ORIGINAL RESEARCH

Isotretinoin-Induced Dyslipidemia: a Single-Center Study in Saudi Arabia

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Purpose: Acne is a chronic inflammatory skin disease with a high prevalence in Saudi Arabia. Isotretinoin is used to treat severe, resistant nodulocystic acne. Side effects include joint discomfort, headache, mucosal dryness, and nose bleeds. Elevated lipids and liver enzymes have also been recorded. The study goal is to identify the prevalence of increased lipid levels during and after isotretinoin use.

Patients and Methods: This retrospective study was conducted in the dermatology polyclinic at King Faisal University, Al-Ahsa, Saudi Arabia. It included adults of different age groups diagnosed with acne vulgaris and treated with oral isotretinoin between January 2021 and December 2022. Parameters included baseline laboratory tests and follow-up laboratory results of cholesterol and triglycerides.

Results: Among 88 patients, 48.9% were aged 21–23 years, with females dominating. In total, 47.7% of patients started using isotretinoin at age 20 years or less, with starting doses ranging from 10 to 20 mg. Fifty percent of the patients had five months or more of treatment duration and only 6.8% of the patients had previously used isotretinoin. For the cholesterol and triglycerides, 87.5% of patients had normal pre-treatment with cholesterol and 90.9% with triglycerides, followed by 81.8% and 95.5% in the second reading, respectively. In the last reading, results were 77.3% for cholesterol and 94.3% for triglycerides.

Conclusion: The study found that most acne patients treated with isotretinoin had normal cholesterol and triglyceride levels at baseline, second, and last readings. The incidence of higher laboratory alterations was low, with 12.5% and 4.5% for cholesterol and triglycerides at baseline, and 18.2% and 3.4% at second, and 22.7% and 5.7% at last readings. Overall, age, gender, age of start of isotretinoin, isotretinoin dose, and previous use of isotretinoin are factors that could affect laboratory readings.

Keywords: acne, lipids, prevalence, roaccutane, triglycerides, cholesterol

Introduction

Acne is a chronic inflammatory skin disease. The factors that lead to lesion formation include increased sebum production, hyperkeratinization, *Cutibacterium acnes* colonization, and the subsequent inflammatory reactions are the main therapeutic targets.[1] In Saudi Arabia, the prevalence of acne vulgaris in 2022 was 53%. About 54% of the female and 50% of the male participants both had acne vulgaris.[2] Acne had a significant negative impact on the quality of life for young ladies, with 85.5% prevalence in the eastern region of Saudi Arabia.[3] Substantial mental health burden is associated with treatment-resistant acne during isotretinoin therapy and the potential impact of medication side effects.[4]

Isotretinoin is a retinoic acid derivative taken orally for the treatment of moderate to severe, nodulocystic acne that is resistant to conventional medications. It primarily works by decreasing the number of sebaceous glands, the amount of the produced sebum, and the bacterial skin microflora.[5]

The possible side effects of isotretinoin including joint discomfort, headache, mucosal dryness, and nose bleeds were the most frequent side effects of isotretinoin treatment, along with lipid profile and liver enzyme changes.[6,7] Interestingly,

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a study conducted in Al-Ahsa, Saudi Arabia, showed that more than half of participants (58.7%) did not consider lipid profile changes as a risk of using isotretinoin.[8]

Following isotretinoin treatment, changes in lipid profile (total cholesterol and triglycerides) and liver enzymes (aspartate transaminase and alanine transaminase) have been recorded.[6,9] A recent study done during 2021 in Qassim University Medical City, Saudi Arabia, showed triglyceride levels and total cholesterol were elevated at the end of treatment course, 12.7% and 9%, respectively. Obesity was the major factor associated with high triglyceride levels, with a significant association between body weight and elevation of triglyceride levels.[10] Our aim in this study is to identify the prevalence of increased lipid levels during and after isotretinoin use in polyclinic patients of King Faisal University, Al-Ahsa, Saudi Arabia.

Materials and Methods

A retrospective cohort design study tobtained the patient data and laboratory test results from the King Faisal University polyclinic records system. Patients of all ages diagnosed with acne vulgaris who were treated with oral isotretinoin in the years of 2021–2022 and who had baseline and follow-up laboratory readings of total cholesterol (TC) and triglycerides (TG) during the treatment course were included in this study. Participants who used isotretinoin for other medical conditions than acne or those with not enough laboratory readings were excluded from the sample population.

Parameters included: age, gender, weight, age of onset of acne, age of start of isotretinoin, commercial type of isotretinoin, the dose of isotretinoin (starting dose, ending dose), duration of treatment, previous use of isotretinoin, baseline laboratory tests, and follow-up laboratory results (second and last reading) of TC and TG. Analysis of TC and TG was based on:

- total cholesterol (TC) is classified as normal (100–200 mg/dL) and high (> 200 mg/dL);

- triglycerides (TG) is classified as normal (37–150 mg/dL) and high (> 150 mg/dL).

The study was approved by the institutional review board committee in King Faisal University.

Statistical Analysis

Categorical variables were presented using numbers and percentages. The relationship between the last triglycerides and cholesterol readings among the demographic and clinical characteristics of patients has been performed using Fischer's exact test. A P-value of ≤ 0.05 was considered statistically significant. The data were analyzed using Statistical Packages for Social Sciences (SPSS) version 26 (IBM Corp., Armonk, NY, USA).

Results

We found 132 patients were treated with isotretinoin. Due to lack of the needed laboratory investigations, we recruited 88 patients.

Sociodemographic Characteristics

Nearly half (48.9%) were aged between 21 and 23 years, with females being dominant (70.5%). A total of 50.7% weighed 51 to 70 kg. Approximately 48.9% had been diagnosed with acne at age of more than 19 years. The use of isotretinoin started at the age of 20 years or less (47.7%). The starting dose mostly ranged from 10 to 20 mg (87.5%), while the ending dose ranged between 30 and 40 mg (51.1%). Half of the respondents (50%) had 5 months or more duration of treatment. The prevalence of patients who had previous use of isotretinoin was 6.8% (Table 1).

Pre, Second, and Last Cholesterol and Triglyceride Reading Levels

Most patients had normal pre-treatment cholesterol (87.5%) and triglycerides (90.9%). The second readings (first to third month) of cholesterol and triglycerides were also mostly normal, with 81.8% and 95.5%, respectively. The last readings (fourth to sixth month) of cholesterol and triglycerides were also normal among 77.3% and 94.3% (Table 2).

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Table 1 Demographic and Clinical Characteristics of the Lipid Profile Patients (n=88)

Study variables	N (%)
Age group	
≤20 years	17 (19.3%)
21–23 years	43 (48.9%)
>23 years	28 (31.8%)
Gender	
Male	26 (29.5%)
Female	62 (70.5%)
Weight (n=75)	
30–50 kg	15 (20.0%)
51–70 kg	38 (50.7%)
>70 kg	22 (29.3%)
Age of onset of acne	
11–15 years	18 (20.5%)
16–19 years	27 (30.7%)
>19 years	43 (48.9%)
Age of start of isotretinoin	
≤20 years	42 (47.7%)
21–23 years	35 (39.8%)
>23 years	11 (12.5%)
Starting dose	
10–20 mg	77 (87.5%)
30–40 mg	11 (12.5%)
Ending dose	
10–20 mg	38 (43.2%)
30–40 mg	45 (51.1%)
>40 mg	05 (05.7%)
Duration of treatment	
<5 months	44 (50.0%)
≥5 months	44 (50.0%)
Previous isotretinoin used	
Yes	06 (06.8%)
No	82 (93.2%)

Table 2 Lipid Parameters (n=88)

Parameters	N (%)
Cholesterol before treatment	
Low	0
Normal	77 (87.5%)
High	11 (12.5%)
Triglycerides before treatment	
Low	04 (04.5%)
Normal	80 (90.9%)
High	04 (04.5%)
Second cholesterol reading (first to the third month)	
Low	0
Normal	72 (81.8%)
High	16 (18.2%)
Second triglycerides reading (first to the third month)	
Low	01 (01.1%)
Normal	84 (95.5%)
High	03 (03.4%)
Last cholesterol reading (fourth to the sixth month)	
Low	0
Normal	68 (77.3%)
High	20 (22.7%)
Last triglyceride reading (fourth to the sixth month)	
Low	0
Normal	83 (94.3%)
High	05 (05.7%)

Notes: Normal cholesterol (100–200 mg/dL) and high (>200 mg/dL). Normal triglycerides (37–150 mg/dL) and high (>150 mg/dL).

Factors Affecting the Reading of Triglyceride Levels

It was observed that a high pre-treatment triglyceride level was significantly more common among the older age group (p=0.047), increasing age of start of isotretinoin (p=0.003) and increasing ending dose (p=0.016) while the last high triglyceride levels were significantly more common among male patients (p=0.025) and those who previously used isotretinoin (p=0.036). No significant relationships were observed between the last triglyceride levels in terms of age group, age of onset of acne, age of start of isotretinoin, starting dose, ending dose, duration of treatment, and weight group (p>0.05) (Table 3).

Table 3 Relationship Between First and Last Triglyceride Reading Among the Demographic and Clinical Characteristics of the Patients (n=88)

Factor	Pre-treatment Triglyceride Level		Last Triglyceride Level	
	Normal, N (%) (n=80)	High, N (%) (n=4)	Normal, N (%) (n=83)	High, N (%) (n=5)
Age group				
≤22 years	44 (55.0%)	0	83 (51.8%)	02 (40.0%)
>22 years	36 (45.0%)	04 (100%)	40 (48.2%)	03 (60.0%)
P-value	0.047**		0.673	
Gender				
Male	25 (31.3%)	01 (25.0%)	22 (26.5%)	04 (80.0%)
Female	55 (68.8%)	03 (75.0%)	61 (73.5%)	01 (20.0%)
P-value	1		0.025**	
Age of onset of acne				
11–15 years	18 (22.5%)	0	16 (19.3%)	02 (40.0%)
16–19 years	25 (31.3%)	0	26 (31.3%)	01 (20.0%)
>19 years	37 (46.3%)	04 (100%)	41 (49.4%)	02 (40.0%)
P-value	0.183		0.591	
Age of start of isotretinoin				
≤20 years	41 (51.2%)	0	39 (47.0%)	03 (60.0%)
21–23 years	31 (38.8%)	01 (25.0%)	34 (41.0%)	01 (20.0%)
>23 years	08 (10.0%)	03 (75.0%)	10 (12.0%)	01 (20.0%)
P-value	0.003**		0.538	
Starting dose				
10–20 mg	72 (90.0%)	02 (50.0%)	73 (88.0%)	04 (80.0%)
30–40 mg	08 (10.0%)	02 (50.0%)	10 (12.0%)	01 (20.0%)
P-value	0.068		0.496	
Ending dose				
10–20 mg	35 (43.8%)	01 (25.0%)	36 (43.4%)	02 (40.0%)
30–40 mg	42 (52.5%)	01 (25.0%)	43 (51.8%)	02 (40.0%)
>40 mg	03 (03.8%)	02 (50.0%)	04 (04.8%)	01 (20.0%)
P-value	0.016**		0.388	
Duration of treatment				
<5 months	49 (61.3%)	02 (50.0%)	43 (51.8%)	01 (20.0%)
≥5 months	31 (38.8%)	02 (50.0%)	40 (48.2%)	04 (80.0%)
P-value	0.644		0.36	

(Continued)

Table 3 (Continued).

Factor	Pre-treatment Triglyceride Level		Last Triglyceride Level	
	Normal, N (%) (n=80)	High, N (%) (n=4)	Normal, N (%) (n=83)	High, N (%) (n=5)
Previous isotretinoin used				
Yes	05 (06.3%)	01 (25.0%)	04 (04.8%)	02 (40.0%)
No	75 (93.8%)	03 (75.0%)	79 (95.2%)	03 (60.0%)
P-value	0.261		0.036**	
Weight				
30–50 kg	13 (18.8%)	0	14 (20.0%)	01 (20.0%)
51–70 kg	36 (52.2%)	01 (33.3%)	37 (52.9%)	01 (20.0%)
>70 kg	20 (29.0%)	02 (66.7%)	19 (27.1%)	03 (60.0%)
P-value	0.432		0.165	

Notes: *P*-value has been calculated using Fischer's exact test. ** Significant at *p*≤0.05 level.

Factors Affecting the Reading of Cholesterol Levels

It was revealed that high pre-treatment cholesterol levels were significantly more common among the older age group (*p*=0.025) and previous usage of isotretinoin (*p*=0.024). On the other hand, the prevalence of patients with high cholesterol levels at the last readings was significantly more common among the older age group (*p*=0.042) (Table 4).

Table 4 Relationship Between First and Last Cholesterol Reading Among the Demographic and Clinical Characteristics of the Patients (n=88)

Factor	Pre-treatment Cholesterol Level		Last Cholesterol Level	
	Normal, N (%) (n=77)	High, N (%) (n=11)	Normal, N (%) (n=68)	High, N (%) (n=20)
Age group				
≤22 years	43 (55.8%)	02 (18.2%)	39 (57.4%)	06 (30.0%)
>22 years	34 (44.2%)	09 (81.8%)	29 (42.6%)	14 (70.0%)
P-value	0.025**		0.042**	
Gender				
Male	21 (27.3%)	05 (45.5%)	19 (27.9%)	07 (35.0%)
Female	56 (72.7%)	06 (54.5%)	49 (72.1%)	13 (65.0%)
P-value	0.290		0.583	
Age of onset of acne				
11–15 years	16 (20.8%)	02 (18.2%)	13 (19.1%)	05 (25.0%)
16–19 years	25 (32.5%)	02 (18.2%)	21 (30.9%)	06 (30.0%)
>19 years	36 (46.8%)	07 (63.6%)	34 (50.0%)	09 (45.0%)
P-value	0.592		0.894	

(*Continued*)

Table 4 (Continued).

Factor	Pre-treatment Cholesterol Level		Last Cholesterol Level	
	Normal, N (%) (n=77)	High, N (%) (n=11)	Normal, N (%) (n=68)	High, N (%) (n=20)
Age of start of isotretinoin				
≤20 years	38 (49.4%)	04 (36.4%)	33 (48.5%)	09 (45.0%)
21–23 years	30 (39.0%)	05 (45.5%)	27 (39.7%)	08 (40.0%)
>23 years	09 (11.7%)	02 (18.2%)	08 (11.8%)	03 (15.0%)
P-value	0.734		0.938	
Starting dose				
10–20 mg	66 (85.7%)	11 (100%)	59 (86.8%)	18 (90.0%)
30–40 mg	11 (14.3%)	0	09 (13.2%)	02 (10.0%)
P-value	0.346		1	
Ending dose				
10–20 mg	34 (44.2%)	04 (36.4%)	29 (42.6%)	09 (45.0%)
30–40 mg	39 (50.6%)	06 (54.5%)	35 (51.5%)	10 (50.0%)
>40 mg	04 (05.2%)	01 (09.1%)	04 (05.9%)	01 (05.0%)
P-value	0.566		1	
Duration of treatment				
<5 months	43 (55.8%)	09 (81.8%)	35 (51.5%)	09 (45.0%)
≥5 months	34 (44.2%)	02 (18.2%)	33 (48.5%)	11 (55.0%)
P-value	0.188		0.8	
Previous isotretinoin use				
Yes	03 (03.9%)	03 (27.3%)	03 (04.4%)	03 (15.0%)
No	74 (96.1%)	08 (72.7%)	65 (95.6%)	17 (85.0%)
P-value	0.024**		0.128	
Weight				
30–50 kg	13 (19.7%)	02 (22.2%)	13 (22.4%)	02 (11.8%)
51–70 kg	33 (50.0%)	05 (55.6%)	27 (46.6%)	11 (64.7%)
>70 kg	20 (30.3%)	02 (22.2%)	18 (31.0%)	04 (23.5%)
P-value	1		0.444	

Notes: P-value has been calculated using Fischer's exact test. ** Significant at p≤0.05 level.

Discussion

Oral isotretinoin treatment might induce a significant rise in lipid profiles indicating the importance of careful monitoring during the duration of therapy. A meta-analysis done in 2016 does not recommend monthly laboratory testing for acne patients who used isotretinoin therapy.[11] However, a recent study demonstrated that although abnormal laboratory results are rare and often do not affect management, the practice of regular laboratory monitoring is still common.[12]

In this study, the lipid profile alterations (TG and TC) were assessed in acne patients treated with oral isotretinoin. The prevalence rates of high levels of cholesterol before treatment and at the first, and at the second follow-ups were 12.5%, 18.2%, and 22.7%, respectively. TG was less affected by isotretinoin therapy than cholesterol. The prevalence rates of high levels before treatment and at the first and second follow-ups for TG levels were 4.5%, 3.4% and 5.7%.

In our study, half of the patients (48.9%) were aged between 21 and 23 years, with females being dominant (70.5%). A similar finding of 200 patients reported that 75% of the patients were female with a mean age of 22–24 years.[13]

Regarding cholesterol level readings, we found that most of the patients had normal pre-treatment (baseline) cholesterol and both second and last follow-up readings (87.5%, 81.8%, and 77.3%, respectively). A retrospective study in Al Qassim, Kingdom of Saudi Arabia (KSA) produced results that corroborate our findings. There were 407 patients with baseline, follow-up, and the end of treatment course laboratory results. TC was normal at baseline with 89.5% of patients and follow-up with 88.6%.[10] On the other hand, a retrospective study in Al Riyadh, KSA of 386 patients had high TC baseline readings as well as 2 follow-up readings (12.1%, 21.8%, and 18.7%, respectively).[14] Also, a study done in Sakarya University, Turkey, found no relation statistically between the third and sixth months of treatment in all parameters including cholesterol and TG.[15]

Regarding triglyceride level readings, we noticed that almost all the patients had a normal baseline (90.9%) and both second (95.5%) and last (94.3%) follow-up readings. The same study done in Al Qassim, KSA showed that TG levels were normal at baseline of patients at 93.5% and at follow-up 83.7%.[10] In contrast, Al Riyadh, KSA study demonstrated high TG levels over time (1.6%, 3.8%, and 4.4%) at baseline and first and second readings, respectively.[14] Another retrospective study of 415 patients also supported significant differences between TG measurements mostly between the second month (23.9%) and the fourth month (27.2%).[16] Many studies supported that high TG levels were associated with the third and sixth months of treatment.[17,18]

In our study, we found that high cholesterol levels of pre-treatment and last readings had a significant relation with the older age group. In contrast, a study of 143 patients revealed that age and oral isotretinoin had no significant effect on cholesterol in the third month of treatment.[19] Abd-Elaziz et al showed that the dose and duration of the treatment had a significant association with higher levels of cholesterol which was not found in our study.[20] Alajaji et al concluded that body weight had no significant effect on cholesterol levels at follow-up and last visit levels which is a similar result in our study.[10]

No significant relationships were observed in our study between the last TG levels in terms of weight group. However, a retrospective study of 204 patients showed that subjects with higher body weight had significantly higher levels of TG.[21] In addition, a previous study showed that triglyceride levels compared with body weight were statistically significant for follow-up and last-visit levels.[10] No relation was found between high TG levels and the dose of isotretinoin in our study, which is similar finding in the previous study.[22]

Strengths

This study compares the following variables: age, gender, weight, dose, duration of treatment, and isotretinoin previous use with lipid parameters, which have not been discussed in previous studies.

Limitations

The limited sample size of the study, and the retrospective character leading to elimination of a number of patients due to lack of regular investigation and recruitment criteria.

Conclusion

Almost all acne patients who were treated with isotretinoin in our study have normal levels of total cholesterol and triglyceride at baseline, second, and last readings. The incidence of higher laboratory alterations of lipid profiles is low. The older age group has a high pre-treatment reading of both total cholesterol and triglyceride levels. Also, older patients have high last-reading cholesterol levels. In addition, previous usage of isotretinoin is associated with high pre-treatment cholesterol levels. High pre-treatment readings of triglyceride have a significant association with an increasing ending dose. While high last-reading triglyceride levels have a significant association with the male gender and those who previously used isotretinoin. Additional confirmatory studies with a larger patient sample will be recommended.

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Data Sharing Statement

Data are available from the corresponding author upon reasonable request.

Ethical Approval and Informed Consent

The study was approved by King Faisal University (protocol code No. KFU-REC-2023-FEB-ETHICS594 and date of 15 February 2023). All data were obtained with permission from the hospital with keeping patients' confidentiality. This study complies with the Declaration of Helsinki.

Disclosure

The authors report no conflicts of interest in this work.

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