treated previously with isotretinoin, were selected and inducted in the study after obtaining an informed consent. Patients suffering from psoriasis, pityriasis rubra pilaris (PRP), hidradenitis suppurativa (HS), ichthyosis for which isotretinoin is a treatment option, patients taking other medications, pregnant and lactating women or patients having thyroid disorders affecting lipid profile were excluded after a thorough history.[6]

The selected patients were prescribed cap isotretinoin 0.5mg/kg per day for 6 months, so the dosage and its impact on patients' serum lipid profile may remain similar in all patients. They were advised to get a fasting lipid profile at the baseline and then after two months of isotretinoin. Triglyceride (TG) and serum cholesterol were classified according to National Cancer Institute Common Terminology Criteria for Adverse Events v 5.0 grading system.[11] Low density lipoproteins (LDL) and high--density lipoproteins (HDL) were assessed according to the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) Guidelines, so any values above or below the reference ranges were considered abnormal. Patients were followed for 6 months. If lipid abnormalities increased more than twice of the baseline during the treatment, the dosage was reduced.

Demographic details of patients including gender, age, marital status, education, and occupation were obtained. Furthermore, each patient was asked about the duration of the disease and counselled for contraception during and one month after cessation of treatment. All results were collected and filled in proforma accordingly by the authors.

After data collection, Statistical Package for Social Science (SPSS) software, version 26 was used for data analysis. Frequency and percentages were determined for the categorical variables. Mean ± standard deviation was calculated for continuous variables. McNemar Bowker test was applied to assess the difference in variables (serum TGs, cholesterol, HDL, and LDL) at the baseline and after 2 months follow-up. The p-value <0.05 was considered as significant.

RESULTS

A total of 214 patients were included in this study. Their age ranged from 14 to 30 years with mean of value 21.94 ± 3.65 years. Of them, 71 (33%) were males and 143 (67%) were females. One hundred and eighteen (55%) had moderate acne and 96 (45%) had severe acne.

Table I: Serum lipid parameters of patients pre and 2-month post-isotretinoin therapy.

Laboratory value	Baseline n (%)	2 Months n (%)	*p-value
Triglycerides			
Normal <150 mg/dl	167 (78)	162 (76)	
Grade 1 (150-300 mg/dl)	44 (21)	50 (23)	0.620
Grade 2 (300-500 mg/dl)	3 (1)	2 (1)	
Cholesterol			
Normal <200 mg/dl	190 (89)	187 (87)	0.629
Grade 1 (200-300 mg/dl)	24 (11)	27 (13)	
HDL			
Low <40 mg/dl	85 (40)	90 (42)	
Normal (40-60 mg/dl)	121 (56)	118 (55)	0.655
High >60	8 (4)	6 (3)	
LDL			
Optimal (<100 mg/dl)	172 (80)	172 (80)	
Borderline high (130-159 mg/dl)	34 (16)	31 (15)	0.185
High (160-189 mg/dl)	8 (4)	11 (5)	

**p-value was calculated by using McNemar Bowker test.*

At the baseline testing, 167/214 (78%) patients had normal (<150 mg/dl) TG levels, 44/214 (21%) patients had values in grade 1 (150-300 mg/dl) range, while TG values of 3/214 (1%) patients were in grade 2 (300-500 mg/dl). After 2 months of therapy, TG values were normal in 162/214 (76%), 50/214 (23%) patients had values in grade 1 range, while TG values of 2/214 (1%) patients were in grade 2 (p = 0.620).

Cholesterol levels of 190/214 (89%) patients were within normal limits (< 200 mg/dl) and 24/214 (13%) had values falling in grade1 (200-300 mg/dl) at the baseline. After two months of taking isotretinoin, 187/214 (87%) patients had their cholesterol levels within normal limits and 27/214 (13%) patients had Grade 1 changes in the lipid profile (p = 0.629, Table I).

Baseline HDL was normal (40–59 mg/dL) in 121/214 (56%) patients, low (<40 mg/dL) in 85/214 (40%) patients, and high (≥60 mg/dL) in 8/214 (4%) patients. After two months of therapy, 118/214 (55%) had normal HDL values, 90/214 (42%) patients were found to have low HDL levels while in 6/214 (3%) patients levels were over 60mg/dl (p = 0.655, Table I).

One hundred and seventy-two out of 214 (80%) patients had optimal (<100 mg/dL) LDL levels, 34/214 (16%) patients had borderline high (130-159), while 8/214 (4%) had high values (160–189 mg/dL) before starting therapy. Two months later, 172/214 (80%) reported values within the normal range, 31/214 (15%) showed levels in the borderline high range and in 11/214 (5%) patient LDL rose to higher range (p = 0.185, Table I).

DISCUSSION

Isotretinoin is widely being used for the treatment of acne vulgaris for around half a century. Various low to conventional daily, alternate day to intermittent dosage regime of systemic retinoid is being practised and has shown clinical benefits in acne patients worldwide.[12] Laboratory monitoring of CBC, LFTs, and FLPs are being performed globally at different intervals without absolute conclusion.[13] As notable changes are not observed in CBCs and LFTs of the patients taking retinoids, routine testing is not performed.[8,14] International studies have

suggested lipid testing as this has been the most common lab abnormality seen in patients while on isotretinoin.[15]

A low dose (0.5 mg) isotretinoin was used in this study for clinical improvement along with better tolerability. FLP testing was done in this study at the baseline and after 2 months while on therapy as supported by a meta-analysis that most abnormalities are observed in the second month of the therapy.[11] In this study, acne patients receiving isotretinoin showed insignificant derangement of lipid parameters and did not require modification in the management. Similar findings were observed in the Saudi population by Al Dhafiri *et al.*[16] They noticed 87.5% and 81.8% normal cholesterol values pre-treatment and 2months post-treatment, respectively. At the baseline and 2 months post-therapy, 90.9% and 95.9% of patients, respectively, had normal TG levels. In another study conducted on Saudi patients, Al-Haddab *et al.* revealed that the TG levels were elevated in 4.4%.[17]

However, Afroz *et al.* drew contrasting conclusion with statistically significant elevation in TG and LDL values and statistically significant decline in the HDL at the baseline and 2 months later.[18] Sarkar *et al.* studied 60 patients who were prescribed isotretinoin, they found that TGs levels were elevated in 16.6% patients and 11.6% reported rise in very low density lipoprotein (VLDL).[15]

This study assessed the impact on lipid profile secondary to isotretinoin administration and it was found that most of the patients maintained their serum lipids within normal ranges while few patients had developed higher grade changes that did not need any treatment modification. The observations made in the study may be helpful in convincing the physicians to start retinoids early rather than prolong use of antibiotics which may increase the risk of antibiotic resistance.[19]

The limiting point in the study was its small sample size and not evaluating their dietary habits. Additional studies would be needed to further study the impact of isotretinoin on the local population.

CONCLUSION

Mild, insignificant alterations in the serum lipids of the acne patients taking isotretinoin were observed in this study. Therefore, isotretinoin is considered as a safe and effective therapeutic option in patients with moderate and severe acne. Although laboratory evaluation can be modified according to individual's specific needs and risk factors.

ETHICAL APPROVAL:

This study was conducted after approval from the Review Board of the Dow University of Health Sciences. (Approval no. TRB-2523/DUHS/Approval/2022/884, Dated: 21st June 2022).

PATIENTS' CONSENT:

Informed consent was obtained from all the patients before conducting the study.

COMPETING INTEREST:

The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:

MS: Writing the original draft, interpretation of data, and discussion of results.
SAA: Conception, study design, and acquisition of data.
TI: Drafting and critical revision of the manu-script.
SB: Proofreading and final approval of the manuscript.
AZ: Data analysis and statistical evaluation.
SI: Literature review and acquisition of data.
All authors approved the final version of the manuscript to be published.

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