Laboratory Tests Need for Plasma Lipids and Liver Enzymes During Oral Isotretioin Treatment

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ABSTRACT Acne is a chronic inflammatory condition of the pilosebaceous unit. Isotretinoin (ISO) is an orally active retinoic acid derivative that is usually used to treat nodulocystic and conglobate types and resistant acne. Routine laboratory tests need when treating patients with ISO is controversial. We retrospectively collected data of 172 patients who received oral ISO for the treatment of acne vulgaris at the Dermatology Clinic of our institution, and we examined biochemical parameters. When we compared pre-treatment and 3rd-month treatment values in terms of serum levels of triglyceride, total cholesterol, LDL cholesterol, AST, and ALT, these parameters were significantly higher at 3rd month. Same laboratory parameters were significantly higher at sixth-month of treatment than those at 3rd-month of treatment. Only HDL cholesterol was significantly lower at third-month of treatment compared with pre-treatment and was lower at sixth-month of the treatment than those at third-month of treatment. However, there was no statistical difference between third-month of treatment and sixth-month of treatment in terms of these all studied parameters.

KEYWORDS Isotretinoin, Plasma Lipids, Liver Enzymes

Introduction

Acne is a chronic inflammatory condition of the pilosebaceous unit. Isotretinoin is an orally active retinoic acid derivative that is usually used to treat nodulocystic and conglobate types and resistant acne. ISO is the only drug effective in all of the pathogenic factors in acne.[1] In many patients, complete and prolonged remission of disease is achieved by a single course of 15-20 weeks.[2]

Teratogenicity is the most critical side effect of ISO. It may cause clinical side effects and laboratory changes also. The most common mucocutaneous side effects include cracked lips, dryness of the skin and nasal mucosa, redness of the skin, eye irritation and deterioration of the acne [3] Poor tolerance to contact lenses, increased S. aureus infection and photophobia are ocular side effects. Less common side effects are, arthralgias, hair loss, fatigue, weakness, and headache, hepatotoxicity, pseudotumor cerebri, acute pancreatitis, hearing and vision impairment, inflammatory bowel disease, hyperostosis, prematüre epiphyseal closure and depression.[2,4,5]

ISO use may also cause an increase in serum levels of liver enzymes (liver aminotransferases) and lipids like triglyceride, total cholesterol and low-density lipoprotein (LDL) cholesterol levels and reduction in levels of high-density lipoprotein (HDL) cholesterol.[1] We retrospectively examined biochemical parameters of serum lipids and serum liver enzymes in acne patients.

Methods

We retrospectively collected data of 172 patients who were admitted to Dermatology Outpatient Clinic of Sakarya University, Training and Research Hospital, The patients with moderate to severe acne vulgaris who received 0.5 mg–1 mg/kg of ISO therapy were included in the study and were retrospectively evaluated. Patients who had a disease or receiving drug therapy that would affect their parameters and patients younger than 15 years of age and older than 45 years of age were excluded from the study. All patients had serum triglyceride, total cholesterol, LDL, HDL, AST, and ALT levels at the time of pretreatment and third month of treatment evaluations. On the other hand, only 94 patients had all studied laboratory parameters at 6th-month evaluation.

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Table 1

	Pre-treatment (mean±SD)	Third month of treatment (mean±SD)	Sixth month of treatment (mean±SD)
Triglycerides	86.4±43.4	115.1±58.9	117.5±72.3
T cholesterol	160.5±32.7	177.1±36.9	183.7±40.1
LDL cholesterol	92.4±28.5	111.0±33.5	114.3±32.6
HDL cholesterol	52.8±12.3	49.0±11.5	48.1±10.7
AST	17.2±4.0	20.1±6.1	21.7±10.7
ALT	14.1±6.1	14.8±8.1	17.8±14.9

Table 2

	Pre-treatment - Third month p value	Pre-treatment - Sixth month p value	Third month - Six month p value
Triglycerides	<0.001	<0.001	0.768
T cholesterol	<0.001	<0.001	0.840
LDL cholesterol	<0.001	<0.001	0.485
HDL cholesterol	<0.001	<0.001	0.182
AST	<0.001	<0.001	0.793
ALT	0.320	0.122	0.299

Results

The mean age of all patients was 22.2±5.6 years (16-68 years). One hundred eighteen patients (68.6%) were female. The mean age of female and male patients was 22.5±4.2, and 20.4±7.5 years, respectively.

When we compared pre-treatment and 3rd-month treatment values in terms of serum levels of triglyceride, total cholesterol, LDL cholesterol, AST, and ALT, these parameters were significantly higher at 3rd month. Same laboratory parameters were significantly higher at sixth-month of treatment than those at 3rd-month of treatment. Only HDL cholesterol was significantly lower at third-month of treatment compared with pre-treatment. HDL cholesterol was lower at sixth-month of the treatment than those at third-month of treatment. However, there was no statistical difference between third-month of treatment and sixth-month of treatment in terms of these all studied parameters (Table 1,2).

Statistic

Analyses were performed using a statistical software package (IBM SPSS Statistics 20, SPSS Inc., an IBM Corp., Armonk, NY). Comparisons between the groups were performed with the Chi-square or Fisher's exact test. Analysis of normality of the continuous variables was performed with the Kolmogorov-Smirnov test. Comparisons between the continuous variables at baseline evaluation, and the third and sixth month of the therapy were performed with the Wilcoxon Signed-Ranks Test. The level of significance was $p< 0.05$.

Discussion

Routine laboratory tests need when treating patients with ISO is controversial according to studies as some of them show severe alterations in serum liver transaminase and lipid levels, but some show minimal effects. [1,6] There is a little evidence about regular biochemical monitoring of liver function and lipid profiles in patients who are treated with ISO. Lipid abnormalities are the most common laboratory abnormality seen with ISO therapy. Zane et al. study of 13,772 patients, they found increased serum lipid and transaminase levels. They suggested that these abnormalities were generally reversible and return to baseline level after two months following the end of treatment.[7] Some other studies reported similar, reversible effects of ISO on transaminase and lipid levels.[8] However, other studies report no effect on lipid and transaminase level with ISO treatment also.[9,10,11] We found serum levels of triglyceride, total cholesterol, LDL cholesterol, AST, and ALT, were significantly higher at the 3rd month and 6th month and HDL cholesterol was significantly lower at third-month and 6th month of treatment.

We agree that laboratory tests prior to the onset of therapy and after 4 weeks should be done to determine the triglyceride response to therapy 12 In this study, we included pretreatment, 3rd and 6th months values and we found increase in serum transaminase and lipid levels (triglyceride, total cholesterol, LDL) and decrease in serum HDL levels that is statistically significant at the 3rd month of treatment. We agree that ISO treatment may increase serum levels of liver enzymes, triglycerides, LDL cholesterol and reduce the level of HDL cholesterol.[1]

Previous reports have suggested that there are small changes

in plasma AST which are maximal after four weeks. It appeared to be dose-related and after four months, the values were within the normal range.[13] Liver function alteration in ISO-treated patients that leads to hepatitis has not been reported.[9]

The increase in triglyceride levels may be related to a reduction in the removal of this lipids from plasma. It also appears to be influenced by the increase in gene expression for ApoE.[1] ISO treatment may increase the risk of metabolic syndrome.[14] Pancreatitis risk during ISO therapy can be considered low. The few reported cases in the literatüre illustrate that pancreatitis is not likely caused by hypertriglyceridemia because elevations were mild to moderate.[12] However, patients with significantly high triglycerides levels should be regularly monitored, and dose adjustments made before pancreatitis occurs.[4] The patient's diet should be restricted to low fat intake and alcohol consumption. There is no correlation found between the oral dose or cumulative dose of ISO and the magnitude of the increase in triglycerides in some reports.[1] Also, no significant increase was found with treatment over long periods. However, Rodondi et al. concluded that persons who develop hypertriglyceridemia during ISO therapy for acne, are at increased risk for future hyperlipidemia and the metabolic syndrome.[15]

Lestringant et al. have stated that in ISO-treated young and healthy patients, significant variations in lipid and lipoprotein levels do not influence the cardiovascular disease risk.[11] Alterations in the lipid profile appear to be transitory, and they return to approximately baseline levels eight weeks after the end of treatment.[8] More frequent monitoring is justified for the patients that have already cardiovascular risk factor.[1]

As conclusion levels for laboratory abnormalities, particularly liver transaminase levels and serum lipids are lacking but very few patients have significantly abnormal responses to isotretinoin therapy therefore regular blood testing throughout therapy is unnecessary.[2] Some authors conclude that limited blood testing should be performed for most patients and more complete blood testing should be reserved to patients that have significant response in liver enzymes, cholesterol or triglycerides.[19,20] We also think that complete blood tests should be done to establish baseline values, and continue blood tests should be done monthly for three months and then should go on monthly ıf there are abnormal responses. If there is no abnormal response for the first three months, blood tests can be done for every two or three months as we found no statistical difference between third-month of treatment and sixth-month of treatment in terms of these parameters This manner should result in considerable savings both in patients time and in blood collection and analysis and cost-effectiveness of the drug therapy.

Competing Interests

None

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