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Evaluation of Lipid profile levels in acne vulgaris on low dose isotretinoin: A prospective study

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Abstract

Aim: 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 low dose isotretinoin treatment.

Materials and Method: A total of fifty patients diagnosed having moderate to severe acne with the age group of 15-45yrs attending dermatology department, was treated with 20mg of isotretinoin daily for 4 months. Blood Samples were collected on day 0, 2nd wk, 1month, 2month, 3month and 4month.

Result: Measured baseline values of cholesterol in continuous therapy group 116.86 ± 23.55, then after at 4wks, 8wk, 12wk, 16wk and at the end of the treatment were increased above the baseline values at every interval. Significant P-value is obtained when compared with the baseline.

There was statistically significant increase in cholesterol, triglycerides, LDL at all the intervals compared with baseline and above normal limit with significant decrease in HDL levels.

Conclusion: Low dose continuous isotretinoin therapy caused increase in cholesterol, triglycerides, LDL above the normal range with grade 1 increase and decrease in HDL levels. Side effects were mild and well tolerated and did not need termination of the treatment. However it is important to educate about the consequences. We advise our specialist that the usage of low dose isotretinoin in moderate to severe acne can be done with minimal concern but close follow up is important.

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Introduction

Acne vulgaris is an extremely prevalent chronic dermatological disorder, affecting 80% of individuals at some point of life time.[1-3] Acne is accompanied with major psychological and social effects and which in turn bring about low self-image, dejection and dwindled quality of life.[4,5] Treating the cases of acne has been changed over the years. Depending on severity and type, appropriate therapeutic agents is selected. They include topical application and oral therapy. Isotretinoin, an oral retinoid and vitamin A derivative is the only medication that acts on all the pathological factors that stimulate acne.[6] Isotretinoin FDA approved drug is recommended for nodulocystic acne, not responding to conventional therapy.[7] Isotretinoin, synthetic retinoid of first generation is regarded as a major significant advance.[8] Isotretinoin, labelled drug, is used to treat severe, moderate acne cases that are resistant to other alternate therapies. Systemic isotretinoin is presently the most dynamic drug for treating severe acne forms, with long term remission rates.[9] The currently accepted conventional dose is 0.5-1mg/kg daily for 16-24wks and gives good results. It is a safe and potent drug but sometimes cause dose dependent side effects such as mucocutaneous lesions and systemic toxic effects such as hyperlipidemia. Dose dependent side effects of the conventional therapy has forced to consider alternative treatment for the betterment of patient. Many low dose treatment alternatives have been identified and formulated. In order to surpass these side effects with conventional regimen and to render regimen economical, low dose regimens for mild/moderate acne has been introduced. Isotretinoin has been in use, in various dosage prescribed daily, intermittent, day therapy so on.[10-12] In literature not many studies are done to evaluate the lipid abnormalities on low dose continuous regimen. So the study is to establish the consequence of low dose isotretinoin on the lipid parameters.

Materials and Method

Source of data: Fifty patients between the age group of 15-45yrs, reporting to the specialty of dermatology, MIMS with moderate to severe acne, according to Indian Acne Grading system is enrolled as subjects after obtaining written consent. The participants over a period of one year were followed up for 16 weeks. The subjects chosen were interviewed. Before starting the treatment and before the sample collection, information about the age, sex, weight, personal and family history of acne was recorded in the patients known language. In case of minors, subject assent and parent's consent was obtained. Ethical committee approval was obtained.

Data collection methodology: A prospective, non-comparative study, 50 patients with moderate to severe acne vulgaris were assessed and indication for oral isotretinoin therapy was recorded. Assessment to grade acne severity was accomplished using Indian acne grading system [Table 1]

Table 1: Indian acne grading system

Mild acne (grade 1)	Comedones<30 Papules <10 No scaring
Moderate acne (grade 2)	Comedones any number Papules>10, Nodules<3 Scarring±
Severe acne (grade 3)	Comedones, papules any number Numerous nodules, scarring

Before starting, the participants were investigated for complete blood count and urine pregnancy test (for female participants of child bearing potential). Prior to the study, initial primary investigation(day 0) like total cholesterol, triglyceride, HDL, LDL done and follow up was carried at the interval of 4weeks for 16 weeks and at the culmination of the intervention. The outcome of regimen and lipid profile variation were assessed at the end of every month for 16weeks.

Inclusion criteria

- Moderate to severe acne cases.
- Patients willing to take isotretinoin therapy.
- Age group between 15-45yrs.
- Subjects willing to give assent and /or consent:

Exclusion criteria

- Gravid women.
- Women with expecting pregnancy.
- Lactating women.
- Hyperlipidemia.
- Allergy to isotretinoin.
- Patients of Diabetes mellitus.

Results

Fifty participants with the age group of 15-45yrs were encompassed in the present research, 23 participants were males and 27 participants were females. Large number of the participants, were in the age group with the mean age 23.4 years in males and 19.2 in females.

The demographic data and severity of acne is summarized in the Table 1.

Table 1: Age, Sex and Grades of participants

	N(%)	Mean age	Moderate	Severe
Male	23(46.0%)	23.4	13	10
Female	27(67.5%)	19.2	15	9

Grading of the lesions was recorded prior to the treatment, during and subsequently at16 weeks of intervention. The incipient mean scores were 80.26% and 88.26% in male and females respectively. During the follow up there were considerable decline in acne load in both sex.

Table 2: Grading of acne

Grade of acne	Baseline	1st month	3rd month	4th month
0	-	-	7%	7%
1	-	12%	80%	90%
2	58%	62%	13%	3%
3	42%	26%	-	-

Mucocutaneous undesired effects were noted in 62.5% of patients. Very frequent unwanted effects is Cheilitis. Less common deleterious effects are in Table 3.

Table 3: Detrimental events on low dose isotretinoin

Side effects	
Cheilitis	20
Xerosis	10
Eye and nasal dryness	8
Hairloss	5
Menstrual irregularities	2
Irritation and redness	4

Total cholesterol, triglyceride, LDL, HDL, were quantified at the incipient stage of the treatment and after 4 months of isotretinoin therapy. Serum levels were monitored at 4weeks, 8weeks, 12weeks, 16weeks and at the end of the treatment. Values are shown in the Table 4.

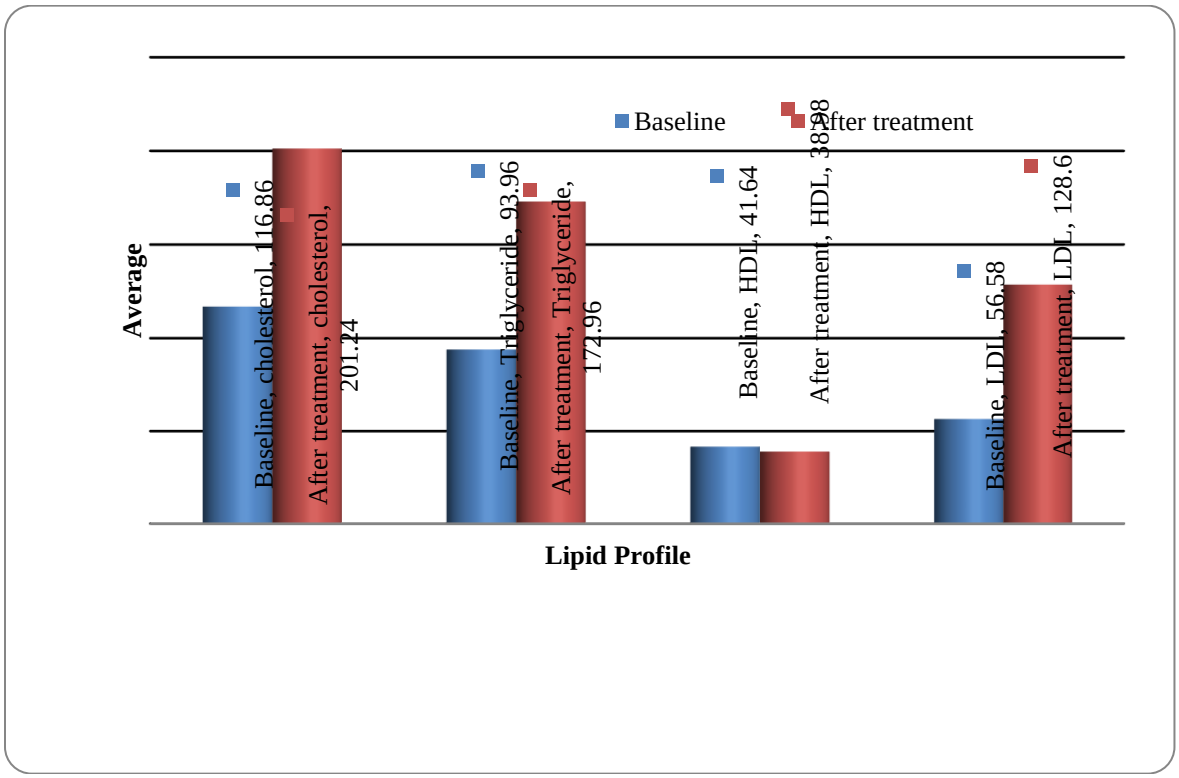
Table 4: Serum Lipid parameters measured at different interruption

	Cholesterol	Triglycerides	HDL	LDL
Baseline	116.86 + 23.55	93.96 ± 19.72	41.64 ± 9.31	56.58 ± 24.30
After 4 weeks	134.62 ± 25.50	111.46 ± 20.62	40.86 ± 8.19	70.04 ± 26.85
After 8 weeks	153.80 ± 24.21	128.06 ± 18.88	41.00 ± 8.28	86.52 ± 24.72
After 12 weeks	173.10 ± 23.76	145.48 ± 17.15	39.80 ± 7.56	103.98± 23.59
After 16 weeks	190.22 ± 24.73	161.20 ± 15.77	39.42 ± 6.52	119.24± 23.91
After 20 weeks	201.24 ± 23.96	172.96 ± 17.73	38.98 ± 5.89	128.60± 23.17

The cholesterol, triglyceride, LDL levels is increased at all the intervals when contemplated with the baseline and the increase was above the normal range with first grade increase. HDL levels is declined at all the periods when compared with the baseline.

Lipid profile prior to and post 4months of continuous isotretinoin therapy.

Lipid	Baseline	After treatment	P-value
cholesterol	116.86± 23.55	201.24± 23.96	<0.0001
Triglyceride	93.96± 19.72	172.96 ± 17.73	<0.0001
HDL	41.64 ± 9.31	38.98 ± 5.89	<0.0001
LDL	56.58 ± 24.30	128.60 ± 23.17	<0.0001



Serum cholesterol, triglycerides, HDL showed appreciable changes on continuous isotretinoin therapy. Values were exalted with reference to the baseline but were above normal level and the dissimilarity was statisically significant with p-value(0.0001).

Discusssion: Isotretinoin ,an isomer of all-trans retinoic acid is a proven effective drug in treating resistant nodular and nodulocystic acne, with reported long term remission.[13] Conventional regimen produces good results but causes dose dependent side effects so many low dose isotretionin has been tired previously.[14,15] In 2016, a systematic review of studies on patients with high dose isotretinoin showed changes in serum transaminases and lipids (TG and total cholesterol), there was no evidence to support monthly testing.[16]

In order to improve tolerability and adverse effect of isotretinoin, we decided to use a modified regimen of fixed 20mg daily isotreinoin. A low dose treatment regimen may be better tolerated as the majority of the adverse effects of tretinoin are dose-dependent.

In our study substantial increment was noticed in the serum cholesterol assay when compared with the baseline. Both men and women showed dramatic increment in the mean level of cholesterol, triglyceride, LDL and decrement in the mean level of HDL. Considering the baseline values, most of these abnormalities during the therapy were in the grade 1 catergory with three of the patients investigated revealed moderate to severe (grade 2) or higher abnormality. Similar variations were seen in total cholesterol, TG, LDL with the P value <0.001. The mild to moderate variations in lipid parameters were generally transient and reversible. The observation in our analysis was in conformance with the study done Ahmadvand et al.[17] The precise means of action of isotretinoin on lipid profile however remains unspecified. some of the studies have experienced the change in the new abnormalities incidence among acne

patients in serum lipid levels when compared with their preceeding normal levels. In study by Amichai et al, changes in lipid parameter above normal and decrease in liver enzymes was determined.[18] In study by Ghalamkarpour et al, patients treated with 0-5mg/Kg/day repoeted statistically significant increase in triglyceride levels with no change in liver enzymes and cholesterol.[19] Isotretinoin therapy has been reported to increase cholesterol, TG, LDL, VLDL and reduce HDL.[20,21] Its been reported that the isotretinoin increase the TG, Chol, LDL but decrease the HDL in their research. According to the reports, serum HDL levels decreases after treatment with tretinoin.[22] Their study is in conformance with our study and reported that no patient was devoid of treatment due to laboratory abnormality.[23,24] Vieira et al noted an increase in AST, ALT and TG levels.[24]

Many studies in literature have reported adverse effects on liver enzymes and lipid profile were reversible. In contrary study done by Brito et al. found no statistically significant changes in liver enzymes, TG, HDL, LDL.[25] Rodondi et al. illustrated a predilection to acquire the metabolic syndrome who had a striking rise in TG levels for the duration of use of oral isotretinoin, in patients implying the contribution of genetic factors.[26] Though the medication being innocuous and acceptable, a regular clinical checkup and laboratory assessment is required. And a better specialist-subject understanding are essential for the effective intervention. Limitation of the study include its sample size and most of our patients were pursued for a short interval.

Conclusion

Our observation demonstrated that low dose oral isotretinoin is an effective safe drug for moderate to severe acne patients, with the lower incidence of side effects and its interference on lipid profile has grade 1 increment. The increase was not severe enough to warrant termination of treatment. But still in practice, laboratory variations should be studied in individual patient. Laboratory alterations can neither suggest an untoward clinical consequence nor absence can impede the possibility of detrimental effects. So patients should be scrutinized on oral isotretinoin regardless of the dosage. Isotretinoin can be securely used in treating acne vulgaris with adequate monitoring, overshadowing the risks. We advise our specialist that the usage of low dose isotretinoin in moderate to severe acne can be done with minimal concern but close follow up is important.

References

1. Lasek RJ, Chren MM. Acne vulgaris and the quality of the life of adult dermatology patients. Arch Dermatol 1998;134:454-458.
2. Tom WL, Friendlander SF. Acne through the ages: case based observations through childhood and adolescence. Clin Pediatr 2008;47:639-651.
3. Akman A, Durusoy C, Senturk M, et al. Treatment of acne with intermittent and conventional isotretinoin: a randomized, controlled multicentre study. Arch Dermatol Res 2007;299:467-473.
4. Kaymak Y, Taner E, Taner Y. Comparison of depression, anxiety and life quality in acne vulgaris patients who were treated with either isotretinoin or topical agents. Int J Dermatol 2009;48:41-46.
5. Strahan JE, Raimer S. Isotretinoin and the controversy of psychiatric adverse effects. Int J Dermatol 2006;45:789-799.
6. Strauss JS, Krowchuk DP, Leyden JJ, et al. Guidelines of care for acne vulgaris management. J Am Acad Dermatol 2007;56:651-663.
7. Roche Laboratories. Accutane insert Document(accessed on January 12,2010.
8. Shahidullah M, Tham SN, Goh CL. Isotretinoin therapy in acne vulgaris: A 10 year retrospective study in Singapore. Int J Dermatol 1994;33:60-3.
9. Layton A. "The use of isotretinoin in acne". Dermato-Endocrinology 2009; Vol. 1 Issue 3.
10. Sardana K, Garg V, Sehgal V, et al. "Efficacy of fixed low- dose isotretinoin with topical clindamycin gel in moderately severe acne vulgaris". J Eur Acad Dermatol Venereol 2009;23(5):556-60.
11. Plewig G, Dressel H, Pfleger M, et al. "Low dose isotretinoin combines with tretinoin is effective to correct abnormalities of acne". J Dtsch Dermatol Ges 2004 Jan;2(1):31-45.
12. Seukeran DC, Cunliffe WJ. "Acne vulgaris in the elderly; the response to low dose isotretinoin". Br J Dermatol 1998 Jul;139(1):99-101.
13. Strauss JS, Thouibaut DM. Disease of the sebaceous glands. In: Freedberg I, Eisen AZ, Wolf K. Dermatology in general Medicine. 5TH ed New York: McGraw-Hill; 1999.p.769-484.
14. Layton AM, Knaggs H, Taylor J, Cunliffe WJ. Isotretinoin for acne vulgaris- 10years later: A safe and successful treatment. Br J Dermatol 1993; 129: 292-296.
15. Wessels F, Anderson AN, Kropman K. The cost-effectiveness of isotretinoin in the treatment of acne. Part 1. A meta-analysis of effectiveness literature. S Afr Med J 1999; 89: 780-784.
16. Lee YH, Scharnitz TP, Muscat J, et al. Laboratory Monitoring during isotretinoin therapy for acne: A Systematic review and meta-analysis. JAMA Dermatol 2016; 152:35-44. Doi:10.1001/jamadermatol.2015.3091.
17. Ahmadvand H, Javanbakht A. "Effects of oral isotretinoin on serum lipids and gamma glutamyltranspeptidase activity in acne vulgaris patients". Afr. J. Pharm 2011, Pharmacol vol. 5 (11). 1338-41.
18. Amichai B, Shemer A, Grunwald MH. Low –dose isotretinoin in the treatment of acne vulgaris. J Am Acad Dermatol 2006; 54:644-646.
19. Ghalamkarpour F, Nasiri S. isotretinoin in treatment of acne: Its efficacy, side effects, and recurrence r of disease. Archives of Iranian Medicine 2006; 9:228-230.
20. Kizilyel O, Metin MS, Elmas OF, et al. Effects of oral isotretinoin on lipids and liver enzymes in acne patients. Cutis. 2014 Nov; 94(5): 234- 238.
21. Da Cunha MG, Batista AL, Macedo MS, et al. Study of lipid profile in adult women with acne. Clin Cosemet Investig Dermatol. 2015 Aug 17;8:449-454.
22. Rasi A, Behrangi E, Rohaninasab M, Nahad ZM. Efficacy of fixed daily 20mg of isotretinoin in moderate to severe scar prone acne. Adv Biomed Res 2014; 3:103.

23. Tallab T, Joharji H, Jazei M, Bahamdan K, Ibrahim K, Karkashan E. Isotretinoin therapy: any need for laboratory assessment? West Afr J Med. 2004;23:273-5.
24. Vieira AS, Beijamini V, Melchiors AC. The effect of isotretinoin on triglycerides and liver aminotransferases. An Bras Dermatol. 2012; 87:382-387.
25. Brito MFM, Pessoa IS, Galindo JCS, et al. Evaluation of clinical adverse effects and laboratory alterations in patients with acne vulgaris treated with oral isotretinoin. An Bras Dermatol. 2010; 85:331-337.
26. Rodondi N, Darioli R, Ramelet AA, Hohl D, Lenain V, Perdrix J, et al. High risk for hyperlipidemia and the metabolic syndrome after an episode of hypertriglyceridemia during 13-cis retinoic acid therapy for acne: a pharmacogenetic study. Ann Intern Med. 2002;136:582-9.