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Southeast Asian Journal of Health Professional

Journal homepage: https://www.sajhp.com/

Case Report

A case report on rosuvastatin-induced myopathy

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ARTICLE INFO

Article history:
Received 14-11-2023
Accepted 11-12-2023
Available online 09-03-2024

Keywords:
HMGCoA
LDLC
CoQ10
Serum C Reatinine Kinase(CK)
Myopathy
CAD

ABSTRACT

Statins are the most commonly used lipid-lowering drugs in cardiovascular patients. Rosuvastatin is a majorly used statin. Rosuvastatin will induce myopathy; it is a rare side effect. In my case report, the patient experiencing muscle cramps for 3 years on and off. He consulted a cardiologist. The doctor advised Atorvastatin. He has been on rosuvastatin for 6 months. From the last 6 months, he has not experienced and myopathy symptoms.

1. Introduction

Statins (HMG-CoA reductase inhibitors) are the mainstay for treating lipid disorders characterized by low-density lipoprotein cholesterol (LDL-C) elevations. Statins have revolutionized the prevention of primary and secondary coronary atherosclerotic disease due to their lipid-lowering properties and other pleiotropic effects that beneficially affect atherosclerotic plaque stability.[1] A class of disorders known as myopathies results in damage to the muscle fibers and weakening of the muscles. Myopathies come in several forms and can be brought on by autoimmune diseases, genetics, or specific drugs. Muscle cramps, stiffness, and weakness are common symptoms. Depending on the particular form of myopathy, treatment options may include alternative medication, physical therapy, or lifestyle modifications. Most patients very well tolerate statins; however, 10 -12% develop muscle-related adverse effects.[2]

1.1. Pathophysiology

There are several potential explanations for statin-induced myopathy, but the precise mechanism is yet unknown. Leading suggestions include depletion of isoprenoids, suppression of ubiquinone or coenzyme Q10 (CoQ10) synthesis, modification or decrease of cholesterol in the sarcolemal membrane, disruption of calcium metabolism, or autoimmune events.

1.2. Depletion of isoprenoid

One proposed mechanism of skeletal muscle cell death is statin-induced isoprenoid deficiency. Isoprenoids are lipids by-products of the HMG-CoA reductase pathway.[5] Farnesyl pyrophosphate (F-PP) and geranylgeranyl pyrophosphate (GG-PP) are the most important isoprenoids in the HMG-CoA reductase pathway (Figure 1).[8] Protein prenylation is the process by which isoprenoids bind to proteins via either farnesylation or geranylgeranylation. Statins reduce the phrenylation of proteins.[6] The reduction of protein prenylation (farnesylation or geranylgeranylation) is thought to increase systolic calcium which activates caspase-3 and leads to cell death. Supporting the role of

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https://doi.org/10.18231/j.sajhp.2024.007

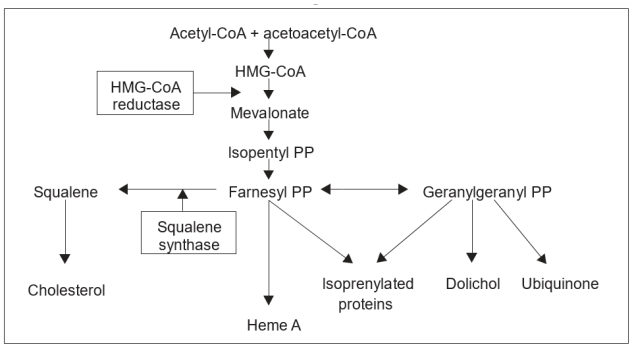

Figure 1: The cholesterol biosynthetic pathway. Statin inhibition of HMG-CoA reductase, the rate-limiting step of cholesterol synthesis, causes a reduction in the production of isoprenoids, most importantly farnesyl PP and geranylgeranyl PP. The reductionof isoprenoids causes a reduction in the production of isoprenylated proteins whose deficiency causes disturbances in cell apoptosis regulation and skeletal muscle cell structure. [3–7]

isoprenoids in statin myopathy is the finding that statin-induced apoptosis in vascular smooth muscle cells is prevented by supplementation with isoprenoids including F-PP and GG-PP. [7,9]

1.3. Ubiquinone inhibition or CoQ10

Ubiquinone or CoQ10 is a constituent of oxidative phosphorylation and ATP production in the mitochondria. [10] Statins inhibit the synthesis of mevalonate, a precursor of CoQ10. Theoretically, statins can cause myopathy by inhibiting the synthesis of CoQ10 in the mitochondria which might compromise the function of the mitochondrial respiratory chain, impair energy production, and ultimately induce myopathy. [10]

1.4. Lower sarcolemmal cholesterol levels

Reduced cholesterol levels cause alterations in myocyte membrane cholesterol. [11] Sarcolemal cholesterol deficiency, as a result of the dynamic equilibrium between membrane and plasma lipids, may adversely modify membrane physical properties, such as membrane integrity and fluidity, thus resulting in membrane destabilization. [12] However, two key findings argue against this mechanism. The first is that myotoxicity does not occur in vitro when cholesterol is lowered by inhibiting squalene synthetase in human skeletal myotubules. [13] The second finding is that inherited disorders of the distal cholesterol synthetic pathway result in reduced cholesterol levels without associated clinical myopathy. [14]

1.5. Disturbed calcium homeostasis

The regulation of calcium (Ca^{2+}) release and uptake is critical for the normal function of muscle cells. [8] L-type calciumchannels mediate the initial increase of intracellular calcium. The sarcoplasmic reticulum's ryanodine receptors are opened by this rise in intracellular Calcium, which results in a significant rise in intracellular Calcium that starts muscle contraction. In a study by Mohaupt et al., muscle biopsies from statin myopathy patients revealed elevated expression of ryanodine receptors 3 (RR3). It is unknown whether elevated RR3 causes or contributes to statin myopathy susceptibility. [4]

1.6. Diagnosis

The NLA does not recommend routine measurement of CPK for all patients before starting statin therapy. [3] However, serum creatinine kinase (CPK) can be advised to patients who are presenting with muscle toxicity. Normal levels of CPK are 55-170 U/L in male,30-145 U/L in females.

1.7. Treatment

Non-statin lipid-lowering drugs such as ezetimibe, colesevelam, pravastatin, fluvastatin, bempedoic acid, pravastatin, PCSK9 inhibitors like inj. Alirocumab, inj. Evolocumab Alternate statins like atorvastatin, Pravastatin, fluvastatin, Pitavastatin will cause less myopathy.

2. Case Presentation

2.1. History of present illness

A 35-year-old male patient came to the hospital with chief complaints of severe muscle cramps at midnight for 3 years on and off symptoms increased since 3 days. These symptoms are developed after the usage of rosuvastatin. He is a known case of hypertension since 5yrs on regular medication cilnidipine, CAD since 3 years on regular medication rosuvastatin and clopidogrel. He came for a regular checkup at cardiology. The doctor advised atorvastatin instead of rosuvastatin.

2.2. Social history

He is married and has 2 sons. He is a financier.

2.3. Allergies

No known foods, medicines, or environmental allergies.

2.4. Past medical history

He had Hypertension since 5 years
CAD since 3 years

2.5. Surgical history

He has no previous surgical history.

2.6. Medication history

Tab. cilnidipine 10mg
Tab. rosuvastatin 20mg
Tab. clopitab 75mg

2.7. Birth history

The patient was the first child and he had normal weight.
Immunization as per schedule.

2.8. Family history

His family history was nill and his brother also suffering with myopathy after using rosuvastatin.

3. Vitals

3.1. General examination

He is cooperative coherent and conscious.

3.2. Vitals

Temp: 98.6F
Blood pressure: 130/90mmhg
Pulse rate: 80/min
Respiratory rate: 22/min
SPO 2:98%

4. Systemic Examination

4.1. Respiratory function

NVBS, bilateral air entry present, no additional sound heard.
He has a normal respiratory rate that is 22/min.

4.2. Gastrointestinal

Per abdomen soft, no tender, no organomegaly noted.

4.3. Cardiovascular

S1 S2 normal
No murmurs heard

4.4. Investigations

CBP: HB-13gms%
WBC-8000c/cmm
PLT-2 lakhs
PCV-40%
CPK mm: 1000 mcg/lit after 2 month atorvastatin 190 mcg/lit
Lipid Profile: T. CHOLESTEROL- 220mg/dl
TRIGLYCERIDES-170mg/dl
LDL-179mg/dl
HDL-60mg/dl
ECG: LVH strain noted.
2-D Echo: Inferiorwall hypokinetic
Grade I diastolic dysfunction

5. Discussion

Statins continue to be the mainstay of the dyslipidemia treatment regimen and a crucial medication for both primary and secondary cardiovascular disease prevention. Doctors can lower the prevalence of statin myopathy by treating each patient differently. A low-dose statin or a statin substation should be administered to patients who have risk factors for statin myopathy, and the dosage should be gradually increased for patients with myopathy, several strategies have been proposed as an alternative to daily statin therapy. Among them are long-acting statins like atorvastatin.

6. Conclusion

Rosuvastatin is the most commonly used lipid-lowering agent for CAD patients considering its efficacy. A rare side effect of rosuvastatin is myopathy. Replacing with other statins which have less myopathy like atorvastatin and other lipid lowering agents will reduce the myopathy.

7. Source of Funding

None.

8. Conflict of Interest

None.

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Cite this article: Sony MD, Rachana N, Sridhar O, Chillara T. A case report on rosuvastatin-induced myopathy. *Southeast Asian J Health Prof* 2024;7(1):28-31.