Pravastatin Induced Myopathy

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Abstract:
Lipid-lowering agents such as HMG-CoA reductase inhibitors (also known as statin drugs) are generally well tolerated.

But a recognized side effect still can happen, We report a case of 47-year-old Iraqi male patient previously known hypothyroid, was not on replacement therapy, as he did not appear after his thyroid functions was checked came in with severe body pain for 10 months got worse in the last three months, started on lipostat (ten months ago) found to have myopathy as evident by high CPK which improved gradually clinically and biochemical after stopping lipostat.

Key words: pravastatin, myopathy

Introduction:
The 3-hydroxy-3-methyl-glutaryl-coenzyme A (HMG-CoA) reductase inhibitors, commonly known as statins are widely used as lipid lowering agents in the primary and secondary prevention of cardiovascular events A recognized side effect of statin use is myotoxicity ranging from mild non-specific myalgia to myositis, which can progress to the rare but life threatening syndrome of acute rhabdomyolysis(1). Uncomplicated myalgia (muscle pain and weakness) is the most common musculoskeletal adverse effect and occurred in about 1-6% of patients receiving statins in controlled trials. Myopathy (characterized by muscle pain and weakness) is the most common musculoskeletal adverse effect and occurred in about 1-6% of patients receiving statins in controlled trials. The risk is dose-related and there are predisposing factors that may increase the risk e.g. multisystem disease, serious infection, hypothyroidism, old age, and small frame.

Case Report:
47 yrs old Iraqi gentleman known case of CAD S/P PTCA 3 months back and hyperlipidemia presented with H/O generalized body weakness for 10 months duration and generalized body ach for 3 weeks duration. He was in his usual state of health 10 months back when he developed generalized body weakness that was gradual in onset, progressive in nature and he had difficulty in getting up of chair or floor, to comb his hair and to climb stairs. For the last 3 months his weakness deteriorated and he developed back pain and bilateral leg pain mainly in thighs followed by upper limb and shoulder pain. Pain was mainly initiated by movements, severe in intensity and aching in nature, not associated with fever. Weakness was not increased with activity or getting worse by the end of the day, history of change in quality of voice for past three weeks became husky. No history of diplopia or decreased visual acuity, paresthesias or sensory symptoms. Difficulty in swallowing; skin rash chest pain, joint pain or swelling no rash, gain about 10 kg in past 7-8 months, increasing appetite for past few months, cold intolerance and constipation, no history of drug abuse. He is not smoker PMH:CAD S/P PTCA 3 months ago
HO Hyperlipidemia, he is on; ECASA 300 mg OD, Plavix 75 mg OD Lipostat 20 mg HS started 10 month ago, ISDN-R 20 mg OD, Vastarel MR 35 mg bid, NTG 0.5 mg prn.

Examination: looks in good general condition, middle aged men, moderate built, a febrile, BP 140/85 mmHg, Pulse 60/min, RR 20/min clinical examination reveals no abnormality apart from mild tenderness on palpation to his thighs and legs, he has no skin rash, diplopia, can count up to twenty loudly.

Examination of other systems-unremarkable, Laboratory: WBC 4700 Hb 15 g/dl, platelets 153,000; BUN 4.4 mmol/L (1.7-8.3); creatinine 98 mmol/L (62-124); calcium 2.4 mmol/L (2.1-2.6); chloride 97 mmol/L (96-110); sodium 133 mmol/L (135-45); potassium 4 mmol/L (3.6-5.1). The creatinine kinase on admission was 3736. He was rehydrated for four days and his kidney function remains stable and in a two months follow-up it came down to 126 after stopping the Lipostat and starting the patient on L-thyroxin 50 mg once daily. He improved gradually with in two months.
Discussion:

The statins are increasingly used to lower the serum cholesterol concentration for both primary and secondary prevention of coronary disease. Statins are both effective and generally safe. Although uncommon, muscle toxicity remains a concern. However, severe myopathy is unusual, affecting 0.1 percent of patients. In patients with normal serum CK, there is no evidence of permanent or progressive muscle injury\(^2\). Myopathic syndromes associated with statin therapy range from myalgias to myositis to overt rhabdomyolysis, which may be associated with acute renal failure\(^3\). 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. Review of 44 cases of statin-associated myopathy found a mean duration of therapy before symptom onset of 6.3 months (range 0.25 to 48 months); approximately two-thirds of patients had onset of symptoms within six months of starting therapy\(^4\). Myalgias and weakness resolve and serum creatine kinase concentrations return to normal over days to weeks after discontinuation of the drug. In the above study, the mean time to resolution of symptoms in 43 patients who discontinued statin therapy was 2.3 months (range 0.25 to 14 months); 58 percent had resolution of symptoms within one month and 93 percent had resolution within six months\(^4\). Clinically significant myopathy, defined as a serum CK elevation more than 10 times normal in association with muscle symptoms, occurred in less than 0.5 percent of patients in the large clinical trials\(^5\). The mechanism by which statins cause muscle toxicity is not well understood. They inhibit the conversion of HMG-CoA to mevalonic acid, which is an important early step in cholesterol synthesis. Statins can also decrease the synthesis of coenzyme Q10 (CoQ10, ubiquinone), which plays an important role in muscle cell energy production. It has been speculated that the reduction in CoQ10 may contribute to statin-induced muscle injury. The susceptibility to muscle injury appears to vary among the different statins. Myositis has been described in less than 0.5 percent overall, primarily occurring at higher doses. With simvastatin, for example, the incidence in clinical trials, in which patients were carefully monitored and some interacting drugs described below excluded, was 0.02 percent at 20 mg/day, 0.07.

Percent at 40 mg/day, and 0.3 percent at 80 mg/day\(^6\). The risk of myopathy appears to be lowest with pravastatin (< 0.1 percent\(^7\). The possible differential sensitivity of statins on striated muscle has been evaluated in cell culture experiments\(^8\). Simvastatin and lovastatin reduced cell viability by 50 percent at concentrations of 1 and 5 \(\mu\)mol/L, respectively; a much higher level of 300 \(\mu\)mol/L was required with pravastatin, suggesting less toxicity. The toxic effect of these agents on dividing myocytes may contribute to the development of myositis. The more hydrophilic statins, pravastatin and rosuvastatin, may have less penetration into muscle than the other more lipophilic statins enhanced susceptibility to statin-associated myopathy occurs in patients with acute or chronic renal failure, obstructive liver disease, and hypothyroidism. The increase in susceptibility to myopathy is substantially greater in patients receiving concurrent therapy with a number of drugs, particularly those that inhibit CYP3A4. These include cyclosporine, gemfibrozil, macrolide antibiotics (eg, erythromycin).

References: