

Does isotretinoin (ISO) Therapy Increase Coagulation Tendency? Evaluation of MPV values and MPV / platelet rate

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ABSTRACT

Introduction/ Purpose: Mean Platelet Volume (MPV), an indicator of platelet activation, is a new risk factor for atherothrombosis and an important marker for the increase in thromboembolic diseases. MPV/ platelet ratio is considered as a risk factor for various diseases such as myocardial infarction. In this study, we aimed to investigate the possible effect of ISO on blood cell counts especially MPV and MPV/ platelet ratio.

Materials and Methods: 75 patients, between the ages of 18-25 with moderate or severe acne vulgaris and using oral isotretinoin (0.5 mg/ kg) were included in the study. Platelet count and MPV values of patients (pre-treatment and 3 months after the treatment) were recorded retrospectively.

Results: The mean age of patients was 23.32 ± 3.44 years. 40 patients were female and 35 were male. MPV levels and MPV/ p ratio of "before treatment period" were significantly higher than the "after treatment period" ($p < 0.001$).

Conclusion: In the literature, alteration in platelet levels under ISO treatment is a controversial issue. Furthermore, it was emphasized that, ISO treatment may be change platelet functions. In our study, MPV values and MPV / p ratio were decreased after ISO treatment. Our data indicates that, the thromboembolic risk of patients with acne vulgaris may reduce after ISO treatment.

Keywords: Acne vulgaris, Isotretinoin, MPV, Platelet, Thromboembolism risk

INTRODUCTION

Acne vulgaris is a chronic inflammatory condition which develops in the pilosebaceous units(1). Isotretinoin (ISO) is an agent and developed for the treatment of severe nodular acne. Long-term remission rates were reported with ISO. ISO treatment requires clinical and laboratory monitoring due to its potential significant adverse events such as visual disturbances, teratogenicity, depression, pancreatitis and hepatotoxicity(3,4). In several case reports ISO was reported as associated with thrombocytopenia, agranulocytosis and leukopenia(4,5). Beside this, in a previous study no abnormalities were found in hemoglobin, white blood cell and platelet counts and the researchers suggested that there is no need to measure these parameters in patients treated with ISO(6). Hematologic adverse effects are uncommon with ISO; however thrombocytopenia can be a serious side effect(6). In the literature, 4 cases of transient thrombocytopenia were reported before(6-9). In this study, we aimed to investigate the possible effects of ISO on MPV values and MPV/ platelet ratio and to determine the coagulation tendency.

MATERIALS AND METHODS

75 patients between the ages of 18-25 with moderate or severe acne vulgaris and using ISO (0.5 mg / kg) were included in the study. We retrospectively reviewed the medical records of patients who received ISO treated for 3 months or more and their laboratory tests which were performed in Afyon Kocatepe University Hospital

from December 2012 to September 2013. Liver function tests, lipid profile, platelet and MPV values of patients (pre-treatment and 3 months after the treatment) were received from the recorded data of the patients. Patients with acute infections, hematologic disorders, smokers or those already undergoing anticoagulant or antiplatelet treatment were excluded. MPV and plt was measured in peripheral blood samples at rutin tests during therapy. MPV and platelet count were analyzed with an Advia 2120 (Siemens Healthcare Diagnostics Inc., Tarrytown, NY, USA) in EDTA within two hours after blood sampling.

Data were analyzed with SPSS version 20 (SPSS Inc, Chicago, IL, USA). To identify the normal distribution, the Kolmogorov-Smirnov test was applied. Student t-test or Mann-Whitney U-test was used where appropriate to compare the differences in laboratory values before treatment and 3 months after the treatment. Statistical significance was assumed for $p < 0.05$.

RESULTS

Of 75 patients, 40 (53.3%) were female and 35 (46.7%) were male. The mean age of the patients were 23.32 ± 3.44 years. Laboratory data of the patients were outlined in Table I.

While MPV values of the patients before treatment were 10.21 ± 3.44 , 3 months after the treatment MPV values were 8.61 ± 1.01 . MPV values of the patients before treatment and 3 months after the treatment showed a statistically significant decrease (Table II)

($p < 0.001$). In addition, while pretreatment mean MPV/platelet ratio was 0.04, posttreatment mean MPV/platelet ratio was 0.03. MPV/platelet ratio was found statistically significant decreased ($p < 0.001$).

Table 1: Laboratory data of the patients

	Pretreatment Mean	Posttreatment Mean	P values
Ast	18.08±4.05	22.2±6.02	0.028
Alt	14.38±6.03	19.05±10.23	0.001
TG	95.56±48.11	123.44±68.88	0.000
HDL	52.22±10.2	48.01±10.50	0.000
LDL	92.45±25.31	111.90±27.32	0.000
VLDL	19.23±9.52	25.65±13.75	0.000

*Data were expressed as mean ± standard deviation

TG: Triglycerides, **HDL:** High density lipoprotein, **LDL:** low-density lipoprotein, **VLDL:** very low-density lipoprotein.

Table 2: Performed prior to and 3 months or more after oral isotretinoin treatment in the results of their laboratory tests values

	Pretreatment mean	Posttreatment mean	P values
MPV*	10.21±3.44	8.61±1.01	$p < 0.001$
Plt*	251.92±55.13	255.86±58.11	>0.05
MPV/Plt	0.04	0.03	$p < 0.001$

*Data were expressed as mean ± standard deviation

MPV: Mean platelet volume **Plt:** platelet

DISCUSSION

ISO is a valuable treatment for a variety of skin conditions including acne vulgaris, rosacea and seborrheic dermatitis. Moreover, it was suggested that ISO treatment reduces the risk of acne relapse in the few studies. The major limiting factor for ISO is its potential adverse effects. Teratogenicity is one of the most significant adverse effects(9,10).

Routine laboratory tests control during ISO treatment has been a subject of debate(5-9). Although there are several studies evaluating lipid profile and liver function tests pre-treatment and post-treatment, it is noteworthy that there is little published knowledge in the literature evaluating the blood count parameters(11,12). The liver function tests and lipid profile of our patients were similar with previous studies.

While it was reported that ISO treatment has no or a little effect on complete blood count parameters in the previous studies, many case reports demonstrated some differences in platelet number. A recent study supported these findings(6-9). In a study by Karadag et al. platelet, MPV, hemoglobin, hematocrit and white blood cell counts were evaluated before and after ISO treatment and a statistically significant decrease was found only in platelet number(13). Kaptanoglu et al. did not find any significant differences in INR and PT values and reported that ISO treatment has no risk for

increase in coagulation(14). Ataseven et al. found that both platelet counts and the mean platelet volume were significantly decreased following the treatment(15).

The association of MPV with several inflammatory diseases has been demonstrated(16,17). Beside this, MPV has a clinical importance in thromboembolic diseases. MPV was found as an important predictor of mortality in acute myocardial infarction and early death in acute pulmonary thromboembolism(18). High MPV shows increased platelet size. MPV and platelet count have usually inverse relationship(19,20). Therefore, an increased MPV/P ratio shows increased MPV and low platelet count status. Increased MPV may be associated with accelerated blood coagulation and low platelet count may also indicate activated coagulation system. Large platelets secrete biologically active substance such as thromboxane A₂, platelet factor 4, thromboglobulin, adenosine triphosphate more than small ones(21-24).

In a study by Gulcan et al. a significant increase in MPV was reported in patients with deep vein thrombosis (DVT) and Cil et al. found MPV as an independent predictor in hospitalized DVT patients(25,26).

In the previous dermatological studies, MPV values were evaluated in chronic urticaria, bullous pemphigoid, psoriasis, recurrent aphthous stomatitis and Behçet's disease(17,27-29). In the same manner, in patients with COPD and in children with chronic idiopathic urticaria significant results were found(30).

Although oral retinoids have been claimed to affect the coagulation process, the mechanism remains still unclear. Prolonged thrombocytopenia with the dose of 60 mg/d of ISO has been reported(5). Several cases of cerebrovascular and thromboembolic events have also been described with high-dose ISO therapy(5,31,32).

MPV and MPV/P ratio may be considered meaningful laboratory markers for the risk of thromboembolism. Actually, MPV/P ratio may have more diagnostic value than MPV alone(21). In our study, decreased MPV values and MPV/P ratio were found in patients with acne vulgaris and using ISO.

As a conclusion in the literature, alteration in platelet levels under ISO treatment is a controversial issue. The activating effect of ISO on megakaryocytes is known(13) 12. Although it was emphasized that platelet functions may also change with ISO treatment; in the previous studies, these data is limited with only a few cases. In our study, MPV values and MPV/ p ratio were decreased after ISO treatment. Our data, indicates that, the risk of patients with acne vulgaris which have thromboembolic process may reduce after ISO treatment.

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