Statin Myopathy
A common cause of chronic pain

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Learning Objectives

• Understand the process to differentiate the three types of statin myopathy.
• Realize the professional boundaries when treating a patient with statin myopathy.
• Review an actual case of statin myopathy.
• Comprehend the Numbers Needed to Treat (NNT).
Opening Statement ...

- Diagnosis is the key to successful treatment!
Benefits of Statins

• Statins appear to drive down the risk of heart attack or stroke by lowering the levels of fatty deposits circulating in the bloodstream.

• Research suggests that the drugs dampen inflammatory processes that can prompt deposits of plaque to break away from blood vessel walls and cause sudden blockages of arteries leading to the heart or brain.

• JOHN D. ABRAMSON and RITA F. REDBERG. Don’t Give More Patients Statins. NYT. Published: November 13, 2013.
Adverse Drug Reactions

• However, the popular profile of statins in terms of efficacy has been maligned by its adverse events.

• The myotoxicity, ranging from mild myopathy to serious rhabdomyolysis, associated with HMG-CoA reductase inhibitors, during treatment of hypercholesterolaemia is of paramount importance.

Caveat Emptor

• Perhaps more dangerous, statins provide false reassurances that may discourage patients from taking the steps that actually reduce cardiovascular disease.

• According to the World Health Organization, 80 percent of cardiovascular disease is caused by smoking, lack of exercise, an unhealthy diet, and other lifestyle factors.

• Statins give the illusion of protection to many people, who would be much better served, for example, by simply walking an extra 10 minutes per day.

JOHN D. ABRAMSON and RITA F. REDBERG. Don’t Give More Patients Statins. NYT. Published: November 13, 2013.
Statin Myopathy

- Statins are associated with adverse side effects of skeletal myopathy.
Statin Myopathy

- Statin treatment reduces ubiquinone levels in the cholesterol synthesis pathway, which may be associated with mitochondrial dysfunction. In addition, reactive oxygen species (ROS) production and apoptosis induced by statins may provide cellular and molecular mechanisms in skeletal myopathy.

Statin Myopathy Symptoms

- The myopathies are neuromuscular disorders in which the primary symptom is muscle weakness due to dysfunction of muscle fiber.
Statin Myopathy Symptoms

• Other symptoms of statin myopathy can include muscle cramps, stiffness, and spasm.
Types of Statin Myopathy

• **Myalgia**—muscle weakness, soreness, tenderness, stiffness, cramping, or aching, either at rest or with exertion, without any elevation in CK.

• **Myositis**—elevated CK with or without muscle symptoms. The “-itis” suffix is unfortunate since myositis does not correspond to inflammation on biopsy.

• **Rhabdomyolysis**—muscle symptoms with a CK level 10 times the upper limit of normal or higher. Evidence of renal dysfunction is not required for the diagnosis, as preexisting renal disease and hydration status are more closely related to kidney damage than the degree of muscle injury.

Physician Denial

Eighty-seven percent of patients reportedly spoke to their physician about the possible connection between statin use and their symptom.

Physician Denial

• Patients reported that they and not the doctor most commonly initiated the discussion regarding the possible connection of drug to symptom (98% vs 2% cognition survey, 96% vs 4% neuropathy survey, 86% vs 14% muscle survey; p < 10^{-8} for each).

• Physicians were reportedly more likely to deny than affirm the possibility of a connection.

CONCLUSIONS

• Since low reporting rates are considered to contribute to delays in identification of adverse drug reactions (ADRs), findings from this study suggest that additional putative cases may be identified by targeting patients as reporters, potentially speeding recognition of ADRs.

Statin Myopathy: A common dilemma

• A focused history and neuromusculoskeletal examination are important in the evaluation of muscle complaints that may be induced by statins.

Neurological Findings

• Diffuse proximal muscle weakness
• Mild hyporeflexia
• Sensory intact

Hip Pain and Weakness

• The typical patient with a statin myopathy is usually older, and complains of pain and stiffness in the muscles of their thighs and buttocks.

• Pate D. Statin Myotosis: A Not-So-Rare Cause of Muscle Pain. *Dynamic Chiropractic* – April 1, 2013, Vol. 31, Issue 07.
Hip Pain and Weakness

- Coronal T2-weighted STIR MRI of the pelvis. Note the edema involving the left gluteus minimus (white arrows at upper right of image).

- Pate D. Statin Myotonia: A Not-So-Rare Cause of Muscle Pain. Dynamic Chiropractic – April 1, 2013, Vol. 31, Issue 07.
Muscle-Related Adverse Effects (MAE)

- Three hundred fifty-four patients (age range 34-86 yrs) who self-reported muscle-related problems associated with statin therapy.

Muscle-Related Adverse Effects (MAE)

- Patients with perceived statin-associated MAEs completed a survey assessing statin drugs and dosages; characteristics of the MAEs; time course of onset, resolution, or recurrence; and impact on quality of life (QOL).

Quality of Life

• The best way of approaching quality of life measurement is to measure the extent to which people's 'happiness requirements' are met (those requirements which are a necessary, although not sufficient, condition of anyone's happiness) those 'without which no member of the human race can be happy.'

Muscle-Related Adverse Effects (MAE)

• Recurrence with rechallenge had a significantly shorter latency to onset (median 2 wks).
• The MAEs adversely affected all assessed functional and QOL domains.
Muscle-Related Adverse Effects (MAE)

- Higher potency statins reproduced MAEs in 100% of 39 rechallenges versus 73% (29/40) with lower potency rechallenges (p<0.01).
- Time course of onset after statin initiation varied (median 14 wks); some MAEs occurred after long-term symptom-free use.
Muscle-Related Adverse Effects (MAE)

CONCLUSION:

• This study complements available information on the properties and natural history of statin-associated MAEs, affirming dose dependence and strong QOL impact.

CONCLUSION:

• The data indicating a dose-dependent relationship between MAE risk and recurrence suggest lower potency statins or discontinuation may bear consideration for ameliorating symptoms.

Number Needed To Treat

• According to The NNT Group, statin drugs given for five years in order to prevent heart disease in people who have no history of heart disease is 104.

• The NNT. “Statins for Heart Disease Prevention (Without Prior Heart Disease). http://www.thennt.com/nnt/statins-for-heart-disease-prevention-without-prior-heart-disease/
Number Needed To Treat

• According to their findings, one in 50 people on statins develops diabetes and one in ten experiences muscle damage as defined as rhabdomyolysis. Undiagnosed muscle pain, such as myalgia wasn’t included.

• The NNT. “Statins for Heart Disease Prevention (Without Prior Heart Disease). http://www.thennt.com/nnt/statins-for-heart-disease-prevention-without-prior-heart-disease/
Number Needed To Treat

• The Mediterranean Diet has an NNT of 61 for preventing, stroke, heart attack or death with no harms noted. So, according to The NNT, the Mediterranean Diet appears to be a better choice than statins for primary prevention of stroke, heart attack or death.

• The NNT. “Mediterranean Diet for Heart Disease Prevention (Without Known Heart Disease).” http://www.thennt.com/nnt/mediterranean-diet-for-heart-disease-prevention-without-known-heart-disease/
Case Report

- A 63 year-old professor experienced a myocardial infarct on February 16, 2013. He endured severe chest and upper thoracic pain for a period of 3 hours due to complete occlusion of the left anterior descending coronary artery, which is known as the “widow maker.” Aspirin and nitroglycerine in the ER did not reduce the pain and morphine reduced the pain from 10/10 to 9.7/10.
Case Report

Angioplasty (One stent implant) restored circulation and the patient recovered without signs of permanent heart damage.
Muscle Pain and Piriformis Syndrome

Approximately 2-4 weeks post surgery the patient experienced severe muscle pains and piriformis syndrome.
Discussion

• How you would manage this patient taking statin medications and presenting with the signs and symptoms of statin myopathy and piriformis syndrome?
Clinical Challenge

- What subjective and objective findings differentiate lumbar radiculopathy and piriformis syndrome due to piriformis compression of the sciatic nerve.
Piriformis Syndrome

• Piriformis syndrome is a neuromuscular condition characterized by a constellation of symptoms that includes hip and buttock pain. The pain is often referred down the back of the leg, sometimes into the medial foot.

Symptoms of Piriformis Syndrome

- Pain in buttocks and affected limb with sitting and rising to stand from seated or squatting position
- Pain and/or paresthesias from sacral area to affected limb
- Change of position does not relieve pain completely
- Increasing pain after sitting for longer than 15-20 minutes (most common symptom)
Symptoms of Piriformis Syndrome

- Weakness in ipsilateral lower extremity
- Contralateral SIJ pain
- Headaches
- Neck pain
- Abdominal, pelvic, and inguinal pain
- Dyspareunia in women
- Pain with bowel movements
Signs of Piriformis Syndrome

- Tenderness in region of SIJ, greater sciatic notch, and piriformis muscle
- Palpable mass in ipsilateral buttock
- Asymmetrical weakness of affected limb
- Presence of Pace, Piriformis, Frieberg, Lasegue, and Beatty signs
- Ipsilateral leg length inequality
- Gluteal atrophy (chronic cases only)
Evaluation and Management of Drug Induced Myopathy and Piriformis Syndrome

• Statin holiday and determine response
• Resume statin medications with reduced dosage and determine response
• Change from one statin medication to another and determine response
• If patient is allergic to statins it might be necessary to discontinue and switch to niacin
• Dietary changes, regular exercise, and stress control is mandatory
Closing Statement ...

• Diagnosis is the key to successful treatment!
Thank You!
• Statins (or HMG-CoA reductase inhibitors) are a class of drugs used to lower cholesterol levels by inhibiting the enzyme HMG-CoA reductase, which plays a central role in the production of cholesterol in the liver, which produces about 70 percent of total cholesterol in the body.

Pre and Post Stent Images