ORIGINAL RESEARCH PAPER
Volume - 10 | Issue - 10 | October - 2021 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A CASE REPORT ON A RARE COMPLICATION OF HMG-COA REDUCTASE INHIBITORS.

Pharmacology

Dr. Sethu Babu Department of Gastroenterology, Krishna Institute of Medical Sciences, Minister Road, Secunderabad - 500003, Telangana, India.

Billakuduru Srija* Pharm D, Bharat Institute of Technology, JNTUH, Telangana, India. *Corresponding Author

Mandhala Sai Krishna Pharm D, Bharat Institute of Technology, JNTUH, Telangana, India.

Kalvakollu Keerthi Pharm D, Bharat Institute of Technology, JNTUH, Telangana, India.

ABSTRACT

Rhabdomyolysis is the rare adverse effect of statin therapy. It is a condition characterized by the damage and breakdown of skeletal muscle. A 66 years old male patient was admitted to the hospital with the chief complaint of pain and weakness in both lower and upper limbs for five days and was diagnosed with statin-induced rhabdomyolysis. The significance of statin-induced rhabdomyolysis in a patient with recent Hepatitis B related Decompensated Chronic Liver Disease with portal Hypertension, and Severe Mitral Regurgitation is highlighted here. Based on this case report, we recommend that clinicians should inform regular follow-up to the patients when prescribing statins.

KEYWORDS

HMG-COA Reductase inhibitors, Statins, Rhabdomyolysis, DCLD.

INTRODUCTION:

Statins are the class of lipid-lowering drugs that inhibits 3-Hydroxy-3-Methylglutaryl Co-Enzyme A (HMG-COA) Reductase, an enzyme necessary for cholesterol formation [1]. These are beneficial in both primary and secondary prevention of ischemic heart disease. They are generally well tolerated, excluding rare but potentially significant adverse effects of elevated liver enzymes and skeletal muscle abnormalities, which can vary from mild myalgia to life-threatening Rhabdomyolysis [2].

Rhabdomyolysis is a rare adverse effect of statin therapy [3]; it is a condition characterized by skeletal muscle damage and breakdown [4] causes by skeletal injury and subsequent release of skeletal muscle substance into the systemic circulation. Plasma contains various intramuscular components, including creatinine phosphokinase (CPK) [5]. Creatinine Phosphokinase is greater than five times the upper limit of normal in mild rhabdomyolysis; severe rhabdomyolysis is associated with myoglobinuria and/or acute kidney injury. Clinically, an increased CPK level is the primary marker used to diagnose Rhabdomyolysis [6]. It was suspected that myoglobin breakdown products have a direct adverse effect on the renal system [5]. This may result in renal complications with Rhabdomyolysis. An etiological factor that is greater than 10%of cases includes myalgia's, muscle weakness, and dark urine [6]. The incidence of statin-induced rhabdomyolysis is low[7] from all causes, at 1.6 per 1,000,000person years, according to the USFDA's adverse event reporting system database; rates of statin-induced rhabdomyolysis in statin prescription range from0.3 to13.5 instances per 1,000,000[8].

Case Presentation:

A 66 years old male patient with a known history of Hepatitis–B related Decompensated Chronic Liver Disease with Portal Hypertension (Nov) and hepatic encephalopathy grade -2 (Dec) and dyslipidemia(on simvastatin for 2 months) was admitted to the hospital with the chief complaints of cramps like pain in both lower limbs and proximal upper arms for five days, and with difficulty in getting up from bed and moving around due to generalized weakness. After that, he underwent series of investigations that showed elevated CPK (59600) and creatinine (3.00mg/dl), metabolic acidosis and hyperkalemia (5.9mmol/L), Mild hyperbilirubinemia with SGOT/SGPT > 2:1, thrombocytopenia. All possible causes related to rhabdomyolysis were ruled out. So, based on the investigations, it was suspected that rhabdomyolysis was induced by statin therapy. As his creatinine levels were elevated, and his urine output was reduced due to acute kidney injury, one of the complications of Rhabdomyolysis. Therefore, simvastatin was with drawn and started with multivitamins and supportive medications and underwent SLED (Sustained Low –efficiency dialysis). Then his body pains were improved, and his CPK level was also come down to the normal range. While undergoing dialysis, he was developed Massive per Rectum (altered fresh blood) along with Hypotension; his condition has deteriorated, then shifted to ICU, and he was succumbed to death due to an episode of Tachycardia with Refractory hypotension.

DISCUSSION:

Statins are used to treat hypercholesterolemia as well as to prevent cardiovascular disease [9]. The cytochrome P450 enzyme system plays a crucial role in the metabolism of statins [2]. Statins, on the other hand, increase the risk of myopathy, which leads to life-threatening rhabdomyolysis. It is a rare side effect, which may lead to Acute Kidney Injury; many other causes include drugs and toxins, hypo/hyperthermia, infections, metabolic /mitochondrial myopathies, electrolyte imbalance, endocrine problems and idiopathic kidney disease[10].

According to Thomas.J.Kiernane. et al. reported, 85 years female with renal impairment and hypothyroidism was started on a high dosage of simvastatin(80mg) for better lipid treatment. She experienced significant muscle weakness and laboratory findings of rhabdomyolysis. Her simvastatin was then stopped to treat her rhabdomyolysis. After five weeks, the renal, hepatic, and myalgia symptoms subsided, and the patient was discharged with no long-term problems. As seen in our case, there is no history of thyroid and simvastatin dosage is 20 mg; he was at high risk due to multiple complications and was succumbing to death[11].

Konstantinos Koskinas.et al. reported a 70 years old female patient with myalgia, primarily effecting upper and lower extremities, for few days. She had been on simvastatin (40mg) for a year. Based on pathogenesis and laboratory evaluation, she was diagnosed with statin-induced rhabdomyolysis. Thus the simvastatin was withdrawn, her vitals were stabilized, and she was discharged. The concerns with the consequences were mentioned to her, and the condition was discussed [12]. But, in our case, simvastatin dosage is 20mg.

Statins are generally well-tolerated, according to a clinical guideline on their use and safety. Elevated liver transaminases (defined as three times the upper limit of normal in most studies) occur in 0.5% to 2.0% of clinical trial subjects and are dose-dependent, while myopathy and muscle-related symptoms, as well as creatinine kinase (CK) elevations, also causes for concern for clinicians [12]. Although the exact mechanism of statin-induced myopathy is unclear, individual genetic susceptibilities and cytochrome P450 interactions are likely to play a role [13]. However, in everyday clinical practice, the safety profile of statins is not well known, as evidenced by the development of rhabdomyolysis in patients moving from one statin to another. Simvastatin is considered to be in the middle of the statin muscle adverse effect spectrum when compared to other statins. It may induce greater rhabdomyolysis than pravastatin or fluvastatin[14].

Based on our knowledge, very less cases of rhabdomyolysis were reported with simvastatin 20 mg. So, here we highlighted that statin-induced rhabdomyolysis with a small dosage of simvastatin within short period.

CONCLUSION:

Statins are safe and effective but result in rare side effects. There are well known and widely used for hypercholesterolemia. Many of the drugs have side effects as well as advantages. Rhabdomyolysis is one of the rare adverse effects of statin therapy, which leads to acute kidney injury. Therefore, physician's while prescribing statins should inform the patient on proper identification of the side effects and follow up for review is necessary for any of the symptoms related to the condition. Early diagnosis, dechallenge, appropriate therapy are all beneficial to reduce the complications and morbidity.

REFERENCES:

1. Ezad S, Cheema H, Collins N. Statin-induced rhabdomyolysis: a complication of a commonly overlooked drug interaction. Oxford medical case reports. 2018 Mar;2018(3):omx104.
2. Williams D, Feely J. Pharmacokinetic-pharmacodynamic drug interactions with HMG-CoA reductase inhibitors. Clinical pharmacokinetics. 2002 Apr;41(5):343-70.
3. Wagner J, Suessmair C, Pfister HW. Rhabdomyolysis caused by co-medication with simvastatin and clarithromycin. Journal of neurology. 2009 Jul;256(7):1182-3.
4. Bagley WH, Yang H, Shah KH. Rhabdomyolysis. Internal and emergency medicine. 2007 Oct;2(3):210-8
5. Fernandez WG, Hung O, Bruno GR, Galea S, Chiang WK. Factors predictive of acute renal failure and need for hemodialysis among ED patients with rhabdomyolysis. The American journal of emergency medicine. 2005 Jan 1;23(1):1-7.
6. Petreski T, Piko N, Petrijan T, Dvoršak B, Hojs R, Bevc S. Statin-Associated Necrotizing Myopathy Leading to Acute Kidney Injury: A Case Report. Case Reports in Nephrology and Dialysis. 2021;11(2):129-35.
7. Antons KA, Williams CD, Baker SK, Phillips PS. Clinical perspectives of statin-induced rhabdomyolysis. The American journal of medicine. 2006 May 1;119(5):400-9.
8. Mendes P, Robles PG, Mathur S. Statin-induced rhabdomyolysis: a comprehensive review of case reports. Physiotherapy Canada. 2014 Apr;66(2):124-32.
9. Mohamed MF, Salameh OK, Saeed AA. Statin-induced rhabdomyolysis, acute kidney injury, and hepatitis leading to death. The American journal of case reports. 2019;20:709.
10. Ezad S, Cheema H, Collins N. Statin-induced rhabdomyolysis: a complication of a commonly overlooked drug interaction. Oxford medical case reports. 2018 Mar;2018(3):omx104.
11. Kiernan TJ, Rochford M, McDermott JH. Simvastatin induced rhabdomyolysis and an important clinical link with hypothyroidism. International journal of cardiology. 2007 Jul 31;119(3):374-6.
12. Koskinas K, Tzellos TG, Gougoulias K, Gougoulias G, Papakonstantinou C, Kouvelas D. Simvastatin-induced rhabdomyolysis: a case study on clinical-decision making based on the evidence-based medicine approach. Archives of Medical Science. 2007;3(3).
13. Pasternak RC, Smith SC, Bairey-Merz CN, Grundy SM, Cleeman JI, Lenfant C. ACC/AHA/NHLBI clinical advisory on the use and safety of statins. Journal of the American College of Cardiology. 2002 Aug 7;40(3):567-72.
14. Sochman J, Podzimkova M. Not all statins are alike: induced rhabdomyolysis on changing from one statin to another one. International journal of cardiology. 2005 Mar 10;99(1):145-6.