Case Report

Rosuvastatin induced rhabdomyolysis – Rare case reported in Batticaloa

Pirasath S.¹*, Jasotharan V.², Sundaresan K. T.³

¹ Post Intern Medical Officer, Teaching Hospital, Batticaloa.
² Medical student, Faculty of Health Care Sciences, Eastern University of Sri Lanka.
³ Consultant Physician, Teaching Hospital, Batticaloa

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We reported a case of rosuvastatin induced rhabdomyolysis in a patient, who presented with one week history of bilateral thigh, back and shoulder pain and easy fatigability associated with passing dark coloured urine for two days. His systemic examination reveals muscle tenderness. His investigations showed high blood urea (147 mg%), serum creatinine (2.4 mol/L), creatine kinase (CK) (21,210 U/L) and with a significant increase in urine myoglobin. Even he has no risk factors; he was diagnosed as rosuvastatin induced rhabdomyolysis associated with acute renal failure. The drug was stopped on the first day of admission and the patient was initiated on intravenous fluid with cautious monitoring of serum electrolytes. On the following days, the level of creatine kinase and serum myoglobin returned toward normal and consequently he was discharged without statins but on dietary therapy. On follow-up evaluation, the patient was symptoms free, his serum creatinine was 0.7 mol/L, whereas his LDL cholesterol was 119mg/dL. The rosuvastatin induced rhabdomyolysis is discussed and the danger of its use in low risk patients is emphasized.

Key Words: Cytochrome P450, rhabdomyolysis, rosuvastatin.

INTRODUCTION

Statins are 3-hydroxy-3-methyl coenzyme A (HMG-CoA) reductase inhibitors that have significant effects on the plasma lipid and lipoprotein profile, lowering total and LDL cholesterol and triglyceride levels and raising HDL cholesterol levels; currently they are the mainstay of dyslipidemia management for the primary and secondary prevention of cardiovascular disease. The use of statins in randomized trials has demonstrated 30% reductions in atherosclerotic end points without serious morbidity [1]. Rosuvastatin is a competitive inhibitor of the enzyme HMG-CoA reductase, having a mechanism of action similar, yet higher efficacy, to other statins [2]. The efficacy of rosvastatin across its dose range of 10 to 40 mg is superior to that of other statins across their dose range, although the safety is similar [3]. Rosuvastatin 40 mg reduced LDL cholesterol levels by 54%, while it increased HDL cholesterol by 13% after 96 weeks [4]. Like other statins, rosuvastatin is associated with a spectrum of adverse events ranging from mild to life-threatening. The most severe adverse event is severe myopathy (ranges from myalgias to rhabdomyolysis), which can cause acute renal failure; this adverse event usually associated with many risk factors. In this report we present a case of rhabdomyolysis induced by low dose of rosuvastatin (10 mg daily) in a 62-year-old Batticaloa man who had no obvious risk factor.

CASE REPORT

A 62 year-old Batticaloa man admitted with one week history of bilateral thigh, back and shoulder pain and easy fatigability associated with passing dark coloured urine for two days. He denied the consumption of grapefruit juice or alcohol abuse and he hadn’t had any exercise before this episode. There was no family
DISCUSSION

Rosuvastatin is a relatively new cholesterol-lowering drug in Sri Lanka as well as in other countries; although highly efficacious, this new statin has generated considerable controversy regarding its safety. In Canada as well as United States, many cases of rosvastatin induced rhabdomyolysis have been reported [5]. Like other statins, rosvastatin can cause life threatening rhabdomyolysis [1]. Our patient presented with bilateral thigh back and shoulder pain and easy fatigability associated with passing dark urine. His serum creatinine was higher than the baseline and his CK was greater than 20 times the upper limit of normal. The incidence of rosvastatin-induced rhabdomyolysis is not known exactly but it was presumed to be low [6] and similar to atorvastatin, pravastatin, and simvastatin [6]; to our knowledge this is the first reported case in Batticaloa and even in low dose of Rosuvastatin (10mg). Although statin induced rhabdomyolysis has been reported at rates of 1 death per 6.6million prescriptions [7], no deaths related to rosvastatin induced rhabdomyolysis were reported in the literature [6]. Heerey et al. [8] estimated that approximately 30% of all users of statins have concomitant prescribed drugs that can inhibit statin metabolism by hepatic cytochrome P450 (CYP) system, potentially leading to rhabdomyolysis. The factors that increase the risk of rosuvastatin induced myopathy or rhabdomyolysis include increased age, renal impairment, hypothyroidism, personal or family history of hereditary muscular disorders, previous history of muscular toxicity with another statin or fibrate, consumption of grapefruit juice (more than 1 L per day), alcohol abuse, being of Chinese or Japanese descent, concomitant use of fibrates. This group of patients should be given rosuvastatin with caution [5]. Our patient had no obvious risk factors; he was 62 years old and non alcoholic and nonsmoker; his baseline creatinine was normal and the calculated creatinine clearance was normal. Rosuvastatin should be discontinued in patients with a creatine kinase level of more than 10 times the ULN with or without muscle symptoms [5]. Liver transaminase levels should be assessed at baseline, at 12 weeks after the start of therapy or an increase in dose, and at 6-month intervals thereafter. The dosage should be reduced or therapy withdrawn if liver transaminase levels exceed 3 times the ULN. Because of the potential for rosuvastatin to increase liver transaminase levels, it should be used with caution in patients with a history of liver disease or alcohol abuse [9]. Overall, persistent elevations in liver transaminase levels are reported in 0.1-0.4% of patients taking rosvastatin 5-40 mg [9]. Similarly, our patient showed high transaminase level which was returned to normal after discontinuation of the drug. Although the exact mechanism of statin-induced rhabdomyolysis is unknown, the implicated mechanisms include the followings: first, the cholesterol synthesis blockage; which makes the skeletal muscle-cell membranes unstable due to low cholesterol content [10]. Second, prenylated protein abnormalities causing imbalances in intracellular protein messaging [11]. Third, coenzyme Q10 deficiency causing abnormal mitochondrial respiratory function [12]. Rosuvastatin induced rhabdom
Rhabdomyolysis in this patient is supported by the following: first, among the drugs used by the patient, there was no drug that known to cause rhabdomyolysis; second: myoglobin and CK were washed out from the blood and returned towards normal within few days after discontinuation of rosuvastatin. In conclusion, although highly efficacious, rosuvastatin has generated considerable controversy regarding its safety; clinicians should maintain an increased level of awareness of the potential for muscle toxicity and rhabdomyolysis, which associated with this new drug even with low dose. Accordingly, Emergent myalgias in patients under rosuvastatin necessitate immediate testing of creatine kinase and myoglobin to exclude life threatening rhabdomyolysis even with low dose.

REFERENCES


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