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Atorvastatin Induced Proximal Muscle Myopathy – Rare Event of Commonly Used Drug

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Abstract

Statins are commonly used drugs for primary and secondary prevention of coronary artery disease. Statins associated muscle adverse events are not uncommon. Myalgias and myopathy occur with a frequency of 2 to 11 percent.1 However, severe myonecrosis and clinical rhabdomyolysis are much rarer (0.5 percent and less than 0.1 percent, respectively) [1,2]. Statin intolerance was neglected during routine clinical practice. We report a case of 58 year old male who developed severe proximal muscle weakness after giving high dose of atorvastatin.

Keywords: Atorvastatin; Coronary Artery Disease; Myonecrosis; Rhabdomyolysis

1. Patient Background

A 58 year old male (weight 63 kg; BMI 21.8 kg/m^2) was admitted in our cardiology department with acute coronary syndrome in form of ST segment elevated inferior wall myocardial infarction. He was started on dual antiplatlets,

beta blockers, anticoagulation and 80mg of atorvastatin. After 3 weeks of discharge, he brought on stretcher in our OPD. On reviewing history, he had difficulty in getting up from sitting position and difficuility in raising arms above the head. He was admitted and through neurological examination done which revealed decrease in power of the proximal muscles of hips and shoulder, severe tenderness present on deep palpation. Power of distal muscles of the extremities was normal. His general physical examination, higher mental functions, cranial nerves, sensory system and all deep tendon reflexes are normal. On investigation, he had FBS 87mg/dl, HB 13gm%, SGOT-351 IU, SGPT-251, Bilirubin 1.2mg/dl, Urea 31mg/dl, creatinine 0.9mg/dl, ESR 120 mm at 1st hour, CRP 74 mg/l (<5 mg/l), Calcium 9.8 mg/dl, phosphorous 2.8 mg/dl, Potassium 4.2meq/l, TSH 1.6 uIU/ml, vitamin D 11ng/ml (30-100ng/ml), CPK 2985 U/L (< 170 U/L), urine examination was normal. He had vitamin D deficiency, raised inflammatory markers and more than 10 times raised CPK, raised liver enzymes.

Possibility of inflammatory myopathy (polymyositis) vs statin induced myopathy was kept. His atorvastatin was stopped and given injectable vitamin D cholicalciferol (600000 IU). After 2 weeks he came to OPD, his weakness was improved he had no difficuility in walking. His lab parameters revealed normalization of CPK 35 U/L, ESR 26 mm at 1sr hour, CRP 10 mg/l, SGOT 21 IU, SGPT 18 IU. So the final diagnosis of atorvastatin induced myopathy was kept with vitamin D deficiency. He was started on 10mg rosuvastatin for secondary prevention coronary artery disease. He was doing well on subsequent follow up visits.

2. Discussion

Terminology around statin-associated adverse muscle events is variable and has changed over time. Statin intolerance as defined by 2014 National Lipid Association Statin Muscle Safety Task Force: [3]

Myalgia – A symptom of muscle-discomfort, including muscle aches, soreness, stiffness, tenderness, or cramps with or soon after exercise, with a normal creatine kinase (CK) level. Myalgia symptoms can be described as similar to what would be experienced with a viral syndrome such as influenza.

- Myopathy – Muscle weakness (not due to pain), with or without an elevation in CK level.
- **Myositis** – Muscle inflammation.
- **Myonecrosis** – Elevation in muscle enzymes compared with either baseline CK levels (while not on statin therapy) or the upper limit of normal that has been adjusted for age, race, and sex:

•Mild – Threefold to 10-fold elevation in CK.

•Moderate – 10-fold to 50-fold elevation in CK.

•Severe – 50-fold or greater elevation in CK.

- **Clinical rhabdomyolysis** – Defined by the Task Force as myonecrosis with myoglobinuria or acute renal failure (an increase in serum creatinine of least 0.5 mg/dL [44 micromol/L]).

The risk of muscle injury is substantially increased when taking a statin that is extensively metabolized by cytochrome P450 3A4 (lovastatin, simvastatin, atorvastatin) together with a drug that interferes with CYP3A4. Pravastatin, fluvastatin, rosuvastatin, and pitavastatin are preferred when concurrent therapy with a strong inhibitor of CYP3A4 cannot be avoided [4,5]. Risk factors associated with development of statin intolerance are old age, female sex, lean body mass, chronic kidney disease, vitamin D deficiency, Hypothyrodism [6]. CYP3A4 inhibitors like diltiazem, verapamil. Amiodarone, Protease inhibitors, cyclosporine, grape fruit juice should be avoided with statins. Concomitant use of fibrates and niacin with statins increase the risk for statin induced myopathy. The diagnosis of symptomatic statin myopathy with laboratory abnormalities (ie, elevated serum CK) is typically straightforward and based on a temporal association for both onset with initiation of statin therapy and resolution with statin withdrawal. However, some patients can have muscle symptoms from statin therapy without an elevation in serum CK, and it can then be difficult to be certain whether muscle symptoms are due to statin therapy. The onset of muscle symptoms is usually within weeks to months after the initiation of statin therapy, but may occur at any time during treatment [7].

CPK levels monitoring not routinely required in patients on statin therapy. It is useful to obtain a baseline CK level for reference purposes prior to starting statin therapy. Patients treated with statins should be alerted to report the new onset of myalgias or weakness. In patients who develop evidence of muscle toxicity while on statin therapy, Assess for drug interactions, and if none is noted, check vitamin D and thyroid function status. Pravastatin and fluvastatin appear to have much less intrinsic muscle toxicity than other statins. In patients who are unable to tolerate daily dosing, dose should be decreased and trial of alternate-day or less frequent dosing (one to two times weekly) of statin therapy (alternate day dosing). There was no role of administering Coenzyme Q10 (CoQ10) for treatment or prevention of statin myopathy. Now a days PCSK9 inhibitors like evolucumab studied in Fourier trial are routinely prescribed for primary and secondary prevention of high risk patients who are statin intolerant [8].

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