Biochemistry- Original article

DOI: http://dx.doi.org/10.18320/JIMD/201603.02103

Journal of International Medicine and Dentistry 2016; 3(2): 103-108

JOURNAL OF INTERNATIONAL MEDICINE AND DENTISTRY

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JIMD

p-ISSN: 2454-8847

e-ISSN: 2350-045X

Study of Lipid Profile Changes in Acne Vulgaris patients on Intermittent Low Dose Isotretinoin

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Abstract:

Acne vulgaris is a common skin disease characterized by comedones, inflammatory lesions, secondary dispigmentation and scarring with a large impact on quality of life. There has been much debate as to whether liver function tests and lipids should be monitored while on therapy. The objective of the study is to evaluate the lipid profile changes in patients with moderate to severe acne on oral intermittent low dose isotretinoin therapy. Setting: Dermatology outpatient clinics, MIMS, Mandya. We included the 50 patients diagnosed with moderate to severe acne. All patients were treated with low dose isotretinoin and followed up in our outpatient clinics for 20 weeks. Patients were subjected to an interview questionnaire which included data on age, gender, previous treatment and liver enzymes. Blood analysis were repeated in the follow-up visits baseline, 4, 8,12,16, 20 weeks. Total cholesterol, triglycerides, HDL, LDL of 50 patients aged 15-40 years receiving isotretinoin for moderate to severe acne were monitored before, during and every month interval for 4 months. There was a statistically significant increase in the levels of total cholesterol, triglycerides, LDL with the decrease in the HDL level when compared with the baseline. The results in the study showed that the use of oral isotretinoin for the treatment of acne resulted in altered total cholesterol, triglycerides, LDL and HDL but the increase in the parameters is mild so as to not interrupt the treatment. Our study show that intermittent isotretinoin therapy has not much effect on the lipid profile and the adverse effects can be treated without interrupting the treatment.

Key words: Acne vulgaris, isotretinoin, lipid profile

Introduction:

Acne, a chronic inflammatory disease of pilosebaceous unit, affects seborrhoeic areas. It is characterized by the development of comedones in the form of erythematous papules, pustules,nodules or pseudocysts. Acne primarily affects adolescents and young adults, but still few individuals experience acne in later adult life.[1] Acne severely affects social and psychologic functioning though neither life threatening nor debilitating.[2] The microcomedo is the primary lesion and etiology ranges from abnormal keratinization, hormonal abnormalities and growth of *Propionibacterium acnes*. The treatment of acne has been changed over years.[3] Different treatments are being used currently, based on the acne severity, among which includes topical and oral antibiotics, hormonal compounds, tretinoin.[4] Oral isotretinoin is clearly more effective than the oral antibiotics in acne and significantly reduces the lesions.[5] Isotretinoin is chemically related to retinoid vitamin A, a fat soluble vitamin stored in high concentration in liver.[6] The exact mechanism of action of isotretinoin is still unknown. Though a safe drug, it has multiple mucocutaneous and systemic side effects and laboratory abnormalities in lipid levels that are dose related and reversible. To overcome these side effects, low dose isotretinoin has been used. Various treatment regimens have been tried nowadays. Low dose isotretinoin has been used in various doses like daily, intermittent, day therapy and so on. There are studies done to evaluate the efficacy of low dose regimens.[7,8,9] Studies have been done with conventional regimens and its

effects on lipid parameters.[10] The aim of the present study is to assess the effect on the variations of total cholesterol, triglycerides, HDL cholesterol and LDL cholesterol in patients with acne vulgaris on intermittent isotretinoin treatment.

Materials and Methods:

A total of 50 patients attending the department of Dermatology, Mandya Institute of Medical Sciences, were included in the study. The study was approved by the Institutional Ethics committee. Eligible patients included males and females aged >15yrs and older with moderate to severe acne. Children below the age of 12 years were not included in the study due to the risk of systemic toxicity. To be included in the study, all sexually active female patients of childbearing potential had to use effective contraception 1month before the onset of therapy and 3 months after the treatment.
Reason for exclusion was any other use of systemic or topical therapy for acne vulgaris, any abnormalities in the laboratory assessment at baseline, known hypersensitivity to isotretinoin, parabene in isotretinoin capsules. All patients were included after written informed consent. After recording detailed demographic data(which included age , sex, age of onset of the disease, duration of disease etc.), the patients were examined under good illumination and were finally graded into mild, moderate and severe on the basis of the severity as described below[7]

- Mild disease: Few to several papules/pustules with no nodule
- Moderate disease: several to many papules/pustules with few to several nodules
- Severe disease: Numerous and /or extensive papules/pustules with many nodules.

The baseline hematological , biochemical investigations that were carried out included haemoglobin estimation(Hb), total and differential leukocyte counts(TLC, DLC), total cholesterol, triglycerides, high density lipoprotein, low density lipoprotein. Haematological investigation was carried out using automated haematology analyser. Estimation of cholesterol was by dynamic extended stability CHOD-POD end point method with lipid clearing agent, Triglycerides by GPO-PAP end point method, HDL by immune-inhibition method, by ERBA Manheim analyzer, LDL by Friedwals's calculation.
The selected patients were assigned to receive 20mg of isotretinoin daily for 7 days in a month for 4 months. The patients were followed up every 2 weeks for the first month and subsequently every four weeks. The study evaluation visits were performed at baseline, at weeks 4, 8, 12, 16 and the end of the treatment.
Statistical analysis: The collected data was entered in the Excel sheet and the data was analysed by using SPSS, Epi-info software and the descriptive statistics Chi-square test, Anova, 't' test was applied

Results:

A total of 50 patients with the age group of 15-30yrs were included in the present study. The demographic data and severity of acne is summarized in the **Table I**.

Table I: Age, sex and grades of participants

	N(%)	Mean age	Moderate	Severe
Male	18(36%)	23.4	8	10
Female	32(64%)	19.2	18	14

The initial mean acne scores were 80.26% and 88.26% in males and females respectively. During the follow-up there was significant decrease in total acne load in both sexes.
Mucocutaneous side effects were noted in 62.5% of patients. Cheilitis was the commonest side effect noted. Other side

Table II: Grading of acne

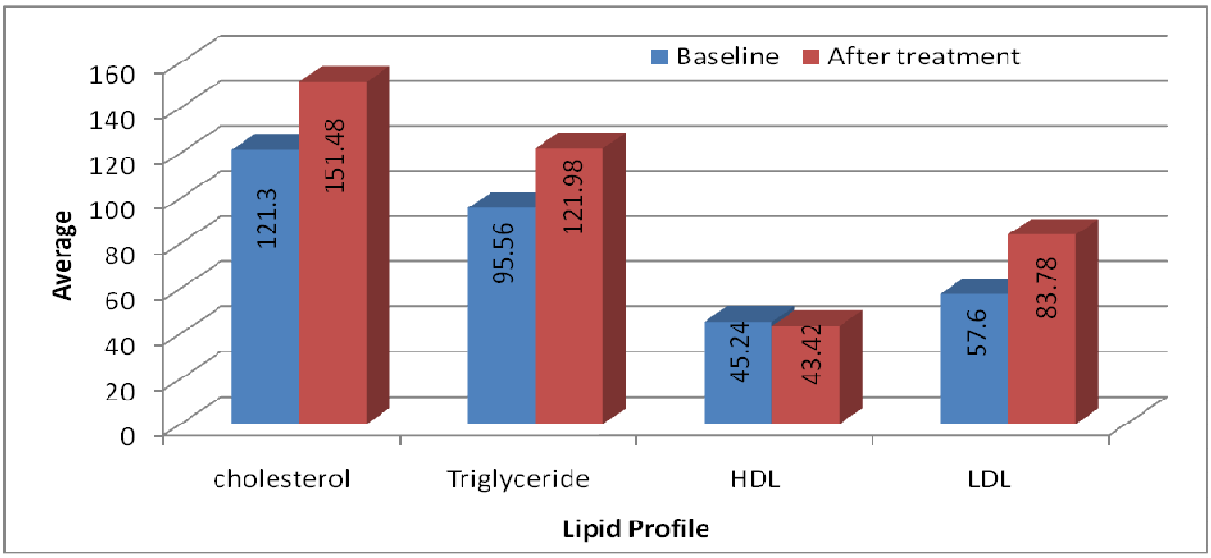
Grade of acne	Week 0	Week 4	Week 12	After 4 months
0	-	-	6%	7%
1	-	12%	80%	89%
2	40%	52%	14%	4%
3	42%	26%	-	-

Table III: Adverse events with isotretinoin

Cheilitis	18
Xerosis	7
Eye and nasal dryness	8
Hair loss	5
Menstrual irregularities	2
Irritation and redness	4

Table IV: Lipid profile before and after 4 months of intermittent isotretinoin treatment

Lipid	Baseline	After treatment	P-value
Cholesterol(Normal range:150-200mg/dl)	121.30± 34.08	151.48± 23.95	<0.0001
Triglyceride (Normal range:60-150mg/dl)	95.56± 45.23	121.98 ± 43.38	<0.0001
HDL (Normal range:30-60mg/dl)	45.24 ± 11.36	43.42 ± 10.07	<0.0001
LDL (Normal range:100-120mg/dl)	57.60 ± 29.40	83.78 ± 24.09	<0.0001



effects are less common and shown in **Table III**.

Serum cholesterol, triglycerides, HDL showed no significant changes on intermittent isotretinoin therapy. Values were elevated when compared with baseline but were within normal levels. (**Table IV**)

Cholesterol:

Measured baseline value of cholesterol in intermittent therapy group were 121.30± 34.08, then after at 4wks, 8wks , 12wks, 16wks and at the end of the treatment were 125.72 ± 33.43, 128.76 ± 29.90, 135.82 ± 27.44, 141.58 ± 25.69 and 151.48 ± 23.95 respectively. There was increase in cholesterol at all the intervals compared with baseline but within normal limit.

Triglycerides:

Measured baseline value of triglycerides in intermittent therapy group were 95.56± 45.23, then after at 4wks, 8wks , 12wks, 16wks and at the end of the treatment were 97.46 ± 43.92, 102.46 ± 43.04, 106.50± 43.78, 111.24± 43.97 and 121.98 ± 43.38 respectively. There was increase in triglycerides at all the intervals compared with baseline but within normal limits.

HDL:

Measured baseline value of HDL in intermittent therapy group were 45.24 ±

11.36, then after at 4wks, 8wks, 12wks, 16wks and at the end of the treatment were 45.46 ± 10.66 , 44.60 ± 10.91 , 45.06 ± 10.58 , 44.58 ± 9.93 and 43.42 ± 10.07 respectively. There was decrease in HDL at all the intervals compared with baseline but within normal limits.

LDL:

Measured baseline value of LDL in intermittent therapy group were 57.60 ± 29.40, then after at 4wks, 8wks, 12wks, 16wks and at the end of the treatment were 60.92 ± 28.24, 63.66 ± 27.18, 69.43 ± 25.78, 73.26 ± 23.96, 83.78 ± 24.09 respectively. There was increase in LDL at all the intervals compared with baseline but within normal limit.

Discussion:

Acne is a near universal disease. In recent years, retinoids has gained wide range clinical use. Isotretinoin has well established efficacy in dermatology. However, retinoid therapy is usually complicated by dose related side effects. Side effects like mucocutaneous toxicity and laboratory abnormalities can compromise patient compliance and necessitate dose reduction or discontinuation of therapy. Retinoid is contraindicated in women likely to become pregnant during therapy and one month after.[11] Successful acne therapy is based on the type and severity of the disease and the rationale use of available treatment options.[12] One study has shown clinical evidence that some plants can be effectively and safely used in acne and skin disease. However, chemical drugs still remains the first choice in the treatment of acne and skin infections.[13]

The main objective of the study was to evaluate the changes in lipid profile at each interval in patients on intermittent low dose isotretinoin.

The study showed that there is increase in cholesterol, triglycerides at all the intervals when compared with the baseline. But the increase is within the normal limits. The exact mechanism of action of isotretinoin on increasing cholesterol and triglycerides are still unknown. Isotretinoin possibly could interact with some essential groups in the active site of the proteins or enzymes in lipid metabolism[14,15] Other studies have reported that isotretinoin increases cholesterol and triglycerides[16], similar to our study. The laboratory abnormalities have been observed in the serum levels during and after the treatment period when compared with the baseline. The HDL levels are observed to be decreased at all the intervals when compared with baseline but within normal limits. Clear studies have not been done to know the incidence of abnormalities in serum lipid levels among patients at baseline. The effectiveness of isotretinoin in treating acne has been well documented.[17,18,19,20]

Our study demonstrated that the laboratory parameters(lipid profile) are not affected much with the intermittent isotretinoin therapy and the adverse effects were not serious and could be treated by conservative methods. Limitations such as the small sample size could affect the results validity.

Conclusion:

Our study has shown that intermittent isotretinoin therapy has not much effect on the lipid profile, and the adverse effects can be treated without interrupting the treatment. As per the data analysed in our study and also as described in the literature, isotretinoin is a safe drug. With the low dose intermittent regimen, isotretinoin is well tolerated with few laboratory side effects. The results obtained with the isotretinoin in patients with moderate to severe acne is excellent which can override the biochemical alterations.

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Conflict of interests: Nil
Source of funding: Nil

Date of submission: 11-05-2016
Date of acceptance: 16-06-2016

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