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Mind and body practices for fatigue reduction in patients with cancer and hematopoietic stem cell transplant recipients: A systematic review and meta-analysis

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ABSTRACT

Purpose: To determine whether non-physical activity mind and body practices reduce the severity of fatigue in patients with cancer or hematopoietic stem cell transplant (HSCT) recipients compared to control interventions.
Methods: We included randomized trials which compared non-physical activity mind and body practices compared with control interventions for the management of fatigue in cancer and HSCT patients.
Results: Among 55 trials (4975 patients), interventions were acupuncture or acupressure (n = 12), mindfulness (n = 11), relaxation techniques (n = 10), massage (n = 6), energy therapy (n = 5), energizing yogic breathing (n = 3) and others (n = 8). When combined, all interventions significantly reduced fatigue severity compared to all controls (standardized mean difference −0.51, 95% confidence interval −0.73 to −0.29). More specifically, mindfulness and relaxation significantly reduced fatigue severity.
Conclusions: Mindfulness and relaxation were effective at reducing fatigue severity in patients with cancer and HSCT recipients. Future studies should evaluate how to translate these findings into clinical practice across different patient groups.

1. Introduction

Cancer-related fatigue (CRF) is a distressing, persistent and subjective sense of tiredness related to cancer or cancer treatments that interferes with usual functioning (Berger et al., 2015). CRF is highly prevalent and can occur throughout the treatment trajectory (Henry et al., 2008; Hofman et al., 2007; Wang et al., 2014; Bower et al., 2000). The cause of CRF is multifactorial and may be related to cancer itself, treatments and comorbidities (Berger et al., 2015; Wagner and Cella, 2004). Hematopoietic stem cell transplantation (HSCT) recipients with and without cancer also experience severe fatigue (Tonosaki, 2012; Graef et al., 2016). Fatigue is an important issue because it reduces quality of life and may lead to the decision to stop cancer treatments (Wang et al., 2014; Bower et al., 2000; Kim et al., 2008).

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Many approaches have been studied for the management of fatigue in cancer patients, including physical activity, psychological interventions and pharmacological approaches (Berger et al., 2015; Bower et al., 2014; Mustian et al., 2017). Another set of interventions include complementary health approaches (NCCIH, 2017). The National Center for Complementary and Integrative Health categorizes complementary health approaches as: (1) natural products such as herbs, vitamins and minerals; (2) mind and body practices; and (3) other approaches including homeopathy and naturopathy. Studying complementary health approaches is important as patients and families are particularly interested in this therapeutic approach, particularly for symptom management (Montross-Thomas et al., 2017).

In the present analysis, we focused on evaluating non-physical activity mind and body practices for fatigue management. Among mind and body practices, yoga, tai chi, and qi gong can be classified as neuromotor physical activities (Garber et al., 2011) and were excluded from the present analysis. Consequently, our primary objective was to determine whether non-physical activity mind and body practices reduce the severity of fatigue among adults and children with cancer or HSCT recipients when compared to control interventions. Our secondary objective was to determine whether the effect of these mind and body practices on fatigue varied by patient, intervention or methodological factors.

2. Methods and materials

For the conduct of this systematic review, we followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement (Shamseer et al., 2015). With the assistance of a library scientist, we searched for randomized trials indexed from 1980 to May 11, 2017 in the following electronic databases: MEDLINE, MEDLINE in-process, EMBASE, Cochrane Central Register of Controlled Trials, CINAHL, and PsychINFO. The search strategy included Medical Subject Heading terms and text words that identified patients with cancer or HSCT recipients who received an intervention to reduce fatigue. Appendix A shows the full search strategies.

2.1. Study selection

Eligibility criteria were defined *a priori*. We included studies if participants of any age had cancer or were HSCT recipients, and if the study was a fully published primary randomized or quasi-randomized trial with a parallel group design. The study had to evaluate an intervention for the prevention or treatment of fatigue. We excluded studies if less than 75% of participants had cancer or were undergoing HSCT; if fatigue was either not an end-point or reported as an adverse effect; if the intervention was direct cancer treatment; and if less than five participants were randomized to any study arm. We did not restrict inclusion by language. For the purpose of this systematic review, we then limited studies to those in which non-physical activity mind and body practices were the intervention being evaluated.

Two reviewers (SO, PDR or LS) independently evaluated the titles and abstracts of studies identified by the search strategy. Any publication considered potentially relevant by any reviewer was retrieved in full and assessed for eligibility by two reviewers (SO, PDR or LS). Inclusion of studies in this systematic review was determined by agreement of both reviewers. Discrepancies between the two reviewers were resolved by consensus and adjudication by a third reviewer if required (LLD or LS). Agreement in study inclusion between the two reviewers was described using the kappa statistic. Strength of agreement was defined as slight (0.00–0.20), fair (0.21–0.40), moderate (0.41–0.60), substantial (0.61–0.80), or almost perfect (0.81–1.00) (Koch et al., 1977).

2.2. Data abstraction and outcomes

Data were abstracted in duplicate by two reviewers (ND, HD or PDR) and any discrepancies were resolved by consensus. If discrepancies could not be resolved by consensus, a third reviewer (LS) adjudicated. We contacted authors in the event of missing primary outcome data.

The primary outcome was self-reported fatigue severity across the fatigue scales used in the primary studies. For studies that used more than one fatigue scale, we selected one scale to be used for analyses based upon an *a priori* developed rule. We selected the most prevalent fatigue scale used across studies (see Appendix B).

2.3. Categorization of non-physical activity mind and body practice interventions and control groups

The interventions were non-physical activity mind and body practices. Practices were classified as: (1) acupuncture and acupressure; (2) mindfulness (practice of enhancing awareness of thoughts, emotions, and experiences) (Anonymous, 2017a); (3) relaxation techniques (such as progressive muscle relaxation and guided imagery); (4) massage therapies; (5) energy therapies (including Reiki, therapeutic touch, and healing touch) (Anonymous, 2017b); (6) energizing yogic breathing; and (7) others. We categorized the duration of the intervention based upon the median duration of all interventions as < 6 weeks vs. ≥ 6 weeks.

Control groups were categorized as follows: (1) usual care or wait list control; (2) sham control (maneuver that mimics the intervention so that patients don't know their treatment assignment); (3) attention control (control that mirrors the time and attention received by those in the intervention group); (4) other mind and body practices; and (5) education.

2.4. Study covariates

We planned to include the following study-level potential covariates: participant age (adult vs. child), cancer diagnosis (breast, colon, other single cancer type or more than one cancer type), inclusion of HSCT patients, timing of intervention (during cancer treatment including hormone therapy, following completion of treatment or both during and following treatment), exclusive enrollment of palliative care patients (as defined by each study), and presence of fatigue at baseline as an eligibility criterion for enrollment (approach to assessment and threshold varied by study).

2.5. Risk of bias assessment

The Cochrane Collaboration's instrument for assessing the risk of bias in randomized trials was used (Higgins and Green, 2011). Elements evaluated were adequate sequence generation, adequate allocation concealment, blinding of participants and personnel, blinding of outcome assessors and lack of attrition bias. We prioritized adequate sequence generation and adequate allocation concealment *a priori* for stratified analyses because of their potential effect on bias (Schulz et al., 1995).

2.6. Data analysis

Data were combined at the study level and not at the individual patient level. We synthesized outcomes if there were at least three studies with outcome data within a stratum. If fatigue scores were missing summary measures, we made the following assumptions to facilitate data synthesis: the mean can be approximated by the median; the range contains six standard deviations, the 95% confidence interval (CI) contains four standard errors, and the interquartile range contains 1.35 standard deviations (Higgins and Green, 2011). The severity of