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Coenzyme Q10 Supplementation for the Treatment of Statin Induced Myalgia

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Coenzyme Q10 Supplementation for the Treatment of Statin Induced Myalgia

Abstract
Background: A significant number of the population is on 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors (statins) because statins are the main pharmacologic drug prescribed for the treatment of hypercholesteremia. Statins also have been shown to reduce the relative risks of coronary events. Statins work by inhibiting the mevalonate pathway. This is the same pathway from which Coenzyme Q10 is synthesized. Coenzyme Q10 is essential for muscle respiration. One of the theories is that statin therapy reduces coenzyme Q10 levels in muscle mitochondria, which leads to myalgia. One of the primary side effects of statin drugs is myalgia which often causes patients to decrease the dosage of the statin or discontinue it. The clinical question of whether coenzyme Q10 can be used in the treatment of myopathic pain caused by statin drug use is a common one encountered by health care providers in primary care. This article is a review of the literature to further address this question.

Methods: A systematic review of the English-language published literature was conducted using MEDLINE, CINAHL and ISI Web of Science using keywords myalgia, muscle pain, myopathy, statin, HMG-CoA, reductase inhibitors, Coenzyme Q10, CoQ10, and ubiquinone. There is very limited research examining the outcome of Coenzyme Q10 for the treatment of myopathy in statin users. Two randomized control studies researching this outcome and one prospective cohort study were retrieved and analyzed for quality and results.

Results: One randomized control study found a significant relationship between the use of Coenzyme Q10 and a decrease in myopathic symptoms, as did the prospective cohort study. However, the other randomized control study found no clinical significance in decreased myopathic symptoms with the addition of Coenzyme Q10. Fewer results were of statistical or clinical significance after the adjustments for known confounders were completed. Limited results showed Coenzyme Q10 supplementation decreased myopathic symptoms in patients on statin medications.

Conclusion: Current guidelines suggest placing patients on the lowest dose of statin medication to control the cholesterol and to decrease side effects like myopathy. Additional randomized trials of larger populations are needed to quantify and qualify possible risks of Coenzyme Q10 supplementation using myopathy as an independent risk factor.

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Coenzyme Q10 Supplementation for the Treatment of Statin Induced Myalgia

Jessica Pomaikai Asherin

A Clinical Graduate Project Submitted to the Faculty of the
School of Physician Assistant Studies
Pacific University
Hillsboro, OR
For the Masters of Science Degree, August 14, 2010

Faculty Advisor: Rob Rosenow, PharmD, OD
Clinical Graduate Project Coordinators: Annjanette Sommers MS, PAC & Rob Rosenow PharmD, OD
Biography

[Redacted for privacy]
Abstract

Background: A significant number of the population is on 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors (statins) because statins are the main pharmacologic drug prescribed for the treatment of hypercholesteremia. Statins also have been shown to reduce the relative risks of coronary events. Statins work by inhibiting the mevalonate pathway. This is the same pathway from which Coenzyme Q10 is synthesized. Coenzyme Q10 is essential for muscle respiration. One of the theories is that statin therapy reduces coenzyme Q10 levels in muscle mitochondria, which leads to myalgia. One of the primary side effects of statin drugs is myalgia which often causes patients to decrease the dosage of the statin or discontinue it. The clinical question of whether coenzyme Q10 can be used in the treatment of myopathic pain caused by statin drug use is a common one encountered by health care providers in primary care. This article is a review of the literature to further address this question.

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Results: One randomized control study found a significant relationship between the use of Coenzyme Q10 and a decrease in myopathic symptoms, as did the prospective cohort study. However, the other randomized control study found no clinical significance in decreased myopathic symptoms with the addition of Coenzyme Q10. Fewer results were of statistical or clinical significance after the adjustments for known confounders were completed. Limited results showed Coenzyme Q10 supplementation decreased myopathic symptoms in patients on statin medications.

Conclusion: Current guidelines suggest placing patients on the lowest dose of statin medication to control the cholesterol and to decrease side effects like myopathy. Additional randomized trials of larger populations are needed to quantify and qualify possible risks of Coenzyme Q10 supplementation using myopathy as an independent risk factor.

Keywords: myalgia, HMG-CoA, reductase inhibitors, Coenzyme Q10
Acknowledgements

To my husband, Ryan: Thank you for your unending love and support throughout this crazy journey they call PA school. Your calm and quiet belief in my abilities encouraged me to overcome many of the hurdles along the way. I love you and I am so excited to get back to sharing the “small things in life” together that I miss most.

To my parents: Thank you both for your continual love, support and unrelenting belief in my abilities. You have opened many doors that have led me to this achievement today. I love you both and am thankful for your influence, guidance and ongoing prayers that I have received throughout my life.

To my fellow classmates: Thank you for continuing to pick me up when I was down and pushing me to keep moving forward. You are an extended family and I am deeply grateful to know you and I look forward to being your colleague out there in the real world.
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List of Abbreviations

HMG-CoA  3-hydroxy-3methylglutaryl coenzyme A
CoQ10    Coenzyme Q10
LDL-C    low-density lipoprotein cholesterol
CK       creatine kinase
PSS      Intensity of myopathic pain
PIS      Interference of pain with daily living activities
SEM      Standard error of the mean
ATP      Adenosine-5'-triphosphate
Coenzyme Q10 Supplementation for the Treatment of Statin Induced Myalgia

BACKGROUND

Overview

A significant number of health care patient population is currently on 3-hydroxy-3methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors (statins). Statins have been shown to reduce the relative risks of coronary events and decrease mortality. Current guidelines also recommend statins as first line therapy for reducing low-density lipoprotein cholesterol (LDL-C). Despite this, adherence to lipid-lowering treatments with statin medication decreases due to the side effects. Because hypercholesterolemia is largely asymptomatic, any unpleasant side effects of pharmacologic agents, such as statins, can decrease compliance.

Myalgia is one of the most frequently reported adverse side affects associated with statin therapy. In two large observational studies, 10-15% of patients had complaints of myopathy. Muscle symptoms usually occur within the first six months of therapy, although they can begin months to years after initiation of treatment. Radcliffe et al addresses the difficulty of defining statin myalgia as it is often inaccurately and inconsistently used throughout the literature. Myalgia is a subjectively reported sensation of muscle pain. Jacobson et al furthered the description of myalgia describing that it manifests as heaviness, stiffness, cramping or weakness that may be persistent, intermittent or occur only during exertion without creatine kinase (CK) elevation. Sometimes this pain can become so severe that it interferes with a patient’s
activities of daily living leading to a reduction in their statin use. Myopathy refers to muscle symptoms with CK elevation, while rhabdomyolysis refers to CK elevations greater than 10,000U/L, usually with renal compromise and urinary myoglobin. Both myopathy and rhabdomyolysis are rare side effects. For the purpose of this paper, myalgia and myopathic pain were identified and measured as the outcome.

There are many identified and well researched risk factors for statin myopathy. The PRIOMO study indicated that patients were at a significantly elevated risk of statin myalgia if they had a personal or family history of this side effect while using lipid-modifying therapy. CK elevation, hypothyroidism, decreased renal and hepatic function also were associated with an increased risk for statin induced myopathy. Law et al also noted advancing age, small body size, female sex and race/ethnicity, especially in Asians due to decreased clearance of the drug, all had associated risk factors for increased occurrence of myalgia. Therefore, when prescribing statin medications these confounding variables must be assessed and discussed with the patient, while encouraging them to report any such side effects.

Statins work by inhibiting HMG-CoA reductase and the mevalonate pathway. Coenzyme Q10 (CoQ10) or ubiquinone is synthesized from mevalonate and tyrosine and is one of several products of the mevalonate pathways. HMG-CoA reductase inhibitors, or statins, block the production of mevalonate from HMG-CoA (see Figure 1). Mevalonate is used to synthesize cholesterol as well as CoQ10. Therefore, statin drugs work by interfering with this pathway, lowering cholesterol and simultaneously lowering CoQ10 levels. There has been extensive evidence that shows that statins lower serum CoQ1- levels. A key component of the mitochondrial respiratory chain is
CoQ10. It participates in electron transport during oxidative phosphorylation in the mitochondria of muscle cells. Accordingly, one of the proposed theories for the cause of myopathy in statin drug users is that CoQ10 deficiency resulting from statin treatment may impair muscle energy metabolism and contribute to the development of myopathy in patients treated with statins. Oral supplementation with CoQ10 has been shown to reverse the decrease in serum CoQ10 levels by statins. In an open label phase I trial in cancer patients Thibault et al evaluated the effect of very high doses of lovastatin (up to 35mg/kg) with or without CoQ10 supplementation 240mg/day. CoQ10 supplementation did not decrease the incidence of musculoskeletal toxicity, however, it did significantly reduce its severity. This study was aimed at the prevention of myopathic pain rather than the treatment of patients already with myopathic pain on statin medications, but it was one of the first to address the theory of coenzyme Q10 supplementation as it correlates to statin myopathy.

**Purpose of Study**

This systematic review examines original research that contributes to the understanding of the supplementation of coenzyme Q10 for the treatment of statin myopathy or myalgia. The question of whether coenzyme Q10 supplementation prevents myalgia and myopathic pain caused by statins is one commonly encountered in primary care. Health care providers who search for evidence based literature and guidelines find little research that address this question directly. Current recommendations for the management of statin myotoxicity are to obtain a baseline serum CK level prior to initiating statin therapy. Measuring follow-up serum CK levels is not recommended unless the patient develops signs or symptoms of myotoxicity which includes myalgia.
The American College of Cardiology, American Heart Association and the National Heart, Lung and Blood Institute recommend following the CK level weekly in a patient with muscle soreness or pain.\textsuperscript{22} If CK exceeds 10x ULN at any time, prompt discontinuation of the statin is indicated.\textsuperscript{22} Consideration should be given to treatment with coenzyme Q10, 60 miligrams (mg) twice daily for two months. \textsuperscript{1,23}

Because of the vast population prescribed and taking statin medications and because of the frequency of myalgia that is reported, it is imperative to remain abreast of the information that is relevant to this question.

METHODS

Search Strategy

In order to gather all of the most pertinent articles related to the chosen topic, a systematic review of the English-language published literature was conducted using MEDLINE, CINAHL and ISI Web of Science using keywords myopathy, muscle pain, myalgia, statin, HMG-CoA, reductase inhibitors, Coenzyme Q10, CoQ10, and ubiquinone. These terms were searched separately as keywords, then combined to form a single search using the “and” command. The extensive online search produced approximately 90 articles that met the combination of at least three of the search words used over the three search engines. This included overlap that produced the same articles on different search engines. Subsequent examination of bibliographic entries in retrieved works yielded additional background information. A total of 28 articles were used in this systematic review.
**Inclusion/Exclusion Criteria**

The search was limited to English language, human population and adult subjects. Studies with a focus on coenzyme Q10 and improvement of endothelial dysfunction, the measurement of CoQ10 levels in plasma or muscle tissues, or the effects of CoQ10 in heart failure, hypertension, diabetes, malignancy and Parkinson’s disease were all excluded. After narrowing the search as described, articles were further investigated and excluded if they did not directly address the correlation of coenzyme Q10 supplementation in the treatment of myalgia of patients who were taking statin medication.

The Jadad score, which is a commonly used set of criteria to assess the validity of articles, could not be applied here because the studies analyzed were not all randomized control trials. Therefore, it became necessary to create an original validity grading scale to more formally assess the group of articles included in the systematic analysis. Using this unique method (see Table 1) a relative score representing quality, validity and reliability in relation to the clinical question was assigned to each article. Each article was given a numeric score according to this set of criteria. This score, ranging from 0-8, was used to represent how much weight should be given to the article in supporting the hypothesis of the clinical question. No studies were eliminated from the review by this score.

**RESULTS**

Because there is very limited research examining the outcome of Coenzyme Q10 for the treatment of myopathy in statin users, two randomized control studies researching
this outcome and one prospective cohort study were retrieved and analyzed for quality and results (see Table 2).

Caso et al.\textsuperscript{1} were the first to publish a clinical pilot study to test whether supplementation with coenzyme Q10 would improve muscle symptoms in patients using statins. In this study, \textit{Effect of Coenzyme Q10 on Myopathic Symptoms in Patients Treated with Statins}, Caso et al.\textsuperscript{1} enrolled 32 patients who were being treated for hyperlipidemia with a HMG-CoA reductase inhibitor (statin) and had reported myopathic symptoms. Eighteen subjects were randomized to the CoQ10 group, while 14 were randomized to the Vitamin E control group. Patients were enrolled only if there were no other identifiable cause of myopathy. Subjects with cofounding variables of hepatic, vascular, renal, endocrine or coagulopathy disease were also excluded. None of the patients enrolled had previously been using coenzyme Q10 or vitamin E before. Caso et al.\textsuperscript{1} stated, “that there were no differences in statin treatment between groups.” There were 11 subjects using simvastatin both in the CoQ10 group and the control group. Three subjects were on atorvastatin in the control group, while four were on atorvastatin in the CoQ10 group. The CoQ10 group also had two patients using pravastatin and one patient on lovastatin. Five subjects in the CoQ10 and four in the vitamin E control group were using medications with analgesic properties prior to and during the intervention period. Both groups were similar for age, weight, height and body mass index. Coenzyme Q10 or vitamin E were supplemented for 30 days, 100mg and 400IU consecutively. Vitamin E was chosen as the placebo for the control group to control for the antioxidant actions of coenzyme Q10 and because both supplements were similar in appearance.\textsuperscript{1}
In addition to measuring plasma concentrations of CK and fasting lipids, this controlled, double-blind randomized trial\(^1\) evaluated myopathic pain before and after treatment with coenzyme Q10 or vitamin E using the Brief Pain Inventory questionnaire. The Brief Pain Inventory measures pain intensity on a 0-10 scale (i.e., 0=no pain and 10=pain as bad as you can imagine). This tool was also used to measure pain interference with daily life on 7 different items (i.e. general activity, mood, walking, working, relations with others, sleeping and enjoyment of life) on a scale of 0-10. Caso et al\(^1\) calculated a Pain Interference Score (PIS) by obtaining average ratings of the 7 interference items. The data were reported as a mean +/- SEM (standard error of the mean). They made comparisons of measurements before and after intervention within the same group using a t-test for paired data. They also made comparisons between the coenzyme Q10 and control treatment groups using a t-test. The authors reported that compliance with either supplement was 100% in both groups.\(^1\)

Caso et al\(^1\) found that plasma cholesterol, LDL cholesterol and triglycerides were similar in both groups before starting the intervention and did not change over the month study period. The authors found that intensity of myopathic pain (PSS) was similar in the coenzyme Q10 group and vitamin E groups before supplementation as was the interference of pain with daily living activities (PIS). The p value for both measurements was >0.05 and were not considered to be significant. No change in pain intensity was observed in the control group using vitamin E supplementation at the end of the trial. However, the change in PSS after the month long intervention with Coenzyme Q10 was significantly different (p=<0.001). In the Coenzyme Q10 group, 16 of 18 patients reported a decrease in their myopathic pain, while only 3 of 14 reported pain relief with
placebo vitamin E. Caso et al\textsuperscript{1} reported that interference of pain decrease with daily activities significantly improved by 38\% +/- 14\% in patients using coenzyme Q10 (p<0.02). The vitamin E control group did not report a significant reduction in pain interference with daily activities.\textsuperscript{1}

Based on the results of this pilot study, Caso et al\textsuperscript{1} suggested that coenzyme Q10 may be beneficial for patients using statins by lessening myopathic symptoms and improving patients ability to perform activities of daily living. A 40\% decrease in muscle pain with Coenzyme Q10 and a 38\% improvement of interference with pain during their daily life activities was also described. The authors went on to state there may be a possible etiologic role of coenzyme Q10 depletion in the pathogenesis of myopathic symptoms in statin-treated patients, supporting the hypothesis that myopathic pain in patients treated with statins is a result of the inability of the mitochondria to supply the ATP (Adenosine-5’-triphosphate) needed for muscle contraction secondary to decreased coenzyme Q10 levels.\textsuperscript{1}

Young et al\textsuperscript{17} conducted a randomized trial to examine the impact of coenzyme Q10 supplementation on statin-induced myalgia. \textit{Effect of Coenzyme Q10 Supplementation on Simvastatin-Induced Myalgia} was a double-blind, placebo-controlled pilot study that enrolled 44 patients with self-reported myalgia who had been unable to continue taking adequate doses of statin therapy secondary to this side effect. Patients who had a history of acute myocardial infarction or cerebral vascular accident within three months, alanine aminotransferase or aspartate aminotransferase >3 times the upper level of normal, a calculated glomerular filtration rate <45 ml/min, decompensated heart failure, warfarin treatment or antioxidant vitamin supplementation were excluded from
the study to control for confounding variables. Prior to randomization, patients underwent a two week washout of conenzyme Q10-supplements and lipid modifying therapies except ezetimibe (n=4).17

Patients in this study were stratified according to the severity of previous myalgic symptoms either as severe or moderate. Young et al17 described severe myalgia as the inability to tolerate a statin dose of 20-40 mg/day within 1 month of commencement and moderate myalgia as development of symptoms at doses >20 mg/day after >1month. Patients were then further randomized within each severity of myalgia to treatment with coenzyme Q10 (200mg/d) or placebo for 12 weeks in combination with simvastatin. The simvastatin therapy was titrated up from a starting dose of 10-20mg/day and then to 40mg/day at 4 week intervals. During each visit, throughout the intervention, fasting blood samples were taken that measured total plasma coenzyme Q10, total cholesterol, triglycerides, high-density lipoprotein cholesterol, creatine kinase electrolytes, renal and liver function and a full blood count. The study17 also measured whole-blood lactate and pyruvate concentrations. Myalgia was assessed daily during the study using a visual analogue scale rating the intensity of pain from 0-100mm that the authors adapted from Landstad et al.24 Using this scale, patients documented the number of sites affected by myalgia and rated the intensity of pain. Patients who experienced significant myalgia reduced their simvastatin dose or discontinued the study medication if they could not tolerate the lowest dose of simvastatin (10mg/d). The study looked at the primary outcomes of the number of patients who tolerated simvastatin 40mg/day at 12 weeks, the number of patients who remained on simvastatin therapy and the change in the myalgia score.17
The results of this study\textsuperscript{17} showed that there were no significant differences observed between the coenzyme Q10 group and the placebo group in the number of patients who tolerated the simvastatin 40mg/d or in the number of patients who remained on simvastatin at any dose. This was also true when each group was stratified according to the severity of previous statin-induced myalgia. The authors also found there to be no differences between the two groups in the change in myalgia score. Therefore, Young et al\textsuperscript{17} felt that they could not demonstrate any significant beneficial effect of coenzyme Q10 supplementation on myalgic symptoms in patients with histories of statin-related myalgia.

Langsjoen et al\textsuperscript{25} chose to supplement 50 patients who were experiencing one or more statin drug side effects, including myalgia, with 240mg on an average of coenzyme Q10 daily and to discontinue statin medication simultaneously in his study \textit{Treatment of Statin Adverse Effects with Supplemental Coenzyme Q10}. This was a prospective analysis of a subset of 50 new cardiology clinic patients who were actively taking statin drug therapy during their initial visit. The authors chose to evaluate patients for five possible categories of statin adverse effects including myalgia with or without muscle weakness. For the purpose of this systematic review, only the outcome of myalgia will be discussed, although fatigue, dyspnea, memory loss and peripheral neuropathy were also analyzed within the study. Initial and follow-up echocardiograms that measured left ventricular size and function was conducted on 28 of 50 patients enrolled. The majority of patients enrolled in the study were on Lipitor or Zocor and on average patients had been using their statin for approximately two years. Sixty-four percent of patients enrolled in the
study complained of myalgia with and without proximal muscle weakness at the beginning of the study.25

Langsjoen et al25 found that fatigue and myalgia were beginning to improve by one month follow-up and significantly by three month follow-up, with myalgia decreasing from 64% to 6% overall.

DISCUSSION

Study Limitations

Much has been written on statins and myopathy and the possible role of CoQ10. The theory that statins cause depletion of CoQ10 in muscles is plausible as statins block the production of mevalonate, one of the precursors of CoQ10.13 These articles are the few that begin to speak to the question of coenzyme Q10 supplementation for the treatment of statin induced myalgia. This body of work reflects a small variety of research methods and their results are of inconsistent quality. When taken together, the two conducted randomized control trial and the prospective cohort study failed to provide a clear answer to the issue. Although two of the studies reported a reduction in statin induced myopathic pain, their results are imperfect secondary to the limitations of the study design.1,25

Caso et al1 was restricted by the lack of placebo control design. While the use of Vitamin E as a placebo was explained, Vitamin E has its own effects on the body’s system and may have affected the measured outcome of myopathic pain. This study1 was also limited by its small study population. Despite the fact that this study was identified as a pilot study, the failure to standardize the dose and type of statin treatment may also
have affected the outcome of the study. Nonetheless, Caso et al\(^1\) did pioneer the exploration of this important clinical question and was able to further the hypothesis that coenzyme Q10 depletion being linked to myopathic pain.

Young et al\(^{17}\) admitted there may have only been a small increase in myalgia scores with either treatment regime, possibly because patients did not experience sufficiently severe myalgia to observe a benefit from coenzyme Q10 supplementation. This same defect may also be applied to Caso et al\(^1\) as they did not standardize pain severity. In Young et al\(^{17}\) patients were previously exposed to the intervention of coenzyme Q10, although a 2 week washout period of coenzyme Q10 was reported. Pre-exposure to the intervention may have skewed the outcome of the trial. Confounding these issues, patients were also able to discontinue or decrease statin supplementation based on their subjective myalgia symptoms, therefore, it is difficult to discern if the decrease in statin drug or the coenzyme Q10 supplementation decreased the myopathy. This study also had a small sample size.

Langsjoen et al\(^{25}\) supported Caso et al\(^1\) in that it did find coenzyme Q10 supplementation to have a positive outcome on statin myopathy. However, this study had an open design, therefore, there was unequivocal bias interpretation of the intervention by the study population or the results of the investigators. This study also had two interventions from the beginning of the trial, discontinuing statin drug therapy and the co-administration of coenzyme Q10. Therefore, as with Young et al\(^{17}\), it is difficult to discern which of the two interventions might have had the positive effect on myalgia outcomes. There were also multiple confounding variables such as age, and disease states that were reported but not accounted for in the results of this study.
**Future Avenues**

Based on the limited research presented here, additional studies are clearly warranted. Future research should follow the lead of Young et al\(^\text{17}\) and Caso et al\(^\text{1}\), with randomized control trials of patients with statin myopathy being treated with coenzyme Q10 and should improve on their foundation by recruiting larger number of participants. Molyneux et al\(^\text{26}\) is accurate in stating that adequately powered randomized controlled trials are now required to establish if there is a role for CoQ10 supplementation in the treatment of statin myopathy. These future studies should better their outcomes by continuing to eliminate confounding variables. Studies should be aimed at including subsets of the population on the same statin drug, dosage and length of use. Furthermore, the supplementation of CoQ10 formulation should be the same, secondary to the bioavailability of the various brands and formulation of CoQ10.\(^\text{27}\) Moreover, the results of these studies should be compared to the results of studies measuring the same variable but on different statin medications.

A more clearly identified definition of myopathy by statin withdrawal and re-challenge should be included in future studies. Simultaneously, a more objective pain scale to measure myopathic symptoms must be used to help standardize previous subjective measurements. Patients should then be compared to groups of patients with more severe levels of myalgia. There is also a need to develop studies that represent subgroups of statin-treated populations for whom Coenzyme Q10 supplementation may be more likely to produce a clinical benefit. The placebo benefit of coenzyme Q10 on
myopathic pain must also be accounted for. Finally, these studies must address and measure any adverse effects of supplementation with coenzyme Q10.

CONCLUSION

Statins are efficacious lipid-lowering agents that are commonly use and considered safe. Statin medications are essential for the treatment of hypercholesterimia as well as for primary and secondary prevention of cardiovascular disease and have been shown to decrease morbidity and mortality in coronary events. In addition to their use in dyslipidemic disorders, the pleiotropic effects of statins have led to wider use in other disorders, such as cancer, stroke and inflammatory conditions. Therefore, the expanded use of statin medication demands awareness, recognition and proper evaluation and treatment of myalgia and myopathy by healthcare providers. The frequency of mild muscle-related symptoms in primary care can be underestimated because physicians might overlook, and patients might fail to report, such symptoms, especially if they are not interfering with activities of daily living. Therefore, the health care provider-patient relationship must work collaboratively to decide how these statin-associated muscle symptoms can be managed so that the patient can maintain the appropriate statin treatment.

Myopathy is one of the chief complaints patients have while taking statin medications. Strategies for managing statin intolerance are numerous. They include changing statins, intermittent dosing, increasing lifestyle modifications and using other LDL-C-lowering agents like bile acid sequestrants and ezetimibe. If myopathy can be treated with Coenzyme Q10 supplementation, the patient can maintain the appropriate
statin medication and continue to gain its benefits without experiencing the myopathy side effect of the drug. Moreover, if it is proven through further research that myopathic pain can be treated with adequate intake of Coenzyme Q10, this supplement may be used as a prophylactic to prevent myopathy. Despite research efforts, the role of coenzyme Q10 supplementation in the treatment of statin induced myalgia remains undetermined.
REFERENCES


24. Landstad BJ, Schuldt K, Ekholm J, Broman L, Bergroth A. Women at work despite ill health: Diagnoses and pain before and after personnel support. A prospective study of


## TABLES

### Table 1: Appraisal Criteria

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<tr>
<td><strong>Confounding Variables Reported and Explained</strong></td>
<td></td>
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</tr>
<tr>
<td>+1: Diagnoses; dietary and lifestyle habits (i.e. smoking);</td>
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<tr>
<td>0: Confounding Variable not explained</td>
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<tr>
<td><strong>Subjects on Same Statin at Beginning of Study</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>+1: Yes</td>
<td>0</td>
<td>1</td>
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</tr>
<tr>
<td>0: No</td>
<td></td>
<td></td>
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<tr>
<td><strong>Subjects on Similar Doses of Statin at Beginning of Study</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>+1: Yes</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>0: No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Researcher Blinded to Control vs. Q10 subjects</strong></td>
<td></td>
<td></td>
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<tr>
<td>+1: Yes</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>0: No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>5/8</td>
<td>7/8</td>
<td>3/8</td>
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</table>
### Table 2: Matrix of Reviewed Literature

<table>
<thead>
<tr>
<th>Author/ Title/ Journal</th>
<th>Population</th>
<th>Intervention</th>
<th>Comparison</th>
<th>Outcome</th>
<th>Validity Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Giuseppe Caso et al. (2007)</td>
<td>Adult Pts. treated for HLD with HMG-CoA reductase inhibitor (statin) reporting myopathic symptoms</td>
<td>Coenzyme Q10</td>
<td>Vitamin E (similar in appearance &amp; antioxidative effect)</td>
<td>-Myopathic Symptoms -Interference with pts ADLs</td>
<td>5/8</td>
</tr>
<tr>
<td>Young, BS et al. (2007)</td>
<td>Adult Patients unable to continue taking adequate dose of Statin secondary to myopathic pain</td>
<td>Coenzyme Q10</td>
<td>Placebo</td>
<td>-# of patients who tolerated simvastatin at therapeutic dose -# of patients who remained on simvastatin therapy -Change in Myalgia Score</td>
<td>7/8</td>
</tr>
<tr>
<td>Langsjoen, P.H et al. (2005)</td>
<td>Adult Statin Drug Users w/AE associated with Statin use</td>
<td>D/C Statin &amp; Begin Coenzyme Q10</td>
<td>None</td>
<td>-Myalgia -Fatigue -Dyspnea -Memory Loss -Peripheral Neuropathy</td>
<td>3/8</td>
</tr>
</tbody>
</table>
FIGURES

Figure 1: The Cholesterol Biosynthetic Pathway

This figure shows where statin medications work on the mevalonate pathway. It also depicts how both cholesterol and coenzyme Q10 are synthesized from the same pathway.