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Review of attrition and adherence in exercise studies following hematopoietic stem cell transplantation

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A B S T R A C T

Purpose: Implementing exercise programs in people receiving high-dose chemotherapy followed by bone marrow (BMT) or hematopoietic stem cell transplantation (SCT) presents unique challenges. This review examines subject attrition rates and reasons for attrition as well as adherence to exercise interventions following BMT/SCT.

Methods: Studies published between January 1985 and December 2012 that prospectively tested an exercise intervention following BMT or SCT were included in the review. Evaluation criteria included: (1) exercise modality; (2) the amount of supervision required to implement the intervention; (3) timing of the intervention; (4) subject attrition rates and reasons for attrition; and (5) exercise adherence rates.

Results: Of the 20 studies reviewed, most tested an aerobic exercise intervention or a combination of aerobic and strength training. Supervised exercise sessions were more commonly used than unsupervised sessions. The overall attrition rate was 18% for the 998 subjects enrolled in the studies. Major reasons for attrition included death, change in health status, protocol issues, personal issues with subjects, and lost to follow-up/no reason provided. Authors of supervised exercise programs rarely published exercise adherence information. Unsupervised exercise programs relied mainly on self-report to document adherence.

Conclusion: Exercise research following BMT/SCT is becoming more sophisticated as researchers build upon the expanding literature base. Questions regarding subject attrition and adherence to exercise interventions must be addressed to identify interventions that are likely to be successful when translated into clinical practice. Subject attrition from exercise studies following BMT/SCT is relatively low. Adherence information for exercise interventions needs to be regularly addressed.

Introduction

The health benefits of exercise are now universally accepted although many people struggle with incorporating exercise into their daily lives (Carlson et al., 2010). In an effort to promote increased physical activity and exercise, the Department of Health and Human Services published the first-ever, Physical Activity Guidelines for Americans ("2008 Physical activity guidelines for Americans," 2008). Simultaneously, interest in the health benefits of exercise among cancer patients has intensified with over 80 randomized clinical trials published (Speck et al., 2010). Some of the documented beneficial effects of exercise include improved functional capacity (Adamsen et al., 2009), improvement in walking ability in exercisers (Yeo et al., 2012), reduced fatigue (Brown et al., 2011; Cramp and Byron-Daniel, 2012; Mishra et al., 2012a; Schwartz et al., 2001), decreased psychological distress (Midtgaard et al., 2005; Mishra et al., 2012a), and improved quality of life (Courneya et al., 2009; Mishra et al., 2012b; Mishra et al., 2012a).

Implementing an exercise program in people with cancer who have received high dose chemotherapy followed by bone marrow transplantation (BMT) or hematopoietic stem cell transplantation (SCT) presents unique challenges. These challenges differ and may be dependent upon a number of factors such as the underlying cancer diagnosis, type of transplant (autologous, allogeneic, matched unrelated donor, or cord), associated medical conditions, such as graft versus host disease, and/or point in the transplant trajectory when the exercise program is implemented. In addition, factors unrelated to cancer or BMT/SCT influence exercise adoption. For example, desire to exercise, time to exercise, and belief in the ability to exercise influence participation and adherence to an exercise program (Arikawa et al., 2012; Courneya et al., 2004, 2012).

Exercise requires work and active participation on the part of the individual. In a research setting, the perceived amount of work

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and burden associated with the exercise program impacts the potential subject's decision to participate in an exercise study. Furthermore, the perceived subject burden influences the subject's desire and/or willingness to continue participation in the study. In people with cancer, this perceived subject burden may be further complicated by cancer and/or treatment related side effects. Following high-dose chemotherapy and BMT or SCT, perceived subject burden becomes even more important given the intensive nature of the treatment. In exercise studies involving people receiving this intensive cancer therapy, minimizing subject attrition and maintaining adherence are two of the biggest challenges facing researchers who are attempting to evaluate the benefits of an exercise intervention.

While the benefits of exercise interventions in people undergoing SCT have been reviewed elsewhere (Wiskemann and Huber, 2008), patient attrition rates and adherence to exercise interventions with SCT have not. This information is important to researchers attempting to design a study, as exercise intervention studies are labor-, cost-, and time-intensive. Furthermore, little information is available to assist researchers in determining subject attrition rates and reasons for the attrition following BMT or SCT. The purpose of this review of the literature is to examine subject attrition rates and reasons for attrition as well as adherence to exercise interventions in people who have received high-dose chemotherapy followed by BMT/SCT. For this review of the literature, subject attrition is defined as subjects who were enrolled in the study but failed to complete all research activities or withdrew from the study for any reason. Exercise adherence is defined as the degree to which the BMT/SCT patient is able to implement and carry out the exercise prescription.

Materials and methods

Publications included in this review were identified through literature searches of PubMed, Embase, and CINAHL from January 1985 through December 2012, using the index terms "bone marrow transplantation," "hematopoietic stem cell transplantation" "cancer" and "exercise". In addition, the references of the studies obtained through computer indexing were examined to locate any additional articles. Meeting abstracts and unpublished studies were not included in the review. This review was limited to adult cancer patients and articles published in English.

Initial phase

The integrative review of the literature was conducted in two phases. The purpose of the initial phase was to provide an overall sense of the literature focused on exercise in people with cancer that received high-dose chemotherapy followed by BMT or SCT. In the initial phase, all retrieved abstracts were reviewed to determine the type of publication. Abstracts were classified as: (1) exercise intervention studies; (2) studies related to exercise and/or BMT or SCT that did not prospectively test an exercise intervention; (3) integrative reviews of exercise intervention studies in bone marrow or hematopoietic stem cell transplant patients; or (4) other types of reviews articles (i.e., clinical reviews, case reports, etc.).

Second phase

In the second phase of the literature review, full articles were retrieved and reviewed for all the abstracts classified as research testing an exercise intervention in BMT or SCT. The purpose of the second phase of the review was to provide an in-depth analysis of subject attrition and adherence to exercise interventions. Research articles meeting the following criteria were included in the second phase of the review: (1) study employed people who had undergone a BMT or SCT; and, (2) study prospectively tested the effects of an exercise intervention on a specified outcome as determined by the investigator(s). The nature of the outcome variable(s) was not limited and included physiological, psychological, and social variables. All studies meeting these predefined criteria were evaluated to determine:

1. The type of exercise intervention: aerobic exercise, strength training, stretching, or a combination of modalities.
2. The amount of supervision required to implement the exercise intervention.
3. Timing of the exercise intervention.
4. Subject attrition rates, defined as the stated number of people who enrolled in the study compared to the final sample size, and the reasons for subject attrition.
5. Adherence rates for supervised, unsupervised or combination (supervised and unsupervised) programs.

Results

Initial phase: overall classification of articles in the exercise and bone marrow/stem cell transplantation literature

One hundred and twenty-seven articles were retrieved from the literature search. The classification of abstracts retrieved during phase 1 is illustrated in Fig. 1. Briefly, the majority of articles were classified as research, but did not prospectively test an exercise intervention ($n = 75$; 59%). This was followed by review articles, such as clinical reviews, exercise intervention studies, case reports, and finally, integrative reviews. Important to this paper, 20 abstracts (16%) were classified as exercise intervention studies.

Second phase: exercise intervention studies in bone marrow/ hematopoietic stem cell transplantation

The full articles for the 20 abstracts classified as research prospectively testing an exercise intervention following BMT or SCT were retrieved and reviewed. Studies using the same sample but reporting different findings in multiple journals were only included once. Fifteen of the 20 articles met the defined inclusion criteria of prospectively testing an exercise intervention. An additional five studies were identified by reviewing reference lists of retrieved articles, bringing the total number of studies included in the review to 20 (Table 1).

Type of exercise and amount of supervision required

The majority of studies tested an aerobic exercise intervention ($n = 7$; 35%) or a combination of aerobic and strength training

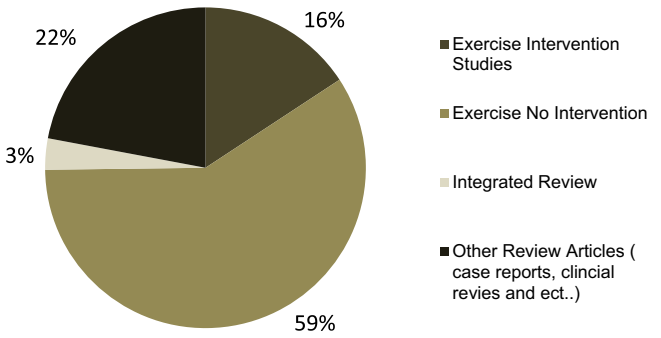

Fig. 1. Results of initial review of exercise in BMT or SCT abstracts ($n = 127$ abstracts).