TFK

Journal of Medical Clinics
Tıp Fakültesi Klinikleri Dergisi

Mart / March **2026**, **9 (1)**
Başvuru / Received: 18.10.2025
Kabul / Accepted: 11.12.2025

https://dergipark.org.tr/tr/pub/atk
https://tipfakultesiklinikleri.aydin.edu.tr

ARAŞTIRMA MAKALESİ **RESEARCH ARTICLE**

Comparison of the Effectiveness of Diet on the Systemic Immune-Inflammation Index in the Treatment of Acne Vulgaris With Isotretinoin

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Abstract

Aim: Acne vulgaris is a systemic inflammatory disease. The consumption of milk and dairy products is considered a triggering factor in the etiopathogenesis of the disease. However, there is also evidence that milk and dairy products may reduce systemic inflammation. The systemic inflammatory development of isotretinoin, which is effectively used in the treatment of acne vulgaris, is controversial. The change in inflammation parameters during isotretinoin treatment with the use of milk and dairy products, which are triggers for acne, will facilitate understanding the effect of diet on the treatment of acne vulgaris.

Materials and Methods: Sixty patients receiving systemic isotretinoin treatment for acne vulgaris were included in the study, and 30 patients were given a diet low in milk and dairy products in addition to their treatment.

Results: When the values of all patients before treatment and at the 3rd month of treatment were examined, a decrease in neutrophil and lymphocyte counts and NLR, and an increase in platelet count and SII were observed, but these changes were not statistically significant. When intergroup changes were examined, no differences were observed in neutrophil, lymphocyte, and platelet counts or in SII and NLR values.

Conclusion: A diet low in milk and dairy products has no effect on neutrophil, lymphocyte, and platelet counts or on SII and NLR values during the treatment of acne vulgaris.

Keywords: *Diet, Milk, NLR, SII*

J Med Clin, 2026; 9(1): 1-5.

Akne Vulgarisin İzotretinoin ile Tedavisinde Diyetin Sistemik İmmün-İnflamasyon İndeksi Üzerine Etkinliğinin Karşılaştırılması

Özet

Amaç: Akne vulgaris sistemik inflamatuar bir hastalıktır. Hastalığın etyopatogenezinde süt ve süt ürünlerinin kullanılması tetikleyici bir faktör olarak görülmektedir. Bununla birlikte süt ve süt ürünlerinin sistemik inflamasyonu azaltabileceğine dair veriler de bulunmaktadır. Akne vulgarisin tedavinde etkin olarak kullanılan isotretinoinin sistemik inflamatuar etkileri tartışmalıdır. Akne tetikleyicisi olan süt ve süt ürünlerinin kullanımı ile isotretinoin tedavisi sırasındaki inflamasyon parametrelerinin değişimi diyetin akne vulgaris tedavisi üzerine etkisini anlamayı kolaylaştıracaktır.

Gereç ve Yöntem: Çalışmaya akne vulgaris nedeni ile sistemik isotretinoin tedavisi alan 60 hasta dahil edilip 30 hastaya tedavilerine ek olarak süt ve süt ürünlerinden fakir diyet verilmiştir.

Bulgular: Tüm hastaların tedavi öncesinde ve tedavinin 3. aydındaki değerleri incelendiğinde nötrofil ve lenfosit sayısının, NLR'nın azaldığı, trombosit sayısının ve Sİİ'nin arttığı izlendi ancak bu değişiklikler istatistiksel olarak anlamlı değildi. Gruplar arası değişiklikler incelendiğinde nötrofil, lenfosit, trombosit sayılarında ve SII, NLR değerlerinde farklılık izlenmedi.

Sonuç: Süt ve süt ürünlerinden fakir beslenmenin akne vulgaris tedavisi sırasında nötrofil, lenfosit, trombosit sayılarında ve SII, NLR değerlerine etkisi bulunamamaktadır.

Anahtar Kelimeler: *Diyet, NLR, SII, Süt*

TFK, 2026; 9(1): 1-5.

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INTRODUCTION

Acne vulgaris is a multifactorial and systemic chronic inflammatory disease whose fundamental steps are excessive sebum secretion, abnormal follicular hyperkeratinization, inflammation, and bacterial colonization (1). Along with hormonal and genetic factors, dietary content is an important factor in the development of acne. It has been observed that diet can alter sebum secretion and composition in the skin. Milk consumption causes an increase in insulin secretion, which stimulates the sebaceous glands. Therefore, a diet low in milk and dairy products is recommended in the treatment of acne vulgaris, a systemic inflammatory disease (2). However, the literature reports that the consumption of milk and dairy products has a weak anti-inflammatory effect (3).

Isotretinoin (13 cis-retinoic acid) is a vitamin A derivative that is effectively used in the treatment of moderate to severe acne vulgaris (4). Although systemic isotretinoin therapy is often well tolerated, it is associated with side effects such as xerosis, cheilitis, conjunctivitis, dyslipidemia, and hepatotoxicity (5). In addition to these side effects, isotretinoin may also increase systemic inflammation (6).

The systemic immune inflammatory index (SII) is a simple, easily accessible, inexpensive biomarker of inflammation calculated using complete blood count parameters. It is calculated as peripheral blood platelet count x neutrophil count/lymphocyte count (P x N/L) (7). The SII has been reported to be associated with disease activity in dermatological diseases, including psoriasis, acne vulgaris, and Behçet's disease (8). This study aimed to investigate the effect of isotretinoin, used in the treatment of acne vulgaris, and milk consumption on inflammation.

MATERIALS AND METHODS

The study population consisted of 60 volunteers aged 18-65 who were selected for the study, received 0.3mg/kg oral isotretinoin treatment, and continued treatment for at least 3 months. were voluntarily selected for the study, were aged 18-65 years, received 0.3 mg/kg oral isotretinoin treatment (low doses of isotretinoin were given because the patients could not tolerate the dryness of their skin), and continued treatment for at least 3 months. Compliance with dietary rules regarding the use of milk and dairy products among patients was monitored through verbal communication. Those who were breastfeeding or pregnant, those aged 18 years, and those with additional diseases associated with systemic inflammation (diabetes, hypertension, psoriasis, lichen planus, etc.) were excluded from the study. The patients were divided into two groups: 30 patients received only isotretinoin treatment, and 30 patients received isotretinoin treatment along with a restricted diet of milk and dairy products. The groups were named Group 1 and Group 2 within themselves;

Group 1: Patients with acne vulgaris received a 3-month course of oral isotretinoin treatment (0.3mg/kg/day) along with a restricted, low glycemic load diet of milk and dairy products.
Group 2: Patients with acne vulgaris received only a 3-month course of oral isotretinoin treatment (0.3mg/kg/day).

Blood samples and biochemical test results obtained from patients for treatment were recorded at the time of application, at the 1st month of treatment, and at the 3rd month of treatment. The SII (neutrophil x platelet/lymphocyte) value was recorded from the hemogram values of the groups.

Statistical analyses were performed using the R 4.3.1 (R Core Team, 2023) program. The normality of the variables was examined using histogram graphs. Descriptive analyses were presented using mean, standard deviation or median (Q1-Q3), frequency, and percentage statistics. The chi-square test was used for the analysis of categorical variables, the t-test for the analysis of numerical variables, and mixed effects models. Least squares means were used for post hoc comparisons. Results with $P<0.05$ were considered statistically significant.

This study was approved by the Sağlık Bakanlığı Türkiye İlaç ve Tıbbi Cihaz Kurumu Ethics Committee on 08/03/2023 with project number 2023/1051.

RESULTS

The study included a total of 60 patients, comprising 6 males and 54 females, who were diagnosed with acne vulgaris and received oral isotretinoin treatment. The patients' ages ranged from 18 to 65 years, with a mean age of 26.10±6.12. When the values of all patients before treatment and at the 3rd month of treatment were examined, a decrease in neutrophil and lymphocyte counts, and an increase in platelet count, NLR and SII were observed, but these changes were not statistically significant (Table 1). No difference was found in neutrophil, lymphocyte, and platelet counts, or in SII and NLR values at the third month of treatment between the groups following and not following a milk and dairy product diet (Table 2).

Table 1. Changes in neutrophil, platelet, lymphocyte, NLR, and SII counts in all patients before and after treatment

	Before treatment	The 3rd month of treatment	p
Neutrophil count	4,56±1,89	4,52±1,70	0,884
Platelet count	281,45±66,04	288,41±73,99	0,274
Lymphocyte count	2,62±0,73	2,57±0,99	0,692
NLR	1,86±0,97	1,89±0,79	0,852
SII	523,10±290,12	541,03±258,94	0,629

Table 2. Changes in neutrophil, platelet, lymphocyte, NLR, and SII levels in all patients before and after treatment between groups

	Group 1	Group 2	p
SII before treatment	**475,72±260,94**	570,49±**313,85**	0,208
SII in the 3rd month of treatment	**502,18±230,96**	**579,87±282,75**	0,248
Neutrophil count in the 3rd month of treatment	**4,14±1,69**	**4,90±1,65**	0,756
Platelet count in the 3rd month of treatment	**296,43±58,96**	**280,40±86,77**	0,406
Lymphocyte count in the 3rd month of treatment	**2,48±0,46**	**2,67±1,33**	0,467
NLR In the 3rd month of treatment	**1,70±0,70**	**2,07±0,85**	0,072

Group 1: Those who follow a milk and dairy product diet during systemic isotretinoin treatment
Group 2: Those who do not follow a special diet during systemic isotretinoin treatment

DISCUSSION

This study evaluated the effect of a restricted diet of milk and dairy products on SII in patients receiving oral isotretinoin treatment for acne vulgaris.

Markers obtained from complete blood counts, which are indicators of systemic inflammation during isotretinoin treatment, have been previously investigated. The effect of isotretinoin on inflammation and MPV and NLR values in patients using isotretinoin were examined at the beginning of treatment and at 3 months, and no significant changes were found. However, a significant increase in platelet count was determined at the 3rd month (9). Demirbaş et al. reported that platelet, lymphocyte, and neutrophil levels decreased with treatment in their study of patients with acne vulgaris who received isotretinoin therapy.(10) In our study, there was an increase in the mean platelet count in both groups at the end of 3 months, but it was not statistically significant.

There are a limited number of studies investigating the effect of isotretinoin on SII. In one study, neutrophil counts and SII levels in patients with moderate-to-severe acne vulgaris prior to isotretinoin treatment were found to be significantly higher than in healthy controls.

After three months of isotretinoin treatment, neutrophil counts and SII in 43 acne vulgaris patients became similar to those in healthy controls (11). Zorlu et al. found that SII decreased with isotretinoin treatment in their study evaluating 361 patients with acne vulgaris (12). In our study, unlike the literature, we observed that isotretinoin treatment did not reduce SII. This may be due to our small sample size and the use of low-dose isotretinoin.

Some studies have shown that milk consumption may contribute to the formation of acne lesions. Although milk has a low glycemic index, it is known to affect the development of acne vulgaris by increasing IGF-1 levels. IGF-1 levels in patients with acne vulgaris have been found to be significantly higher than in healthy individuals (13). Milk contains growth factors and anabolic steroids that support growth in dairy-fed calves. This factor indicates that milk has a stimulating effect on acne lesions. Some hormones found in milk, such as IGF-1, 5α steroid, and α-lactalbumin, are thought to affect the pilosebaceous unit (14).

The relationship between the consumption of milk and dairy products and inflammation is contradictory; in addition to its anti-inflammatory effect, it has also been reported to be associated with inflammatory diseases (15). To our knowledge, there is no study in the literature comparing the effects of a restricted diet of milk and dairy products, which cause inflammation, with isotretinoin therapy used in the treatment of acne vulgaris on SII. Our study is the first to compare in detail the effects of a diet restricted in milk and dairy products, which cause inflammation, with those of isotretinoin therapy on SII.

Our study has certain limitations. These include the large number of female participants and the limited follow-up periods and the use of low-dose isotretinoin.

In our study, although the neutrophil count and SII values of our patients with acne vulgaris in the group on a restricted diet of milk and dairy products during isotretinoin treatment were lower at the end of the third month compared to before treatment, this was not statistically significant. This finding may be due to the small sample size and short follow-up period. In conclusion, although a diet low in milk and dairy products may have an anti-inflammatory effect during isotretinoin treatment, our findings are not statistically significant. Long-term data with a larger sample size is needed.

Author's contributions: Conceptualization: HG, FÖ, İÖ; Writing: HG, İÖ, FÖ; Review: ZISG, RÖK; Editing: ZISG, RÖK; Proofreading: FÖ, ZISG, RÖK

Conflict of interest: The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. All authors have read and approved the final version of the manuscript.

Ethics approval: This study was approved by the Sağlık Bakanlığı Türkiye İlaç ve Tıbbi Cihaz Kurumu Ethics Committee on 08/03/2023 with project number 2023/1051. The study was designed in accordance with the principles of the Declaration of Helsinki.

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