Original paper

The Impact of Isotretinoin on Platelet and White Blood Cell Count in Patients with Acne Vulgaris

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Abstract

Background: Acne is a multifactorial inflammatory disorder and represents a spectrum range from a pair of blackheads and pustules to severe nodulocystic fulminant acne. The severity of the disease differs from patient to patient; therefore, For the treatment of acne, isotretinoin is frequently utilized. Isotretinoin, however, may cause triglyceride and cholesterol levels in the blood to rise and may interfere with liver function tests. Also, the impact of isotretinoin on hematological parameters is still debatable and is examined by looking at alterations to the blood chemistry profile and haematological parameters of acne patients who are on isotretinoin. This study was aimed to show the effect of Isotretinoin on WBC and platelet count in a patient with acne vulgaris.

Methods: This comparative study was conducted in a Clinic at the Department of Dermatology in two hospitals, Salahaddin hospital and the general hospital, in Tikrit city, Iraq. One hundred sixteen patients were selected. Patients suffer from acne and are divided equally (58 patients each) into one of the two treatment regimens (Isotretinoin and doxycycline). Group one was given oral Isotretinoin 0.5mg/kg divided twice daily for six months, and Group two was given doxycycline 100 mg twice daily for the same period.

Results: Among the 116 cases included in the study, (36) were male, and (80) were female. The mean age of group one was 21.97±4.87 years, and in group two, it was 21.72±4.95years. The mean platelet counts increased, whereas the white blood cell count decreased after isotretinoin treatment. But without any statically significant association.

Conclusions: This study's results revealed no statistically significant effect of white blood cells and platelet count after therapy by Isotretinoin.

Keywords: Acne, Isotretinoin, white blood cells and platelet.

Introduction

Acne vulgaris (AV) is a common chronic inflammatory disorder of the pilosebaceous unit. It is a polymorphic disorder characterized by forming comedones that are (whiteheads) or (blackheads), papules, pustules, nodules, and pseudocysts. In some cases, it is accompanied by scarring. Usually appears on the face, forehead, chest, shoulders and upper back. [(1)].

Acne is a condition that affects the adolescents commonly and is usually resolved by the mid-twenties, and it is of multifactorial etiology. Acne can present as non-inflammatory lesions, inflammatory lesions, or a mixture of both [(2)]

Healthy skin appears to have some natural self-disinfecting mechanisms that are responsible for the disappearance of living organisms implanted in it. The skin flora consists mainly of an Aerobic and aerobic bacterium; diphtheria is classified nowadays in the genus Propionibacterium [(3)]. Healthy skin carries many these diphtheroids.

It is concluded that Propionibacterium acnes outnumbers the aerobic flora by (10-100) folds, mostly in areas where there are large sebaceous follicles.

The only treatment for acne vulgaris that addresses all key etiological variables is isotretinoin. It affects cell-cycle development, cellular differentiation, cell survival, and apoptosis to accomplish this astounding efficacy. It has anti-inflammatory characteristics, considerably reduces sebum production, impacts

comedogenesis, lowers surface and ductal P. acnes, and influences comedogenesis [4].

Within six weeks, sebum production is drastically reduced by 90% at a dose of 0.5–1.0 mg/kg/day. Isotretinoin, unlike tretinoin (all-trans retinoic acid), has little to no affinity for cellular retinol-binding proteins or retinoic acid nuclear receptors (RARs and RXRs). It can, however, function as a pro-drug that is internally transformed into compounds that are nuclear receptor agonists for RAR and RXR. [5].

When isotretinoin is used, it might result in aberrant modifications to hematological parameters such leukopenia, neutropenia, thrombocytopenia, thrombocytosis, and neutropenia. [6]

Hematological parameter changes are typically not notable in terms of frequency or severity. Patients with a clinical suspicion of an abnormality have been recommended to have their white blood cell count and platelet count monitored while taking isotretinoin. [6]

Furthermore, the use of isotretinoin has been linked to serious medical disorders like severe thrombocytopenia. For maximum safety, it is advised to acquire a complete blood count before and throughout isotretinoin treatment. It is questionable, though, whether hematological guidelines should be followed throughout isotretinoin therapy. There is disagreement over how frequently to check the total blood count when taking isotretinoin. [7]

At least five different biologically active isotretinoin metabolites have been identified, including all-trans-RA (tretinoin), all-trans-4-oxo-retinoic acid (4-oxo-tretinoin), 9-cis retinoic acid, and 9-cis-4-oxo-retinoic acid. Studies looking at sebum excretion rates in people with severe acne have indicated that, compared to the same dose of oral isotretinoin over 4 weeks, 4-oxo-isotretinoin only results in a 70% mean reduction in sebum excretion after 4 weeks. Moreover, isotretinoin is more effective at reducing sebum than both 9-cis and all-trans retinoic acids [4].

Patients and method

A Comparative Study of treatment acne by isotretinoin with other patients treated by systematic antibiotics. The study was carried out from October 2019 to March 2020. The total sample of this study was included 116 patients (acne vulgaris), who were selected by non-random sampling method according to specific criteria that were included in the study as a convenience sample and divided into two groups:

- Group one: 58 Patients with (acne vulgaris) were diagnosed by a dermatologist in the hospital's dermatology department and treated with 0,5 mg/kg isotretinoin divided dose daily for 7 months.
- Group two: 58 patients attending the same hospital as group one has (acne vulgaris) without previous history of treatment by isotretinoin but treated with doxycycline 100 mg twice daily. Those participants match group one in gender and age (± 5 years).

Inclusion criteria Patients aged 13 to 35 years suffering from moderate to severe acne vulgaris and without any systematic treatment for the previous three months.

Exclusion criteria:

Patients treated with any type of systemic antibiotics and oral retinoids within three months prior to the study, patients treated with any topical medication such as adapalene and tazarotene within one month prior to the study, patients not willing to participate, pregnant women and nursing mothers, patients treated with any type of systemic antibiotics and oral retinoids within three months prior to the study, and patients with the systemic disease (stomach, liver, pancreas disease).

A structured questionnaire for data collection includes the full history, age, weight, height, duration of the disease, occupation, aggravating factors, relieving factors, past medical history, family history, drug history, type of food, site of lesions (mainly the face) with the close physical examination which dermatologists did to evaluate the severity of acne. A detailed history, cutaneous examination, and baseline follow-up investigations (WBC and platelet count) related to isotretinoin and doxycycline use were all done in the hospital laboratory. These patients were prepared before the time of the study, consent was taken from the patients, and they were followed up during the treatment period. According to females, pregnancy is prevented by two contraceptive methods. Both groups are investigated with the same investigations.

Laboratory Tests: Lipid profile, serum cholesterol, Platelet count, WBC count, Liver transaminase test (SGOT, SGPT), and a pregnancy test were done at the hospital's laboratory.

Results

In this study, 116 patients with acne vulgaris were included: 80 (69%) females and 36 (31%) males. The total sample was divided into two groups. Each one included 58 patients of acne vulgaris, group 1 treated with isotretinoin, and patients group 2 treated with doxycycline. Regarding platelet count, the result of the study showed no difference among study groups at the beginning (mean is 266) and without statically significant (p=0.934), while the platelet count after one month was more among group one than group two (mean 269.14 and 264.33 respectively), and without statically significant difference (p=0.574). Also, the platelet counts after three months and seven months. The result showed no statically significant association (p= 0.806 and 0.393), as shown in Table 1

Table 1. correlation between platelet count and study groups

Platelet count	group	N	Mean±SD	P value
Before treatment	1	58	266.00±48.735	0.934[NS]
	2	58	266.72±50.530	
After 1 month	1	58	269.14±41.041	0.574[NS]
	2	58	264.33±50.408	
After 3 months	1	58	269.28±36.777	0.806[NS]
	2	58	267.28±49.743	
After 7 months	1	58	274.02±34.976	0.393[NS]
	2	58	267.48±46.336	
T-test was *: significant at p ≤ 0.01 N: number of cases; SD: standard deviation; S: significant; NS= Non significant				

Regarding WBC count, the result of the study showed no difference among study groups at the beginning (mean count 8.36 and 8.45) and without statically significant (p=0.924), while the WBC count after one month was more among group one than group two (mean 7.64 and 7.64 respectively), and without statically significant difference (p=0.145). Also, the WBC counts after 3 months and 7 months. The result showed no statically significant association (p= 0.063 and 0.891), as shown in Table 2.

Table 2. correlation between white blood cell count and study groups (V:value at each visit).

WBC	*groups*	*N*	*Mean±SD*	*P value*
V0	*1*	*58*	*8.36±1.491*	*0.924*
	2	*58*	*8.45±7.271*	
V1	*1*	*58*	*8.17±1.211*	*0.145*
	2	*58*	*7.64±2.487*	
V2	*1*	*58*	*8.04±1.253*	*0.063*
	2	*58*	*7.42±2.099*	
V3	*1*	*58*	*8.20±1.026*	*0.891*
	2	*58*	*8.33±7.122*	
T-test was *: significant at p ≤ 0.01 N: number of cases; SD: standard deviation; S: significant; NS= Non significant				

Regarding the treatment side effect, the study showed that the most common side effect was lip dryness (22.4%) and gastric pain (12.1%). In the current study, the distribution of side effects according to groups showed no statistically significant association (p= 0.278), as shown in Table 3.

Table 3. Distribution of study sample according to side effect of treatment

Variable	Groups	Groups 1	Groups 2	Total	P value
side effect	epistaxis	4	1	5	0.278[NS] df=7 x^2= 8.670a
	gastric pain	6	7	13	
	headache	2	3	5	
	Lip dryness	16	10	26	
	mood change	5	5	10	
	nausea	2	3	5	
	non	23	29	52	
Total		58	58	116	
Pearson Chi-Square, significant at p ≤ 0.05 N: number of cases; S: significant; NS= Non significant					

The result of the present study shows an increase in the level of SGPT and S. cholesterol after one month in group 1, while the other group who received isotretion had no changes in the result, as showed in Table 4.

Table 4. Distribution of study sample according to laboratory test. (n=58)

laboratory test	No.	Mean
$SGOT_0$	58	16
$SGOT_1$	58	18
$SGPT_0$	58	36.4
$SGPT_1$	58	98
TG_0	58	100
TG_1	58	65
$SCHOL_0$	58	165
$SCHOL_1$	58	270

Discussion

It has been reported that isotretinoin has particularly played a role in causing thrombocytopenia, thrombocytosis, agranulocytosis, and leukopenia by affecting hematological parameters [8,9]. In the present study, orally administered ISO to patients with acne vulgaris resulted in increased hemogram parameters involving thrombocyte and PCT levels and decreased leukocyte and neutrophil levels. And without any statically significant association.

In the literature, ISO has been shown to have various and contradictory effects on platelet count and volume. For example, Karadag et al. reported only a

moderate increase in the platelet levels of 70 patients in their study. No, variation in the other hematological parameters (Hb, Hct, MPV, and WBC) per ISO therapy [10].

On the other hand, Retinoic acid promotes the synthesis of hematopoietic progenito, the hematovascular system's progenitor; it is derived from human embryonic stem cells [11]. In the present study, increased levels of platelets after the fourth month of the treatment were detected. Michaelson et al. reported significantly decreased levels of leukocyte and neutrophil in patients using ISO for acne. Similarly, Friedman et al. reported a case where leukopenia and neutropenia were associated with ISO therapy [12].

During isotretinoin medication, Lee et al. evaluated the laboratory alterations in patients with acne vulgaris. The WBC count was statistically significantly lower when isotretinoin was used. Unfortunately, due to a lack of information, analyses of hemoglobin, hematocrit, and PLT counts were not possible [13].

According to Ataseven et al., MPV and PLT numbers decreased dramatically during isotretinoin therapy [14]. Moreover, Gencoglan et al. assessed hematological variables while treating acne vulgaris with isotretinoin. WBC count and neutrophils fell throughout the first month, rose during the second month, then fell once more at the conclusion of the therapy. The first month of treatment saw an increase in platelet count, followed by a decrease. MCV rose with therapy [15].

Inflammatory indicators and hematological parameters were studied by Seckin et al. in relation to the effects of isotretinoin. Three months after starting isotretinoin therapy, hemoglobin levels and platelet counts doubled, and the width of the distribution of red blood cells dramatically shrank. In addition, isotretinoin raised the rate of platelet lymphocytes while decreasing the rate of neutrophil lymphocytes. Although not statistically significant, these changes still occurred [16].

Similar to this, Ataseven et al. observed no significant variations in neutrophil count, lymphocyte count, or neutrophil/lymphocyte ratio in acne vulgaris patients who received isotretinoin. [17].

In present study showed that the most common side effect was lip dryness (22.4%), and after that was gastric pain (12.1%) and followed by headache. These results are similar to a study reported by Alison. L et al. who confirmed that the treatment by isotretinoin has a wide range of side effects, nonetheless, the majority are predictable and infrequently interfere with the patient care. The typical mucocutaneous adverse effects are dosage-dependent and can be managed with dose adjustment, extra symptomatic therapy, or both. Teenagers frequently have mood fluctuations, including depression. This has also been observed in isotretinoin-treated acne patients. Two studies examined incidental side effect reports to the FDA in the USA. [18].

For acne patients exposed to oral isotretinoin, a more recent controlled case cross-over research found a relative risk for depression of 2.68 (95% CI = 1.03 to 3.89) [19].

The mucocutaneous adverse effects are dose-dependent and are typically manageable by using lip balms and moisturizers on a regular basis. Other systemic adverse effects, such as headache, are typically successfully managed by dose reduction and concurrent use of aspirin or non-steroidal anti-inflammatory medicines (NSAIDs). [20].

Conclusion

There is no effect of isotretinoin on platelet, and white blood cells count in patients with acne vulgaris. Treatment of acne vulgaris with isotretinoin is safe. There are slight changes in white blood cell and platelet count in the isotretinoin therapy group compared to those treated with antibiotics.

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