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Original Research Article

EFFECTS OF ISOTRETINOIN ON PLATELET COUNT AND MEAN PLATELET VOLUME DURING TREATMENT OF ACNE VULGARIS

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Abstract: *The most effective systemic therapy for acne is Isotretinoin. However, Isotretinoin has many side effects, including known side effects like dryness, palmoplantar exfoliation, rash, teratogenicity, raised intraocular pressure, and deranged liver functions and lipid profile. Its lesser-known side effects include its effects on platelet count and mean platelet volume (M.P.V.). This Quasi-experimental case series was conducted to observe the change in platelet count and mean platelet volume in patients taking Isotretinoin for acne vulgaris, attending the dermatology outpatient department at Jinnah Hospital Lahore from May 10th 2016 to November 9th 2016. After ethical committee approval and informed consent, subjects of acne vulgaris with an indication for Isotretinoin were included in the study from O.P.D. Relevant demographic and clinical details were recorded in a standardized predesigned proforma. Citrated blood samples were taken under aseptic conditions. Baseline platelet counts and mean platelet volume were determined using an auto-analyzer in the pathology laboratory of Jinnah hospital Lahore. All the patients were advised to take daily Isotretinoin at a dose of 0.5 mg/kg for 12 weeks. Platelet counts and mean platelet volume were again measured after twelve weeks after the start of treatment. A total of 100 patients completed the study. The age of the patients ranged from 18 to 60 years with a mean + sd age of 27.26+5.88 years. Out of these 41%(n=41) were male and 59%(n=59) were females. The severity of acne was measured using Global Acne Grading System (G.A.G.S.). It was recorded that 62%(n=62) had moderate, 22%(n=22) had severe while 16%(n=16) had very severe acne vulgaris. The mean pre-treatment platelet count was 271273+9139 c/µL, while 259192+11717 c/µL was post-treatment. The mean difference was 12080+8140 c/µL, and the p-value was 0.001. The mean platelet volume was 10.63+1.01 fl as pre-treatment and 9.77+1.01 fl as post-treatment. The mean difference was 0.85+0.04 fl, and the p-value was 0.001. We concluded that Isotretinoin decreases platelet count and means platelet volume in patients receiving isotretinoin treatment for acne vulgaris.*

Keywords: Acne vulgaris, Isotretinoin, change in mean platelet count, mean platelet volume.

Introduction

Acne is one of the most common skin problems, and even though it does not cause physical disability, it can cause significant psychological morbidity (Albuquerque et al., 2014; Borovaya et al., 2013; Simonart, 2012; Williams et al., 2012). Acne treatments aim to prevent follicular hyperproliferation, increased sebum production, Propionibacterium acnes proliferation, and inflammation (Simonart, 2012; Williams et al., 2012). Isotretinoin, commonly known as (Karadag et al., 2013) cis-retinoic acid, has been used successfully to treat severe intractable nodular acne since the 1980s. Oral Isotretinoin works against the inflammatory and bacterial processes that contribute to the development of acne vulgaris. The therapy causes the sebaceous glands to shrink, significantly reducing the amount of sebum released. P. acnes, a sebum-dependent bacteria that play a significant role in the inflammation associated with acne vulgaris, is suppressed when sebum production is reduced. When taken orally, Isotretinoin prevents formation by stimulating keratinocyte differentiation and normalizing desquamation (Ataseven and Ugur Bilgin, 2014; Borovaya et al., 2013; Simonart, 2012).

Even though systemic retinoids are very effective medications, they are linked with a significant risk of major side effects. The most common forms of adverse reactions that may occur when using this

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medicine are mucocutaneous (dryness, palmoplantar exfoliation, rash, and dermatitis), gastrointestinal (inflammatory bowel sickness), and ocular illnesses (conjunctivitis, dry eyes) (Laroche et al., 2007). Besides these side effects, Isotretinoin has been linked to various test anomalies (Vieira et al., 2012). In a 2014 study published by Arzu Ataseven and Aynur Ugur Bilgin, they investigated the effects of Isotretinoin on platelet count and mean platelet volume in acne vulgaris patients. The study's subjects had moderate to severe acne and were administered an isotretinoin dose ranging from 0.5 to 1 mg/Kg for three months. The laboratory findings for hemoglobin (Hb), hematocrit (Hct), platelet count (P.L.T.), mean platelet volume (M.P.V.), and total leucocyte count (T.L.C.) were recorded before and three months after the study's completion. Following isotretinoin therapy, it was revealed that both the number of platelets and the mean platelet volume had significantly decreased (Ataseven and Ugur Bilgin, 2014). The difference in mean platelet count was 11880 $\pm$ 2997 (c/L) (p=0.019), whereas the difference in mean platelet volume was 0.85 ± 0.07. (p=0.001). Because the fall in platelet counts and mean platelet volume happened simultaneously, it was inferred that the effect of Isotretinoin was through bone marrow suppression (Ataseven and Ugur Bilgin, 2014).

After three months of treatment with Isotretinoin, a Caucasian lady who was 27 years old and had been diagnosed with acne experienced acute thrombocytopenia and high levels of transaminases, according to a case report written by Moeller KE and Toumasc. The generally asymptomatic patient reported that they were suffering from rectal bleeding. Her platelet count was 44000 c/L after 3.5 months of treatment with Isotretinoin at a dose of 60 mg per day. Before treatment, her platelet count was average (Moeller and Touma, 2003). In a different study by Lee T. Zane and colleagues on analyzing laboratory abnormalities that occurred during isotretinoin therapy for acne vulgaris, significant increases in the cumulative incidence of abnormalities were seen in serum lipids and transaminase levels during isotretinoin treatment. Still, they did not occur in hematological parameters. This was in comparison to the baseline values. Platelet count was evaluated in 7959 patients, of whom platelet counts were within the normal range in 98.6 percent of cases, low in 0.41 percent of cases, and high in 1.00 percent of cases (Zane et al., 2006).

My research is based on the idea that even though systemic retinoids are potent drugs, they could still harm the body because of how they interact with them. They can cause significant problems with the blood and more common problems that can be treated and fixed, like problems with the mucocutaneous, gastrointestinal, and ophthalmic systems. So far as I know, we couldn't find any articles in the Pakistani medical literature that looked at the effects of Isotretinoin on platelet counts or M.P.V. levels in people taking it to treat acne vulgaris. The goal of this study is to look into the M.P.V. levels and platelet counts of people who are being treated for acne vulgaris with Isotretinoin. This will tell us how to keep track of the baseline platelet count and mean platelet volume, and we'll look at it again three months after the treatment has started. When giving Isotretinoin, it will also be helpful to know that thrombocytopenia can cause effects that could be life-threatening.

Methods

This Quasi-experimental case series study was conducted at the Dermatology outpatient department, Jinnah hospital, Lahore, from May 10th 2016, to November 9th 2016. The sample size was estimated as 100 patients with a 95% confidence level, d=0.02, and taking expected mean ± S.D. of mean change in platelet volume, i.e., 0.85 ± 0.07 in patients receiving isotretinoin treatment for acne vulgaris. . Diagnosed cases of acne vulgaris according to operational definition, having G.A.G.s score of above 18 (moderate, severe and very severe acne), both males and females, aged 18-60 years were included in this study through consecutive nonprobability sampling.

Patients had contraindications to the use of Isotretinoin determined by history (e.g., pregnancy, hypersensitivity to Isotretinoin); patients with clinical splenomegaly, diabetes, chronic liver disease, congestive cardiac failure, and myocardial infarction determined by history and those patients taking aspirin or any other antiplatelet medications, determined by history were excluded from the study.

After ethical committee approval and informed consent, subjects of acne vulgaris with an indication for Isotretinoin were included in the study from O.P.D. Relevant demographic and clinical details were recorded in proforma. Citrated blood sample from each patient was taken under aseptic conditions and sent to the pathology lab at Jinnah hospital Lahore. In the laboratory, baseline platelet counts and mean platelet volume were determined using an auto-analyzer. All the patients were advised to take daily Isotretinoin at a dose of 0.5 mg/kg for 12 weeks. Platelet counts and mean platelet volume were again measured after twelve weeks after the start of treatment. All the information was recorded in a structured proforma. The mean change in platelet count and volume was measured per operational definitions.

The data collected was entered and analyzed in the S.P.S.S. version 17. Mean with standard deviation was calculated for quantitative variables like age, pre

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and post-treatment platelet count, and platelet volume. Frequency and percentages were calculated in the case of categorical variables like Gender and severity of acne. Paired sample t-test was used to determine the significant difference in mean change in platelet counts and mean change in platelet volume at the end of 12 weeks of treatment. The data were stratified for age, Gender, and severity. Post-stratification paired sample t-test was applied. A p-value <.05 was taken as significant.

Results

A total of 100 cases fulfilling the inclusion criteria were enrolled to determine the effects of Isotretinoin in terms of mean change in platelet count and mean platelet volume in patients receiving Isotretinoin.

The age range of the patients included in the study was 18-60 years. Mean + sd age was calculated as 27.26+5.88 years. (Figure No. 1). Age distribution of the patients showed that 69 % (n=69) were between 18-30 years of age while 31 % (n=31) were between 31-60 years of age.

Gender distribution shows that 41 % (n=41) were male and 59 % (n=59) were females. (Figure No. 2).

Frequency of severity of acne was recorded as 62 % (n=62) had moderate, 22 % (n=22) had severe, while 16 % (n=16) had v. severe acne vulgaris. (Figure No. 3)

The mean pre-treatment platelet count was 271273±9139 c/µL while 259192±11717 c/µL post-treatment. The mean difference was 12080±8140 c/µL, and the p-value was 0.001. The mean platelet volume was 10.63±1.01 fl pre-treatment and 9.77±1.01 fl post-treatment. The mean difference was 0.85±0.04 fl, and the p-value was 0.001. (Table No. 1). The data was stratified for age, Gender, and severity of acne. Post-stratification paired sample t-test was applied. There was a significant difference across age, Gender, and severity of acne (p-value <.05).(TableNo.2)

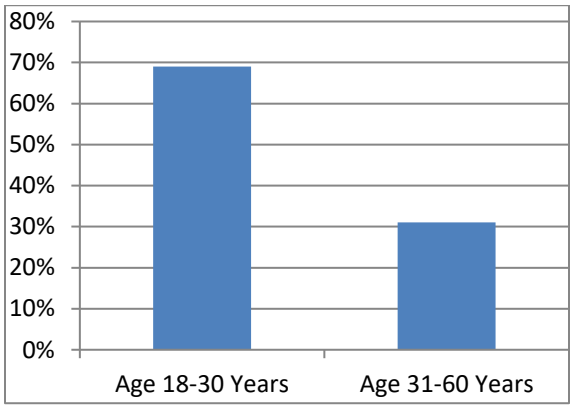

Figure 1 Distribution of age groups

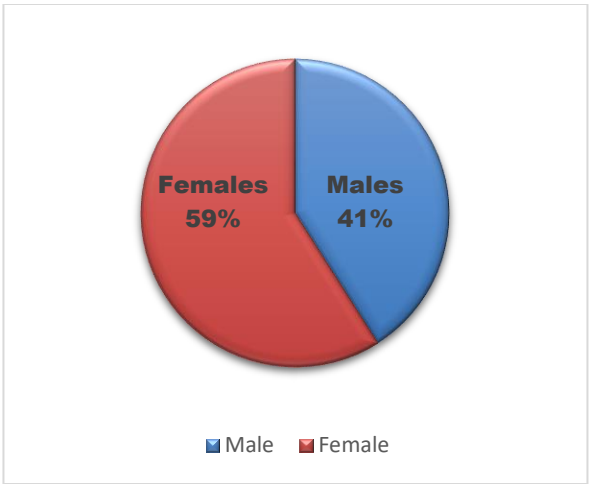

Figure 2 Distribution of gender

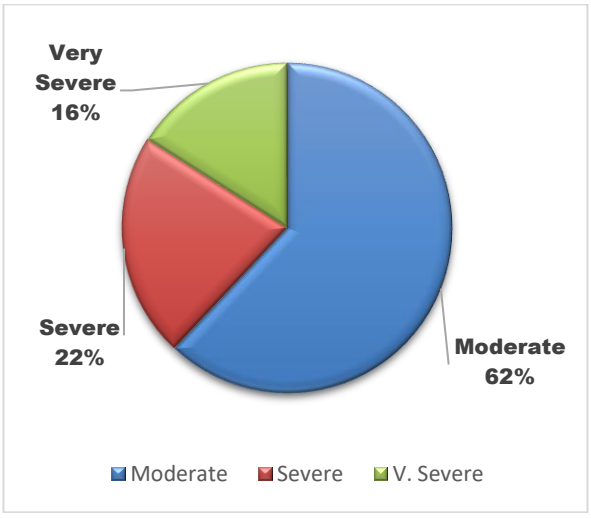

Figure 3 Distribution of patients according to the severity of acne

Discussion

Acne vulgaris, if treated effectively, can avoid scarring on both the emotional and physical levels. The treatment plan will change depending on the severity of the illness. When it comes to comedonal acne, topical treatments are typically sufficient, but when it comes to inflammatory acne, oral treatments are typically required in addition to topical treatments. Systemic antibiotics are the most common medication prescribed and have a history of producing excellent results. When treating moderate to severe acne, systemic retinoids, particularly Isotretinoin, have proven to be the most successful systemic therapies.

Along with its usefulness, it comes with a host of undesirable effects. Other than teratogenicity, the most severe side effect, its most prevalent, acceptable, and reversible adverse effects are difficulties with the gastrointestinal tract, the mucocutaneous system, and the eyes.

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Table 1 Mean pre- and post-platelet count and platelet volume

Platelet count/platelet volume	Pre-treatment		Post-treatment		Mean difference		P value
	Mean	SD	Mean	SD	Mean	SD	
Platelet count	271273	9139	259192	11717	12080	8140	0.001
Platelet volume	10.63	1.01	9.77	1.01	0.85	0.04	0.001

Table 2 Stratification of data according to age groups, Gender, and severity

variables	Construct	Platelet count/platelet volume	Pre-treatment		Post-treatment		Mean difference		P value
			Mean	SD	Mean	SD	Mean	SD	
Age	18-30 years	Platelet count	271173	9346	258702	12866	12470	9759	0.0001
		Platelet volume	10.59	1.00	9.74	1.00	0.85	0.04	0.001
	31-60 years	Platelet count	271496	8807	260283	8723	11213	1280	0.01
		Platelet volume	10.71	1.03	9.85	1.05	0.85	0.04	0.01
Gender	Male	Platelet count	273083	9036	259511	14858	13571	12556	0.001
		Platelet volume	10.59	0.99	9.73	1.00	0.86	0.04	0.001
	Female	Platelet count	270015	9074	258971	9054	11044	1305	0.001
		Platelet volume	10.66	1.02	9.80	1.03	0.85	0.04	0.001
Severity	Moderate	Platelet count	271000	9284	258311	13033	12688	10266	0.001
		Platelet volume	10.69	1.03	9.84	1.04	0.85	0.05	0.000
	Severe	Platelet count	274137	67103	262906	64466	11231	3069	0.001
		Platelet volume	10.81	2.81	9.95	2.61	0.87	0.21	0.001
	Very severe	Platelet count	269959	8615	258974	8638	10985	1375	0.001
		Platelet volume	10.32	0.90	9.45	0.89	0.86	0.04	0.01

Rarely can it induce significant hematologic derangements, such as a drop in platelet count, anemia, or a reduction in the number of white blood cells in the blood. The current study sought to learn more about the effects of systemic Isotretinoin on platelet count and mean platelet volume in our participant population. We could not locate any study papers in the Pakistani medical literature that evaluated the platelet counts and M.P.V. levels of individuals receiving Isotretinoin for treating acne

vulgaris. Patients receiving Isotretinoin at a dose of 0.5 mg/kg for acne vulgaris had their M.P.V. levels, platelet counts checked at the start of the study, and then they were reevaluated after 3 months of treatment. In our study, which included 100 patients, platelet counts before and after treatment were examined, and the results revealed a mean difference of 12080 + 8140 c/L. Similarly, the difference in M.P.V. before and after treatment was 0.85+0.04 fl. The p values for both differences suggested that they were statistically significant. Because the fall in platelet counts and mean platelet volume happened simultaneously, it was inferred that the effect of Isotretinoin was through bone marrow suppression.

When we compared our findings to those of a prior study, we discovered that the difference in mean platelet count between before and after treatment was 118802997 (c/L) ($p < 0.019$), and the change in mean platelet volume was 0.850.07 ($p < 0.001$).

(Ataseven and Ugur Bilgin, 2014) Our research produced findings that were consistent with these findings.

After three months of therapy with Isotretinoin, a white lady who was 27 years old was reported to have had acute thrombocytopenia and high levels of transaminases; according to a case report by Moeller KE and Toumasc, the generally asymptomatic patient reported that they were suffering from rectal bleeding. Her platelet count was 44000 c/L after 3.5 months of treatment with Isotretinoin at a dose of 60 mg per day. Before treatment, her platelet count was average (Moeller and Touma, 2003). Even though their platelet counts dropped, none of our patients experienced bleeding complications due to the treatment.

However, the findings of a few other studies are not consistent with these findings. In their investigation into the laboratory findings of 94 individuals, Bruno and colleagues could not identify any evidence of any hematological abnormalities. 73 Platelet counts were found to be within the normal range in 98.6 percent of patients, decreased in 0.41 percent of patients, and high in 1.00 percent of patients in another study that was conducted by Lee T. Zane and colleagues on the analysis of laboratory abnormalities during isotretinoin therapy for acne vulgaris (Zane et al., 2006).

Another 2013 study discovered that 10% of all patients (n = 253) had increased platelet counts.

74 According to another case report submitted by Jansen and Altmeyer, one patient taking Isotretinoin developed thrombocytosis. 75 However, isotretinoin-induced thrombocytosis can be produced by the influence that IL-6 has on platelet formation, and it is considered that the action of Isotretinoin on platelets is not understood.

Our investigation and reference study showed no significant differences when we compared the changes in platelet count and mean platelet volume between the various age groups. These findings were consistent with the findings of our reference study.

(Ataseven and Ugur Bilgin, 2014) Similarly, there was no significant difference in the results between the various genders and the severity of acne, and these results were also equivalent to the findings of our reference study. The primary drawback of our study is that only a limited number of patients who presented to the Outpatient Department at Jinnah Hospital in Lahore participated in our research.

Taking into account the findings of our research and the studies mentioned above, we believe that there is a mixture of data available; nonetheless, our findings indicate a considerable drop in both the platelet count and the mean platelet volume. In addition, we kept in mind that the findings we obtained are preliminary and need to be confirmed by the findings of other regional research. While it is helpful for us to be aware of the potentially life-threatening effects of thrombocytopenia while administering Isotretinoin, it is equally helpful for us to be aware of the potential benefits of this condition. It could be helpful to establish some standards for monitoring the platelet count and mean platelet volume at baseline and then reevaluate the situation after three months of administering medication.

Conclusion

We concluded that patients taking Isotretinoin for acne vulgaris experience a drop in platelet counts and mean platelet volume. Since the mean platelet volume and platelet counts both declined concurrently, it was determined that Isotretinoin's impact was due to the suppression of bone marrow.

Conflict of interest

The authors declared absence of conflict of interest.

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