Exercise for Fatigue Management in Hematopoietic Stem Cell Transplantation Recipients

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Fatigue is a commonly reported symptom of patients who have undergone hematopoietic stem cell transplantation (HSCT). Fatigue in the HSCT recipient has multiple possible causes, including deconditioning, anemia, and medications. Regardless of the cause, fatigue impacts patients' well-being, ability to reintegrate into their normal lifestyle, physical recovery from transplantation, and overall symptom management. The authors discuss the current evidence regarding exercise for the management of fatigue in this population and lay the groundwork for developing an evidence-based intervention.

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Hematopoietic stem cell transplantation (HSCT) is the umbrella term for bone marrow transplantation, peripheral blood stem cell transplantation, autologous transplantation, allogeneic transplantation, and umbilical cord transplantation, with the distinction being the source of the stem cells. HSCT includes an intensive conditioning regimen using high-dose chemotherapy with or without total body irradiation followed by a period of severe myelosuppression to create marrow space for the engraftment of the transplanted stem cells. Toxicities from the conditioning regimen can include nausea, vomiting, diarrhea, mucositis, alopecia, and increased risk of bleeding and infection. HSCT, considered a more aggressive treatment compared to standard cancer therapies, often increases the risk of fatigue, a common symptom reported among the HSCT population (Gielissen et al., 2007). Gielissen et al. (2007) found that 35% of long-term HSCT survivors ($\bar{X}$ = 9.3 years post-HSCT) continued to experience severe fatigue when compared to the general cancer population that experienced a decline in severe fatigue over time.

Background and Significance

The National Comprehensive Cancer Network ([NCCN], 2013) defined cancer-related fatigue (CRF) as "a distressing, persistent, subjective sense of tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning" (p. 2). The reported incidence of CRF ranges from 4%–91% (Lipman & Lawrence, 2004) to as high as 80%–99% (Evans & Lambert, 2007). Patients with cancer describe fatigue as abnormal, distressing, and unrelieved by rest in contrast to healthy people who conceptualize fatigue as being a normal regulating process (Glaus, Crow, & Hammond, 1996). Cancer fatigue is multidimensional and, unfortunately, the etiologic mechanisms have not been fully elucidated. Cancer, cancer treatments, cachexia, anemia, muscle wasting, and inflammation have been shown to contribute to CRF (Evans & Lambert, 2007). In addition, CRF is not always resolved at the conclusion of therapy or when evidence of disease no longer exists (Prue, Rankin, Allen, Gracey, & Cramp, 2006). Current management of CRF is guided by consensus and recommendations, but no definitive standard exists. NCCN (2013) provides guidelines for the management of CRF, documented to be one of the most prevalent complications of cancer and its treatment. Management of CRF with exercise has received a lot of attention in the literature. Exercise has been reported to improve psychological and physical health in patients with CRF (Hacker, 2009). A systematic review and meta-analysis by Cramp and Daniel (2008) concluded that exercise can benefit patients with CRF during and after cancer treatment. Conversely, a systematic review and meta-analysis of 30 studies published by Jacobsen, Donovan, Vadaparampil, and Small (2007) found no statistical significance for the use of exercise in the management of CRF. Kangas, Bovbjerg, and Montgomery (2008) reviewed 17 studies and found benefit from psychological and exercise-based intervention for CRF.

Concerns exist about the safety of allowing HSCT recipients to participate in an exercise program. Etler et al. (2009) initially described the concern as the potential risk of bleeding and tissue damage resulting from exercise secondary to severe cytopenias during treatment. Elter et al. (2009) studied the safety of implementing an exercise intervention in 12 patients with severe pancytopenia who suffered no bleeding episodes even with platelet counts less than 10,000, and no critical tachycardias with hemoglobins