Facilitating Exercise Adherence for Patients With Multiple Myeloma

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Physical exercise is being recognized widely as being beneficial for healthy individuals (Healthy People 2010: Understanding and Improving Health, 2000) and is becoming a part of therapy for many patients with cancer (Mock, 2001). However, prescribing individually tailored exercises and tracking patients’ abilities and commitments to adhere to a program of exercise throughout the course of treatment require greater time and effort than typically are available to busy practitioners. In an effort to better understand the barriers to exercise for patients receiving treatment for multiple myeloma (MM), the authors conducted a feasibility/pilot study to test the suitability of home-based exercise therapy and autologous peripheral stem cell transplantation for these patients receiving high-dose chemotherapy and stem cell transplantation consisted of aerobic and strength-building components. The program was home-based, and patients performed exercises without direct supervision. On average, the patients completed the six-month exercise prescription 75% of the time. Overall trends showed that all 14 patients in the exercise group improved in several areas of testing, and the test results of all 10 patients in the usual-care group declined. Flexibility and simplicity are essential when designing exercise programs for patients, and encouragement and support also are needed to help patients adhere to prescribed exercise.

Key Words: exercise, multiple myeloma

Benefits of Exercise for Patients With Cancer

Benefits of exercise for patients with cardiovascular disease, diabetes, pulmonary disease, and arthritis are well documented (Braden, 1990; Glasgow et al., 1992; McGavin, Gupta, & McHardy, 1976; Pollock et al., 2000; Stewart, 2002). Patients with cancer frequently experience lack of energy and loss of physical performance and strength. Evidence to support programmed exercise during cancer treatment is growing. Researchers have found that exercise can alleviate patients’ fatigue and improve physical performance and psychological outlook (Dimeo, 2001; Dimeo, Fetscher, Lange, Mertelsmann, & Keul, 1997; MacVicar, Winningham, & Nickel, 1989; Mock, 2001). With cancer, patients frequently experience lack of energy and loss of physical performance and strength. Evidence to support programmed exercise during cancer treatment is growing. Researchers have found that exercise can alleviate patients’ fatigue and improve physical performance and psychological outlook (Dimeo, 2001; Dimeo, Fetscher, Lange, Mertelsmann, & Keul, 1997; MacVicar, Winningham, & Nickel, 1989; Mock, 2001).
et al., 1997). Because previous research has focused on aerobic exercise (Dimeo et al., 1996; Dimeo, Rumberger, & Keul, 1998; Dimeo, Stiegitz, et al., 1997; Friendenreich & Courneya, 1996; MacVicar et al.; Mock et al., 1994, 2000; Pinto & Maruyama, 1999; Portenoy & Itri, 1999; Schwartz, 2000) and because patients with cancer who have skeletal muscle wasting may not obtain maximum benefit from aerobic exercise training, the researchers in the current study included strength resistance training in the exercise program for patients with MM.

### Multiple Myeloma: Disease and Treatment

MM is part of a spectrum of diseases labeled plasma cell dyscrasias. Plasma cells are responsible for forming antibodies against bacteria and foreign proteins. In MM, for reasons that are unclear, these cells lose their ability to respond to controlling signals from a hierarchy of immune cells. Plasma cells then divide and form abnormal proteins, which results in damage to bone, bone marrow, or other organs of the body. As myeloma cells increase in number, they damage and weaken bones, causing pain and fractures. Bone pain can make moving difficult for patients. When bones are damaged, calcium is released into the blood. This may lead to hypercalcemia, which can cause loss of appetite, nausea, thirst, fatigue, muscle weakness, restlessness, and confusion. Myeloma cells prevent bone marrow from forming normal plasma cells and other white blood cells that are important to the immune system. Therefore, patients may not be able to fight infection and disease. Patients with MM may develop renal failure as excess antibody proteins and calcium prevent the kidneys from filtering and cleaning the blood properly (Lokhorst, 2002).

The majority of patients with MM have anemia at initial presentation; 62% have hemoglobin less than 12 g/dl, and 25% present with hemoglobin less than 8.5 g/dl. Anemia generally is normochromic and normocytic and results from inadequate production of red blood cells, presumably from displacement by excessive numbers of abnormal plasma cells, shortening of red blood cell survival, and renal insufficiency (Kyle, 1975). Anemia may contribute to fatigue and result in a reduction of physical activity.

Patients receiving conventional treatment for MM have a median survival of less than three years (Barlogie et al., 1997). Tandem autologous peripheral blood stem cell transplantation improves the chance for partial or complete remissions and longer survival, with the possibility that some patients may be considered cured (Tricot et al., 2002). Initial chemotherapy consists of a cycle of the following combinations of chemotherapy agents: VAD—vincristine, doxorubicin, and dexamethasone; DCEP—dexamethasone, cyclophosphamide, etoposide, and cisplatin; and CAD—cyclophosphamide, doxorubicin, and dexamethasone, followed by peripheral blood stem cell collection and a second course of DCEP. Four to six weeks after the last induction cycle, patients receive high-dose melphalan and stem cell transplantation. Two to four months after the first stem cell transplantation, patients undergo a second course of high-dose melphalan and stem cell transplantation. Following the transplant phase, patients undergo consolidation with DPACE (dexamethasone, cisplatin, doxorubicin, cyclophosphamide, and etoposide) or DT PACE (the T stands for the addition of thalidomide) every three months for one year, followed by maintenance therapy with interferon and dexamethasone (with or without thalidomide) for another year and then interferon (with or without reduced-dose thalidomide) onward. Half of the patients at the authors’ institution are randomized to receive thalidomide during induction, post-transplant consolidation, and maintenance therapy. Side effects from these agents that interfere with exercise adherence include nausea, vomiting, anemia, fatigue, dizziness, headache, peripheral neuropathy, cardiac arrhythmia, sleep disturbances, diarrhea or constipation, and myalgia.

The majority of patients treated at the authors’ center receive this aggressive treatment as outpatients and are admitted to the inpatient hospital setting only for severe complications of their disease or its treatment. However, patients undergoing induction and consolidation treatments in their hometowns where outpatient support may be limited often are hospitalized to receive chemotherapy. These hospitalizations can contribute to physical deconditioning that increases fatigue. Fatigue and wasting occur in 50% of patients with MM (Lokhorst, 2002). As patients receive aggressive treatment, fatigue occurs in almost 100%. Thus, patients with MM are susceptible to virtually all treatment-associated complications that other patients with cancer experience, including sleep disturbances and fatigue.

Patients enrolled in the treatment program at the University of Arkansas for Medical Sciences in Little Rock were assessed for inclusion into this feasibility/pilot study. Patients 40 years of age or older who were not at high risk for pathologic fracture and were not currently participating in an exercise program were invited to participate in the feasibility/pilot exercise study. Diagnosis of high risk for pathologic fracture was based on skeletal surveys with lytic lesions in critical parts of the body, spine, or extremities. Consenting patients were assigned randomly to either an exercise group or a usual-care group.

### Feasibility/Pilot Exercise Study

Twenty-four patients enrolled in the study, with 14 subjects in the exercise group and 10 in the usual-care group. Because of time and funding constraints, the feasibility/pilot exercise study ended before another six subjects enrolled. The study subjects, 10 women and 14 men, all Caucasian, ranged in age from 42–74 years, with a mean age of 55 years.

The researchers collected aerobic capacity, strength, fatigue, sleep, mood, and anthropometric measurements at three different times: about three months before the first transplant, when receiving the first transplant, and about three months after the first transplant. These times were when the patients returned to the center for treatment. After the first testing period, patients in the exercise group received individualized exercise prescriptions and patients in the other group received usual care as prescribed by their physicians. Usual care at this center included encouragement to remain active and walk 20 minutes at least three times per week.

The prescribed exercise programs consisted of an aerobic component (usually walking, but sometimes running or cycling depending on fitness and desires of patients) and strength resistance training (using exercise stretch bands). The programs were home based, and patients performed their exercises without supervision. Patients in the exercise group received a set of color-coded exercise stretch bands with varying resistances and a booklet illustrating the exercises.

Keeping a weekly exercise log helped patients track the frequency, intensity, and duration of the exercises they performed (see Figure 1). Based on patients’ documented exercise performance, programs could be altered to best accommodate their physical functioning (e.g., if a patient was feeling very fatigued, the researchers lowered the intensity of the exercises [i.e., changed color of band], reduced the number of repetitions, and decreased the length or rate of the walk). No injuries were sustained as a result of the exercise regimens. One patient reported a broken central venous catheter stitch that she suspected might have occurred during the course of exercise testing. Subsequently, the researchers put more emphasis on instructions regarding putting no pressure on central venous catheter insertion sites during exercise testing. At two separate repeat testing
times, the researchers decided that certain portions of exercise testing would be deferred because of a patient’s physical condition at the time.

Patients assigned to the exercise group faxed the researchers copies of their weekly exercise logs. Patients assigned to the usual-care group faxed their activity logs weekly, which allowed the researchers to control for possible bias created by additional contact with healthcare providers.

The Exercise Prescription

To ensure that each patient in the exercise arm of the study met personally with an exercise physiologist, each patient was escorted to the testing site. This first meeting provided the exercise physiologist with an opportunity to test each patient and establish baseline aerobic and strength ability and lean body mass estimates. Prior to testing, each patient rode a stationary bicycle for 8–10 minutes. After this warm-up period, each patient completed a series of stretching exercises. After stretching, the patient performed a series of strength tests, including leg extension, chest press, double leg press, arm pull, and leg curl, all using Keiser pneumatic equipment. Each patient walked on a treadmill, and researchers used the modified Balke protocol to determine his or her fitness level (Tonino & Driscoll, 1988). The Balke protocol is a procedure for assessing cardiovascular health using a graded treadmill exercise test in which the treadmill speed is held constant and its slope increased, with the incremental increases in work so closely spaced as to approach continuity (Dorland’s Illustrated Medical Dictionary, 2002). To measure each patient’s body composition, the researchers used the Bod Pod® (whole body plethysmography, Life Measurement, Concord, CA). This test provided each patient’s percent and actual body fat weight and percent and actual lean body weight.

After testing, the exercise physiologist gave each patient an exercise program based on his or her health and exercise history, as well as strength levels and aerobic capacity determined during the baseline testing. Figure 2 illustrates a sample of an exercise prescription. Each patient received a set of exercise stretch bands; however, only patients who showed significant strength during baseline testing received black bands. Overall, most patients used the green, red, and blue bands during the exercise program. When patients had episodes of extreme fatigue, they completed the exercise prescription using yellow bands. Throughout the six months of training, a member of the research team attempted to contact patients each week via telephone to determine whether modification of exercise prescriptions was needed. In addition, patients contacted the research team through a toll-free phone number to request help with their exercise programs.

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**Figure 1. Sample of Exercise Log**

**Figure 2. Sample of an Exercise Prescription**

easily could carry and use the exercise stretch bands in small hotel rooms, where many of them stayed during treatment. The exercise stretch bands were equipped with easy-to-hold plastic handles and ranged from 2–27 pounds of resistance (see Figure 4). Figure 5 shows the pounds of resistance for various colored exercise stretch bands.

Each patient in the exercise group received a set of exercise bands; however, only patients who showed significant strength during baseline testing received black bands. Overall, most patients used the green, red, and blue bands during the exercise program. When patients had episodes of extreme fatigue, they completed the exercise prescription using yellow bands. Throughout the six months of training, a member of the research team attempted to contact patients each week via telephone to determine whether modification of exercise prescriptions was needed. In addition, patients contacted the research team through a toll-free phone number to request help with their exercise programs.

**Figure 3. Borg Scale (Rate of Perceived Exertion)**
Results and Patient Experiences

The researchers had planned for each patient to be in the study for about six months. One patient assigned to exercise died from disease progression. Six other participants left the study before the second testing period, two because of disease progression and four for personal reasons; three of these were in the exercise group and four in the usual-care group. Measurements taken on individuals who had been in the study for less than 2.5 months were not used in data analysis for comparisons with baseline measurements.

Because of the small sample size in the feasibility study, the only endpoint that achieved statistical significance was the positive effect of exercise on lean body weight. However, the following trends suggest that individualized exercise programs for patients receiving aggressive treatment for MM are feasible and may be effective in decreasing fatigue and mood disturbance and improving sleep.

- The exercise group gained lean body weight, but the usual-care group lost lean body weight.
- The exercise group gained muscle strength, but the usual-care group lost muscle strength.
- The exercise group lost fewer minutes on the treadmill than the usual-care group.
- The exercise group showed a decrease in fatigue, whereas the usual-care group did not.
- Mood disturbance scores decreased for both groups.
- The total minutes of nighttime sleep increased for the exercise group and decreased for the usual-care group, and the percent of time asleep while in bed at night increased for the exercise group but decreased for the usual-care group.
- Daytime sleepiness decreased for both groups as the minutes of daytime sleep increased.

Patients enrolled in this study had poor sleep characteristics. Their sleep efficiency (i.e., percentage of time sleeping during the time one tries to sleep) was 70.2% for men ($n = 14$) and 82.3% for women ($n = 10$). Maladaptive sleep behaviors frequently develop among patients with cancer who are encouraged to sleep and rest to recuperate (Graydon, Bubela, Irvine, & Vincent, 1995; Irvine, Vincent, Graydon, & Bubela, 1998; Richardson & Ream, 1997).

Muscle wasting is a common feature of cancer, and dexamethasone therapy increases the risk for muscle weakness and osteoporosis. Resistance exercise increases muscle mass and reduces muscle wasting associated with a variety of catabolic conditions and may have a positive effect on cancer-related muscle wasting (al-Majid & McCarthy, 2001). The finding that the exercise group maintained lean body weight whereas the usual-care group lost lean body weight supports a positive effect of a combination of aerobic and resistance exercise for patients with cancer. These findings are clinically important because treatment for MM includes dexamethasone, which can cause muscle wasting.
The researchers’ conceptual approach was that, with increased muscle strength, patients may be able to maximize their aerobic capacity and physical activity. Increased physical activity may increase the homeostatic sleep drive to increase nighttime sleep and thus relieve cancer-related fatigue. More information on results will be reported in another publication (Coleman et al., in press).

During weekly phone conversations with the researchers, the patients in the exercise group described their exercise routines as motivating and challenging and also indicated that the weekly phone calls were a motivating factor. Although prescriptions were adjusted during treatment based on patients’ endurance and physical abilities, most patients completed their prescribed exercises. On average, the exercise group completed the six-month exercise prescription 75% of the time. In the general population, only half of individuals who begin exercise programs still are exercising at the end of six months (Ohio State University, 2000; Paterson, 2003; Titzer, 2003).

In the current study, a 47-year-old female patient who was enrolled in the exercise group performed her exercise prescription more than 90% of the time. In addition to the prescription, the patient performed a significant amount of nonprescribed activities. These activities included carrying lumber, walking an additional 20 minutes while at a construction site, and lifting tools and supplies that weighed in excess of 20 pounds. During her treatment, she did require decreases in exercise amounts and times; however, she continued to maintain or increase her baseline prescription. A 63-year-old man completed more than 50% of his exercise prescriptions during the six-month program. During the treatment of his cancer, he became severely fatigued and struggled to complete his prescription. On-one-one consultation provided him with individualized instruction and provided the physiologist an avenue for modifying the prescription, which enabled the patient to complete it successfully. During final testing, none of his scores changed dramatically; however, he did maintain baseline scores, whereas many patients in the usual-care group experienced a decrease from baseline.

**Barriers and Suggestions to Facilitate Exercise Adherence**

**Lack of support:** When the researchers tested patients at baseline, they encouraged a family member or significant other to attend. They also included this person in the explanation of the testing and the exercise demonstrations. Patients who exercised with someone suggested that this helped them complete their exercises. As the literature suggests, support is essential in maintaining an exercise program (Ohio State University, 2000; Titzer, 2003), and this study suggests that this remains true with individuals with MM who are receiving treatment.

**Time:** Recent studies suggest that time constraints are the number one barrier to lack of vigorous physical activity, with other barriers being personal health, laziness, cultural barriers, and lack of past experience with exercise (Brownson, Baker, Housemann, Brennan, & Bacak, 2001; Eyler et al., 2002; Juarbe, Turok, & Perez-Stable, 2002; Saxena, Borzekowski, & Rickert, 2002; Stutts, 2002; Walcott-McQuigg, Zerwic, Dan, & Kelley, 2001). During the weekly phone calls, the exercise physiologist helped patients determine how to fit exercise into their routines. In addition, the researchers instructed the patients to break up the exercises throughout the day to allow for flexibility.

**Weakened immune system:** MM and its treatment weaken the immune system. Patients should stay out of crowds and away from people with colds or other infectious diseases. When prescribing aerobic exercise, the researchers instructed immunocompromised patients to walk or jog on treadmills in their homes or in their neighborhoods and avoid gyms and malls for exercising.

**Fatigue and therapy-induced side effects:** As with most cancer treatments, patients being treated for MM experienced many side effects that interfered with completing their exercise prescriptions. To keep the patients involved in some activity, even during the worst time of treatment, the researchers tailored prescriptions to their abilities. For example, some patients only needed to complete eight chair stands throughout the day for their exercise. This small amount of movement provided them with a task that they could complete and feel successful in achieving. The most important part of the exercise program was to keep patients involved and performing some type of prescribed exercise. Encouragement was given to increase portions of healthy, nutritious foods when exercise was increased. The patients also were instructed to keep themselves hydrated by replacing fluids lost while exercising.

**Important Factors to Consider**

Exercise prescriptions are an important part of patients’ care plans to improve strength, endurance, flexibility, and general well-being. When determining exercise plans, several factors should be considered.

**Patient selection:** Patients with MM vary in clinical status and risk for injury. Exercise programs may not be appropriate for patients at high risk for pathologic fractures or may need modification to minimize the risk of fracture. Patients participating in prescribed exercise programs need ongoing assessment of their risk for pathologic fractures.

**Exercise support from a family member or friend:** In planning exercise prescriptions, healthcare professionals always should try to include a family member or friend who can be involved in the exercise or who will be a positive support for encouraging exercise. Many patients enrolled in the study suggested that they exercised more when someone else exercised with them. If patients do not have an eager support person and are not immunocompromised, suggest that they participate in a group exercise program available in their communities or current residences that can be tailored to meet their exercise needs without compromising group exercise goals. Recommending weight levels, offering instruction on rate of exertion, and modifying exercises that meet the predetermined goals can accomplish this.

**Exercise equipment:** The equipment needed to perform prescribed exercise can facilitate or inhibit adherence. The researchers provided the patients with equipment that was lightweight, easy to use, and easy to pack in a suitcase. When prescribing exercise programs, healthcare professionals should be sure that patients will be able to perform the exercises at any location and that the equipment is a facilitator to exercising, not a barrier.

**Motivation:** Most people who begin exercise programs require some form of motivation. Without it, long-term adherence drops significantly. People with a life-threatening illness must have not only internal motivation but also external motivation from many sources, including friends, family members, and peers. However, the patients enrolled in this study suggested that the motivation they received from healthcare team members was highly influential. Based on this information, the authors encourage healthcare providers to include plans for motivational contacts with patients when prescribing exercise.

**Modifying exercises:** Exercise prescriptions must be easily adaptable to patients’ courses of treatment and their improvements and declines in ability. For the patients in this study, ability levels changed weekly. By using a variety of exercises and resistance levels, the researchers could change prescriptions to accommodate patients' evolving needs.
accommodate patients without them having to learn new exercise programs. Patients were able to keep exercising and complete their exercises, which, in turn, helped them to feel successful in their exercise programs, regardless of intensity level. In addition, many of the exercises were modified because of medical history or medical devices being used for treatment. For example, some patients experienced discomfort with their central venous catheters when performing chest exercises or exercises that required them to lift their hands over their heads. In these instances, exercises were modified to work the targeted muscles without causing discomfort to patients.

Conclusions and Discussion

The pilot/feasibility study demonstrated that patients with MM who are undergoing aggressive treatment with high-dose chemotherapy and stem cell transplantation can implement personalized, home-based exercise programs successfully without direct supervision and without injuring themselves. Most patients completed their prescribed endurance and strength exercises each week throughout six months of participation in the study. The flexibility of prescriptions, simplicity of the exercise equipment, and frequent encouragement from healthcare professionals contributed to successful implementation of the program. The trends identified in this pilot/feasibility study suggest that patients participating in individualized exercise programs during cancer treatment can maintain or improve their fitness levels. The encouraging results from this study have allowed the researchers to expand the eligibility criteria in the current study to include patients with more significant bone marrow transplantations of intensity level. In addition, many of the exercises required them to lift their hands over their heads. In these instances, exercises were modified to work the targeted muscles without causing discomfort to patients.

References


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Rapid Recap

**Facilitating Exercise Adherence for Patients With Multiple Myeloma**

- Patients with cancer frequently experience lack of energy along with loss of physical mobility and strength, and growing evidence supports programmed exercise during cancer treatment.
- Patients with multiple myeloma (MM), in particular, are at risk for impaired mobility and strength secondary to infiltration of myeloma cells, which can cause bone pain and lytic lesions.
- Prolonged hospitalization (e.g., for high-dose chemotherapy followed by stem cell transplantation) also contributes to physical deconditioning and fatigue experienced by patients with MM.
- Dexamethasone therapy places patients at risk for muscle weakness and osteoporosis.
- Barriers to exercise adherence among patients with cancer include lack of support, time constraints, weakened immune systems that preclude group exercise classes, and fatigue.
- Factors to consider when prescribing exercise to patients with MM include patient selection (e.g., patients at risk for pathologic fractures may need modified exercise programs), availability of support from a family member or friend, exercise equipment that is obtained easily and likely to be used, and the need to motivate patients to exercise.