

Case Report: Rehabilitation of a 65 Year-Old Female with Statin-Induced Rhabdomyolysis

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Abstract

Statin-induced rhabdomyolysis is a debilitating condition of muscle breakdown that can lead to severe functional limitations. Prior reports of physical therapy treatment have focused on athletes and military personnel following acute exertional rhabdomyolysis, however there is minimal information for treatment of statin-induced rhabdomyolysis in the geriatric population. A 65 year-old female with a diagnosis of rhabdomyolysis due to the interaction of atorvastatin and clarithromycin was seen in an out-patient orthopedic clinic for weakness, fatigue, and difficulty completing daily tasks. The treatment approach was adapted from work based on previous military programs in managing acute exertional rhabdomyolysis by decreasing the pace and intensity of the exercises to accommodate an elderly patient, but still maintaining a focus on achieving active range of motion before progressing to isotonic exercises and functional activities. Primary outcome measures included the Timed Up and Go (TUG), 6 Minute Walk Test (6MWT), and 5 Time Sit to Stand (5xSTS). By discharge all outcome measures demonstrated improvement and the patient was able to return to work.

Keywords: Rhabdomyolysis, rehabilitation, older adult, case report

1. Introduction

Statin-induced rhabdomyolysis is a potentially life threatening medical condition characterized by the disruption of the plasma membrane of skeletal muscle leading to the leakage of intracellular components, such as myoglobin and creatine kinase (CK), into the blood and urine (Aschenbrenner & Venable, 2012; Baxter & Moore, 2003; Torres, Helmstetter, Kaye, & Kaye, 2015). The cause of this condition is the interaction of certain antibiotics and the statin medication, particularly clarithromycin and atorvastatin (Lee & Maddix, 2001; Li et al., 2015; Magee, Medani, Leavey, Conlon, & Clarkson, 2010; Mendes, Robles, & Mathur, 2014; Petrov, Yatsynovich, & Lionte, 2015). The severity of rhabdomyolysis can range from asymptomatic laboratory findings to acute renal failure and can potentially lead to death (Allsion & Bedsole, 2002). The clinical signs of this syndrome include elevated CK (above 10,000 U/L), dark colored urine, muscle weakness, and myalgia (Aschenbrenner & Venable, 2012; Mendes et al., 2014). The most common physical complaints are fatigue, weakness, and myalgia (Torres et al., 2015). Immediate medical management is focused on the prevention of acute renal injury (Blaiher, Lishner, & Elis, 2011; Chatzizisis et al., 2010; Torres et al., 2015). Depending on the severity, statin medication is either stopped completely (if serum CK levels are >10x the upper limit of normal) or reduced (if serum CK levels are <10x the upper limit of normal) (Chatzizisis et al., 2010).

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Statin medication, either the same or different, can be resumed at the same or lower dose if no symptoms of rhabdomyolysis reoccur (Chatzizisis et al., 2010). If symptoms reoccur then statin medication is to be suspended. Prolonged muscle weakness and fatigue are common among those who have been diagnosed with rhabdomyolysis, regardless of the etiology. Patients may find it difficult to complete activities of daily living (ADLs) due to muscular fatigue and weakness, as well as decreased endurance. Physical therapy can be used to help those who are recovering from the secondary effects of rhabdomyolysis. Due to the wide variety of physical and functional impairments that these patients can present with, it may be difficult to develop a comprehensive plan of care based on the needs of the patient. Previous work has been done following acute exertional rhabdomyolysis in athletes and military personnel (Baxter & Moore, 2003; O'Connor, Brennan, Campbell, Heled, & Deuster, 2008; Randall, Butler, & Vance, 1996; Tietze & Borchers, 2014). A protocol based on the work of Randall et al has been used to treat acute exertional rhabdomyolysis due to intense push-up training, allowing the individual to return to physical activity (Baxter & Moore, 2003). The treatment program was broken into 4 phases. Phase 1 consisted of AROM exercises and was completed when full AROM was achieved. Phase 2 consisted of steady state work on an upper body ergometer (UBE) and was completed once 15 minutes of continuous low intensity (30 watts) work was achieved. Phase 3 consisted of isotonic weight exercises focusing on the upper body musculature to perform push-ups. Phase 4 was return to normal activity and was initiated once push-ups were performed without modification.

The Consortium for Health and Military Performance (CHAMP) guidelines are similar to the work of Randall et al. The CHAMP protocol contains 3 phases; phase 1 is primarily rest, phase 2 is light activity with follow-up care, and phase 3 is gradual return to regular training/activity if no clinical symptoms are present (O'Connor et al., 2008; Tietze & Borchers, 2014). The consensus of the reports is to begin with low level exercises and gradually increase the level of intensity in order to help patients return to prior level of function. There are currently no evidence based guidelines for and no scientific literature about physical therapy management specific to older adult patients diagnosed with statin-induced rhabdomyolysis. The purpose of this case report was to describe the adaption of the treatment approach for younger patients with acute exertional rhabdomyolysis specific to the upper body and apply it to an older adult with statin-induced rhabdomyolysis involving the upper and lower extremities

2. Case Description

The patient was a 65-year-old female medically diagnosed with rhabdomyolysis one month prior to the start of physical therapy. The patient's primary language was Greek and at times she had difficulty speaking and understanding English. This made communication difficult at times, but was not a significant barrier to care. Additional time was required in order to explain procedures during the examination and during intervention sessions. Past medical history included hyperlipidemia, but was otherwise insignificant.

The etiology of the rhabdomyolysis was a drug interaction of atorvastatin and clarithromycin. The patient was hospitalized for 2 weeks after becoming weak to the point of being unable to get out of bed. All medications were stopped upon admission to the hospital. No physical therapy was administered during her hospital stay. The patient was discharged from the hospital after being stabilized with serum CK levels returning to normal. Upon discharge the patient received home physical therapy, which continued until she was referred to outpatient physical therapy 4 weeks later.

The patient was seen in an outpatient clinic for the episode of care. The chief complaints were a feeling of weakness all over her body, fatigue, and a fear of falling due to the weakness in her legs. She reported that she felt pain in her legs and as if "they were going to give out" when she would walk or go up/down stairs. No falls were reported. At time of initial evaluation the patient was not taking medications for cholesterol per physician orders. Prior to the onset of weakness, the patient was an owner and manager of a family restaurant. Job duties included management of staff, greeting customers, and most of the time spent on her feet walking around the restaurant. No functional limitations were reported prior to the onset of rhabdomyolysis. She was not able to return to work at the time of initial evaluation and reported functional limitations in household ambulation, prolonged community ambulation, dressing, cooking, general mobility issues, and stair navigation. Frequent rest breaks were required in order to perform prolonged activities such as grocery shopping. She lived with her husband who was able to assist her when needed. She did not use any assistive devices at the time of evaluation, but was using a walker and straight cane after discharge from the hospital. The main goals of the patient were to return to work and "stop feeling tired and weak all the time".

The case report was approved by the Midwestern University Institutional Review Board and the patient was informed about the purpose of this case report and signed an Institutional Review Board approved consent form.

3. Examination

3.1 Systems Review

Integumentary, neurologic, and cardiovascular examinations were all unremarkable.

3.2 Observation/Gait

The patient displayed a slouched posture while seated, with rounded shoulders and increase thoracic kyphosis. During gait the patient displayed excessive trunk lean in the frontal plane as a compensation for weak hip abductors bilaterally. Decreased toe off bilaterally was observed as well. The weak hip and lower extremity strength may have contributed to increased trunk movement as a compensatory strategy. At times the patient did not clear her toe from the ground and would stumble, but not fall.

3.3 Range of Motion

Active range of motion (AROM) was measured using a universal goniometer. Measurements were taken due to decreased upper and lower extremity range motion during gross screening and because of the patient's concern of decrease upper extremity mobility, specifically impairing her ability to complete ADLs. At the time of initial evaluation, it was suspected that AROM would be decreased secondary to muscle based on the patient's subjective reports and medical diagnosis. AROM measurements were used to guide the progression of the intervention plan, based on the literature (Baxter & Moore, 2003; Randall et al., 1996). Intrarater reliability ($r = 0.8-0.89$) has been shown to be higher than interrater reliability ($r = 0.58-0.86$) for AROM measurements (Boone et al., 1978). Active range of motion measurements throughout the episode of care are listed in table 1 (Norkin & White, 2009).

Table 1. Active Range of Motion Measurements(Norkin & White, 2009)

Motion	Initial Evaluation		3 weeks		6 weeks	
	Right	Left	Right	Left	Right	Left
Shoulder Flexion	0-90	0-85	0-147	0-145	0-147	0-145
Shoulder Abduction	0-90	0-90	0-143	0-140	0-143	0-140
Elbow Flexion	0-120	0-120	0-130	0-130	0-130	0-130
Hip Flexion	0-120	0-120	0-120	0-120	0-120	0-120
Knee Flexion	15-101	15-101	0-115	0-115	0-115	0-125

3.4 Muscle Strength

Manual muscle testing (MMT) was used to confirm that the suspected decrease in AROM was due to muscle weakness and not due to soft tissue hypomobility. Strength was measured using the 12 point scale (scores ranging from 0-5) from Kendall (Kendall, McCreary, & Provance, 2005a). Interrater reliability for upper extremity MMT ranges from fair to good with intraclass correlation coefficients (ICC) ranging 0.55-0.72 (Hayes, Walton, Szomor, & Murrell, 2002). Intrarater reliability ranges from good to excellent (ICC =0.79-1.00) (Hayes et al., 2002). However, MMT lacks the sensitivity and diagnostic accuracy to detect true strength deficits, especially with higher MMT grades (score = 5/5)(Bohannon, 2005; Bohannon & Corrigan, 2000). Strength scores are listed in table 2 (Kendall, McCreary, & Provance, 2005b).

Table 2. Manual Muscle Testing Scores

Motion	Initial Evaluation		3 weeks		6 weeks	
	Right	Left	Right	Left	Right	Left
Shoulder Flexion	2+	2+	4	4	4+	4+
Shoulder Abduction	2+	2+	3	3	4	4
Elbow Flexion	3+	4	4+	5	5	5
Elbow Extension	3	3+	4+	4+	5	5
Hip Flexion	3+	3	4	4	4	4
Hip Abduction	2+	2+	4	4	4	4
Knee Flexion	4	3+	4	4+	4	4+
Knee Extension	3+	3+	3+	4+	3+	4+
Plantarflexion*	5 partial repetitions	5 partial repetitions	20 repetitions	20 repetitions	20 repetitions	20 repetitions

*Plantarflexion grading based on 20 single leg repetition test in order to achieve 5/5 grade
MMT scores based on Kendall (Kendall et al., 2005b)

3.5 Functional Assessment

Decreased functional mobility was a major concern of the patient and therefore it was important to conduct three functional tests; the 6 Minute Walk Test (6MWT), Timed Up and Go (TUG), and 5 Time Sit to Stand (5xSTS). The 6MWT was used due to the patient's complaint of reduced endurance and fatigue during prolonged activity, noted specifically in the lower extremities. This test has been shown to have moderate correlation with lower leg strength ($r = 0.67$) and gait speed ($r = 0.52$), as well as excellent test-retest reliability ($r = 0.95$) (Harada, Chiu, & Stewart, 1999). The TUG was the primary outcome measured used as the patient stated that she had a fear of falls and was active in the community prior to the onset of rhabdomyolysis. The TUG has been shown to have good predictive ability for ADL disability and difficulty in higher level tasks in community-dwelling older adults (Donoghue, Savva, Cronin, Kenny, & Horgan, 2014). A score of 20 seconds indicated a higher probability of ADL disability (probability = 0.43) and a score of 13 seconds indicated a lower probability of disability (probability = 0.09) (Donoghue et al., 2014). Good sensitivity (0.87) and specificity (0.87) in predicting falls has been shown with the TUG (Shumway-Cook, Brauer, & Woollacott, 2000). The 5xSTS was used to assess functional lower extremity strength and as another falls risk assessment. The patient's concern of weakness in her legs and a feeling of "giving out" were the primary reason for using the 5xSTS. This test has excellent reliability (ICC= 0.89) and moderate sensitivity ($r = 0.66$) and specificity ($r = 0.55$) (Tiedemann, Shimada, Sherrington, Murray, & Lord, 2008). It is a valid measure of functional mobility in older adult women (Pearson's correlation coefficient = 0.64, $p < .001$) (Goldberg, Chavis, Watkins, & Wilson, 2012). A score greater than 11.4 seconds on the 5xSTS indicates an increased risk for falls (Bohannon, 2006). The results of the tests are listed in Table 3.

Table 3. Functional Assessments Scores

Functional Assessment	Initial Evaluation	3 weeks	6 weeks
Time Up and Go (seconds)	26.2	12.2	9.2
6 Minute Walk Test (meters)	149*	389	434
5 Time Sit to Stand (seconds)	54.77	14.36	13.93 s

*Patient stopped at 4 minutes and 52 seconds due to fatigue

4. Clinical Impression

Based on the previously mentioned history and examination findings, the patient was at a high risk for falls due to the generalized weakness and unsteadiness secondary to rhabdomyolysis. The rhabdomyolysis induced muscular weakness was causing high fatigability as well. Gait abnormalities and instability made prolonged ambulation difficult. Decreased muscle strength and endurance, loss of balance, and decreased AROM all impacted the patient's functional status in her occupation as a restaurant owner and her ability to participate in her family life. A plan of care based on previous work with military personal was modified to incorporate a whole body treatment approach and to address the balance deficits noted(Baxter & Moore, 2003; Randall et al., 1996).

5. Interventions

The plan of care was based on the previous work of Randall et al, as well as Baxter and Moore(Baxter & Moore, 2003; Randall et al., 1996). Modifications were made to those treatments parameters to include both upper and lower extremities exercises from the beginning of care. Balance and functional activities were incorporated earlier in this treatment to address ADL difficulties. Low level aerobic exercise was initiated early on to address decreased activity tolerance, as opposed to waiting until full AROM was achieved. The use of patient feedback to monitor the intensity level, rather than objective measures, was another modification made to the protocols.

The patient in this case was seen twice a week for 6 weeks. The frequency of treatment sessions was determined by the patient's availability and to allow for adequate muscle recovery. No treatment was given on the day of initial evaluation as the functional tests performed left the patient exhausted. Since the patient reported feeling weak all over, an exercise program focusing on major muscle groups of both the upper and lower extremities was developed with the goals of returning to work and being able to complete ADLs independently. Rest breaks were given frequently throughout the plan of care and the patient was carefully monitored so as to not exacerbate symptoms.

During the initial treatment sessions, AROM and individual muscle strengthening exercises were implemented. As AROM began to improve and individual muscle strength began to increase, treatment shifted towards more functional activities and whole body training, such as sit to stand exercises and lifting objects from ground to overhead. The functional activities were based on the functional deficits found during the examination and designed to allow the patient to meet her goals. Individual muscle strengthening exercises and AROM exercises were given as a home exercise program (HEP) to help to continue to make progress in those areas. The HEP was monitored continuously and adjusted based on the patient's response. During the final weeks of therapy an emphasis was placed on balance exercises. Balance was the patient's primary concern at this point as she reported feeling unsteady performing ADLs. Upper body endurance training began on the first treatment session with the UBE and lower body endurance on the second session with recumbent bike. Duration was kept to a short period and intensity was self-selected as to not completely exhaust the patient. Time was gradually increased throughout the plan of care in order to increase the patient's endurance. The general treatment progression over the course of 6 weeks is shown in table 4. HEP progression is listed in table 5. Handouts of exercises with descriptions were provided when changes were made to HEP and at discharge.

Table 4. Weekly treatment progression

Session	Treatment approach	Rationale
1-2	AROM for upper extremities and low intensity lower extremity strengthening, short duration UBE.	Focusing on achieving full AROM and increasing lower extremity strength to help with ambulation. Short duration aerobic activity to improve endurance.
3-4	Continue with AROM and lower extremity strengthening, add in upper extremity resistance exercises and recumbent bike.	Upper extremity strengthening and increase cardiovascular training to improve added to improve ADL completion.
5-6	Increased number of stepping activities, additional hip strengthening and balance exercises were added to previous plan of care. Discontinue with AROM exercises	Enhance lower extremity strength and balance to address functional deficits of ambulation and ADL completion. Full functional AROM was achieved and no longer required to perform during treatment sessions.
7-8	Increase difficulty of balance exercises to include unstable surfaces, increase duration of endurance exercises, additional overhead exercises were added. Continue lower extremity strengthening.	Progress cardiovascular exercises to increase endurance. Overhead exercises were added to help with ADL completion and work requirements.
8-9	Continue with previous treatment protocols, increasing balance exercise difficulty.	Addressed balance deficits and performed exercises to be included in HEP prior to discharge.
	Review and perform HEP. Patient was discharged to HEP.	Finalize HEP in order to continue progression outside of physical therapy.

AROM: Active Range of Motion
 HEP: Home Exercise Program
 ADL: Activity of Daily Living

Table 5. Home exercise program progression.

Session	Exercises	Rationale
1-2	Sit-to-stand, cervical retraction	Increase lower extremity strength, decrease forward head posture
3-4	Gastronomies/soles and pectorals major stretch	Improve upper and lower body flexibility
5-9	No changes made to HEP as patient returned to work and reported more physical activity throughout the day.	Patient increased physical activity at home and work on her own.
Discharge	Bilaterally shoulder internal/external rotation, D2 PNF (flexion, abduction and external rotation), standing row with <i>TheraBand</i> added to upper extremity HEP. Standing hip flexion/extension/abduction and side stepping with <i>TheraBand</i> added to lower extremity HEP.	Upper and lower body strengthening of major muscles in order to enhance ADL completion. PNF given to strengthen in functional motions.

HEP: Home Exercises Program
 PNF: Proprioceptive Neuromuscular Facilitation
 ADL: Activity of Daily Living

6. Outcomes

At the conclusion of 6 weeks the patient was discharged from physical therapy to an independent HEP. The patient's 6MWT, TUG, and 5xSTS scores improved from the initial evaluation. The TUG score decreased from 26.2 seconds, placing her at a high risk for falls at initial evaluation, to 9.2 seconds (norm = 8.0 seconds), placing her at a low risk for falls and functional disability. This was a 64.9% improvement in her score from baseline. The patient was unable to complete the 6MWT on initial evaluation and by discharge was able to complete the full time and walk 434 meters (1425 feet) (minimal detectable change = 58 meters [190 feet]), but was still below the age and gender mean value of 538 meters (1765 feet) (Perera, Mody, Woodman, & Studenski, 2006). Based on the 6MWT she was still demonstrating an impaired aerobic capacity and limited community ambulation. The 5xSTS time decreased from 54.77 seconds to 13.92 seconds. Her fall risk based on the TUG and 5xSTS decreased from a high to a low risk. Active range of motion and muscle strength steadily improved throughout the course of treatment (Table 2 and 3). The patient reported improved ease of washing hair and dressing herself. She was able to play with her grandchildren on the floor, which she was unable to do prior to physical therapy. Stair navigation improved from initially using a step-to pattern to using a reciprocal pattern. Lateral trunk lean during gait decreased and increased toe off was demonstrated. Subjectively, balance had improved since the beginning of therapy, but had not returned to prior level per patient report. Return to work occurred during the 3rd week of treatment for only a few hours each day, 2-3 days per week. By the end of therapy she was able to return to work daily, but with reduced hours. Subjectively, the patient noted improved endurance as she was able to complete her job duties, taking fewer rest breaks throughout the day compared to the start of therapy. The patient was discharged to a HEP at the conclusion of 6 weeks.

7. Discussion

Following the treatment parameters reported previously for military personnel with acute exertional rhabdomyolysis, a program for an older adult with statin-induced rhabdomyolysis was developed to address upper and lower extremity weakness and decreased functional ability. This approach still emphasized early AROM, but addressed functional activity deficits and impaired aerobic capacity early on as well. Exercise selection was based on the impairments noted during the examination and progressed as the patient tolerated in order to develop upper and lower strength without exacerbating muscle breakdown. At the end of 6 weeks, the patient's functional capabilities improved from baseline and she was able to complete ADLs with greater ease. Although many of the patient's physical abilities improved throughout the treatment period, balance deficits and decreased endurance remained following treatment. Her 6MWT was below the cut-off score for her age and she reported that prolonged ambulation was difficult. This may be attributed to the severity of rhabdomyolysis and the amount of muscle tissue breakdown. More sessions of physical therapy were recommended by both the referring physician and physical therapist to address the functional deficits, but were denied by the patient's insurance company. To address the remaining deficits, a HEP was given focusing on balance and muscle strengthening exercises for the whole body.

Patient intrinsic motivation was a major factor in the positive results of treatment. There were many personal goals that the patient wanted to accomplish, including return to work and the ability to play with her grandchildren. Her high level of motivation led to greater adherence to her HEP and to advice of the physical therapist in order for her to achieve those goals. The patient verbally reported performing her HEP multiple times a week and following the guidelines set by the physical therapists in order to "not over do anything". A number of examination tools were used to assess the functional limitations described by the patient. Active range of motion was measured and used as a guide for treatment based on the previous reports for treatment of acute exertional rhabdomyolysis, and because of patient subjective reports of decreased functional mobility (Baxter & Moore, 2003; Randall et al., 1996). It was suspected that the decrease of AROM was due to muscle weakness based on the primary diagnosis of statin-induced rhabdomyolysis. Manual muscle testing was then performed in order to confirm the suspected muscle weakness. However the limitations of MMT mentioned previously do not make the best way to measure strength (Bohannon, 2005; Bohannon & Corrigan, 2000). A more quantitative approach to measure muscle strength would have been to use hand held dynamometry. It is a valid way to measure strength in older adults (ICC = 0.44-0.85) and age related normative values have been reported, which would have aided in objectively quantifying the progress of the patient (Arnold, Warkentin, Chilibeck, & Magnus, 2010; Backman, Johansson, Hager, Sjoblom, & Henriksson, 1995; Bohannon, 1997; van der Ploeg, Fidler, & Oosterhuis, 1991).

Muscle strength, especially in the lower extremities, is associated with functional mobility in older adults (Akbari & Mousavikhatir, 2012; Moreland, Richardson, Goldsmith, & Clase, 2004). The ability to rise from a chair, climb stairs, or to be able to ambulate wherever needed safely is vital to the independence of the older adult (McCarthy, Horvat, Holtsberg, & Wisenbaker, 2004). In order to assess overall lower extremity strength and functional mobility, the 5xSTS was conducted. To assess balance and functional mobility the TUG was performed and to measure aerobic capacity the 6 MWT was performed. It was important to have an objective form of measuring the changes in function throughout the treatment. It is important to have a well-rounded, objective examination when treating an older adult as single measures do not accurately depict the functional mobility of the patient.

A substantial limitation to this case study was the lack of objective measurement of the patient's exercise intensity throughout the course of treatment. The patient was informed to exercise at a self-selected pace, with the only guidelines being to stop exercise if pain was felt and to prevent over exertion. Using the rating of perceived exertion (RPE) scale would have been an objective way to monitor exercise intensity. The RPE has been shown to be a reliable method to quantify exercise intensity for both aerobic and resistance training (Day, McGuigan, Brice, & Foster, 2004). Row et al reported that during resistance training, a RPE score of 14-16 would elicit strength and power gains, while a score of 13 or lower would be useful for improving power in older adults (Row, Knutzen, & Skogsberg, 2012). Instructing the patient to select a load that would match a score 13 would have been a more objective way to measure exercise intensity and progression. A physical therapy intervention plan for an older adult with statin-induced rhabdomyolysis was developed based on the work with younger patients with acute exertional rhabdomyolysis. This approach remained similar to previous case reports, prioritizing full AROM before resistance training and developing activity tolerance prior to return to normal activity, but was adapted to treat the whole body and address balance deficits as well (Baxter & Moore, 2003; Randall et al., 1996). Although the specific exercises and goals of therapy may be different between older adults and younger patients, the general approach to treatment is similar. Regardless of etiology or age, physical therapy aimed at achieving full, available AROM and then gradually restoring strength and activity tolerance can benefit patients with rhabdomyolysis.

The treatment described is not meant to serve as an exclusive guideline in treating patients with statin-induced rhabdomyolysis, but to help guide future treatments for patients regardless of age or etiology and serve as a suggestion for future research. There are currently no clinical trials examining the effectiveness of this treatment or any other kind of physical therapy interventions to restore function to patients with statin-induced rhabdomyolysis. Future work may want to address to the optimal treatment approach for patients with rhabdomyolysis and to specifically meet the needs of the older adult population.

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