

**A CASE REPORT ON ROSUVASTATIN INDUCED NEW ONSET DIABETES
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ABSTRACT

Background: Statins are synthetic analogues of HMG-CoA primarily used to treat hyperlipidaemias with raised low density lipoproteins (LDL) and total cholesterol levels, which may lead to atherosclerotic plaque, Myocardial infarction (MI) and mortality in patients with known ischemic heart disease (IHD). They competitively inhibit the conversion of HMG-CoA to mevalonate by acting on HMG-CoA reductase enzyme. Generalised adverse effects of statins include myositis, myopathy, and elevated aminotransferase levels. But the incidence of statins induced diabetes mellitus is rare and is mainly due to long term use. However, recent meta-analyses of previous studies done with statins have shown that these drugs could induce new onset diabetes mellitus (NODM), especially in subjects prone to diabetes: obese, females, older age, Asian descent, and those with pre-diabetes or the metabolic syndrome. **Case presentation:** We report a case of young male who presented to us with complaints of uncontrolled diabetes mellitus after prolonged use of Rosuvastatin. **Conclusions:** He was diagnosed as a case of new onset non insulin dependent diabetes mellitus (NIDDM) after blood investigations.

KEYWORDS: Rosuvastatin, IHD, NIDDM, NODM, Aminotransferase, Myositis.**BACKGROUND**

Rosuvastatin belongs to the class of Lipid-lowering drugs. Statins are analogues of HMG-CoA. These drugs inhibit the activity of HMG-CoA reductase, which is responsible for conversion of HMG-CoA to mevalonic acid. Elevated levels of mevalonic acid leads to increase in LDL synthesis, thus statins decrease the synthesis of LDL and increase the clearance of LDL from plasma. Atorvastatin and Rosuvastatin are long lasting inhibitors. Other uses of statins include improved clinical outcomes of Alzheimer's disease and prevention of the prostate cancer, whereas undesirable actions include migrating primordial germ cells and contraindication in pregnancy. Myalgia, gastrointestinal disturbances, raised concentrations of liver enzymes; insomnia and rash are the common adverse drug reactions. More serious adverse effects include rhabdomyolysis, angio-oedema and diabetes mellitus upon prolonged use.

CASE PRESENTATION

A 45 year old male presented with complaints of swelling in right upper back region for the last 3years. There was no history of pain, fever, trauma, vomiting and headache. He was not a known case of diabetes mellitus, hypertension, thyroid disorder or any other chronic disease. He was a known case of atherosclerosis and has undergone with stent implementation 5years back and was upon regular medication with metoprolol, aspirin, rosuvastatin, since surgery was performed.

Metoprolol was prescribed to prevent systolic dysfunction and to enhance ventricular filling as patient is a known case of coronary artery disease. Upon examination of the swelling, doctor planned for surgery and advised patient to admit in the hospital to perform the surgical prophylaxis. Doctor advised the patient to stop the intake of rosuvastatin and aspirin two days prior to treatment. During the day of surgery, patient's blood glucose level was tested in order to exclude the risk of surgical site infection and the random blood sugar (RBS) was found to be 656 mg/dL which was very high and the surgery is halted. Further investigations revealed that patient's glycosylated haemoglobin (HbA1c) were found to be 11.7% which indicates abnormal control. The patient's average blood glucose levels for a span of seven days was found to be 290 mg/dL and it has been indicated that patient's sugar levels increases gradually in the morning and decreases during night. Patient has been started treatment with human actrapid insulin (HAI) to decrease elevated blood glucose levels at a dose of 50 units in 50cc normal saline for three times a day until RBS reaches 160 mg/dL. On further inquiry, the patient gave history of rosuvastatin intake for 5 years (20 mg/day) for atherosclerosis. A provisional diagnosis of rosuvastatin induced non insulin dependent diabetes mellitus was made and the patient was asked to stop rosuvastatin. The patient was also started on a course of gemfibrozil which is a fibrate and causes marked reduction in circulating very low density lipoproteins

(VLDL) and modest reduction in LDL-c by 10%. Patient was prescribed with glimester oral preparation at a dose of 1 mg twice a day to control blood glucose levels. There was improvement in glucose levels after three months of stopping statin therapy. The patient was advised to take carbohydrate free diet in order to decrease the episodes of hyperglycaemia.

DISCUSSION

Some experimental studies support the hypothesis that statins may cause diabetes by altering glucose homeostasis through both impaired insulin secretion and diminished insulin sensitivity. Glucose is the most important signal for insulin release. Glucose is transported into the beta cells through glucose transporters 2 (GLUT2). Inside beta cells, glucose is phosphorylated to glucose-6-phosphate by enzyme glucokinase. Following further metabolic steps, adenosine triphosphate (ATP) is produced which closes ATP sensitive potassium channels. Resulting membrane depolarisation leads to calcium influx through L-type calcium channels causing exocytosis of insulin containing granules. Adiponectin is an insulin sensitising and anti-inflammatory cytokine released from adipocytes. Rosuvastatin and simvastatin have been shown to decrease plasma adiponectin levels and insulin sensitivity. Multiple mechanisms may lead to impairment of glycemic control and risk of NODM with statins. Further studies are needed to confirm these hypotheses.

CONCLUSION

A 45 year old male presented with complaints of swelling in the right upper back region, he was a known-case of atherosclerosis and was upon regular medication with metoprolol, aspirin and rosuvastatin since surgery was performed. Upon examination of the swelling doctor planned for surgery and patient's blood glucose levels were tested in order to exclude the risk of surgical site infections and the random blood sugar was found to be 656 mg/dL and surgery is halted. Further investigations revealed that patient's HbA1c was found to be 11.7%. On further inquiry, the patient gave history of rosuvastatin intake for 5 years. A provisional diagnosis of rosuvastatin induced non insulin dependent diabetes mellitus was made and the patient was asked to stop rosuvastatin. The patient was also started on a course of Tab. Gemfibrozil 600mg twice a day along with glimester oral preparation at a dose of 1 gm twice a day to control blood glucose levels. There was improvement in glucose levels after three months of stopping statin therapy.

LIST OF ABBREVIATIONS: IHD, NIDDM, NODM, LDL, MI, HbA1c, RBS, VLDL, GLUT2, ATP, HAI.

CONSENT TO PARTICIPATE: Patient has been explained about his medical condition and permission has been taken from the individual in order to publish the article and assured the patient that identity will not be revealed.

ETHICAL APPROVAL: IRB approval is not obtained as it is a single case report and patient is not a part of clinical trial.

CONSENT FOR PUBLICATION: Written and signed consent form is collected from the patient after proper explanation.

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