

The Role of Serum Lipids in Predicting Suicidal Ideation in Isotretinoin Therapy for Acne

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ABSTRACT

Background: Previous studies have demonstrated that lipids could play a role in suicidal ideation and the pathogenesis of psychiatric diseases. The present study aims to investigate the correlation between variations in serum lipid concentration, a side effect of isotretinoin (ITT), psychiatric symptoms, and suicidal ideation in acne vulgaris patients under ITT treatment.

Methods: The study was completed with 41 acne patients. Patients were analyzed with the sociodemographic and clinical data form, Beck depression inventory (BDI), Beck anxiety inventory (BAI), Beck Suicidal Ideation Scale (BSS), and Brief Psychiatric Rating Scale (BPRS) at the beginning and on the third month of treatment. Lipid levels [serum total cholesterol (TC), triglyceride (TG) and high-density lipoprotein cholesterol (HDL)] were measured using the automatic chemistry analyzer (Beckman AU-5800). Serum low-density lipoprotein cholesterol (LDL) values were estimated with the Friedewald formula.

Results: A statistically significant correlation was determined between the BSS scores and TC, TG, and LDL parameters at the beginning of treatment and the control date. Thus, it was determined that there was a negative weak correlation between BSS and TC parameters ($r=-0.403$; $P=.009$), a moderate negative correlation between BSS and TG ($r=-0.526$; $P < .001$), and a weak negative correlation between BSS and LDL ($r=-0.421$; $P=.006$). Furthermore, there were statistically significant changes between the BDI and BAI scores at the beginning of treatment and the third month ($P=0.016$ and $P=.001$, respectively). Although an increase was observed in BSS and BPRS after the treatment compared to pretreatment, the increase was not statistically significant.

Conclusion: The present study findings revealed that serum lipid levels could be associated with psychiatric side effects in patients under ITT treatment. But, this must not be the only way to detect the risk when we consider that serum lipid levels that have been associated with suicidal ideation, depression, and several psychiatric diseases have the potential to be an important indicator. In this context, our preliminary results open the doors to a new perspective in this regard, using the concept of blood lipid optimization. These findings need to be considered preliminary and supported by large samples.

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INTRODUCTION

Acne vulgaris is a chronic inflammatory disease of the pilosebaceous unit. It is the most prevalent skin disease that affects approximately 85% of the 12- to 24-year old population. The disease is characterized by clinically noninflammatory lesions, inflammatory lesions with open and closed black heads, papules, pustules, and, less frequently, nodules. Ductal hyper-keratinization, increase in sebum production, microorganisms, and inflammation are the most important etiopathogenesis factors.¹

The correlation between acne and mood has been investigated for a long time. While emotional stress could exacerbate acne, patients could also experience

psychological and psychiatric problems due to acne.² Psychological problems induced by acne vulgaris could include depression, dysmorphophobia, social problems, anger, and anxiety. The treatment of acne could include topical or both topical and systemic treatments based on the severity of the disease.³ Isotretinoin (13-cis retinoic acid) (ITT) is a commonly used treatment and effective retinoid on all pathogenesis factors in acne.^{4,5} Studies have shown that xerosis, eczematous lesions, mucocutaneous events such as itching, and hyperlipidemia were among the most common adverse effects of ITT treatment.⁶ Although ITT is the most effective treatment option in severe acne,

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ITT treatment has been associated with certain physical and mental disorders including depression.⁷

In fact, due to the comorbidity of acne and psychiatric disorders, effective treatment of acne could be expected to improve the mental condition of the patient.⁷ However, systemic ITT treatment led to psychological problems such as depression and suicidal ideation in patients.^{6-9,11}

In severe acne, ITT is the most effective treatment option. However, teratogenic and psychiatric problems limit the use of ITT in treatment.⁸ Psychiatric side effects such as depression, suicidal ideation, and suicide attempts are the most concerning problems. Genetic vulnerability and central nervous system (CNS) influence via vitamin A synthesis are the most important biological factors in psychiatric adverse effects of ITT.^{9,10} Oral synthetic retinoids such as ITT were suggested to affect CNS via vitamin A synthesis. It was shown that excessive Vit A release could lead to lethargy, depression, cyclothymia, sleep disorders, skin variations, hair loss, headaches, bone and joint pain, irritability, and psychosis.^{11,12} This effect, which could be on the neurotransmitter system and secondary messengers, could induce psychiatric symptoms by changing neuroplasticity. Furthermore, in addition to the immediate neurochemical effects, behavioral changes could be observed weeks or even months later, such as the late onset of the effect of antidepressants.⁹ This could provide insight into the onset of psychiatric symptoms months after the initiation of ITT treatment. Most studies conducted to analyze the correlation between suicide and ITT reported that the suicide risk starts between the second and fourth months after the treatment.⁸

However, certain studies emphasized that the correlation between ITT and psychiatric symptoms was quite weak; ITT even improved psychological symptoms, and non-drug factors were more significant.^{13,14} The correlation between psychiatric symptoms and ITT has been controversial, and conflicting results have been reported, indicating that certain biological or personal factors could be effective in the development of psychiatric problems during ITT treatment, which should be investigated further.^{13,14}

The impact of ITT on serum lipid profile is among the well-defined adverse effects. Hypertriglyceridemia, hypercholesterolemia, and high liver enzyme levels were observed in about 15%-25% of the patients treated by ITT. Lipid levels decrease rapidly after the treatment.¹⁵

MAIN POINTS

- Previous studies suggest an association between isotretinoin and suicide.
- Isotretinoin treatment could affect the lipid levels.
- Lipids could be associated with psychiatric adverse effects and suicide ideation.
- Lipids may be associated with suicidal ideation in isotretinoin treatment.

The correlation between serum lipid levels and psychiatric disorders has been studied intensively. A correlation was determined between low serum cholesterol level and depression in different populations.^{16,17} There is a well-defined correlation between low serum cholesterol levels and violence, suicidal behavior, and depression. It was suggested that lipids had psychiatric effects via cell membrane activity, on sex hormones, neurotransmitters, monoamine oxidase (MAO) enzyme systems, and especially low CNS serotonin activities.^{18,19} Thus, it was suggested that high testosterone levels in men and low estrogen levels in women could alleviate suicide risk.²⁰ In panic disorder, it was determined that serum lipid levels were higher than controls, as opposed to depression, violence, and suicidal behavior.¹⁰ It was demonstrated that especially low total cholesterol (TC) and LDL²¹ levels could be associated with suicidal behavior in psychiatric disorders.²²⁻²⁴ Furthermore, studies also indicated that there could be a correlation between lipid levels and suicide risk in individuals without a history of psychiatric illness.²⁰

Investigation of biomarkers and modifiable risk factors associated with suicide is a significant and important issue. Lipids are of great interest in this research.²⁰ Certain studies have reported a correlation between suicidal behavior and serum lipid levels in depression and bipolar disorder patients.^{25,26} Certain studies have emphasized that the serum lipid profile could be a biomarker in the prediction of suicidal behavior.²⁰⁻²⁴

Serum lipid levels could change during ITT treatment. Psychiatric side effects are a concerning and controversial issue in ITT treatment, which could hinder effective treatment. However, the literature review revealed no study that analyzed the correlation between psychiatric outcomes and serum lipid levels in acne vulgaris patients under ITT treatment.

Thus, the current study aimed to determine the correlation between serum lipid levels and psychiatric problems in acne vulgaris patients under ITT treatment, based on the idea that lipids could be associated with psychiatric adverse effects and suicide ideation, and ITT treatment could affect the lipid levels.

MATERIAL AND METHODS

The Study Sample

The local Ethics Committee of Fırat University approval was obtained before the study (Protocol number of ethics committee approval: 04-03/18; Date: February 15, 2018). The informed consent form was signed by all participants prior to the study. A careful anamnesis and detailed clinical examination were conducted before the patients were included in the study. Sixty-three patients who met the study criteria and were treated in our clinic for acne vulgaris were included in the study prospectively. However,

the study was completed with 41 patients since certain patients could not conclude the study due to various reasons (e.g., meeting regular check-up requirements, systemic treatment interventions, and discontinuing the treatment). Lipid profile control was included in routine examinations during ITT treatment of acne patients. The lipid levels of the patients [TC, LDL, high-density lipoprotein cholesterol (HDL), and triglyceride (TG)] were determined, and simultaneously Beck Depression Inventory, Beck Anxiety Inventory, Brief Psychiatric Rating Scale, and Beck Suicidal Ideation Scale were applied at the beginning of the treatment and during the third month check-up. Study inclusion criteria included voluntary participation in the study, 18-65 years of age, acne vulgaris diagnosis, lack of a concomitant dermatological disease or a systemic or psychiatric disease, lack of a significant physical pathology that could affect the existing dermatological symptoms, and the informed consent form. Exclusion criteria included the presence of a serious physical illness and psychological disorders (e.g., depression, bipolar disorder, and schizophrenia), a history of alcohol and substance abuse or addiction, previous cholesterol-lowering treatment, an endocrinological condition, medicine use during the previous 2 weeks, and obesity.

Blood Samples and Laboratory Analysis

Venous blood samples were collected after at least 12 hours of fasting to determine serum lipid levels. Patients were required to avoid taking medicine (e.g., beta-blockers, diuretics, steroid drugs, etc.) and a lipid-lowering diet was required for at least 2 weeks before the blood samples were taken at the beginning of the treatment and before the check-ups. Patient blood and biochemical test results (laboratory examinations such as complete hemogram, liver function tests, and basic lipid profile) were recorded after the routine patient controls. To determine serum levels of lipids, venous blood samples were obtained at 08.00-10.00 AM In the patients, blood was collected after fasting for 10-12 hours. Lipid levels (serum total cholesterol, triglyceride, and HDL) were measured using the automatic chemistry analyzer (Beckman AU-5800). Serum low-density lipoprotein cholesterol (LDL) values were estimated with the Friedewald Formula.

Data Collection Instruments

Sociodemographic and Clinical Data Form: A sociodemographic and clinical data form developed by the authors was applied to the participants. The form was a semi-structured questionnaire that included sociodemographic data such as age, gender, marital status, educational level, occupation, place of residence, income level, family type, and clinical data such as the duration of the disease and the presence of psychosocial stressors at the onset of the disease.

Beck Depression Inventory (BDI): It is a 4-point Likert-type self-rating scale developed by Beck to determine

depression risk and depressive symptom levels. The Turkish language validity and reliability of the scale was conducted by Hisli.²⁷ Reliability coefficients were 0.90 and over for Beck Depression Inventory in this study.

Beck Anxiety Inventory (BAI): The scale includes 21 items. Each question is scored between 0 (never) and 3 (severe), and a high score indicates high anxiety. The scale was developed by Beck et al.²⁸ and adapted into Turkish language by Ulusoy et al.²⁹ The reliability coefficient of the Beck Anxiety Inventory was calculated as 0.88

Brief Psychiatric Rating Scale (BPRS): The scale was developed by Overall and Gorham³⁰ to determine the severity of psychotic and certain depressive symptoms. It is sensitive to changes as its main goal is to measure changes during pharmacological treatment. Reliability coefficients were 0.93 and over for Brief Psychiatric Rating Scale in this study.

Beck Suicidal Ideation Scale (BSS): The 20-item scale was developed by Beck in 1973.³¹ The scale includes 15 scored and 5 unscored items, which analyze the expectations of the individual during the suicide attempt. Each item is scored between 0 and 2 points. After the data are collected for each item during the interview, the interviewer selects the most adequate option in the scale. The total score varies between 0 and 30, and the sum of the scores obtained in the items is the total scale score. The validity and reliability of the scale in Turkish language was studied by Dilbaz et al.³² In this study, the reliability coefficient was 0.92 for BSS.

Statistical Analysis

Statistical Package for Social Science Statistics software for Windows, version 24.0 (IBM SPSS Corp.; Armonk, NY, USA) was employed in data analysis. Frequencies and percentages were analyzed to determine the distributions based on the gender, marital status, education level, income level, place of residence, and occupation of the patients. The means and SDs were analyzed to determine the age, disease duration, BA, BD, BI, BPRS, TC, TG, LDL, and HDL of the study participants. A 1-sample Kolmogorov-Smirnov test was applied to examine the distribution of variables. When the distributions of the variables examined within the scope of the study were examined $P > .05$ values were found for all depression scores and blood lipid levels parameters, and it was determined that the variables showed a normal distribution. For this reason, parametric tests were applied.

A paired samples *t*-test was applied to determine whether there were statistically significant differences between the baseline and third month BA, BD, BSS, BPRS, TC, TG, LDL, and HDL data.

The delta variable was calculated as the difference between the post-treatment values and pre-treatment values.

Furthermore, a Pearson correlation coefficient was conducted to determine the statistically significant correlations between the differences between the baseline and third month BA, BD, BSS, BPRS, TC, TG, LDL, and HDL levels. The findings were considered significant at 95% ($P < .05$) CI.

RESULTS

Sociodemographic patient data revealed that 85.4% ($n=34$) were female and all were single. The demographic characteristics of the patient group are presented in Table 1.

The findings revealed a statistically significant difference between the baseline and third month TC, LDL, and HDL parameters. Total cholesterol increased by 10.88 after the treatment, LDL increased by 8.80 after treatment, and HDL decreased by 4.1 after the treatment ($P=.010$,

Table 1. Sociodemographic Characteristics of the Studied Group

Demographic Data	n	%
Gender		
Females	35	85.4
Males	6	14.6
Marital		
Single	41	100.0
Married	-	-
Education		
Literate	1	2.4
Secondary education	2	4.9
High school	13	31.7
Licence	25	61.0
Residential area		
Rural	4	9.8
Town	5	12.2
City	32	78.0
Economical situation		
Low	4	9.8
Middle	36	87.8
High	1	2.4
Occupation		
Housewife	1	2.4
Student	30	73.2
Officer	1	2.4
Employee	1	2.4
Private occupation	5	12.3
Unemployed	3	7.3
Disease Onset Age		
Under 18 years old	24	58.5
Between 18 and 25	17	41.5

Table 2. Changes in Serum Lipid Values at the Beginning of Treatment and at the Third Month Values

		Mean ± SD	Difference	P
TC	Baseline	152.24 ± 27.34	10.88	.010*
	Third month	163.12 ± 36.73		
TG	Baseline	97.97 ± 48.47	7.46	.148
	Third month	105.43 ± 51.08		
LDL	Baseline	83.90 ± 23.20	8.80	.022*
	Third month	92.70 ± 33.66		
HDL	Baseline	49.34 ± 8.85	-4.1	.000*
	Third month	45.24 ± 7.26		

HDL, high-density lipoprotein cholesterol; LDL, low-density lipoproteins; TC, total cholesterol; TG, triglycerides. Paired-samples *t*-test. * $P < .05$. Bold values: $P < 0.05$ were considered significant.

$P=.022$, $P < .001$, respectively). However, there was no statistically significant difference between the baseline and third month TG levels ($P=.148$) (Table 2).

Paired-samples *t*-test was conducted to determine the statistical significances between the baseline and third month BA, BD, BSS, and BPRS findings. The findings revealed a statistically significant difference between the baseline and third month anxiety levels ($P=.001$). The baseline BA scale score ($\bar{x}=8.39 \pm 7.67$) increased by an average of $\bar{x}=2.70$ on the third month ($\bar{x}=11.09 \pm 7.77$). Thus, although both the baseline and third month anxiety scores were at “mild anxiety” levels, an increase was observed in the total scale score after the treatment. A statistically significant difference was observed between the baseline and third month depression scores ($P=.016$). The baseline BD scale score ($\bar{x}=8.73 \pm 8.19$) increased by an average of $\bar{x}=0.61$ after the treatment on the third month ($\bar{x}=9.34 \pm 8.05$). Thus, an increase was observed in the depression scale score on the third month after the treatment when compared to the baseline score (Table 3).

Although there were increases in suicidal ideation scale and BPRS scores after the treatment, the increase was not statistically significant ($P > .05$) (Table 3).

The most significant findings of the current study included the correlation between the changes in BA, BD, BSS, and BPRS scale scores and the TC, TG, LDL, and HDL levels on the third month after the treatment.

When the relationship between pre- and post-treatment blood lipid levels and depression was examined, no significant correlation was found between pre- and post-treatment BD and BA scores and blood lipid levels ($P > .05$). However significant correlations were determined between posttreatment BSS scores and TC, TG, and LDL values. Accordingly, a weak negative correlation was detected between BSS and TC ($r=-0.247$; $P=.020$), a weak negative correlation with TG ($r=-0.186$; $P=.045$), and a weak negative relationship with LDL ($r=-0.289$; $P=.017$). Also, significant correlations were determined

Table 3 Differences Between the Measurements of the Psychiatry Inventories at the Beginning of Treatment and at 3 Months

		Mean ± SD	Difference	P
BA	Baseline	8.39 ± 7.67	2.70	.001*
	Third month	11.09 ± 7.77		
BD	Baseline	8.73 ± 8.19	0.61	.016*
	Third month	9.34 ± 8.05		
BSS	Baseline	3.80 ± 4.16	0.51	.103
	Third month	4.31 ± 4.34		
BPRS	Baseline	12.53 ± 11.69	0.61	.352
	Third month	13.14 ± 11.88		

BA, Beck anxiety; BD, Beck depression; BPRS, Brief Psychiatric Rating Scale; BSS, Beck Suicidal Ideation Scale. Paired-samples *t*-test. **P* < .05. Bold values: *P* < 0.05 were considered significant.

between pretreatment BSS scores and TC, TG, and LDL values. Accordingly, a weak negative correlation was detected between BSS and TC (*r* = -0.154; *P* = .036), a weak negative correlation with TG (*r* = -0.135; *P* = .042), and a weak negative relationship with LDL (*r* = -0.254; *P* = .017).

No statistically significant correlation was determined between ΔBA and parametric changes (*P* > .05). Similarly, no statistically significant relationship was identified between ΔBD and parametric changes (*P* > .05) (Table 4).

Statistically significant correlations were determined between ΔBSS and ΔTC, ΔTG, and ΔLDL parameters. Thus, there was a weak negative correlation between ΔBSS and ΔTC (*r* = -0.403; *P* = .009), a moderate negative correlation between ΔBSS and ΔTG (*r* = -0.526; *P* < .001), and a weak negative correlation between ΔBSS and ΔLDL (*r* = -0.421; *P* = .006) (Table 4).

Statistically significant correlations were identified between ΔBPRS and ΔLDL and ΔTC parameters. There was a weak positive correlation between ΔBPRS and ΔTC parameters (*r* = 0.401; *P* = .009), and a weak positive correlation between ΔBPRS and ΔLDL parameters (*r* = 0.467; *P* = .002).

DISCUSSION

The principal finding of the present study was the correlation between psychiatric symptoms, especially

Table 4 Relationship Between Psychiatric Inventories Scores and Serum Lipid Parameters

		ΔBA	ΔBD	ΔBSS	ΔBPRS	ΔTC	ΔTG	ΔLDL	ΔHDL
ΔBA	<i>r</i>	1.000							
	<i>P</i>								
	<i>n</i>	41							
ΔBD	<i>r</i>	.493*	1.000						
	<i>P</i>	.001							
	<i>n</i>	41	41						
ΔBSS	<i>r</i>	.079	.157	1.000					
	<i>p</i>	.622	.326	.					
	<i>n</i>	41	41	41					
ΔBPRS	<i>r</i>	.500*	.276	-.250	1.000				
	<i>P</i>	.001	.080	.116	.				
	<i>n</i>	41	41	41	41				
ΔTC	<i>r</i>	.114	.041	-.403*	.401*	1.000			
	<i>P</i>	.476	.799	.009	.009				
	<i>n</i>	41	41	41	41	41			
ΔTG	<i>r</i>	-.200	-.203	-.526*	.166	.476*	1.000		
	<i>P</i>	.209	.204	.000	.300	.002	.		
	<i>n</i>	41	41	41	41	41	41		
ΔLDL	<i>r</i>	.205	.098	-.421*	.467*	.922*	.349*	1.000	
	<i>P</i>	.199	.541	.006	.002	.000	.025	.	
	<i>n</i>	41	41	41	41	41	41	41	
ΔHDL	<i>r</i>	-.131	-.045	.073	.160	.475*	.016	.311*	1.000
	<i>P</i>	.413	.779	.651	.319	.002	.922	.048	.
	<i>n</i>	41	41	41	41	41	41	41	41

BA, Beck anxiety; BD, Beck depression; BPRS, Brief Psychiatric Rating Scale; BSS, Beck Suicidal Ideation Scale; HDL, high-density lipoproteins; LDL, low-density lipoproteins; TC, total cholesterol; TG, triglycerides. Pearson correlation coefficient. **P* < .05.

suicidal ideation, and low serum lipid levels (TC, TG, and LDL). Also, a statistically significant difference was observed between the baseline and third month BD and BA scores. Furthermore, although increases were observed in BSS and BPRS scores after the treatment, these increases were not statistically significant.

Several studies have investigated the factors that could increase the suicide risk in patients under ITT treatment.^{8,9,13,14,33} Certain studies reported that several factors such as female gender, previous psychiatric treatment, psychiatric treatment history in the family, absence of supportive factors, and ethnicity increased the risk of suicide. There was no clear consensus on the impact of any factor, and controversial results were reported in the literature. Singer et al³⁴ reported in a retrospective study based on FDA reports that depressive side effects accounted for 42.3% of the psychiatric adverse effects associated with ITT treatment. Monthly mental check-ups of psychiatric side effects, which are mostly observed in the 10-19 age group (52.5%), were recommended by the authors. Certain studies demonstrated that depression and suicidal ideation induced by ITT could be related to BDNF (brain-derived neurotrophic factor) and folic acid treatment, and dose reduction could be beneficial.⁷

The determination of the correlation between ITT and psychiatric symptoms is problematic due to several factors such as exclusion of patients with a psychiatric disease anamnesis in the studies, similar to the present study, the fact that research has been conducted by both psychiatrists and dermatologists, lack of double-blind studies due to the skin dryness adverse effect of ITT, and preference of ITT in severe acne cases with psychiatric symptoms.⁹ Thus, several controversial findings have been reported on the psychiatric side effects of ITT.^{8,9,13}

Although Brenner et al¹¹ reported that there was a strong correlation between ITT use and psychiatric side effects based on the psychiatric literature, several dermatological studies could not evidence this correlation and reported that ITT had a therapeutic effect on psychiatric symptoms.^{9,35} Although increases were observed in depression and anxiety scores after treatment in the current study, the increases were not significant in suicidal ideation and BPRS scores. This could suggest that factors other than depression could also affect suicidal ideation. Thus, serum lipid levels, which were associated with impulsivity and suicidal ideation, could be considered.

Retrospective studies on ITT treatment reported a possible correlation between ITT and depression, while prospective studies emphasized that there was no evidence on development of depression.^{8,9,13} In the current study, an increase was observed in the depression scale scores on the third month after the treatment when compared to baseline. However, it should be noted that this increase was lower than the anxiety scores.

One of the most frequently detected laboratory abnormalities during ITT treatment is hyperlipidemia.^{6,36} This rate is reversed when treatment is terminated. Certain studies reported that 50% of the patients had elevated TG and 30% had elevated cholesterol levels.³⁷ Due to the correlation between serum lipid levels and psychiatric disorders and suicide, it could be suggested that the changes in lipid levels observed during ITT treatment could be associated with psychiatric symptoms.

Certain studies emphasized the association between serum lipid levels and impulsivity, depression, or suicide attempts. In previous studies conducted by our group, it was determined that low serum leptin, ghrelin, and cholesterol levels could be associated with impulsive and suicidal behavior, and even violent suicide attempts in individuals with schizophrenia²⁵ and those who committed suicide.^{25,26,38} Two meta-analyses on the correlations between serum lipid levels and suicide markers^{39,40} were published recently. Wu et al³⁹ emphasized that individuals with suicidal tendencies and psychiatric patients exhibited lower total serum cholesterol and TG levels. However, Bartoli et al⁴⁰ reported that the correlation was controversial and could be significant in patients with a history of psychiatric disease. Although the focus has been on suicidal behavior and low serum cholesterol levels, other publications emphasized that this correlation was controversial.⁴¹ Although clarifying this relationship seems to be difficult, when considering the importance of cholesterol on neuron membranes, decreased cholesterol might be affecting neurotransmitter levels related to depression, resulting in depressive symptoms and impulsivity. Perhaps, routine lipid screening could not be justified in the evaluation of suicide risk; however, it could be beneficial to consider the lipid profile in routine controls in acne patients treated with ITT with a significant suicide risk.

The correlation between suicide, a global public health problem, and anxiety and susceptibility to anxiety is well known.⁴² In a previous meta-analysis, susceptibility to anxiety and its subscales were associated with suicide risk and ideation.⁴² Furthermore, depression symptoms are not the sole predictors of suicide attempts. However, focusing only on depression symptoms as a predictor of suicide in patients under ITT treatment could lead to the neglect of suicide risk. The current study findings demonstrated that anxiety symptoms increased more than depressive symptoms in patients treated with ITT, and this increase was associated with suicidal ideation. Thus, anxiety symptoms should be considered and followed up as well as depression when monitoring the psychological symptoms and suicidal risk in patients under ITT treatment.

The correlation between psychiatric symptoms and ITT is clear. However, a successful ITT treatment in severe acne could also improve psychiatric symptoms. The

analysis of depressive symptoms and suicidal ideation, which are significant concerns for dermatologists in ITT treatment, could with a multidisciplinary approach that would include a psychiatrist in the early period, and consideration of routine blood lipid level follow-up could resolve this issue.

Suicidal behavior is quite complex and multidimensional. The contradicting findings reported by studies on the correlation between ITT and suicidal behavior could be induced by this complexity. To date, it has been suggested that the best way for clinicians to evaluate suicide risk is to screen for suicide histories in the anamnesis of the patients and their families.¹⁹ It could be suggested that this method is still valid for patients under ITT treatment. The relative protective effect of hyperlipidemia and the potential benefits of optimizing lipid levels could be beneficial for clinicians in monitoring psychiatric symptoms during ITT treatment. Thus, there is still a need for further parameters that could be employed as biomarkers.

The other view about the development of psychiatric symptoms, namely vulnerability, is an interesting approach since individual cases differ in the development psychiatric symptoms, complicating the situation. These have been explained with genetic traits and a history of psychiatric treatment in the patient and the family. However, no previous study has investigated the correlations between individual differences, biomarker data, or serum lipid levels.

The correlation between psychiatric symptoms and ITT is still debated. Serum lipid levels are affected during ITT treatment. The correlation between the onset and exacerbation of psychiatric diseases and serum lipid levels has been studied in several studies. This is the first in the literature where the correlation between the significant psychiatric adverse effects of ITT treatment and serum lipid levels in acne patients is studied.

Limitations

First, suicide attempts could be measured; however, recognition of suicidal ideation is only possible with scales, which may not always lead to accurate results. Second, although we only included metabolically healthy individuals in the study, it was not possible to completely exclude the effects of other biological factors that affected lipid serum levels. Finally, lipid subclasses could play different roles in suicide risk; however, we routinely checked lipid parameters in the current study. Thus, it should be accepted that we could not exclude all clinical and complex psychosocial models that could affect the correlation between serum lipid levels and suicide attempts.

Thus, the most significant issue for the clinicians is to decide in which patients and in which cases psychiatric assistance is required or treatment of ITT should

be discontinued. For this purpose, parameters that can be measured precisely are required. Especially individuals with a history of psychiatric treatment and genetic burden are the most important group for lipid optimization.²⁰ As mentioned above, suicidal behavior is quite complex and multidimensional, with contradicting results reported by studies on the correlation between ITT and suicidal behavior. To date, it seems the best way for clinicians to evaluate suicide risk is to screen for suicide histories in the anamnesis of the patients and their families. But, this should not be the only way to detect the risk, when we consider that serum lipid levels that have been associated with suicidal ideation, depression, and several psychiatric diseases have the potential to be an important indicator. In this context, our preliminary results open the doors to a new perspective in this regard, using the concept of blood lipid optimization. These findings need to be considered preliminary and supported by large samples.

Ethics Committee Approval: This study was approved by Ethics Committee of Firat University (Approval No: 04-03/18, Date: February 15, 2018).

Informed Consent: Informed consent form was obtained from the all participants who agreed to take part in the study.

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