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Changes in muscle strength in individuals with statin-induced myopathy: A summary of 3 investigations

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BACKGROUND: There are inconsistent findings regarding muscular weakness in individuals with statin-induced myalgia.

OBJECTIVE: We used rigorous muscle testing to compare findings from 3 investigations in 3 different study populations to determine if statin myalgia is associated with measurable weakness.

METHODS: In all 3 studies, we measured maximal isometric handgrip strength, resting respiratory exchange ratio (RER), and knee extensor isometric and isokinetic force. In 2 of the 3 studies, elbow flexor isometric and isokinetic force and knee endurance fatigue index were also assessed. Knee extensor and elbow flexor measurements were obtained using an isokinetic dynamometer. Resting RER was measured using a metabolic breath-by-breath collection method. Measurement outcomes were compared on vs off drug.

RESULTS: In study 1, 18 participants fit the criteria for statin myalgia. Participants taking atorvastatin 80 mg daily had significantly lower muscle strength in 5 ($P < .05$) of 14 measured variables. Participants on placebo (N = 10) with myalgia had significantly lower muscle strength in 4 ($P < .05$) of 14 measured variables. In study 2, 18 participants tested positive for statin-induced myalgia when receiving simvastatin 20 mg daily and displayed no significant muscle strength changes (all $P > .05$). In study 3, 11 patients with statin-induced myalgia completed the study and had a significant decrease in 2 ($P < .05$) of 10 leg muscle strength variables. In all 3 studies, no significant changes were shown for handgrip strength or RER (all $P > .05$).

CONCLUSION: Our results indicate that after a short-term treatment with statin therapy, a rigorous muscle strength protocol does not show decrements of muscle strength in subjects with statin myalgia. Short-term treatment with statin therapy is not common in clinical practice. Thus, future studies should examine the effects of prolonged statin therapy on muscle strength.

Introduction

The most frequently reported side effect of treatment with hydroxymethylglutaryl-coenzyme A reductase inhibitors or statins is muscle symptoms, such as myalgia,

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cramps, and weakness.[1,2] However, quantitative observations of muscular weakness in those with statin-induced myalgia are inconsistent because of the lack of rigorous muscle strength measurements used in studies investigating statin myalgia. Studies examining changes in muscular strength in individuals with statin-induced myalgia are imperative because of the potential effect these symptoms may have on medication adherence, quality of life, physical activity, and, in older adults, ability to perform the activities of daily living necessary for functional independence. The purpose of the current report was to summarize and compare findings from 3 investigations using 3 different populations in which we used rigorous muscle strength testing techniques to determine if statin myalgia is associated with measurable weakness.

Methods

Overview

In all 3 studies, maximal isometric handgrip strength was measured 3 times using a handgrip dynamometer in a seated position, with 3-second contractions and 1-minute rest between contractions. Isometric handgrip strength is an indicator of overall muscular strength.[3] Elbow flexor and knee extensor isometric and isokinetic force at 60°/s and 180°/s were measured (N-m) as well as knee endurance fatigue index[4] using the Biodex System 3 isokinetic dynamometer (Biodex Medical, Shirley, NY) following procedures outlined by Pincivero et al.[5] The Biodex System 3 is a valid and reliable measure of dynamic muscle function.[6] Knee endurance fatigue index was used as a measure of muscular endurance.[4] Fasted resting respiratory exchange ratio (RER) was measured using TrueOne 2400 metabolic measurement system (Parvo Medics, Inc, Sandy, UT) by a breath-by-breath collection method. Participants sat quietly in a chair breathing normally for 6 minutes while gas collection is conducted through a sterilization breathing apparatus. RER at rest was used to assess potential changes in oxidative metabolism and subsequent fuel utilization due to statin therapy at rest, which could have potentially limited submaximal exercise tolerance.[7]

Study 1: The effect of statins on muscle performance

The statins on muscle performance study was a large, multisite, clinical trial with a double-blind, random assignment design in which we randomized healthy individuals to 80 mg of atorvastatin or placebo.[8,9] Participants were considered "myalgic" if all the following were met: (1) they developed new or increased muscle pain, cramps, or aching, unassociated with exercise; (2) symptoms persisted for at least 2 weeks; (3) symptoms resolved within 2 weeks of stopping the study drug; and (4) symptoms reoccurred within 4 weeks of restarting the study medication. Muscle strength and endurance as well as resting RER changes were assessed at the beginning of the study (off drug) and after 6 months of placebo or atorvastatin treatment (on drug) or, in the patients with myalgia, at the point in which muscle symptoms reoccurred during the rechallenge phase (Fig. 1). A paired *t* test was used to compare pre-to-post muscle strength and endurance and RER changes in the statin- and placebo-treated subjects.

Study 2: A randomized trial of coenzyme Q10 in patients with statin myopathy

The coenzyme Q10 (CoQ10) study was a large, clinical trial in which we enrolled patients with a self-reported history of myalgia who were confirmed mylagic by a randomized, double-blind, crossover, run-in phase where muscle symptoms developed with 20 mg of simvastatin but not placebo. The run-in phase was used to ensure that myalgia symptoms were statin associated before being enrolled into the trial. We then assessed RER, muscle strength, and symptoms before and after patients with myalgia were randomized to blinded treatment with simvastatin + placebo or simvastatin + CoQ10 (Fig. 1). For the purposes of this report, only results from the simvastatin + placebo group were used for comparison with the other studies. A paired *t* test compared pre-to-post muscle strength and RER changes.

Study 3: Changes in muscle strength in patients with statin myalgia

We enrolled patients into a nonrandomized trial from the Hartford Hospital Cholesterol Clinic who reported a history of statin-associated myalgia, confirmed by physician discretion in which participant's statin type and dose prescribed varied (Table 1). We tested muscle strength and endurance as well as resting RER changes on vs off the prescribed statin (Fig. 1). Duration of patient treatment on statin ranged from 2 months to 7 years and off statin from 2 months to 1 year.[10] A paired *t* test compared leg muscle strength and endurance and RER changes on vs off drug.

Results

Study 1

We enrolled 420 participants, and 28 of those enrolled fit the criteria for myalgia. Eighteen myalgics were on statin, and 10 myalgics were taking placebo. In the overall sample of 420 participants, no muscle changes were shown ($P > .05$). Participants with myalgia had significantly lower muscle strength in 5 of 14 measured variables compared with asymptomatic participants on atorvastatin (Table 2). Participants on placebo who were considered myalgic had