RESEARCH PAPER | Biochemistry | Volume : 5 | Issue : 7 | July 2015 | ISSN - 2249-555X

Effects of Statin Therapy on Plasma Glucose and Glycated Hemoglobin

KEYWORDS: Statin, HbA1c, Hypercholesterolemia, diabetes

*Shashi R.M. Yadav	A.D. Deepak	Vijay K. shah
Department of Biochemistry, MGM Medical College, KamotheNavi Mumbai. *Corresponding Author	Department of Biochemistry, MGM Medical College, KamotheNavi Mumbai	Department of Biochemistry, MGM Medical College, Kamothe Navi Mumbai

ABSTRACT *Introduction:As statin acts by inhibiting rate limiting step in cholesterol biosynthesis, is most commonly employed drugs in hypercholesterolaemic patients. Beside its several beneficial effects in coronary heart patients, it is supposed to confer an increased risk of developing diabetes. Thus there is need of proper investigations and demonstrations of such adverse effects of statin therapy. Therefore, this study was undertaken to monitor the adverse effects of statin therapy on hypercholesterolemic patients.*

Objective: The present study evaluated the effects of statin therapy on plasma glucose and glycated haemoglobin in non-diabetic patients.

Method:A total of 40 patients were recruited in the study after obtaining informed written consent.They weredivided into two groups. Group 1 included subjects to be prescribed with statin and Group 2 included subjects with 3 months prescription of statin drug.Biochemical parameter like plasma glucose was estimated by colorimetric method on autoanalyser and HbA1c by Immunoturbidimetric method by D10 analyser.

Result: There were statistically significant differences found in glycemic and lipid profiles in group 1 and group 2 (0.001). There were significantly decreased levels of total cholesterol, triacylgltcerol, LDL and VLDL (0.001) while significantly increased levels of HbA1c (0.001) in group 2 than in group1. Similarly there were significantly increased levels of plasma glucose and HbA1c (0.001) in group 2 than in group 1.

Conclusion: We suggest from our study that patients on statin therapy should have a frequent monitoring of plasma glucose levels and HbA1c levels to avoid complications like Hyperglycaemia, Myopathy, Hepatotoxicity, Cataract and many more.

INTRODUCTION

Statins are the most effective & best tolerated agents for treating dyslipidemias which are reversible competitive inhibitors of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, and catalyzes an early rate limiting step in cholesterol biosynthesis.[1]Because of these properties, statins have become the most widely prescribed lipid-lowering drugs in patients with elevated serum cholesterol levels. [2]

Several clinical trials have documented the efficacy and safety of statins in reducing fatal and non-fatal coronary heart disease (CHD) events whereas rates of adverse events in all such trials were also followed same in the placebo groups and those receiving active drug. This was also true with regard to non-cardiac illness.[1]

Subjects with Impaired fasting glucose (IFG) are at higher risk for type-2 diabetes & cardiovascular diseases. Therefore, the issue of Statin adverse impact on glucose homeostasis in individuals with IFG remains crucial and needs to be further investigated.[3]

Yet, trial data and meta-analyses indicate that statins confer an increased risk of developing diabetes. Particularly, recent overviews indicate that all statin agents are associated with a modest increase in the risk of incident type 2 diabetes (hazard ratio 1.09, 95% CI 1.02–1.17), and that intensive-dose therapy may be associated with somewhat higher risk than moderate dose therapy (hazard ratio 1.12, 95% CI 1.04–1.22). For these reasons, on March 1, 2012, the United States Food and Drug Administration (FDA) added a warning regarding diabetes risk to the labelling of all statin agents and similar concern has been raised by European drug authorities. These regulatory changes have engendered controversy in the lay and medical press as to whether the cardiovascular benefit of treatment with statins exceeds the diabetes risk, particularly in primary prevention, a setting in which these agents have seen increasing use. The Justification for Use of statins in Prevention: an Intervention Trial Evaluating Rosuvastatin (JUPITER) trial provides a contemporary opportunity to address this issue directly. [4]

Therefore, we intended to study the effects of Statin therapy, besides its hypolipidemic effect, on plasma Glucose and HbA1c of the patients in our hospitals.

Aim: To Study the Effect of Statin therapy on Plasma Glucose, Glycated haemoglobin and Lipid profile

Objectives:

- To estimate plasma glucose,HbA1c levels and Lipid Profile.
- To study the effect of statin therapy on the above biochemical parameters pre & post statin therapy in hyperlipidaemic group.

MATERIAL &METHODS

I. Necessary approval from the Institutional Ethics Committee was obtained before initiating the study.

Volume : 5 | Issue : 7 | July 2015 | ISSN - 2249-555X

II. Study site
The study was conducted at the departments of Biochemistry and Medicine, MGM Medical College & Hospital, Kamothe, Navi Mumbai, India.

III. Study period
The study was an observational study completed over a period of 12 months,

From February 2014 to February 2015.

IV. Study design : Prospective , observational study

V. Sample size: 40 patients prescribed with statin class of drugs were taken for the study

VI. Patient selection

Inclusion Criteria:
- Patients of age group between 30-60 yrs.
- Patients with Hypercholesterolemia.

Exclusion criteria:
- Known diabetic case.
- On treatment with corticosteroids along with statin drugs.
- Patients on major immunosuppressive drugs.
- Patients with complaints of Myopathy, Musculodystrophy and Renal failure.

VII. Study Procedure :
• Blood samples was collected for Plasma Glucose, HbA1c and Lipid profile

- ❖ During initial phase of statin therapy.
- ❖ 2 months after statin therapy.

RESULTS
Table 1 shows anthropometric and clinical characteristics of Group-1 and Group-2. There were significant differences in the parameters considered.

Table 1: Descriptive and comparative statistics fordifferent groups by student t-test

Parameters	Group-1	Group-2	p-value
Cholesterol mg/dl	182.83±27.89	133.65±24.74	<0.001
Triglycerides mg/dl	141.39±51.45	106.85±30.95	<0.001
High Density Lipoprotein (HDL) mg/dl	33.23±6.1	39.91±3.8	<0.001
Low Density Lipoprotein (LDL) mg/dl	121.41±30.31	76.6±24.23	<0.001
Very Low Density Lipoprotein (VLDL) mg/dl	28.25±10.41	21.36±6.21	<0.001
Fasting Plasma Glucose mg/dl	105.72±16.8	127.81±22.03	<0.001
Glycated Hemoglobin (%)	5.57±0.47	6.23±0.69	<0.001

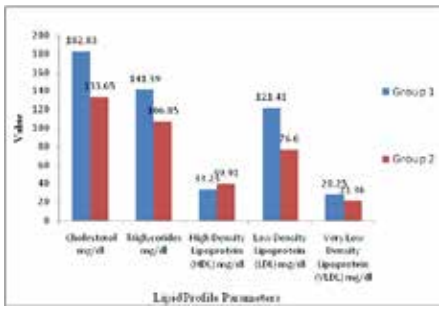

Fig 1 Shows: Evaluation of lipid profile of non diabetic Patients
There were significantly decreased levels of total cholesterol, triacylglycerides, LDL and VLDL (<0.001) while significantly increased levels of HDL-Cholesterol (<0.001) in Group-2 as compared to that in Group-1 which can also be seen in Figure 1.

There were significantly increased in levels of fasting plasma glucose and HbA1c (<0.001) in group-2 as compared to that in group-1.

The comparison was done using paired sample t test. The level of significance was set at 5%. All p values less than 0.05 were treated as significant. The analysis was performed using statistical software IBM SPSS 20.0.

DISCUSSION
The present study includes total forty subjects whose levels of serum lipid profile, plasma glucose and whole blood HbA1c observed in group-1 was compared with those observed in group-2.

We estimated serum lipid profile and got significantly decreased levels of total cholesterol, triacylglycerides, LDL and VLDL (<0.001) while significantly increased levels of HDL-Cholesterol (<0.001) in Group-2 as compared to that in Group-1. Our results are in accordance with Li et al[6] and Kostapanos et al[3] who got significantly decreased levels of Cholesterol, TG, LDL and VLDL, and significantly increased levels of HDL in group-2 than in group-1.

We also estimated plasma glucose and found significantly increased levels of fasting plasma glucose (0.001) in group-2 than that of in group-1.Our results showed resemblance to the results of Sukhija et al[7] and Yada et al[8] who found significantly higher levels of FPG in group-2 than in group-1.

The estimated values of whole blood glycated haemoglobin (HbA1c) were found to be significantly increased (0.001) in group-2 than in group-1.Our results were also supported by Daida et al[9] and Rajpathak et al[10] who observed significantly increased levels of HbA1c in group-2 than in group-1.

CONCLUSION
Our study revealed increased levels of plasma glucose and whole blood HbA1c after 3 months of statin therapyin subjects who were non-diabetic at the start of therapy, also landing of some patients into diabetic category. If statins are to be given to a diabetic patient with hypercholesterolemia it surely may require modification in the treatment of diabetes otherwise it may cause severe complications relatedto diabetes mellitus.Therefore patients on statin therapy should have a frequent monitoring of plasma glucose levels and HbA1c levels to avoid complications like

Volume : 5 | Issue : 7 | July 2015 | ISSN - 2249-555X

Hyperglycaemia, Myopathy, Hepatotoxicity, Cataract and many more.

REFERENCE

1. Goodman & Gilman's The Pharmacological Basis of Therapeutics; 10th edition, 2001: 984, 988. | 2. Bonetti P.O., Lermanc L.O., Napolid C., Lermana A.; Statin effects beyond lipid lowering -are they clinically relevant?; European Heart Journal (2003) 24, 225–248 | 3. Kostapanos M.S., Milionis H.J., Agouridis A.D., Rizos C.V., Elisaf M.S.; Rosuvastatin treatment is associated with an increase in insulin resistance in hyperlipidaemic patients with impaired fasting glucose; Int J ClinPract 2009, 63(9): 3108-1313. | 4. Ridker P.M., Pradhan A., MacFadyen J.G., Libby P., Glynn R.J.; Cardiovascular Benefits and Diabetes Risks of Statin Therapy in Primary Prevention; Lancet. 2012 August 11; 380(9841): 565–571. doi: 10.1016/S0140-6736(12)61190-8 | 5. Friedwald WT, Levy, RI, Fredrickson DS; Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge; ClinChem 1972; 18:499-502. | 6. Junli J., Zhechen M., Xinchen, Fang C.H.; Rapid Effects of Simvastatin on Lipid Profile and C - reactive protein in Patients with Hypercholesterolemia; Clin. Cardiol. 26, 472–476 (2003) | 7. Sukhija R., Prayaga S., Marashdeh M., Bursac Z., Kakar P., Bansal D. et al; Effect of Statins on Fasting Plasma Glucose in Diabetic and Nondiabetic Patients; Journal of Investigative Medicine & Volume 57, Number 3, March 2009 | 8. Yada T., Nakata M., Shiraishi T., Kakei M.; Inhibition by simvastatin, but not pravastatin, of glucose-induced cytosolic Ca2+ signalling and insulin secretion due to blockade of L-type Ca2+ channels in rat islet b-cells; British Journal of Pharmacology (1999) 126, 1205 ± 1213 | 9. Daida H., Takayama T., Hiro T., Yamagishi M., Hirayama A., Saito S. et al; High HbA1c levels correlate with reduced plaque regression during statin treatment in patients with stable coronary artery disease: Results of the coronary atherosclerosis study measuring effects of rosuvastatin using intravascular ultrasound in Japanese subjects (COSMOS); Cardiovascular Diabetology 2012, 11:87 doi:10.1186/1475-2840-11-87. | 10. Rajpathak S. N., Kumbhani D. J., Crandall J., Barzilai N., Alderman M., Ridker v; Statin Therapy and Risk of Developing Type 2 Diabetes: A Meta-Analysis; Diabetes Care 32:1924–1929, 2009. |