
Case report

The Association Between Statin Drugs and Kidney Injury

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Abstract

Introduction. Statins are widely prescribed lipid-lowering agents that significantly reduce cardiovascular morbidity and mortality. They are frequently prescribed as first-line drugs for the primary and secondary prevention of coronary, cerebral and peripheral ischemic vascular events. Although effective and tolerated by most patients, myotoxicity is a rare but well-documented adverse effect of all statins that usually occurs within weeks or months. The aim of this presentation is to review the pathophysiological mechanisms and diagnosis of statin associated myotoxicity, focusing on the most effective strategies for statin intolerance clinical management. Hence, we present two different cases of statin induced rhabdomyolysis with different treatment, one with help from medium cut off (MCO) dialyzer, and the other with conservative approach with a lot of fluids and diuretic stimulation.

Case reports. The first case is a 68 years old male, on chronic therapy with atorvastatin proposed from cardiologist after having heart problems three years ago. One month before the hospital admission, the patient had elevated creatine kinase and myoglobin, and statin was removed from the therapy. The initial myoglobin level was 700ng/ml and creatine kinase 1500U/L. An excessive fluid parenteral administration was initiated with over 3000ml with an additional oral intake. While under hospital treatment, 24h diuresis was measured between 2300ml up to 4500ml. On the day of discharge, his creatine kinase was 300U/L, myoglobin 200ng/ml and serum creatinine was 138μmol/L. He was instructed for a regular checkup thereafter.

The second case was also a 69 years old male, with chronic kidney disease (CKD) and congestive heart failure with 35% EF. A week before admission the patient has felt problems with walking, pain in the muscles and on three days before the actual hospital admission he was treated in the nearby hospital and transferred because of an acute worsening of the CKD for further treatment. At the admission, the creatine kinase level was 57904U/L.

Because of the highly elevated waste products (urea and creatinine) a treatment with hemodialysis was initiated. A total of 11 hemodialysis was performed, and in 7 of them MCO dialyzer was used. Creatinine kinase level has declined up to 243 U/L. No proper creatine decline has been managed and the patient was discharged with the need for chronic hemodialysis treatment with regular checkups for eventual discharge from the chronic hemodialysis program (CHDP).

Conclusion. We can say that the choice of statin in patients with kidney disease is complex and depends on specific risk factors. This fact is important for choosing the right treatment in these patients. The data and conclusions may help guide future clinical practice and research in this area.

Key words: statins therapy, rhabdomyolysis, kidney injury, medium cut off membrane, myoglobin

Introduction

Statins are widely prescribed lipid-lowering agents that significantly reduce cardiovascular morbidity and mortality. They are competitive inhibitors of HMG-CoA-reductase (3-hydroxy-3-methylglutaryl-CoA reductase) and thereby reduce cholesterol synthesis, so they are frequently prescribed as first-line drugs for the primary and secondary prevention of coronary, cerebral and peripheral ischemic vascular events [1-3]. Although effective and tolerated by most patients, myotoxicity is a rare but well-documented adverse effect of all statins that usually occurs within weeks or months. However, their use is occasionally associated with adverse muscular effects, ranging from mild myalgia to severe rhabdomyolysis. Statin-induced rhabdomyolysis is a rare but potentially life-threatening condition characterized by muscle breakdown, elevated creatine kinase levels, and risk of acute kidney injury. The mechanism of statin-associated myotoxicity is not entirely certain, but toxicity is dose-dependent and several risk factors have been identified. Indeed, any

clinical case of statin-induced myotoxicity can be seen as multifactorial [3-5].

The aim of this presentation is to give an update on pathophysiological mechanisms and diagnosis of statin associated myotoxicity, focusing on the most effective strategies for statin intolerance clinical management, including new emerging alternative therapies. This review aims to improve diagnostic and therapeutic approaches in order to increase statin adherence and reduce cardiovascular events [5].

Case report

Here in, we present two different cases of statin induced rhabdomyolysis with different treatment, one with help from medium cut off (MCO) dialyzer, and the other with a conservative approach with a lot of fluids and diuretic stimulation.

Case 1

We report a case of 68 years old male, on chronic therapy with atorvastatin proposed from cardiologist after having heart problems three years ago.

One month before the hospital admission, the patient had an elevated creatine kinase and myoglobin, and statin was removed from therapy. It was given parenteral fluids and vitamin therapy four days through daily visits in hospital. On the second control one month after daily hospital treatment creatine kinase and myoglobin were insignificantly depleted showing no regression and decision was made for hospital treatment. On the admission day the myoglobin level was 700ng/ml and creatine kinase 1500U/L. The other laboratory findings were as follows: hemoglobin 109..112g/L, erythrocytes 3.39..3.49, hematocrit 0.31..0.32, BUN 5.7..4.7 mmol/L, creatinine 138..134μmol/L, creatine kinase 2028..1087U/L, myoglobin 229..206ng/ml, CRP 1.7..2.9. An excessive fluid parenteral administration was initiated with over 3000ml with an additional oral intake. Diuretics were used only the first day and during the hospitalization the 24h diuresis was measured between 2300ml up to 4500ml. On the day of discharge, his creatine kinase was 300U/L, and myoglobin 200ng/ml. Serum creatinine was 138μmol/L. He was instructed for a regular checkup afterwards. regular checkup thereafter.

Case 2

The second case was also a 69 years old male with chronic kidney disease (CKD) and congestive heart failure with 35% EF. A week before admission the patient has felt problems with walking, pain in the muscles and on three days before the actual hospital admission he was treated in the nearby hospital and transferred because of an acute worsening of the CKD for further treatment. At the admission, the creatine kinase level

was 57904U/L. The other laboratory findings were as follows: hemoglobin 119..71.91g/L, erythrocytes 3.82..2.26..2.88, hematocrit 0.35..0.22..0.26, BUN 30.8..5.9..8.3mmol/L, creatinine 762..329..573μmol/L, creatine kinase 7904..1089..243U/L, myoglobin 615..1071..362 ng/ml, CRP 1.1..22..17.1, AST 1137..62U/L, ALT 693..152U/L.

Because of the highly elevated waste products (urea and creatinine) a treatment with hemodialysis was initiated. A total of 11 hemodialysis was performed, and in 7 of them MCO dialyzer was used. Creatinine kinase level has declined up to 243 U/L. No proper creatine decline has been managed and the patient was discharged with the need for chronic hemodialysis treatment with regular checkups for eventual discharge from the chronic hemodialysis program (CHDP). Urine output has slowly corrected from 200ml/24h up to 1250ml/24h. No other direct cause for the rhabdomyolysis has been confirmed.

Discussion

Understanding the risk factors, clinical presentation, and management of acute kidney injury (AKI) is essential for clinicians to balance the benefits of statin therapy with patient safety. Here we present two case reports treated at our clinic, in one case with the rare use of specific MCO dialyzer and a positive clinical outcome. The patients can rapidly develop severe rhabdomyolysis associated with rosuvastatin therapy while suffering from AKI. Although we were not able to obtain rosuvastatin plasma levels, even without such data, according to the standard semiquantitative causality assessment, rosuvastatin could have been classified as the "probable" cause of rhabdomyolysis in our patient [4]. Statins are generally safe for patients with normal kidney function, but it carries an increased risk of kidney-related side effects, including proteinuria and hematuria, especially at high doses and for people with pre-existing kidney disease. Dosage adjustments are necessary for patients with severe CKD [6,7].

While all statins can affect the kidneys, rosuvastatin has shown a slightly higher risk of kidney issues compared to atorvastatin, with risks increasing with higher doses. An increase in protein (proteinuria) and blood (hematuria) in the urine was observed in clinical trials, particularly with higher dosages. These effects are often temporary and generally do not lead to a decline in overall kidney function.

Our patients have both proteinuria and hematuria, but after they stopped therapy with statins, the urine status was normalized. Some studies published in the Journal of the American Society of Nephrology found that rosuvastatin users had a 15% higher risk of kidney failure requiring replacement therapy (dialysis or transplantation) compared to those taking atorvastatin.

In rare cases, the statin side effect rhabdomyolysis (muscle breakdown) can lead to severe kidney damage or AKI. This risk is higher in individuals with pre-existing kidney problems.

High-dose rosuvastatin has been linked to renal tubular toxicity, a non-rhabdomyolysis-related injury to the kidney's filtering tubules [8,9].

The prescribing guidelines for rosuvastatin emphasize extra caution when treating patients with existing kidney issues. For patients with severe CKD, defined as a creatinine clearance (CrCl) or estimated glomerular filtration rate (eGFR) below 30 mL/min, the dose should be started at 5 mg and does not exceed 10 mg daily [10,11].

Patients with an eGFR below 30 have a significantly higher risk of proteinuria and hematuria when taking rosuvastatin compared to those with normal kidney function. Research suggests that other statins may be safer for kidney health, though studies have mixed results [12,13].

A large 2022 observational study comparing rosuvastatin to atorvastatin showed that rosuvastatin was associated with a higher risk of kidney harm, particularly at higher doses [6].

Atorvastatin seems to have a renoprotective effect. In one study, high-dose atorvastatin appeared to have more protective effects on the kidneys compared to high-dose rosuvastatin. Despite some comparative differences, statins as a class have been shown to have overall renoprotective effects and are important for managing cardiovascular risk in patients with CKD [10].

The choice of statin in patients with kidney disease is complex and depends on specific risk factors. A large percentage of patients on lipid lowering therapies have CKD, and data regarding renal outcomes associated with high doses of statins in this population are limited. We found that nearly half of patients with CKD are on inappropriately high doses of rosuvastatin when considering their kidney function. Further research into long term outcomes and statin dosing in this patient population is needed [14,15].

Conclusion

This case report provides important clinical insights into the management of statin-induced rhabdomyolysis and emphasizes the need for personalized approaches in statin therapy, especially in patients with underlying kidney conditions. The choice of statin in patients with kidney disease is complex and depends on specific risk factors. This fact is important for choosing the right treatment in these patients. The data and conclusions may help guide future clinical practice and research in this area.

Conflict of interest statement. None declared.

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