Choosing between Atorvastatin and Rosuvastatin in Statin induced Myopathy

KSBS Krishna Sasanka[1], TY. Sri Hari[2], Anjaly Mary Varghese[3], Sree Sudha TY[4]

ABSTRACT

Introduction: Statins are the widely prescribed lipid lowering drug which reduces the cardiovascular morbidity and mortality. Though well tolerated generally, these drugs can cause severe muscle weakness and elevated creatinine kinase (CK) often termed as statin induced myopathy.

Case report: We report a case of a 67-year-old male patient, a known case of diabetes, hypertension was taking tab. Atorvastatin for 10 years. He complained of cramping pains in both legs and spasm consecutively for 3 months of Atorvastatin intake. Physician advised to stop using Atorvastatin for 8 days and there were no complaints of myopathy during these days. Afterwards, the patient was restarted half dose of Atorvastatin. Atorvastatin then symptoms reappeared, but with less severity. Later on changing the medication to Rosuvastatin, myopathy was relieved and elevated investigatory values got resolved.

Conclusion: We report this case to emphasis on fostering a pharmacovigilance approach in all the treating clinicians in identifying drug induced myopathy and the rationale of using rosuvastatin in reversing the atorvastatin induced myopathy.

Keywords: Atorvastatin, Rosuvastatin, Myopathy, Pharmacovigilance, ADR.

INTRODUCTION

Lipid evaluation as an integral part of the diagnostic workup for many cardiovascular diseases (CVD) as there is established link between the atherosclerosis and CVD. The hypolipidemic drugs group 'Statins' (HMG-CoA reductase inhibitors) are the mainstay of treatment of lipid disorders that are characterized by elevations in low-density lipoprotein cholesterol (LDL-C).[1] Statins generally safe and well tolerated, work by reducing cholesterol- an indispensable ·structural component of biological membranes. They may alter muscle cell membrane function[2-7], perhaps to the extent that electrical properties may get altered, or membrane integrity be compromised. In rabbit skeletal muscle following statin treatment, electrical myotonia has been observed.[5] Clinically 10-12% of patients develop muscle related adverse effects with the use of statins.[1] More serious muscular adverse events are rare, and the incidence of myopathy is 1.2 per 10,000 person-years observed in the general population.[6] Multiple pharmacologic agents, including certain antibiotics, beta-blockers, corticosteroids, can also induce myotoxic effects[8-9], and combining administration of such drugs with a statin could increase the risk of myopathy. It is known that the risk of myopathy increases with increased statin dose and also with statin-fibrate combination.[10]

Symptoms of statin-induced myopathy include a blend of myalgias, muscle tenderness, muscle weakness. Incidences of tendon pain and nocturnal leg cramps may also occur in some.[7,11] The most severe adverse effect of statins encountered is myotoxicity, in the form of myopathy, myalgia, myositis or rhabdomyolysis. Clinically statin toxicity is identified as myalgia or muscle weakness with creatine kinase (CK) levels greater than 10 times the normal upper limit. Multiple pathophysiological mechanisms may lead to statin myotoxicity.

CASE REPORT

A 67-year-old male patient, a known diabetic and hypertensive for the last 30 years, came to Neurology department with chief complaints of myopathy (leg cramping pains, spasm) since 3 months (September-November 2018). Patient was on Tab. Metformin 1000 mg, Inj. Insulin 30 IU/day, Tab. Clopidogrel 75 mg, Tab. Cilnidipine 10 mg, Tab. Telmisartan 40 mg. Patient underwent regular check and had uneventful life. Based on his lipid profile (raised triglycerides-hypercholesterolemia), physician prescribed Tab. Atorvastatin 20 mg OD at night in 2008, which he continued to take for a long 10 years. There were no complaints of myopathy in his medical history previously. From September till November 2018, he experienced severe leg pain and consulted a neurologist.

On general examination, vitals were normal. There was no history of concomitant use of drugs (like herbal or homeopathic medicines taken without a prescription) or any alcohol intake. On CNS examination, there was no neurological deficit and orientation was normal. On CVS examination, S1 S2 present. On respiratory examination, there was normal vesicular breath sounds. On GIT examination, no organomegaly noticed. Physician decided to rule out the cause of myopathy which could be due to diabetes or drug atorvastatin induced.

[1]Senior Resident, Dept. of ENT & HNS, AIIMS, Raipur, [2]DNB Family Medicine, Senior Registrar (MICU-I), Krishna Institute of Medical Sciences (KIMS), Secunderabad, Telangana, [3]Assistant Professor, Dept. of Pharmacology, Santhiram Medical College, Nandyal, AP, [4]Senior Resident, Dept. of Pharmacology, AIIMS, Raipur., India

Corresponding author: Dr. KSBS Krishna Sasanka, Senior Resident, Department of ENT & HNS, AIIMS, Raipur, India

How to cite this article: Sasanka KSBSK, Hari TYS, Varghese AM, Sree Sudha TY. Choosing between atorvastatin and rosuvastatin in statin induced myopathy. International Journal of Contemporary Medical Research 2021;8(3):C1-C3.

DOI: http://dx.doi.org/10.21276/ijcmr.2021.8.3.14

Findings of Neurological Examination and investigations

Nerve conduction - electromyogram/nerve conduction velocity (EMG/NCV) studies were normal and no neuropathic or myoneural abnormalities detected. Radiculopathy absent. Vitamin B12, Vit B1, Vit B6, Vit D all are within normal ranges. Proximal muscle weakness and wasting present, raised creatine kinase myocardial band (CK-MB), increased uric acid and potassium levels. The routine blood investigations like complete blood picture- CBP, liver function test- LFT, renal function test - RFT, complete urine examination (CUE) were within normal range.

From the history taken, neurological examination and lab investigation findings, the diagnosis was 'atorvastatin induced myopathy'. Doctor advised to stop tablet Atorvastatin immediately and accordingly Atorvastatin was stopped for 8 days and there were no complaints of myopathy during these days. Afterwards, the patient started taking half tablet of Atorvastatin 10 mg and the symptoms reappeared, but with less severity. Physician put him on Tab. Rosuvastatin 10 mg OD at night from the end of November 2018. Soon myopathy was relieved and elevated investigative values turned normal.. No similar complaints arose from patient thereafter and he continues to be on Rosuvastatin. This case was reported as drug induced myopathy to local ADR monitoring center at Santhiram medical college and general hospital, Nandyal, Kurnool. Temporal relationship between the drug and event is evident and dechallenge positive as patient's myopathy was resolved on stopping the offending drug and rechallenge positive as the same drug when taken again induced myopathy in the patient. Casualty assessment based on UMC scale concluded this case to be a certain type of adverse drug reaction (ADR) reported to national and international ADR/ pharmacovigilance monitoring centers via vigiflow.

DISCUSSION

Hyperlipidemia refers a condition where there is elevated lipid levels in the blood. Statins are inhibitors of HMG-CoA reductase, the enzyme that catalyzes the rate-limiting step in cholesterol biosynthesis. Atorvastatin and rosuvastatin are relatively most efficacious for the treatment of hypercholesterolemia, and hence frequently prescribed. Statins can cause elevations in muscle enzymes and produce muscle symptoms including myalgia, weakness, myopathy, myositis, and, in some cases, rhabdomyolysis (statin intolerance). Some of the leading theories for statins induced myopathy include isoprenoid depletion, inhibition of ubiquinone or coenzyme Q10 (CoQ10) synthesis, decreased or altered sarcolemma membrane cholesterol, disturbed calcium metabolism or autoimmune phenomena.

A recently published study of the Dutch reported that among rosuvastatin users (101470) and other statin users (37396) did not demonstrate increased myopathy incidence or rhabdomyolysis with rosuvastatin when compared with other statins.[12] Rosuvastatin has less risk of myopathy than atorvastatin (lowest with pravastatin), probably due to its hydrophilic properties and minimal metabolism by CYP3A4. It also shows greater hepatoselectivity than lipophilic agents, as well as a reduced potential for uptake by peripheral cells. Lipophilic statins may enter peripheral tissues by passive diffusion, hence more likely to penetrate muscle and cause myotoxic effects; relatively hydrophilic agents may have a reduced potential for myotoxic events compared with lipophilic agents.[13-16] Atorvastatin, simvastatin, lovastatin, fluvastatin, cerivastatin and pitavastatin are relatively lipophilic compounds.[17] The rate and extent of absorption of atorvastatin is affected by time-of-day administration, hence best administered in the evening, when the rate of endogenous cholesterol synthesis is highest; in contrast pharmacokinetic properties of rosuvastatin remain unaffected and can be given any time.[18-19]

CONCLUSION

All statins are not equal, with the risk of myopathy. Avoid prescribing or combining known myopathy inducing drugs. Choose safer alternatives, carefully weighing the benefit-risk. During patient reviews, continue to monitor the patients for any signs of myotoxicity and recommend screening of creatine kinase at the onset and routinely as a biomarker for muscle damage.[10,20] Neurologic examination is also important to rule out myopathy.[21] Physicians and pharmacovigilance teamed up can help in identifying ADR, report them and eventually revivify safe drug practices, benefiting the patient and the physician mutually.

REFERENCES

1. Bruckert E, Hayem G, Dejager S, et al. Mild to moderate muscular symptoms with high-dosage statin therapy in hyperlipidemic patients. The PRIMO study. Cardiovasc Drugs Ther 2005;19:403-14
2. Levy Y, Leibowitz R, Aviram M, et al. Reduction of plasma cholesterol by lovastatin normalizes erythrocyte membrane fluidity in patients with severe hypercholesterolaemia. Br J Clin Pharmacol. 1992;34:427–430.
3. Morita I, Sato I, Ma L, Murota S. Enhancement of membrane fluidity in cholesterol-poor endothelial cells pre-treated with simvastatin. Endothelium. 1997;5:107–113.
4. Lijnen P, Celis H, Fagard R, et al. Influence of cholesterol lowering on plasma membrane lipids and cationic transport systems. J Hypertens.1994;12:59–64.
5. Sonoda Y, Gotow T, Kuriyama M, et al. Electrical myotonia of rabbit skeletal muscles by HMG-CoA reductase inhibitors. MuscleNerve. 1994;17:891–897.
6. Philips PS, Haas RH, Bannykh S, et al. Statin-associated myopathy and normal creatine kinase levels. Ann Intern Med. 2002;137:581–585.
7. Gaist D, Rodrı´guez LAG, Huerta C, et al. Lipid-lowering drugs and risk of myopathy: a population-based follow-up study. Epidemiology.2001;12:565–569.
8. Le Quintrec JS, Le Quintrec JL. Drug-induced myopathies. Baillieres Clin Rheumatol. 1991;5:21–38.
9. Pasternak RC, Smith SC Jr, Bairey-Merz CN, et al. ACC/AHA/NHLBI clinical advisory on the use and safety of statins. Circulation. 2002;106:1024–1028.
10. Kuncl RW: Agents and mechanisms of toxic myopathy.

CurrOpinNeurol, 2009, 22, 506–515.
11. Sirvent P, Mercier J, Lacampagne A: New insights into mechanisms of statin-associated myotoxicity. CurrOpinPharmacol, 2008, 8, 333–338.
12. McAfee AT, Ming EE, Seeger JD, et al. The comparative safety of rosuvastatin: a retrospective matched cohort study in over 48,000 initiators of statin therapy. Pharmacoepidemiol Drug Saf 2006; June 8
13. Masters BA, Palmoski MJ, Flint OP, et al. In vitro myotoxicity of the 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors, pravastatin, lovastatin, and simvastatin, using neonatal rat skeletal myocytes. ToxicolApplPharmacol. 1995;131:163–174.
14. Gadbut AP, Caruso AP, Galper JB. Differential sensitivity of C2- C12 striated muscle cells to lovastatin and pravastatin. J Mol CellCardiol. 1995;27:2397–2402.
15. Nakahara K, Kuriyama M, Sonoda Y, et al. Myopathy induced by HMG-CoA reductase inhibitors in rabbits: a pathological, electrophysiological, and biochemical study. ToxicolApplPharmacol. 1998;152:99–106.
16. Reijneveld JC, Koot RW, Bredman JJ, et al. Differential effects of 3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors onthe development of myopathy in young rats. Pediatr Res. 1996;39:1028–1035.
17. Davidson M.H. Rosuvastatin: a highly efficacious statin for the treatment of dyslipidaemia. Expert Opin. Invest. Drugs 2002;11:125–141.
18. Cilla D.D. Jr, Gibson D.M., Whitfield L.R., Sedman A.J. Pharmacodynamic effects and pharmacokinetics of atorvastatin after administration to normocholesterolemic subjects in the morning and evening. J. Clin. Pharmacol. 1996;36604–609.
19. Martin P.D., Mitchell P.D., Schneck D.W. Pharmacodynamic effects and pharmacokinetics of a new HMG-CoA reductaseinhibitor, rosuvastatin, after morning or evening administration in healthy volunteers. Br. J. Clin. Pharmacol. 2002;54472–477.
20. Smith CC, Bernstein LI, Davis RB, et al. Screening for statin-related toxicity: the yield of transaminase and creatine kinase measurementsin a primary care setting. Arch Intern Med. 2003;163:688–692.
21. Antons KA, Williams CD, Baker SK, et al. Clinical perspectives of statin induced rhabdomyolysis. Am J Med 2006; 119:400–409.

Source of Support: Nil; **Conflict of Interest:** None

Submitted: 21-01-2021; **Accepted:** 15-02-2021; **Published:** 26-03-2021