CLINICAL VIGNETTE

Rosuvastatin Associated Acute on Chronic Kidney Failure

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Introduction

Rosuvastatin is FDA approved for use at dosages ranging from 5mg to 40mg daily. Lower starting doses of 5mg to 10mg daily are recommended in patients with severe chronic kidney disease, particularly those with creatinine clearances less than 30 ml/min. However, nearly half of patients with chronic kidney disease are on higher than recommended dosing when considering kidney function.[1,2] We present a patient with chronic kidney disease who received high dosing of rosuvastatin who developed rhabdomyolysis and worsening kidney failure requiring hemodialysis.

Case Presentation

A 61-year-old female had stage 4 chronic kidney disease, type 2 diabetes mellitus, hypertension and multivessel coronary artery disease requiring multiple percutaneous coronary interventions. Her atorvastatin 80mg was changed to rosuvastatin 40mg to improve low-density lipoprotein reduction. Her creatinine was 1.75 mg/dL and creatinine clearance 38 ml/min at the time. She had gradual worsening of her kidney function over the next four months, with an increase in creatinine to 2.83 mg/dL and decrease in creatinine clearance to 23 ml/min. She then developed an abrupt worsening of kidney function and was admitted for hyperkalemia and acute-on-chronic renal failure. Admission potassium was 6.3 mmol/L which had increased from 4.5 mmol/L one week prior. Creatinine was 7.85 mg/dL which increased from 2.83 mg/dL one week prior. She had concomitant acute hypoxic respiratory failure due to pulmonary edema requiring BiPAP. She required emergency hemodialysis. Additional labs showed new transaminitis with ALT 207 U/L and AST 427 U/L, elevated total creatine phosphokinase 33,730 U/L and urinalysis with 3+ blood, 17 RBC per uL. Home medications included aspirin, carvedilol, clopidogrel, furosemide, glimepiride, insulin glargine and lispro, isosorbide mononitrate, linaclotide, losartan, nifedipine, pantoprazole, pregabalin, rosuvastatin and sitagliptin. Rosuvastatin dosing was 40mg daily. She was diagnosed with rhabdomyolysis and acute-on-chronic kidney failure with rosuvastatin being the probable cause. Rosuvastatin was discontinued. Respiratory failure resolved. Total creatine phosphokinase normalized. Kidney and liver function returned to baseline but urine output remained low. She was continued on outpatient hemodialysis pending renal recovery. She was restarted on atorvastatin 80mg daily, which was well tolerated.

Discussion

Patients with chronic kidney disease are at higher risk for cardiovascular disease than the general population and dyslipidemia is a modifiable risk factor.[3] The Kidney Disease: Improving Global Outcomes (KDIGO) organization recommends statin or statin/ezetimibe treatment in adults aged 50 years and older with an estimated glomerular filtration rate (eGFR) < 60 ml/min/1.73 m^2 not treated with chronic dialysis or kidney transplantation.[4]

Generally, lipid lowering medications are considered safe and effective. Rosuvastatin is a highly potent hydroxymethylglutaryl–coenzyme A reductase inhibitor. Shin, et al reported that pre-approval clinical trials showed proteinuria and hematuria mostly in patients on rosuvastatin 80mg which was subsequently discontinued. 10% and 5% of patients on 40 mg also developed dipstick hematuria ≥+ and proteinuria ≥++, compared with 2%–4% and 0.4%–2% of patients on any dose of atorvastatin. The risks increased in special populations such as those with chronic kidney disease where systemic drug concentrations could be significantly higher. Therefore, the FDA recommends a starting dose for rosuvastatin of 5 mg and a maximum dose of 10 mg in patients with severe chronic kidney disease, such as those with a creatinine clearance <30 ml/min.[1]

Shin, et al reported rosuvastatin risk in patients with severe chronic kidney disease in a large cohort study of nearly 1 million patients initiating statin therapy from 40 health care systems in the United States. He found patients treated with rosuvastatin had a slightly higher risk of hematuria, proteinuria and kidney failure with replacement therapy. Patients with eGFR <30 ml/min per 1.73 m^2, 80% started rosuvastatin with higher doses than the FDA-recommended starting dose of 5 mg. Forty-four percent received initial rosuvastatin doses that exceeded the maximal recommended dose of 10 mg, 30% with 20mg and 14% with 40mg. A rosuvastatin dose-risk gradient was found consistently for both hematuria and proteinuria. He concluded that greater care was needed in the prescribing and monitoring of rosuvastatin, particularly in patients receiving high doses and those with severe chronic kidney disease.[1]

Conclusion

Patients aged 50 years and older with chronic kidney disease are recommended to be on statin therapy for lipid management. While rosuvastatin is a potent hydroxymethylglutaryl–coen-

zyme A reductase inhibitor, it can have adverse effects at higher doses in patients with severe chronic kidney disease. The FDA recommended starting dose for rosuvastatin is 5 mg with a maximum dose of 10 mg in patients with severe chronic kidney disease, such as those with a creatinine clearance <30 ml/min. However, nearly half of patients in this population were found to be on higher than recommended dosing. Greater awareness of rosuvastatin recommended dose adjustments is needed in patients with severe chronic kidney disease.

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