Statins and Myalgia: A Case Report of Pharmacovigilance with Implications for Physical Therapy

**Background and Purpose.** Physical therapists work with patients who are taking medications in virtually every health care setting. Patients may present with complaints of pain from both musculoskeletal and non-musculoskeletal origins. Medication used in many situations may have a significant effect on the health of the patient and may alter the clinical presentation or course of the patient’s symptoms. Statins are a group of antilipemic drugs that reduce LDL-cholesterol in the blood by inhibiting the 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) - reductase which is an early (and rate-limiting) step in cholesterol biosynthesis. There is a wide body of medical literature that associates the adverse reaction of myalgia and the more serious reaction of rhabdomyolysis with statin medications. Physical therapists spend sufficient time with the patient to perform good pharmacovigilance.

**Case Description.** The patient was a 53-year old female who complained of right-sided knee pain and constant bilateral thigh pain. She was referred for physical therapy with a musculoskeletal diagnosis of osteoarthritis of both knees. The physical therapist recognized that the constant myalgic symptoms could be related to a recent increase in the dosage of atorvastatin calcium (Lipitor). The patient was referred to her primary care physician.

**Outcomes.** After receiving physical therapy interventions, the patient’s right-sided knee signs and symptoms were improved, but the constant myalgic symptoms were unchanged. The patient was referred to her primary care physician who discontinued the atorvastatin calcium. Four weeks following the discontinuation of atorvastatin calcium the myalgic thigh complaints were fully resolved.

**Discussion.** Physical therapists may treat patients with pain from both musculoskeletal and non-musculoskeletal origins. Adverse reactions to medications may masquerade as musculoskeletal problems. While generally well tolerated, statins are associated with myalgia. This case report demonstrates the important role the physical therapist can play in monitoring the drug-safety regimen.

**Key Words:** Statins, Myalgia, Pharmacovigilance, Physical Therapy

David J Trumbore
INTRODUCTION

In almost every health care setting, physical therapists examine and treat patients who are taking medication. Boissonnault reported that 40% of the patients receiving physical therapy interventions are taking anti-inflammatorys and 28% take narcotics. Furthermore, up to 90% of ambulatory elderly patients take at least one medication, most take two or more. An important part of the screening process is to recognize that a patient’s complaint of pain may be from predictable or unpredictable adverse reactions or interactions from the medication regime.

Pharmacovigilance is the practice of monitoring the safety of a drug-therapy regime. In addition, it can be defined as “watchfulness in guarding the safety of drugs.” Physical therapists spend considerable amount of time with their patients. Therefore, they are uniquely positioned to screen for adverse drug reactions and can apply knowledge of pharmacodynamics and pharmacokinetics to ensure proper pharmacovigilance for their patients.

Statins and Hyperlipidemia

Hyperlipidemia refers to a group of metabolic abnormalities resulting in combinations of elevated serum total cholesterol (hypercholesterolemia), elevated low-density lipoproteins, elevated triglycerides (hypertriglyceridemia) and decreased high-density lipoproteins. These abnormalities are the primary risk factors for atherosclerosis and coronary artery disease. Data from phase I of the National Health and Nutritional Examination Survey III (NHANES) showed that 49% of the adult US population had cholesterol concentrations of ≥ 5.2 mmol/L and that approximately 8% of the population use cholesterol lowering medications.

The association between increased total and low-density lipoprotein cholesterol levels and the development of atherosclerotic diseases in general and coronary heart
The efficacy of statin medications for lipid lowering and reducing the risk of coronary heart disease is well established. Statins are a group of drugs that reduce LDL-cholesterol in the blood by inhibiting the 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) – reductase that normally regulates cholesterol synthesis in the liver. Statins lower the total cholesterol level by reducing LDL-cholesterol by about 25-40% and reducing triglycerides to some extent, while raising HDL-cholesterol by a small amount.

Lipitor (atorvastatin calcium) is a synthetic lipid-lowering agent and is a frequently prescribed statin. While Lipitor and other statins are generally well tolerated, there is a wide body of medical literature that associates the adverse reaction of myalgia and the more serious reaction of rhabdomyolysis with statin medications. Terminology used to describe statin-induced muscular adverse events is inconsistent. For example, myopathy has been defined as muscle pain, tenderness or weakness associated with abnormal elevations in creatine kinase (CK) levels (> 10 times the upper limit of normal), whereas the American College of Cardiology/American Heart Association/National Heart, Lung and Blood Institute (ACC/AHA/MHLBI) task force considers myopathy to be a general term for disease of the muscle.

The incidence of myotoxic events appears to be dose-dependent and symptoms of mild myalgia to frank rhabdomyolysis ranges from 1% to 7% depending on the definition used. These musculoskeletal adverse reactions account for 10% to 14% of statin-related adverse events reported to the International Drug Information System. Myalgia is the most common myotoxic event, comprising 6% to 14% of adverse events associated with statins. Pasternak et al described the following factors that may increase the risk of
myopathy: multisystem disease, being female, age greater than 80 years, peri-operative periods and hypothyroidism. While myotoxic effects can occur with statin therapy, when they are detected early they can usually be reversed with withdrawal of treatment.

Concerns about adverse reactions from other medications such as corticosteroids and fluoroquinolones have been reported in physical therapy literature. However, there is little physical therapy literature reporting on myalgia and statins.

In an attempt to locate all articles published in physical therapy literature pertinent to this case report, an Internet search of the MEDLINE database was performed. MEDLINE offers the best access to the core physical therapy literature. Various combinations of the key words statin, statins and myalgia were used. None of the 64 retrieved articles were from physical therapy journals/literature. Next, various combinations of the key words statin, statins and adverse reaction and muscle were used. Only one of the 285 retrievable abstracts was from physical therapy journals/literature.

A manual search of the following three physical therapy journals was performed: Physical Therapy, Journal of Orthopedic and Sports Physical Therapy (JOSPT) and Orthopaedic Physical Therapy Practice. A search from January 1993 through February 20056 did not yield any additional articles reporting on the topic of statins and myalgia.

Hyperlipidemia is a common condition that is often treated with statin medications. It is estimated that more than 76 million prescriptions were filled for statins in 2000. Therefore it is likely that physical therapists will treat patients who are taking a statin. The purpose of this case report is two-fold. The first purpose is to highlight that physical therapists are uniquely positioned to apply knowledge of
pharmacokinetics and pharmacodynamics toward the application of pharmacovigilance. The second purpose is to report on the potential adverse reaction of myalgia in patients who are taking a cholesterol lowering statin.

CASE DESCRIPTION

The patient was a 53-year old female who complained of pain and stiffness in the right knee. Six weeks after being evaluated by her primary care physician, she developed an onset of constant bilateral thigh pain. She was diagnosed with osteoarthritis (OA) of the right and left knees and was referred for physical therapy by her orthopedic surgeon.

Chronology of Events Prior to the Initial Physical Therapy Examination

Ten Weeks Prior (1st Primary Care Physician Visit)
The patient was evaluated by her primary care physician (PCP) for complaints of constant pain in the right knee. The patient reported mild intermittent pain in the right knee for several years with a recent exacerbation of her symptoms. The patient related the recent increase in her right knee pain to an increase in her activity level. She was prescribed Ibuprofen and instructed to decrease her activity level.

Six Weeks Prior (2nd Primary Care Physician Visit)
After four weeks of taking Ibuprofen, the patient returned to her family physician noting only a mild decrease of pain in the right knee. Anteroposterior (AP) and lateral x-rays of the right knee were taken in the physician’s office and the patient was told she had “arthritis in the right knee”. The patient was instructed to continue taking the Ibuprofen and to apply warm compresses.

Four Weeks Prior
Two weeks later, the patient developed a constant “flushing” type pain in the anterior aspect of both thighs. The patient called the primary care physician with the new complaint and was referred to an orthopedic surgeon.

Three Weeks Prior
An orthopedic surgeon evaluated the patient and ordered magnetic resonance imaging (MRI) for both knees. The Ibuprofen was discontinued and Naprosyn was prescribed. The patient was instructed to reduce her activity level and to apply ice to both knees.

One-Week Prior
During a follow up visit with the orthopedic surgeon, the patient reported that her right knee pain and constant bilateral thigh pain were unchanged. The results of the MRI were
reviewed, and she was diagnosed with OA of both knees. The patient was referred for physical therapy. She was instructed to continue taking Naprosyn and was scheduled to receive viscosupplementation with hyaluronate therapy.

**Initial Physical Therapy Examination**

**[History]**

The patient complained of constant pain in the right knee. She rated the intensity of the pain as 2/10 at rest and 5/10 during and after weight bearing activities. Morning stiffness was prominent, and the patient described difficulty transitioning from prolonged sitting to standing. The patient reported increased pain in the right knee after weight bearing for approximately five minutes. This prevented her from going for walks and attending social events that involved prolonged sitting or standing. Furthermore, she experienced increased pain in the right knee while cooking and cleaning, and her husband began doing these tasks for her.

In addition to the right-sided knee pain, the patient also complained of a constant bilateral anterior thigh pain. This pain was described as a “flushing” sensation and was unchanged by position or motion. The intensity of the bilateral constant thigh pain was rated 3-4/10.

The review of systems (ROS) was unremarkable. The past medical history (PMH) was significant for hypertension, hypercholesterolemia and insomnia. The patient had no newly prescribed medications and her current medication regime included metoprolol (Lopressor), atorvastatin calcium (Lipitor) and zolpidem tartate (Ambien). An X-ray report of the right knee described moderate degenerative changes in the medial compartment with slight patellar tilt and possible mild chondromalacia patella. Finding from a MRI of the right reported were as follows: moderate degenerative arthritis in the
medial compartment with mild degeneration of the medial meniscus, intact lateral meniscus, intact anterior and posterior cruciate, medial and lateral collateral ligaments, and moderate joint effusion. With the exception of mild chondromalacia patella, the MRI of the left knee was unremarkable.

[Physical Examination]

The patient did not appear to be in any acute distress. She ambulated with a slightly antalgic gait on the right without the use of ancillary support. The patient was 1.57 m tall and weighed 70.3 kg. Body mass index (BMI) was 28.3. The patient’s blood pressure was 145/92 mm Hg and resting heart rate was 76 bpm, regular and without murmur.

The right knee was slightly warm and there was a positive fluctuation test as described by Magee. The right medial joint line was tender to palpation. Goniometric measurements were taken according to the NASM Guidelines. Active right knee extension was WNL and active knee flexion was limited to 115 degrees. Passive right knee extension was WNL and active knee flexion was limited to 120 degrees. There was mild crepitus associated with both active and passive ROM of the right knee. The end range of knee flexion was painful and had a capsular end feel as described by Cyriax. Manual muscle testing (MMT) as described by Daniels and Worthingham was 4+/5 for right knee flexion and extension. Forward lunge testing, as described by the International Weight-Lifting Association (IWA), resulted in a stride length of 20 inches with 30 degrees of knee flexion (Appendix 1).

The following special tests for the right knee as described Magee were negative: varus and valgus stress test, Lachman test, anterior drawer test for the anterior and
posterior cruciate ligament, McMurray test, bounce home test and modified Helfet test. Movement and special testing of the right knee did not alter the right thigh pain.

Examination of the left knee was unremarkable. Movement and special testing of the left knee did not produce or alter any of the patient's symptoms. There was no ecchymosis, erythema or effusion on examination of the left knee. Left knee flexion and extension strength was 5/5. Active and passive ROM of the left knee was WNL and pain free. Special tests for ligamentous instability and the menisci were negative.

Findings from the lower quarter screen (LQS) were unremarkable. Lumbar ROM was WNL. With the exception of moderate discomfort in the L4-5 region at the end range of lumbar extension, all lumbar motions were pain free. Sacroiliac compression and gapping joint stress tests were negative. Active and passive ROM of both hips and ankles were within normal limits. Strength of the ankle and hips was 5/5 bilaterally. Active, passive and resistive motions of the lumbar spine, and both hips, knees and ankles did not alter the bilateral constant thigh pain. Sensation in the L2-S2 dermatomes was intact to light touch. Patellar and Achilles deep tendon reflexes (DTR) were both 2+. Palpation of the abdominal quadrants was benign.

Evaluation

Based on the data gathered from the patient history, physical examination and review of the diagnostic study reports, an early hypothesis was developed. The origin of the patient’s right-sided knee pain and stiffness was believed to be from OA of the right knee. The origin of the bilateral constant thigh pain was uncertain. However, the physical therapist believed the bilateral thigh myalgia was not from musculoskeletal
origin and that the diagnosis of bilateral knee OA would not account for the full spectrum of the patient’s symptoms.

In the past ten weeks prior to the initial physical therapy examination, the patient had been evaluated by a physician four times. The most recent evaluation was by an orthopedic surgeon one week prior to her initial evaluation. Diagnostic studies did not reveal any serious pathology. Additionally, the patient appeared to be otherwise in good health, her ROS was unremarkable and with the exception of constant thigh myalgia, she did not present with any “red flags”. In light of this, it was felt that physical therapy interventions could be implemented for a 4E preferred practice pattern despite complaints of pain from an unknown origin.32

Based on the early hypothesis, a plan of care was developed. Interventions known to have a mitigating effect on the signs and symptoms of osteoarthritis would be implemented for both lower extremities. Symptoms related to OA would be expected to be improved by the physical therapy interventions, while symptoms of non-musculoskeletal origin would likely be unaffected.

**Intervention**

There were five components to the patient’s treatment program: (1) patient education, (2) recommendation of chondral protective oral supplements, (3) recommendation of a supportive device, (4) generalized resistive training program, and (5) patient specific exercise prescription.

*Patient Education*

Patient education is an important intervention for patients with OA.33 The patient was provided with general information regarding osteoarthritis of the knee. She was
informed that OA is a common form of arthritis and can be a major source of disability.\textsuperscript{34} Patients with OA typically have pain that worsens with weight bearing activities and generally have stiffness associated with rest.\textsuperscript{33} The patient was encouraged to lose weight as weight loss has been shown to decrease joint stress and pain and improve the ability to exercise. Data has shown that a twelve-pound weight loss can decrease the chance of developing osteoarthritis in women by 50\%.\textsuperscript{35, 36} Furthermore, the patient was cautioned to avoid high impact activities that involved running, jumping and prolonged kneeling.

**Recommendation for Chondro-Protective Oral Supplements**

Glucosamine and chondroitin sulfate are endogenous molecules in articular cartilage with synergistic action when taken together. Glucosamine is thought to stimulate chondrocyte and synoviocyte metabolism and chondroitin sulfate is believed to inhibit degradative enzymes and prevent the formation of fibrin thrombi in periarticular tissues.\textsuperscript{33} Some considerable difference of opinions regarding the use of chondro-protective oral supplements exits. However, there is compelling research, multi center randomized controlled clinical trials and systematic reviews with meta-analysis demonstrating effective pain relief and increased function without toxicity or side effects.\textsuperscript{33, 34, 37-44} The patient was recommended to take 1 gram of Glucosamine and 1,200 mg. of chondroitin sulfate per day, as these are standard recommended dosages.\textsuperscript{33}

The author recognizes that the scientific community is somewhat skeptical about supplements because of quality control issues. Supplements are not Food and Drug Administration (FDA) regulated as compared to pharmaceuticals. There are no government-regulated requirements for testing the safety or efficacy prior to marketing. However, the FDA does have the power to remove a dietary supplement from the market.
if it is proven unsafe. Another frequent criticism of the dietary supplement industry is that there are no requirements to follow good manufacturing practices (GMP), a process which when in place, guarantees high quality and batch-to-batch consistency.45

The following instructions on the risks and benefits of oral glucosamine and chondroitin sulfate, as well as concerns about their manufacturing, were given to the patient: (1) Because food supplements such as glucosamine and chondroitin sulfate are not regulated by the FDA, their quality and actual content can vary. Therefore, a reputable brand that follows GMP, and by inference is supported by the Arthritis Foundation, was recommended to the patient.46 (2) The patient was informed about the apparent short-term safety of supplementation with glucosamine and chondroitin sulfate, the relatively low cost of these agents and their apparent efficacy in ameliorating the symptoms of OA. (3) The patient was given standard warnings about the incomplete nature of the research of these agents at this time. (4) Lastly, the patient was told to discontinue using the supplement and to contact her physician should any adverse symptoms appear.37

Supportive Device

The use of walking poles has been shown to reduce both vertical ground reaction forces and knee extensor angular impulse moments.47 The patient was instructed to use a single point cane in the left hand to reduce joint forces through the right knee.33

Generalized Resistive Training Program

Traditionally, hypertensive patients have been discouraged from performing resistance training for fear of precipitating a cerebral vascular event or placing an excessive demand on a myocardium that already displays left ventricular dysfunction.
Such fears have arisen primarily as a result of the marked pressure response elicited during an acute bout of heavy resistance exercise.\textsuperscript{48} Contrary to what might be expected, studies investigating the impact of long-term participation in resistive training on resting blood pressure have generally failed to document a deleterious effect. Indeed, longitudinal training studies have shown that chronic resistance training may modify resting blood pressure in a favorable manner.\textsuperscript{49}

The cause of disability from osteoarthritis is complex. However, poor musculature and aerobic conditioning are important contributors to loss of function. Patients with OA have weaker musculature than age and gender matched controls. It has been suggested that muscle weakness and decreased proprioception may lead to or hasten the progression of OA by causing instability of the joint.\textsuperscript{50} Such instability is thought to alter the biomechanics of the joint resulting in destruction of cartilage. Numerous studies have examined the effects of resistive training on muscle strength, pain, physical function and health-quality of life in patients with arthritis. Data is consistent and compelling that resistance training improves muscle strength, balance, and function, thereby reducing dependency and disability.\textsuperscript{33, 51-54} Thus, resistance training has the potential to improve clinical outcomes in patients with arthritis.

Furthermore, patients with OA often have unfavorable risk factors and profiles for heart disease. Individuals with lower-extremity OA tend to be more obese, less fit and hypertensive with higher fasting glucose levels and lower high density lipoprotein levels than age-matched controls.\textsuperscript{55} Much of this can be attributed to the low level activities of persons with arthritis.\textsuperscript{48} Collectively, this data suggests that patients with OA are at higher risk for heart disease, hypertension and osteoporosis and that they would benefit
from resistive training. Moreover, there is no apriori reason to believe that patients affected with arthritis would not gain the same benefits as their counterparts who do not have musculoskeletal disorders. Therefore, this author believes that a structured generalized resistance training program has a very important therapeutic role in the treatment of OA.

The patient was instructed to perform the following general resistive exercises: dumbbell bench press, dumbbell curl, dumbbell shoulder press, seated cable latissimus pulldowns, and stability ball trunk flexion. Brooks\textsuperscript{56} describes proper performance of these exercises. After a brief warm-up of scapular retraction and protraction exercises performed with resistive bands, the patient performed one set of 10-12 repetitions of each exercise at 60\% of her one-repetition maximum (1-RM). Recent meta-analytical research indicates that this is the optimal training volume for an untrained individual.\textsuperscript{57, 58} The gold standard for determining training loads is the one-repetition maximum (1-RM).\textsuperscript{59, 60} However, 1-RM muscle strength testing may be contraindicated in individuals who have no previous weight lifting experience.\textsuperscript{60, 61} An alternative method to the 1-RM for determining proper training loads is the estimation of a 1-RM. Submaximal repetition testing for determining training loads has been shown to be effective.\textsuperscript{60} Because the patient had no prior resistive training experience, the ten repetition maximum testing was used to determine the proper training load (Appendix 2).\textsuperscript{62}

\textit{Patient Specific Exercise Prescription}

Range of motion, strength and proprioception exercises are valuable interventions for OA.\textsuperscript{33, 50, 63, 64} Quadriceps strengthening can improve function and decrease knee pain.\textsuperscript{65-67} Proprioceptive, agility and perturbation training activities may improve
treatment effectiveness in patients with OA by allowing them to return to higher levels of activity in shorter time periods. Perturbation and proprioceptive training activities may provide an opportunity to adapt to potentially destabilizing loads on the knee during rehabilitation, ultimately allowing faster return to recreational activities.64

Specific therapeutic interventions consisted of moist heat to the right knee followed by closed chain supervised therapeutic exercises (CCSTE) for both lower extremities.68 Ice was applied to the right knee following the CCSTE. The patient performed 5-7 minutes of stationary bicycling using a light to moderate tension as a warm up. After the warm up, she performed the following CCSTE:

- Forward, reverse and lateral lunges [12-15 repetitions] 69
- Standing chair box squat [12-15 repetitions] 70
- Double leg balance (DLB) and visual tracking (VT).71
- Standing heel raises [12-15 repetitions]

During the first 4 weeks of treatment, the patient performed one set of each exercise. Both the DLB and the VT were performed for 1 minute each while standing on an inflatable domed balance-training device. During weeks 5-8, the patient performed two sets of each exercise.

Outcomes

The patient received physical therapy treatments three times weekly for four weeks. The patient was re-evaluated four weeks after initiating physical therapy treatment. After four weeks of treatment, the patient was without complaints of pain in the right knee at rest and rated the pain in the right knee as 3-4/10 following activity. The patient reported being able to stand and walk for 15-20 minutes before experiencing an increase of pain in her right knee. The anterior thigh pain was unchanged. The right knee
was no longer warm but was still slightly swollen. Passive right knee extension was WNL and active knee flexion was limited to 125 degrees. Right hamstring and quadriceps strength was 5/5. The patient was able to lunge to 24 inches at 65 degrees of knee flexion without pain. The patient had resumed cooking activities but was still unable to clean and continued to decline social activities that required prolonged standing or sitting. Improvement in pain, ROM, and strength of the right knee, coupled with the lack of change in the constant bilateral thigh myalgia, strengthened the early hypothesis.

The patient was re-examined after receiving eight more physical therapy treatments during the next four weeks. The patient was without complaint of pain in the right knee while at rest. Mild stiffness still occurred after sitting more than 30 minutes. She reported being able to stand and/or walk approximately 30-40 minutes without experiencing pain in the right knee. Pain after 30-40 minutes of activity was rated 1-2/10. Functionally, the patient has resumed cooking and cleaning, but continued to withdraw from social activities because of the anterior thigh pain. Active and passive ROM of right knee was WNL for flexion. Hamstring and quadriceps strength was 5/5. The right knee was no longer swollen or warm, although she continued to be mildly tender over the right medial joint line. The patient was able to lunge to 26 inches at 90 degrees of knee flexion without pain.

The physical therapist believed the early hypothesis was supported by the substantial improvement in the right-sided knee symptoms and lack of improvement in the bilateral thigh myalgia. The patient was discharged after eight weeks of physical therapy interventions. At this juncture, the physical therapist believed that the patient’s right-sided knee symptoms were sufficiently improved and that the patient could
maintain or improve upon her current status by following her discharge instructions. Furthermore, the myalgic thigh symptoms had not improved in the last eight weeks and the physical therapist did not feel the myalgic symptoms would be improved by further physical therapy interventions. During the discharge interview, the patient was encouraged to attend her scheduled follow up appointment with her orthopedic surgeon and to speak with her primary care physician regarding the constant thigh myalgia. She was instructed to continue to take the glucosamine and chondroitin and to perform her patient specific exercises 2-3 times weekly.

Two weeks after being discharged, the patient returned to the clinic with a prescription from the orthopedic surgeon requesting four more weeks of physical therapy treatment. The patient was re-examined in order to determine if her status had changed since discharge. The patient’s complaints, functional status and clinical findings were unchanged from when she was discharged two weeks prior.

Considerable time was spent questioning the patient regarding the onset of the anterior thigh pain. The patient recalled that during her 2nd Primary Care Physician Visit the dosage of her atorvastatin calcium (Lipitor) was increased from 20 mg. to 40 mg. The onset of her bilateral thigh myalgia occurred two weeks following this dosage increase. Potential adverse reactions to atorvastatin calcium (Lipitor) were reviewed in the Nursing 2004 DRUG Handbook. Myalgia is listed as a potential musculoskeletal adverse reaction. Furthermore, patients are advised to inform the prescriber of any onset of muscle pain, malaise or fever.

The physical therapist did not feel that further physical therapy interventions were warranted. The patient’s clinical presentation was unchanged from her status two weeks
prior when she was discharged from physical therapy. Although she continued to have complaints of constant bilateral thigh myalgia, these symptoms were not improved by previous physical therapy interventions. Patient-teaching information from NDH2004 Plus! on atorvastatin calcium (Lipitor) was printed and given to the patient (Appendix 3). NDH 2004 Plus! is a mini CD that accompanies the Nursing 2004 DRUG Handbook. It is a computer program that allows the clinician to easily create and print patient-teaching instructions. The patient observed that in the past her PCP had not responded well to dialogue with other health care professionals. Therefore, the patient was instructed to call her primary care physician regarding her onset of myalgic thigh symptoms subsequent to the increased dosage of her atorvastatin calcium (Lipitor). The patient was asked to call the physical therapy clinic to confirm that she had made an appointment with the primary care physician regarding this matter.

Two weeks later, the patient called and indicated she had been evaluated by her PCP. The atorvastatin calcium (Lipitor) was discontinued to evaluate how it would affect the patient’s myalgic thigh complaints. The patient reported approximately a 50% reduction in the constant bilateral thigh myalgia since discontinuing the atorvastatin calcium (Lipitor). During a follow up conversation three weeks later, the patient stated that her myalgic thigh complaints were fully resolved. She indicated that she would remain off the atorvastatin calcium (Lipitor) for a total of twelve weeks and then would receive clinical laboratory testing to evaluate serum cholesterol levels. The PCP would consider prescribing a different statin to control her hypercholesterolemia based on future cholesterol levels.
Discussion

Because the vast majority of patients take medications, it is important for physical therapists to recognize potential adverse reactions from the patient’s medication regime. While generally well tolerated, statin medications are associated with the potential adverse reaction of myalgia and the more serious reaction of rhabdomyolysis. There is a paucity of physical therapy literature reporting on adverse reactions to statins. Clinicians who spend the most time with the patient must monitor both therapeutic response and adverse reactions to the drug-therapy regime. Therefore, physical therapists must have a working knowledge of pharmacology and are uniquely positioned to ensure pharmacovigilance.

The data gathered during the initial physical therapy examination of the right knee supported the diagnosis of OA of the right knee. However, the onset and clinical presentation of the bilateral constant thigh myalgia was inconsistent with the known clinical presentation of OA. The working hypothesis was that the right-sided knee symptoms were due to OA of the knee, while the origin of the constant thigh myalgia was uncertain. Interventions known to be effective for OA were implemented for both lower extremities. Symptoms related to OA were expected to improve, while symptoms from a non-musculoskeletal origin were not expected to improve.

After eight weeks of physical therapy interventions, the patient was without complaint of pain in the right knee while at rest. Right-sided knee pain was minimal following weight bearing activities. Range on motion of the right knee was WNL and hamstring and quadriceps strength was 5/5. Additionally, the patient’s overall functional status was improved. However, the complaint of constant thigh myalgia was unchanged.
The patient’s response to treatment supported the early hypothesis. After eight weeks of treatment, the patient was discharged as it was believed that she had achieved maximum benefit from a formal physical therapy program. Her discharge instructions were reviewed, and she was instructed to contact her primary care physician regarding her myalgic complaints.

The patient was re-examined after being referred for further physical therapy by the orthopedic surgeon. After a lengthy inquiry regarding the onset of the patient’s symptoms, the physical therapist first learned of the change in the dosage of the patient’s statin. This was the first point in the patient’s physical therapy treatment that a potential adverse reaction to a statin medication was considered. The patient was instructed to contact her PCP regarding who discontinued the atorvastatin calcium (Lipitor). Approximately four weeks after discontinuing the atorvastatin calcium (Lipitor), the patient’s myalgic thigh complaints were fully resolved.

In addition to this case report highlighting the role that physical therapists can play in pharmacovigilance, an important clinical lesson was learned. During the initial patient interview, the patient’s medications listed on the health history questionnaire (HHQ) were reviewed. The patient indicated she was not taking any prescribed, over the counter (OTC) or nutraceutical supplements that were not listed on the HHQ. However, the patient was not asked if there had been any change in any changes in the dosages of her current medications. If this question had been asked, the association of an adverse myalgic reaction to a statin medication was likely to have been considered earlier.
Summary

While other factors may have contributed to this patient’s outcome, this case report highlights the role the physical therapist can play in pharmacovigilance. Physical therapists generally spend considerable time with their patients. Therefore, they are uniquely positioned to apply knowledge of pharmacokinetics and pharmacodynamics in order to monitor the safety of the drug-therapy regime.

Adverse reactions from medication must be considered in the differential diagnosis process. While statin medications are generally well tolerated, myalgia is a known adverse reaction. When patients begin taking a new statin or a current statin dosage is increased, physical therapists should be aware of the potential for a myalgic reaction. Myalgic reactions in patients taking a statin should be reported to the patient’s physician.

References


64. Fitzgerald GK, Childs JD, Ridge TM, Irrgang JJ. Agility and perturbation training for a physically active individual with knee osteoarthritis. *Phys Ther* 2002; 82:372-82.


Appendix 1
Description of the Forward Lunge Test as described by the IWA

- Client stands with the feet parallel to each other.
- Feet should be approximately shoulder width apart.
- Client is instructed to maintain the back in a straight or slightly arched position and on keeping the body as vertical as possible while performing the lunge test.
- Client is instructed to step forward with the involved leg allowing the knee to bend to the point of discomfort.
- Stride length is the distance between the great toe of the involved and uninvolved leg.
- Goniometric measurement of knee flexion is taken to determine the amount of tolerable knee flexion.
- The test is performed three times. The most favorable effort is recorded.

Appendix 2
The Ten Repetition Maximum Testing Protocol as described by the Professional Health and Fitness Institutes Certified Strengthening and Conditioning Instructor Certification (CSCI)

Instruct the client to warm up with light resistance that allows five to ten repetitions

- One-minute rest.
- Determine a load that allows the client to perform fifteen repetitions.
- Two-minute rest.
- Determine a load that allows the client to complete ten repetitions by adding
  - 2.5-5% of upper body
  - 5-10% for lower body exercises.
- If the client was successful have them take a four minute rest and attempt to make a load increases.
  - 2.5-5% for upper body
  - 5-10% for lower body.
- If the client was unsuccessful have them take a four-minute rest and attempt to make a load decrease.
  - 2.5% for upper body
  - 5-10% for lower body.
Appendix 3
Patient Teaching Printout from Nursing 2004 DRUG Handbook

atorvastatin calcium Lipitor

Averse reactions
CNS: headache, asthenia, insomnia.
CV: peripheral edema.
EENT: rhinitis, pharyngitis, sinusitis.
GI: abdominal pain, dyspepsia, flatulence, nausea, constipation, diarrhea.
GU: urinary tract infection.
Musculoskeletal: arthritis, arthralgia, myalgia.
Respiratory: bronchitis.
Skin: rash.
Other: infection, flulike syndrome, allergic reaction.

Interactions

Contraindications
Contraindicated in patients hypersensitive to drag and in those with active liver disease or conditions associated with unexplained persistent elevations of serum transaminase levels. Also contraindicated in pregnant and breast-feeding women and in women of childbearing age who are at risk for becoming pregnant.

Patient teaching

- Teach patient about proper dietary management, weight control, and exercise. Explain the importance of these factors in controlling elevated lipid levels.
- Warn patient to avoid alcohol.
- Tell patient to inform prescriber of adverse reactions, such as muscle pain, malaise, and fever.
- Advise patient that drug can be taken at any time of day and without regard to meals.
- Alert: Inform woman that drug is contraindicated during pregnancy because of potential danger to the fetus. Advise her to notify prescriber immediately if pregnancy occurs or is suspected.

*Liquid contains alcohol. fCanada | Australia §U.K. OTC Over the counter
Reactions may be common, uncommon, life-threatening, & COMMON AND LIFE-THREATENING

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