International Journal of Medical Research Professionals
P-ISSN: 2454-6356; E-ISSN: 2454-6364
DOI: 10.21276/ijmrp

IJMRP

Original Research Article.

Association of Lipid Abnormalities with High-Sensitivity C – reactive Protein In Patients Treated with Atorvastatin in a Tertiary Care Hospital

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ABSTRACT

Background: Disorder in lipid metabolism is one of the main determinants of cardiovascular risk. The primary target of lipid management is to achieve low-density lipoprotein cholesterol at goal. Statin therapy lowers the risk of cardiovascular events by reducing plasma cholesterol levels, and practice guidelines for patients with known cardiovascular disease emphasize the importance of reaching target goals for low density lipoprotein cholesterol.

Subjects and Methods: The study included total 50 cases among which 30 were males and 20 were females. Total of fifty dyslipidemic subjects were included in this study to explore residual lipid abnormalities and subclinical inflammation on statin therapy.

Results: Atorvastatin have significant effect on lowering of hs-CRP levels (P=0.001), reducing LDL-C levels (P=0.04), elevating HDL-C levels (P=0.02) along with reducing TC (P=0.02) and TG (P=0.05) levels in obese T2DM patients. This study showed a strong and significant positive correlation between the serum hsCRP Levels with the total serum cholesterol (p<0.006, r=0.38) and significant positive correlation of triglycerides with hsCRP (p=0.01, r=0.36).

Conclusion: Treatment with atorvastatin leads to a significant reduction in plasma Total cholesterol, LDL cholesterol and TG, a lowering of plasma CRP and an improvement in endothelial dysfunction.

Keywords: Lipid Abnormalities, hs-CRP, Atorvastatin.

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Article History:

Received: 13-08-2019, **Revised:** 16-09-2019, **Accepted:** 02-10-2019

Access this article online	
Website: www.ijmrp.com	Quick Response code
DOI: 10.21276/ijmrp.2019.5.6.044	

INTRODUCTION

Cardiovascular diseases (CVDs), the leading causes of death in the world are rising rapidly in low- and middle-income countries.[1] CVDs are the most prevalent cause of morbidity and mortality among patients with type1 or type2 diabetes.[2] Disorder in lipid metabolism is one of the main determinants of cardiovascular risk. The primary target of lipid management is to achieve low-density lipoprotein cholesterol at goal.[3] Statin therapy lowers the risk of cardiovascular events by reducing plasma cholesterol levels, and practice guidelines for patients with known cardiovascular disease emphasize the importance of reaching target goals for low density lipoprotein cholesterol.[4] For the management of dyslipidemia, statins or fibrates are commonly used. Statins (HMG~CoA reductase inhibitors) reduce cardiovascular diseases risk by approximately 23% per every 1 mmol/l (~39 mg/dl) low-density lipoprotein cholesterol lowering.[5] Atorvastatin, at doses ranging from 2.5 mg to 80 mg daily, can reduce low-density lipoprotein cholesterol by 25% with the lowest dose and up to 60% with the maximal dose.[6] Beside lipid parameters, high sensitivity C-reactive protein– an inflammatory cytokine and an independent predictor of cardiovascular disease.[7] is claimed to be reduced by statin treatment.[8] The US Food and Drug Administration approved a new use for statin therapy among those with elevated hsCRP and one additional risk factor, and the Canadian Cardiovascular Society recently issued new national guidelines indicating that statin therapy should be offered to those at "intermediate risk" who have elevated levels of hsCRP, even if low-density lipoprotein cholesterol levels are low.[9] Though proven befit of statin on cardiovascular diseases risk, patients with dyslipidemia remains at high risk for cardiovascular events even after low-density lipoprotein cholesterol, blood pressure and HbA1c target have been achieved.[10] My aim was to evaluate the effects on high-sensitivity C-reactive protein levels and lipid profile in Patients Treated with Atorvastatin.

SUBJECTS AND METHODS

This study was conducted in the Department of Medicine, Narayan Medical College and Hospital, in collaboration with the Department of Biochemistry, during the period of Nine months i.e.,

from November, 2018 to July, 2019. The study included total 50 cases among which 30 were males and 20 were females. This study was conducted before starting the current study. Sample size calculation was done according to standard methods available. Newly diagnosed Patients with dyslipidemia, not taking any medications (neither hypolipidemic drugs nor any other drugs like thiazide diuretics, glucocorticoids etc. that can alter the lipid profile) were included in the study. and Patients with infection, stroke, myocardial infarction, major surgery, mal-absorption, severe allergy, cancer, severe illness, liver dysfunction, chronic kidney disease, pregnancy, edema, oral contraceptive users and steroid or Non-steroidal anti-inflammatory drugs users were excluded from the study. Blood samples were obtained from the antecubital vein with the subject sitting comfortably in a chair in a quiet room and transfused into vacuum tubes containing EDTA in the morning after an overnight fasting period. After separation, blood samples were centrifuged for 5 minutes at 2500 rpm to obtain serum. Then serum was aliquoted into 2 microtubes, one preserved for lipid profile measurements and another was preserved at -20oC for hs-CRP estimation until analysis. Total cholesterol, Triglycerides, HDL-c, LDL-c were analyzed on Erba Autoanlyzer and hsCRP by sandwich ELISA technique using hs-CRP kit. Statistical analysis was done using IBM, SPSS Statistics-22 software.

Table 1: Baseline clinical characteristics of study subjects:

Parameters	Mean±SD / Number
Age in years	45 ± 12.02
Male:Female ratio	30:20
Body mass index (Kg/m2)	27.4 ± 6.5
Hypertension	39 (78%)
Systolic blood pressure (mm Hg)	124 ± 22.6
Diastolic blood pressure (mm Hg)	84 ± 16.05
Diabetes mellitus (%)	42 (84%)
Smoker	7 (14%)

Table 2: Effects of atorvastatin on hs-CRP and lipid profile:

Biochemical Parameters	Baseline	Atorvastatin after treatment
	(Mean ± S D)	(Mean ± S D)
Total cholesterol	256.3 ± 56.8	190.51 ± 36.2
Triglycerides	176.24 ± 45.4	160.2 ± 24.36
HDL-c	42.3 ± 11.42	50.7 ± 13.4
LDL-c	166.56 ± 34.7	88.64 ± 14.5
hs-CRP	2.84 ± 0.6	1.72 ± 0.2

(Statistically Significant at p value <0.05) *NS: Statistically not Significant

Table 3: Correlation between lipid abnormalities with hs-CRP with the in dyslipidemic patients:

Parameters	Correlation coefficient (r)	p-value
TC	0.38	0.006
TG	0.36	0.01
HDL-c	-0.14	0.33*
LDL-c	0.30	0.03

*Statistically significant (p<0.05); *NS: Statistically not Significant

RESULTS AND DISCUSSION

Total of fifty dyslipidemic subjects were included in this study to explore residual lipid abnormalities and subclinical inflammation on statin therapy. All the subjects used statin (Atrovastatin, 10 mg per day). Baseline clinical characteristics of the study subjects are shown in [Table-1]. Dyslipidemia is a prominent one among the traditional biochemical risk factors of CVDs.

Elevated TG, total cholesterol, and LDL cholesterol as well as decreased HDL cholesterol has been implicated with a variably increased risk of CVDs both in cross-sectional and prospective studies.[11] The nature and extent of dyslipidemia, however, may vary depending on the ethnic, cultural and environmental background of a particular population.

For the management of lipid abnormalities, statin and fibrates are commonly used in our population. Some studies have identified residual CVD risk on therapy in different population[12]; no study has yet been carried out to explore the prevalence of lipid abnormalities on stable statin therapy in this population. In the present teaching hospital-based study on south Indian population,

50 statin treated subjects were included. Among the study subjects most of them (84%) were diabetic, 78% were hypertensive and 14% had a habit of smoking [Table-1]. [Table-2], On statistically analyzing, it is clearly indicated that atorvastatin has significant effect on lowering of hs-CRP levels (P=0.001), reducing LDL-C levels (P=0.04), elevating HDL-C levels (P=0.02) along with reducing TC (P=0.02) and TG (P=0.05) levels in obese T2DM patients.

This study showed a strong and significant positive correlation between the serum hsCRP Levels with the total serum cholesterol ($p<0.006$, $r=0.38$) and significant positive correlation of triglycerides with hsCRP ($p=0.01$, $r=0.36$). A statistically non-significant and weak negative correlation is seen between the serum hsCRP levels and HDL-C ($p=0.33$, $r= -0.14$) Table-3. On the other hand, LDL-C showed a statistically significant positive correlation with serum hsCRP level ($p=0.03$, $r=0.30$). Several mechanisms by which statins improve endothelial dysfunction have been investigated, and it has been shown that statins have pleiotropic properties that complement their cholesterol-lowering effects.[13] One of these pleiotropic properties is the anti-inflammatory effect of statins. Atorvastatin has a direct anti-inflammatory effect on the vessel wall in animal models[14], and statin therapy has been shown to lower CRP levels in patients with hypercholesterolemia and combined hyperlipidemia.[15] We have shown, for the first time, that atorvastatin also reduces CRP levels in patients with type 2 diabetes, and the magnitude of reduction in CRP correlated with the degree of improvement in endothelium-dependent vasodilation. This would support the hypothesis that the improvement in endothelium-dependent vasodilation in our diabetic patients might be partly mediated by the anti-inflammatory effect of atorvastatin. We cannot exclude the possibility that other mechanisms might also be involved. There is both in vitro and in vivo evidence to show that the effect of statins on endothelial dysfunction is related not only to the lowering of LDL, but also to a direct effect on NO production. Statins have a direct effect on endothelial NO synthase (eNOS) expression and cause upregulation of eNOS with increased bioavailability of NO in vivo.[16]

Statins can also reverse the inhibitory effect of oxidized LDL on eNOS. In addition to the effect on NO, statins have been shown to reduce the synthesis of endothelin- 1, a potent vasoconstrictor, by endothelial cells.[17] The metabolites of atorvastatin have potent antioxidant activities on LDL in vitro, protect HDL against oxidation, and have a paraoxonase-sparing effect.[18] All these additional pleiotropic properties of statins are independent of their cholesterol-lowering effect, and this may explain why we did not find a significant correlation between the magnitude of LDL lowering and the degree of improvement in endothelium dependent vasodilatation. As a categorical variable, hsCRP has potential as a marker of future cardiovascular disease risk. However, the influence of age and gender should be taken into account in its application to the prediction of cardiovascular disease risk.

CONCLUSION

These findings suggest that the treatment with atorvastatin leads to a significant reduction in plasma Total cholesterol, LDL cholesterol and TG, a lowering of plasma CRP and an improvement in endothelial dysfunction. The screening of patients with elevated CRP levels may identify patients who have an increased risk for cardiovascular events although the use of CRP levels as a predictor of cardiovascular events is not well defined for patients who already qualify for statin treatment because of lipid abnormalities. Thus, screening of patients with dyslipidemia for elevated blood hs-CRP levels may be done to identify those patients with an increased risk for future development of atherosclerosis as well as bad cardiovascular events at earlier stages so that they can changes their life style, food habit etc. to resist the further aggravation of dyslipidemic status as well as catastrophic cardiovascular events.

REFERENCES

1. Miranda JJ, Kinra S, Casas JP, Davey Smith G, Ebrahim S. Noncommunicable diseases in low- and middle-income countries: context, determinants and health policy. Trop Med Int Health 2008; 13: 1225-34.

2. Matheus AS, Tannus LR, Cobas RA, Palma CC, Negrato CA, et al. Impact of diabetes on cardiovascular disease: an update. Int J Hypertens 2013: 653-789.

3. Carreiro-Lewandowski E. Update on selected markers used in risk assessment for vascular disease. Clin Lab Sci 2004; 17: 43-9.

4. National Cholesterol Education Program; Executive summary of the third report of the National Cholesterol Education Program (NCEP) expert panel on detection, and treatment of high blood cholesterol in adults (Adult Treatment Panel III). JAMA 2001; 285:2486-97.

5. Pichandi S, Pasupathi P, Raoc YY, Farook J, Ambika A, et al. The role of statin drugs in combating cardiovascular diseases. Int. J. Cur. Sci. Res. 2011; 1: 47-56.

6. Nawrocki JW, Weiss SR, Davidson MH, Sprecher DL, Schwartz SL, et al. Reduction of LDL Cholesterol by 25% to 60% in Patients with Primary Hypercholesterolemia by Atorvastatin, a New HMG-CoA Reductase Inhibitor. Arteriosclerosis, Thrombosis, and Vascular Biology 1995; 15: 678-82.

7. Pearson TA, Mensah GA, Alexander RW, Anderson JL, Cannon III RO, et al. Centers for Disease Control and Prevention; American Heart Association. Markers of inflammation and cardiovascular disease: application to clinical and public health practice. A statement for healthcare professionals from the Centers for Disease Control and Prevention and the American Heart Association. Circulation 2003; 107: 499-511.

8. Nissen SE, Tuzcu EM, Schoenhagen P. Reversal of Atherosclerosis with Aggressive Lipid Lowering (REVERSAL) Investigators. Statin therapy, LDL cholesterol, C-reactive protein, and coronary artery disease. N Engl J Med. 2005; 352: 29-38.

9. Genest J, McPherson R, Frohlich J, Anderson T, Campbell N, et al. Canadian Cardiovascular Society/Canadian guidelines for the diagnosis and treatment of dyslipidemia and prevention of cardiovascular disease in the adult - 2009 recommendations. Can J Cardiol 2009; 25: 567-79.

10. Fruchart JC, Sacks F, Hermans MP, Assmann G, Brown WV, et al. The Residual Risk Reduction Initiative: a call to action to reduce residual vascular risk in patients with dyslipidemia. Am. J. Cardiol. 2008; 102: 1K-34K.

11. Verschuren WM, Jacobs DR, Bloemberg BP, Kromhout D, Menotti A, et al. Serum total cholesterol and long-term coronary heart disease mortality in different cultures. Twenty-five-year follow-up of the seven countries study. JAMA 1995; 274: 131-6.

12. Strang AC, Kaasjager HA, Basart DC, Stroes ES. Prevalence of dyslipidaemia in patients treated with lipid-modifying drugs in the Netherlands. Part of the dyslipidaemia international survey. Neth J Med 2010; 68: 168-74.
13. Davignon J, Laaksonen R. Low-density lipoprotein-independent effects of statins. Curr Opin Lipidol 1999; 10:543–59.
14. Bustos C, Hernandez-Presa MA, Ortego M, Tunon J, Ortega L, Perez F, Diaz C, Hernandez G, Egido J. HMG-CoA reductase inhibition by atorvastatin reduces neointimal inflammation in a rabbit model of atherosclerosis. J Am Coll Cardiol 1998; 32:2057–64.
15. Jialal I, Stein D, Balis D, Grundy SM, Adams-Huet B, Devaraj S. Effect of hydroxymethyl glutaryl coenzyme a reductase inhibitor therapy on high sensitive C-reactive protein levels. Circulation 2001; 103:1933–5.
16. Kaesemeyer WH, Caldwell RB, Huang J, Caldwell RW. Pravastatin sodium activates endothelial nitric oxide synthase independent of its cholesterol- lowering actions. J Am Coll Cardiol 1999; 33:234–41.
17. John S, Schlaich M, Langenfeld M, Weihprecht H, Schmitz G, Weidinger G, Schmieder RE. Increased bioavailability of nitric oxide after lipid lowering therapy in hypercholesterolemic patients: a randomized, placebo controlled, double-blind study. Circulation 1998; 98:211–6.
18. Hernandez-Perera O, Perez-Sala D, Navarro-Antolin J, Sanchez- Pascuala R, Hernandez G, Diaz C, Lamas S. Effects of the 3-hydroxy-3-methylglutaryl- CoA reductase inhibitors, atorvastatin and simvastatin, on the expression of endothelin-1 and endothelial nitric oxide synthase in vascular endothelial cells. J Clin Invest 1998; 101:2711–9.
19. Aviram M, Rosenblat M, Bisgaier CL, Newton RS. Atorvastatin and gemfibrozil metabolites, but not the parent drugs, are potent antioxidants against lipoprotein oxidation. Atherosclerosis 1998; 138:271–80.

Source of Support: Nil.

Conflict of Interest: None Declared.

Cite this article as: S. R. Hanamshetty. Association of Lipid Abnormalities with High-Sensitivity C – reactive Protein In Patients Treated with Atorvastatin in a Tertiary Care Hospital. Int J Med Res Prof. 2019 Nov; 5(6): 202-05.
DOI:10.21276/ijmrp.2019.5.6.044