Evaluating the Differences Among Dermatologists' Approaches to Abnormal Laboratory Results of Patients Using Oral Isotretinoin Treatment for Acne

Sezgi Sarıkaya Solak, Hande Yelgen, İmran Boğa[1]

Department of Dermatology, Trakya University, School of Medicine, Edirne, Turkey, [1]Trakya University, School of Medicine, Edirne, Turkey

Abstract

Background: Oral isotretinoin is one of the most frequently used treatment options in moderate and severe acne. Abnormal laboratory results may occur during the treatment and there may be differences in approach to these abnormal laboratory results among dermatologists. **Aim:** In this study, we aimed to retrospectively evaluate the differences in approach to abnormal laboratory results and treatment modifications of dermatologists during oral isotretinoin treatment. **Materials and Methods:** Data of 207 patients who had oral isotretinoin treatment for acne between January 2013 and October 2020 were included in this study. Baseline and follow-up laboratory results were reviewed. All treatment modifications were noted and evaluated with relevant literature. **Results:** Among 207 patients, 28 (13.5%) had treatment modifications due to the abnormal laboratory results, and all of them were due to elevation of lipid and liver enzyme levels. The dose was reduced in 24 (11.6%) patients and the treatment was discontinued in 4 (1.9%) patients. Treatment modification was not compulsory in the vast majority of patients (26 of 28) according to the relevant literature. **Conclusion:** The results of the present study showed that unnecessary treatment modifications due to the abnormal laboratory results can be made by dermatologists during oral isotretinoin treatment for acne. Educational programs for dermatologists and more detailed guidelines may prevent these unnecessary treatment modifications.

Keywords: Abnormal, acne, isotretinoin, laboratory, treatment

Introduction

Oral isotretinoin is one of the most effective treatments for the management of moderate to severe acne. Although it has some adverse effects that are generally mild, it is considered a safe treatment option. The most commonly observed adverse effects are mucocutaneous effects related to dryness, such as cheilitis, xerosis of the skin and dermatitis.[1] Abnormal blood tests, including liver function test abnormalities, hyperlipidemia and changes in complete blood count, are other relatively frequent adverse effects.[1,2]

The literature contains little consensus in terms of guidelines for the frequency of laboratory monitoring of patients receiving oral isotretinoin treatment.[3] Moreover, it is unclear when the treatment should be stopped or the dosage decreased in the case of abnormal laboratory results. Due to the different recommendations of various medical resources on oral isotretinoin treatment, dermatologists may also differ in their approach to monitoring and following up with patients using oral isotretinoin. In this study, we aimed to evaluate the responses of dermatologists to the abnormal laboratory test results of patients being treated with oral isotretinoin for acne.

Submission: 04-04-2022 **Revision:** 28-07-2022
Acceptance: 04-08-2022 **Web Publication:** 15-03-2023

Access this article online

Quick Response Code:

Website: www.tjdonline.org

DOI: 10.4103/tjd.tjd_58_22

Address for correspondence: Dr. Sezgi Sarıkaya Solak, Trakya Üniversitesi, Deri ve Zührevi Hastalıklar Anabilim Dalı, Edirne, Türkiye.
E-mail: sezgisarikaya@gmail.com

How to cite this article: Sarıkaya Solak S, Yelgen H, Boğa İ. Evaluating the differences among dermatologists' approaches to abnormal laboratory results of patients using oral isotretinoin treatment for acne. Turk J Dermatol 2023;17:16-8.

Materials and Methods

We conducted a retrospective study of the acne patients receiving oral isotretinoin treatment who admitted to Trakya University Hospital between January 2013 and October 2020. The study was approved by the Trakya University Ethics Committee (TUTF-BAEK 2021/258). We evaluated the demographic, clinical and laboratory data of acne patients who received oral isotretinoin for at least 4 months. The laboratory tests were conducted before treatment and monthly thereafter. Patients who completed a minimum of two laboratory tests during the treatment course were included in the study. There was one professor, one associate professor, four assistant professors and five residents in the department of dermatology during the study period. The faculty members had their academic degrees for at least four years. Residents with at least two years of dermatology training were allowed to make treatment modification decisions on their own. Otherwise, treatment modification decisions were made by faculty members.

Laboratory test results of the patients, including complete blood count (CBC), serum lipids (triglycerides [TG], total cholesterol, low-density lipoprotein cholesterol [LDL-C], high-density lipoprotein cholesterol [HDL-C]), liver enzymes (aspartate aminotransferase [AST], alanine aminotransferase [ALT]) were reviewed manually. Patients who have any baseline abnormal laboratory results prior to oral isotretinoin initiation were excluded from the study.

In patients with any abnormal laboratory results, we evaluated and recorded the treatment modifications as followings: no treatment modification, treatment interruption, reduction of dose, and treatment termination. We further reviewed the medical records to identify the reasons for changes in treatment management and evaluated whether the treatment modifications made in these patients were appropriate according to the recommendations in previous literature.[4,5] Values that we used to evaluate the appropriateness of the treatment modifications were, dose reduction if two-to-three-fold elevation in liver enzymes and drug discontinuation if there is more than three-fold elevation in liver enzymes; dose reduction if TG levels exceeds 500 mg/dl and drug discontinuation if TG levels exceeds 800 mg/dl.[4,5] In our literature review, we found no information or recommendation about the modifications that should be made, if total cholesterol and LDL-C level abnormalities occur during the oral isotretinoin treatment.

Results

A total of 207 acne patients using oral isotretinoin were included in the analyses. 150 (72.4%) of the patients were female and 57 (27.5%) were male. The mean age of the patients was 24.99 ± 5.03 years. Treatment modification due to the abnormal laboratory test results occurred in 28 (13.5%) patients, with 24 (11.6%) dose reduction and four (1.9%) treatment termination [Table 1].

There were no treatment modifications due to the CBC abnormalities. All modifications (n = 28, 13.5%) were due to the elevation in serum lipids and liver enzymes. The reasons of the treatment modifications were distributed as following: 10 (4.8%) patients for total cholesterol elevation, six (2.9%) patients for TG elevation, four (1.9%) patients for LDL-C elevation, four (1.9%) patients for ALT elevation, and four (1.9%) patients for AST elevation [Table 1].

Treatment modifications were made in the first month of treatment in four patients (14.3%), in the second month in eight patients (28.6%) and in the third, fourth and fifth months in five patients (17.8%) in each group.

When the patients who underwent a treatment modification (n = 28, 13.5%) were further evaluated, we found that treatment modification was not mandatory in 26 (12.6%) patients according to the literature.[4,5] These patients' laboratory abnormalities were mild-to-moderate and did not meet the abovementioned criteria to make a modification. Treatment modification was appropriate in two (%0.9) patients [Table 1]. These two patients had more than threefold and fivefold liver enzyme elevation; therefore, oral isotretinoin treatment was terminated.

Discussion

In this study, we found that 13.3% of acne patients had their treatment modified, including dose reduction (11.4%) and treatment termination (1.9%), due to abnormal laboratory results during oral isotretinoin treatment. Total cholesterol (4.7%) and TG (2.8%) elevation were the most common reasons leading to treatment modifications. In the majority of the patients who had treatment modification, the laboratory abnormalities were mild, and based on the literature, treatment modification was not compulsory.[4,5] In two patients (0.9%), both of whom had liver enzyme elevations, the decision to modify treatment was compatible with the recommendations provided in the literature.

Table 1: Treatment modificiations made by dermatologists due to the abnormal laboratory results during oral isotretinoin treatment

	High total cholesterol levels	High triglyceride levels	High LDL levels	ALT	AST	Total number (%)
Number of patients with treatment modification (%)	10 (35.7)	6 (21.4)	4 (14.3)	4 (14.3)	4 (14.3)	28 (100)
Number of patients with dose reduction (%)	10 (42)	4 (17)	4 (17)	2 (8)	4 (17)	24 (85.7)
Number of patients with treatment discontinuation (%)	-	2 (50)	-	2 (50)	-	4 (14.3)

It is known that an elevation in serum lipids is the most common laboratory abnormality observed during oral isotretinoin treatment.[2,6] Similarly, the most common reason for treatment modification (4.7%) was the elevation of total cholesterol levels in our study. A systematic review and meta-analysis demonstrated that high-risk or severe abnormalities in total cholesterol levels are rare.[2] However, to our knowledge, there is no specific information or recommendation in the published guidelines regarding the total cholesterol and LDL-C threshold levels that require treatment modification.[3,7] The lack of detailed and clear information on total cholesterol and LDL-C levels in the literature may explain the physicians' dose reductions in the presence of mild to moderate total cholesterol and LDL elevations in our study. We suggest that providing specific values for the total cholesterol and LDL-C levels that should prompt treatment modifications are required in the guidelines, as are currently provided for TG and liver enzyme levels, and that this information would avoid unnecessary treatment modifications by making physicians feel more comfortable with continuing treatment without making any changes. Moreover, providing this information would reduce the number of laboratory tests conducted to check for abnormal values. Thus, both the cost and the stress of blood draws would also be reduced.

In our study, other reasons for treatment modifications included elevated TG levels (2.8%), AST levels (1.9%) and ALT levels (1.9%). The literature provides recommended threshold values for both TG and liver enzymes to indicate when treatment modifications are required during oral isotretinoin treatment.[4,5,7,8] The existence of these kinds of specific criteria undoubtedly has an effect on dermatologists' decision-making processes. However, our study showed that treatment changes were made for some patients who did not meet the published criteria and who had clinically insignificant TG or liver enzyme elevations. Treatment modification was appropriate in only two (0.9%) patients with liver enzyme elevations. There may be several reasons that dermatologists take this approach. First, dermatologists and/or patients may feel anxious about side effects such as hepatitis and pancreatitis due to elevated TG or liver enzyme levels, even though the patient's TG and liver enzyme levels are mild or moderate. Second, current guidelines contain differences that may lead to confusion among dermatologists, resulting in unnecessary treatment changes.[3] A study that assessed dermatologists' actions in response to commonly seen laboratory abnormalities during oral isotretinoin treatment showed that they relied on a wide variety of sources to help them make decisions.[9] These sources included residency training, personal experience, comprehensive drug books, drug company package inserts and evidence-based guidelines. Differences in the information provided by various sources, may lead to difficulties in decision-making and inappropriate treatment modifications among dermatologists. As suggested by Barbieri *et al.*,[10] the provision of education and up-to-date information to dermatologists by dermatology societies on the management of patients using oral isotretinoin would reduce inappropriate treatment modifications.

The present study has some limitations. First, due to the retrospective design of the study, the sources that dermatologists relied on when making the decision to modify patients' treatment could not be evaluated. Second, the single-center design of the study limits the generalization of the findings.

In conclusion, the results of the present study show that in some patients who receive oral isotretinoin therapy and have commonly seen laboratory changes, inappropriate treatment changes are made. Providing specific values or threshold levels for abnormal laboratory results in published guidelines and organizing regular educational programs that provide current information on oral isotretinoin management may prevent unnecessary treatment modifications by dermatologists.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Vallerand IA, Lewinson RT, Farris MS, Sibley CD, Ramien ML, Bulloch AGM, *et al*. Efficacy and adverse events of oral isotretinoin for acne: A systematic review. Br J Dermatol 2018;178:76-85.
2. Lee YH, Scharnitz TP, Muscat J, Chen A, Gupta-Elera G, Kirby JS. Laboratory monitoring during isotretinoin therapy for acne: A systematic review and meta-analysis. JAMA Dermatol 2016;152:35-44.
3. Dessinioti C, Zouboulis CC, Bettoli V, Rigopoulos D. Comparison of guidelines and consensus articles on the management of patients with acne with oral isotretinoin. J Eur Acad Dermatol Venereol 2020;34:2229-40.
4. On SC, Zeichner J. Isotretinoin updates. Dermatol Ther 2013;26:377-89.
5. Park H, Skopit S. Safety considerations and monitoring in patients treated with systemic medications for acne. Dermatol Clin 2016;34:185-93.
6. Hansen TJ, Lucking S, Miller JJ, Kirby JS, Thiboutot DM, Zaenglein AL. Standardized laboratory monitoring with use of isotretinoin in acne. J Am Acad Dermatol 2016;75:323-8.
7. Landis MN. Optimizing isotretinoin treatment of acne: Update on current recommendations for monitoring, dosing, safety, adverse effects, compliance, and outcomes. Am J Clin Dermatol 2020;21:411-9.
8. Karadağ AS. Sistemik İzotretinoin. Turkderm-Turk Arch Dermatol Venereol 2020;54:34-40.
9. Hobson JG, Cunningham MJ, Lesiak K, Lester EB, Tegeder AR, Zeeck E, *et al*. Isotretinoin monitoring trends: A national survey of dermatologists. J Drugs Dermatol 2017;16:557-64.
10. Barbieri JS, Shin DB, Wang S, Margolis DJ, Takeshita J. The clinical utility of laboratory monitoring during isotretinoin therapy for acne and changes to monitoring practices over time. J Am Acad Dermatol 2020;82:72-9.