

Evidenced Based Critically Appraised Topic
Adverse Effects of Statins and Exercise
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Clinical Scenario

A 60 year old male presents to the clinic for a physical to renew his CDL license. He is in excellent physical condition, BP 110/80, denies any cardiac or respiratory history. Patient has never smoked, and only has an occasional drink. The patient however has a significant family history of heart disease. His father died at age 55 of a massive heart attack, and his mother died at the age of 62 from a stroke, with a history of HTN. Lab reports show elevated total cholesterol at 217 mg/dl, and an elevated LDL at 156 mg/dl. The patient already takes Aspirin 81mg a day, red yeast rice, and Omega-3 fish oil. It is recommended that the patient start a low dose of Simvastatin. The patient expresses hesitation in starting a Statin because he heard that it can cause a lot of muscle aches.

Clinical Question

Does regular exercise reduce the muscle pain patients often experience when starting statin therapy compared to patients who do not exercise?

Articles

Di Stasi, S., MacLeod, T., Winter, J., & Binder-Macleod, S. (2010). Effects of statins on skeletal

muscle: A perspective for physical therapists. *Physical Therapy*, 90(10), 1530-1542.

Simple, S. J. (2012). Statin therapy, myopathy and exercise--a case report. *Lipids in Health*

and Disease, 11, 40-42.

Summary and Appraisal of Key Evidence for Article 1

Di Stasi et al., (2010) conducted a peer-review on the use of statins, exercise, and muscle injury providing a Level 1, Grade A level of evidence. Statin treatments have been shown to exacerbate exercise-induced skeletal muscle injury. The extent of statin-influenced myopathies during exercise is still under investigation. Exercise-induced muscle damage and increased serum levels of creatine kinase (CK) increase as a result of damage to the muscle tissue following intense, prolonged exercise, especially exercises that are weight bearing and include eccentric muscular contractions. Myocytes that are affected by exercise induced muscle damage release intracellular substances, such as CK, into the blood; therefore, CK levels are a commonly used marker to determine skeletal muscle damage. Individual CK level responses vary and may be influenced by multiple factors, such as genetics, level of athletic performance, and types of exercises being performed. The exact mechanisms or pathways through which statins adversely affect the skeletal muscles during exercise are not fully understood. The ubiquitin proteasome pathway is one possible mechanism for statin induced muscle myopathy during exercise. Up regulation of the ubiquitin proteasome pathway during eccentric exercise has been shown to be associated with increased muscle injury, decreased muscle strength, and a decrease in myofibrillar protein.

Summary and Appraisal of Key Evidence for Article 2

Simple, (2012) gave a case report to assess the effects of statins and exercise on myopathy providing a Level 1, Grade A level of evidence. Reducing high cholesterol levels through pharmacotherapy is a key goal for patients with dyslipidemia. Despite the controversy surrounding statins they remain one of the most widely prescribed groups of lipid-lowering drugs simply because of their effectiveness. Serious adverse side effects are rare, however, myopathy symptoms including fatigue, weakness, cramps and muscle pain are commonly reported by patients. These symptoms may be exacerbated in patients who exercise and be prevalent in as many as 75% of athletes who take the drug. The underlying mechanism(s) responsible for the statin-induced myopathy is unclear, however there is evidence that statins may up regulate muscle cell apoptosis, inflammation and protein catabolism in response to eccentric exercise. Creatine kinase (CK), another indirect marker of muscle damage is significantly elevated in statin users following exercise when compared to non-statin users. Statin therapy may negatively affect the stability of skeletal muscle cell membranes. This may in part explain why CK is elevated following exercise, particularly strenuous or unaccustomed exercise. The more pronounced muscle damage may up-regulate inflammation which in turn could account for the longer recovery time that exercising patients experience. Clinicians and rehabilitation practitioners should be aware of the prevalence and potential negative effects that statin therapy has on patients (even in low doses) and in particular on those patients that regularly engage in physical activity. It is arguable that this is even more pertinent for patients who were previously sedentary and then begin exercising as part of their chronic disease rehabilitation plan. The paradox which exists for these patients is that physical activity which is supposed to improve functionality and quality of life may actually exacerbate the myopathy if they are taking statins. This makes adherence to physical rehabilitation programs a challenge.

Results

The results of the articles indicate that statins may negatively affect the stability of skeletal muscle cell membranes, and adding strenuous exercises can exacerbate damage to the muscles even further. However, the extent of statin-influenced myopathies during exercise is still under investigation. Further research is recommended at this time.

Clinical Bottom Line

According to these two articles, statins remain one of the most widely prescribed groups of lipid-lowering drugs despite their adverse effects simply because of their effectiveness. Statins may induce myopathy, inflammation, and protein catabolism in response to exercise. However, further research is necessary to determine the actual extent of muscle damage, and what can be done to reduce this adverse effect. If exercise truly does increase statin-induced myopathy our patients will be less likely to comply with our treatment plan of pharmacotherapy and exercise to lower their risk of CVD.

Implications for Practice

I would recommend lifestyle modifications for my patients with an increased risk of heart disease, and closely monitor their triglyceride, cholesterol, LDL, and HDL levels. If the patient is unable to control their levels after trying red yeast rice, omega-3 fish oil, and possibly niacin I would recommend starting them on a low dose statin. Regardless of the increased risk for myopathy I would still recommend regular exercise. I would encourage the patient to come in for a follow up in 2-4 weeks to monitor their tolerance of the new medication, and then follow up 3 months later to reevaluate their lipid panel and check their creatine kinase level to monitor for muscle damage.