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Review Article

Physical Exercise Interventions in Patients Undergoing Allogeneic Haematopoietic Stem Cell Transplantation

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Abstract

Allogeneic haematopoietic stem cell transplantation (allo-HSCT) patients experience several problems, such as physical, psychological, and psychosocial side effects, during the transplantation phase. Physical exercise has recently been proposed as a method that assists HSCT patients in their recovery from the decline in physical fitness, worsening of psychological status, and impaired quality of life. The number of studies describing the promising role of physical exercise programs as non-pharmacologic adjuvant therapy for patients with cancer has increased. In this review, we describe the effects of physical exercise on the psychological well-being as well as distress, fatigue, physical functioning, and other outcomes in allo-HSCT patients. Thus, we believe that physical exercise therapy may be helpful and advantageous for patients undergoing allo-HSCT.

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- Physical functioning

INTRODUCTION

Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is increasingly being used as treatment for hematopoietic diseases worldwide [1,2]. This treatment has disease specific 5-year survival rates ranging from 5 to 80% [3]. The standard procedure for myeloablative allo-HSCT entails a conditioning regime of high-dose chemotherapy, often in combination with total-body irradiation, followed by infusion of stem cells harvested from donor bone marrow or peripheral blood [4]. This procedure results in a 2- to 4-week period of cytopenia (severe leukopenia and thrombocytopenia). The patient is hospitalised in a single-bed isolation room for a period of 4–6 weeks, as the severely depressed bone marrow function increases the risk of bleeding, infection, and anaemia, resulting in weakness, fatigue, shortness of breath, and insomnia [5]. Currently, complications for patients with haematological malignancies are frequently reported [6], and allo-HSCT treatments are themselves associated with numerous somatic, psychological, and psychosocial side effects [7]. Pre and post HSCT, patients experience substantial physical, psychological, and psychosocial distress, and deterioration in quality of life (QOL). Complications caused by the transplantation emerge at different stages of the treatment. During the pre-transplant (conditioning) phase, side effects of high-dose chemotherapy and/or radiation include nausea, emesis, diarrhoea, loss of hair, cystitis/bladder infection, and mucositis [8]. During the post-transplant phase, complications resulting from graft versus host disease include skin rash, bronchiolitis, nausea, emesis, diarrhoea, and jaundice, which cause weakness [9]. As a result of graft versus host disease and its treatment process, patients are often subjected to prolonged periods of immobilization and bed rest that lead to loss of strength and endurance [10]. We showed that allo-HSCT patients had lower QOL as well as deteriorated physical function after transplantation compared to those before transplantation [11].

Over the past few years, the number of studies describing the promising role of physical exercise programs performed as non-pharmacologic adjuvant therapy for patients with cancer has risen [12-14]. Physical exercise constitutes a potentially promising adjuvant intervention for HSCT patients because of its multidimensional effectiveness. The purpose of this review was to summarize and show the effects of exercise interventions administered before, during, and after HSCT on QOL, psychological well-being and distress, fatigue, physical functioning, and other outcomes.

Exercise intervention studies

To date, 22 studies on the effects of exercise in patients prior to, during, or after HSCT have been published. As a rule, exercise interventions were implemented during and/or after the hospitalization phase. Some studies evaluated the effects

of endurance training, whereas only a few studies investigated the specific effects of isolated resistance training. The majority of studies (n = 10) investigated the effects of a combination of endurance and resistance training, with two studies including relaxation exercises as a third part of their intervention model.

Exercise intervention period

The onset timing of physical exercise intervention for allo-HSCT patients varies, and can occur in one of three phases: conditioning (before HSCT) [12-20], post engraftment (after HSCT) [21-24], or hospital discharge [25-31]. Recently, physical exercise intervention has been increasingly initiated during the conditioning phase (chemotherapy and radiation therapy regimen). In a previous study, we observed that patients who underwent allo-HSCT had significantly lower body mass index and physical function compared to those in the normal population, even before undergoing the transplantation [32]. We also showed that roughly half of the study population had sarcopenia before undergoing allo-HSCT [33]. On the basis of these findings, we concluded that physical exercise should be initiated as soon as possible during the hospitalization of allo-HSCT patients. Recent guidelines for cancer survivors' exercise prescription provided by the American College of Sports Medicine did not report any contraindications to starting an exercise program for patients undergoing either autologous or allogeneic HSCT [34]. The ideal time for safely and effectively starting an exercise program for HSCT patients, as well as the appropriate type, frequency, intensity, and duration of the program have not been identified. In a previous study, we showed that physical exercise is beneficial and can be performed safely in patients with cytopenia undergoing allo-HSCT [5]. Physical exercise, even if it is only mild, should be performed by allo-HSCT patients as early as during the conditioning period, as it may help prevent the deterioration of physical function after transplantation.

Types of exercise intervention

Physical exercise intervention is usually fully [12,14-22,24-26,30] or partially supervised [13,31] in patients undergoing allo-HSCT. Interestingly, Shelton et al. reported higher endurance and gait speeds in supervised training groups than in patient-directed training groups [27]. Wilson et al. [28] investigated the effects of home-based aerobic exercise programs, and found that 84% of the participants completed the exercise programs at the prescribed intensity and duration. Physical exercise intervention for patients undergoing allo-HSCT typically involves a combination of aerobic training (treadmill, cycle, walking, or stair climbing) and resistive exercises with weights or elastic bands [12-14,19-22,24,26,27]. Other common physical exercise programs have incorporated educational [27] and psychoeducational [14,23] elements with low intensity bed exercises for stretching and relaxation breathing [15,16]. In our study, we performed one-on-one (physical therapist and patient) physical therapy involving resistance, stretching, and aerobic exercises for cytopenic patients during their hospitalization [5]. Physical therapists can usually vary the exercise frequency, intensity, and duration based on patient conditions and complaints on a given day. For allo-HSCT patients, a physical exercise regimen combining different types of exercise may be recommended. However, if the patient is unable to execute a self-directed exercise regimen, one-on-one physical therapy may be more appropriate.

Quality of life

Several studies have examined the effects of physical exercise on the QOL of patients undergoing allo-HSCT [13,14,17,22,26,28,30]. Most of these studies used the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire [13,14,17,26,30,31], while other studies used the Cancer Rehabilitation Evaluation System [22,24], and another used the Medical Outcomes Study 36-Item Short Form [28]. Most studies revealed significantly higher QOL scores for the allogeneic physical exercise intervention group than for the allogeneic control group [13,14,17,22]. On the other hand, Hacker et al. [30] and Knols et al. [26] observed no significant differences between the QOL scores of the physical exercise and control groups following physical exercise intervention. Wilson et al. [28] observed higher QOL scores pertaining to 'vitality/fatigue' outcomes; however, the results were not compared to those in a control group. We also investigated the QOL of patients undergoing allo-HSCT using the Medical Outcomes Study 36-Item Short Form questionnaire, and demonstrated that the frequency of physical therapy corresponded with the extent of decline in QOL [5]. Several reports have examined the effects of physical exercise on QOL; however, to date, these effects have not been confirmed in HSCT patients [5,13,14,17,22].

Fatigue

The effect of physical exercise on fatigue in patients undergoing allo-HSCT was assessed using the following questionnaires: the Functional Assessment of Cancer Therapy-Anaemia scale [14,26], Functional Assessment of Cancer Therapy-Fatigue [25] scale, Brief Fatigue Inventory [25,27], Multidimensional Fatigue Inventory [13], Piper Fatigue Scale [15], and Fatigue Symptom Inventory [28,35]. Knols et al. [26] did not observe a statistically significant decline in fatigue between the intervention and control groups. Moreover, Shelton et al. [27] reported that the decline in fatigue observed after physical exercise was not statistically significant, and the favourable changes in the intervention group's fatigue levels observed by Jarden et al. [14] were also not statistically significant. On the other hand, Wilson et al. [28] and Carlson et al. [25] reported significant improvement in fatigue symptoms following physical exercise, and Wiskemann et al. [13] demonstrated significant differences in fatigue levels between the intervention and control groups at the end of the physical exercise intervention. Moreover, Kim et al. [15] described a significant decline in the level of fatigue in the relaxation breathing exercise group compared to that in the control group. We also investigated fatigue using the Piper Fatigue Scale, and observed that post-HSCT fatigue levels were significantly higher than pre-HSCT levels in allo-HSCT patients. Increased fatigue is often observed in allo-HSCT patients, and physical exercise intervention might be useful and beneficial in alleviating this increased fatigue.

Psychological function and distress

Some studies have examined the effects of physical exercise on the psychological function and distress levels of patients undergoing allo-HSCT [13,14,18,25]; in these studies,

psychological function was evaluated using the Profile of Mood States [13,25], or the Hospital Anxiety and Depression Scale [13,14]. Wiskemann et al. [13] demonstrated a significant reduction in anxiety and depression levels in the intervention group compared to those in the control group. Defor et al. [18] showed significant differences in physical and emotional well-being between the exercise and control groups at the time of discharge. However, Jarden et al. [14] observed no significant difference in the anxiety and depression levels between the groups following physical exercise intervention. Additionally, Carlson et al. [25] did not observe a reduction in depression levels following physical exercise intervention. We investigated anxiety and depression levels in patients undergoing allo-HSCT using the Hospital Anxiety and Depression Scale, and observed no differences between pre-HSCT and post-HSCT [11]. It seems that anxiety and depression levels are not significantly increased in allo-HSCT patients, and are not significantly affected by physical exercise.

Physical functioning

Physical functioning has been evaluated through various methods that usually involve the following three aspects: aerobic capacity [12,14,20,21,25,28], muscle strength [12,14,19-21,26,31], and functional capacity [13,14,26,27,29]. In previous studies, aerobic capacity was evaluated using a treadmill or bicycle. A significant increase in aerobic fitness was observed after the physical exercise intervention compared to that before the intervention [25,28]. Furthermore, the physical exercise group demonstrated significantly better aerobic fitness compared to that in the control group [12,14,21]. Muscle strength was evaluated as upper and lower body strength using a hand-held dynamometer and resistance equipment, and a significant increase in muscle strength was observed in the physical exercise group compared to that in the control group, following physical exercise intervention [12,14,19-21,26]. Functional capacity was evaluated using the 6-min walk test, 50-foot walking time, and repeated sit-to-stand movement. While one study reported no significant increase in functional capacity after physical exercise intervention [29], several other studies described a significant increase in functional capacity in the physical exercise group compared to that in the control group, following physical exercise intervention [11,12,21,22]. In our study, we showed that the high-frequency physical therapy group of allo-HSCT patients exhibited significantly less decline in muscle strength and functional capacity compared to the decline exhibited by the low-frequency physical therapy group [5]. Overall, physical exercise intervention may be useful and beneficial for maintaining physical functioning in allo-HSCT patients.

OTHER OUTCOMES

Jarden et al. [23] evaluated data on five symptom clusters: mucositis, cognitive, gastrointestinal, affective, and functional clusters. The experimental group showed significant reduction in the symptoms severity in all clusters except for those subsumed under the affective cluster. Knols et al. [26] showed a reduction in the incidence of diarrhoea, and no significant effects were found in the study by Baumann et al. [12] for lung function.

CONCLUSION AND FUTURE RESEARCH

This review summarized the effects of physical exercise intervention in patients undergoing allo-HSCT. According to previous research, exercise intervention may help patients reduce the loss of or maintain aerobic and functional capacity, as well as muscle strength. Some studies have also indicated that exercise interventions have multidimensional benefits, including improved QOL and reduced fatigue. Therefore, exercise intervention may help allo-HSCT patients to not only maintain physical function during treatment but also improve QOL and alleviate fatigue symptoms. Future research needs to give more consideration to the different donor types in HSCT such as human leukocyte antigen (HLA)-matched sibling donors and HLA-haploidentical donors, because different treatment modalities and disease types have a varied influence on patients' initial condition and have a strong impact on physical function, QOL, and fatigue.

REFERENCES

1. Yoshimi A, Suzuki R, Atsuta Y, Iida M, Lu DP, Tong W, et al. Hematopoietic SCT activity in Asia: a report from the Asia-Pacific Blood and Marrow Transplantation Group. Bone Marrow Transplant. 2010; 45: 1682-1691.
2. Passweg JR, Baldomero H, Gratwohl A, Bregni M, Cesaro S, Dreger P, et al. The EBMT activity survey: 1990-2010. Bone Marrow Transplant. 2012; 47: 906-923.
3. Copelan EA. Hematopoietic stem-cell transplantation. N Engl J Med. 2006; 354: 1813-1826.
4. Gratwohl A, Baldomero H, Horisberger B, Schmid C, Passweg J, Urbano-Ispizua A; Accreditation Committee of the European Group for Blood and Marrow Transplantation (EBMT). Current trends in hematopoietic stem cell transplantation in Europe. Blood. 2002; 100: 2374-2386.
5. Morishita S, Kaida K, Setogawa K, Kajihara K, Ishii S, Ikegame K, et al. Safety and feasibility of physical therapy in cytopenic patients during allogeneic haematopoietic stem cell transplantation. Eur J Cancer Care (Engl). 2013; 22: 289-299.
6. Wiskemann J, Huber G. Physical exercise as adjuvant therapy for patients undergoing hematopoietic stem cell transplantation. Bone Marrow Transplant. 2008; 41: 321-329.
7. Grulke N, Albani C, Bailer H. Quality of life in patients before and after haematopoietic stem cell transplantation measured with the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Core Questionnaire QLQ-C30. Bone Marrow Transplant. 2012; 47: 473-482.
8. Tabbara IA, Zimmerman K, Morgan C, Nahleh Z. Allogeneic hematopoietic stem cell transplantation: complications and results. Arch Intern Med. 2002; 162: 1558-1566.
9. Gillis TA, Donovan ES. Rehabilitation following bone marrow transplantation. Cancer. 2001; 92: 998-1007.
10. Kovalszki A, Schumaker GL, Klein A, Terrin N, White AC. Reduced respiratory and skeletal muscle strength in survivors of sibling or unrelated donor hematopoietic stem cell transplantation. Bone Marrow Transplant. 2008; 41: 965-969.
11. Morishita S, Kaida K, Yamauchi S, Wakasugi T, Yoshihara S, Taniguchi K, et al. Gender differences in health-related quality of life, physical function and psychological status among patients in the early phase

following allogeneic haematopoietic stem cell transplantation. Psychooncology. 2013; 22: 1159-1166.

12. Baumann FT, Zopf EM, Nykamp E, Kraut L, Schüle K, Elter T, et al. Physical activity for patients undergoing an allogeneic hematopoietic stem cell transplantation: benefits of a moderate exercise intervention. Eur J Haematol. 2011; 87: 148-156.

13. Wiskemann J, Dreger P, Schwerdtfeger R, Bondong A, Huber G, Kleindienst N, et al. Effects of a partly self-administered exercise program before, during, and after allogeneic stem cell transplantation. Blood. 2011; 117: 2604-2613.

14. Jarden M, Baadsgaard MT, Hovgaard DJ, Boesen E, Adamsen L. A randomized trial on the effect of a multimodal intervention on physical capacity, functional performance and quality of life in adult patients undergoing allogeneic SCT. Bone Marrow Transplant. 2009; 43: 725-737.

15. Kim SD, Kim HS. Effects of a relaxation breathing exercise on fatigue in haemopoietic stem cell transplantation patients. J Clin Nurs. 2005; 14: 51-55.

16. Kim SD, Kim HS. A series of bed exercises to improve lymphocyte count in allogeneic bone marrow transplantation patients. Eur J Cancer Care (Engl). 2006; 15: 453-457.

17. Baumann FT, Kraut L, Schüle K, Bloch W, Fauser AA. A controlled randomized study examining the effects of exercise therapy on patients undergoing haematopoietic stem cell transplantation. Bone Marrow Transplant. 2010; 45: 355-362.

18. DeFor TE, Burns LJ, Gold EM, Weisdorf DJ. A randomized trial of the effect of a walking regimen on the functional status of 100 adult allogeneic donor hematopoietic cell transplant patients. Biol Blood Marrow Transplant. 2007; 13: 948-955.

19. Mello M, Tanaka C, Dulley FL. Effects of an exercise program on muscle performance in patients undergoing allogeneic bone marrow transplantation. Bone Marrow Transplant. 2003; 32: 723-728.

20. Jarden M, Hovgaard D, Boesen E, Quist M, Adamsen L. Pilot study of a multimodal intervention: mixed-type exercise and psychoeducation in patients undergoing allogeneic stem cell transplantation. Bone Marrow Transplant. 2007; 40: 793-800.

21. Hayes SC, Davies PS, Parker TW, Bashford J, Green A. Role of a mixed type, moderate intensity exercise programme after peripheral blood stem cell transplantation. Br J Sports Med. 2004; 38: 304-309.

22. Hayes S, Davies PS, Parker T, Bashford J, Newman B. Quality of life changes following peripheral blood stem cell transplantation and participation in a mixed-type, moderate-intensity, exercise program. Bone Marrow Transplant. 2004; 33: 553-558.

23. Jarden M, Nelausen K, Hovgaard D, Boesen E, Adamsen L. The effect of a multimodal intervention on treatment-related symptoms in patients undergoing hematopoietic stem cell transplantation: a randomized controlled trial. J Pain Symptom Manage. 2009; 38: 174-190.

24. Hayes S, Davies PS, Parker T, Bashford J, Newman B. Quality of life changes following peripheral blood stem cell transplantation and participation in a mixed-type, moderate-intensity, exercise program. Bone Marrow Transplant. 2004; 33: 553-558.

25. Carlson LE, Smith D, Russell J, Fibich C, Whittaker T. Individualized exercise program for the treatment of severe fatigue in patients after allogeneic hematopoietic stem-cell transplant: a pilot study. Bone Marrow Transplant. 2006; 37: 945-954.

26. Knols RH, de Bruin ED, Uebelhart D, Aufdemkampe G, Schanz U, Stenner-Liewen F, et al. Effects of an outpatient physical exercise program on hematopoietic stem-cell transplantation recipients: a randomized clinical trial. Bone Marrow Transplant. 2011; 46: 1245-1255.

27. Shelton ML, Lee JQ, Morris GS, Massey PR, Kendall DG, Munsell MF, et al. A randomized control trial of a supervised versus a self-directed exercise program for allogeneic stem cell transplant patients. Psychooncology. 2009; 18: 353-359.

28. Wilson RW, Jacobsen PB, Fields KK. Pilot study of a home-based aerobic exercise program for sedentary cancer survivors treated with hematopoietic stem cell transplantation. Bone Marrow Transplant. 2005; 35: 721-727.

29. Morris GS, Brueilly KE, Scheetz JS, de Lima MJ. Adherence of stem cell transplant recipients receiving glucocorticoid therapy to an exercise-based rehabilitation program. Support Care Cancer. 2012; 20: 2391-2398.

30. Hacker ED, Larson J, Kujath A, Peace D, Rondelli D, Gaston L. Strength training following hematopoietic stem cell transplantation. Cancer Nurs. 2011; 34: 238-249.

31. Hacker ED, Larson JL, Peace D. Exercise in patients receiving hematopoietic stem cell transplantation: lessons learned and results from a feasibility study. Oncol Nurs Forum. 2011; 38: 216-223.

32. Morishita S, Kaida K, Ikegame K, Yoshihara S, Taniguchi K, Okada M, et al. Impaired physiological function and health-related QOL in patients before hematopoietic stem-cell transplantation. Support Care Cancer. 2012; 20: 821-829.

33. Morishita S, Kaida K, Tanaka T, Itani Y, Ikegame K, Okada M, et al. Prevalence of sarcopenia and relevance of body composition, physiological function, fatigue, and health-related quality of life in patients before allogeneic hematopoietic stem cell transplantation. Support Care Cancer. 2012; 20: 3161-3168.

34. Schmitz KH, Courneya KS, Matthews C, Demark-Wahnefried W, Galvão DA, Pinto BM, et al. American College of Sports Medicine roundtable on exercise guidelines for cancer survivors. Med Sci Sports Exerc. 2010; 42: 1409-1426.

35. Wilson RW, Jacobsen PB, Fields KK. Pilot study of a home-based aerobic exercise program for sedentary cancer survivors treated with hematopoietic stem cell transplantation. Bone Marrow Transplant. 2005; 35: 721-727.

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