Cover Page

Official Title:

The Effect of 30-Minute Mindful Breathing in Reducing Fatigue Symptom among Patients with Haematological Cancer – A Randomized Controlled Trial.

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Title:

The Effect of 30-Minute Mindful Breathing in Reducing Fatigue Symptom among Patients with Haematological Cancer – A Randomized Controlled Trial.

Version Number:

1.1

Version Date:

2 July 2019.

Time Frame:

1 August 2019 to 31 July 2021.

Project Focus:

This project aims to study the effectiveness of 30-minute mindful breathing as a non-pharmacological intervention to reduce fatigue symptom among patients with haematology cancer, such as leukaemia, lymphoma, multiple myeloma, myeloproliferative disease and myelodysplastic syndrome.

Problem Statement:

Fatigue is the most prevalent symptom of haematological cancer, as well as the commonest side-effect of haematological cancer treatment such as cytotoxic chemotherapy or marrow suppressive agents. In addition, fatigue may persist for years or remained for life in patients who successfully achieved haematological cancer remission post cytotoxic chemotherapy or

haemopoeitic stem-cell transplantation. Fatigue has significant negative impact on patients' quality of life, daily activities, employment, social relationships and mood. Non-pharmacological treatment particularly exercise and psychological interventions significantly improve cancer-related fatigue, but it may be contraindicated or not practical in patients with haematological cancer. On the other hand, studies have shown that pharmacological treatment does not confer significant benefit in cancer-related fatigue. Therefore, an intervention that can effectively reduce the fatigue symptom in patients with haematological cancer and practical to perform in local setting is urgently needed.

Hypothesis:

A single session of 30-minute mindful breathing significantly reduces the fatigue symptom among patients with haematological cancer.

Patients with haematological cancer are satisfied with 30-minute mindful breathing and willing to practise this intervention in their daily life.

Research question:

1. How effective is single session of 30-minute mindful breathing in reducing fatigue symptom among patients with haematological cancer?
2. Do patients with haematological cancer satisfy and willing to practise 30-minute mindful breathing in their daily life?
3. How effective is 30-minute mindful breathing in reducing fatigue symptom among patients with active haematological cancer versus those with haematological cancer in remission?

Literature Review:

Haematological cancer includes leukaemia, lymphoma, multiple myeloma, myeloproliferative diseases and myelodysplastic syndrome.[1,2] In 2018, haematological cancer accounts for 10% of all malignancies and 9.5% of malignancies-related mortality.[3]

National Comprehensive Cancer Network (NCCN) defined cancer-related fatigue (CRF) as a distressing persistent subjective sense of physical, emotional, or cognitive tiredness or exhaustion associated with cancer or cancer-related treatment that is disproportional to recent activity and interferes with usual functioning.[4] Fatigue is the most prevalent symptom of haematological cancer, as well as the commonest side-effect of haematological cancer treatment such as cytotoxic chemotherapy or marrow suppressive agents.[5-10] In addition, fatigue may persist for years or remained for life in patients who successfully achieved haematological cancer remission post cytotoxic chemotherapy or hemopoeitic stem-cell transplantation.[11-14] CRF has significant negative impact on patients' quality of life, daily activities, employment, social relationships and mood.[15]

Management of CRF in patients with haematological cancer remained challenging despite studies have reported non-pharmacological treatment, particularly exercise and psychological interventions may significantly improve CRF.[16,17] First, exercise is contraindicated in patients with anaemia, thrombocytopenia, active infection, bone lesion and risk of falls.[18] Second, attending psychological interventions such as cognitive-behavioural therapy, psycho-educational therapy, supportive-expressive therapy and mindfulness-based stress reduction therapy in outpatients setting can be tiring, as well as time and cost consuming because these interventions are delivered in multiple sessions over months. Third, pharmacological treatment such as methylphenidate, modafinil and corticosteroid in CRF is still lack of strong evidence and not without side-effects.[17]

Mindfulness involves paying attention on purpose, in the present moment and non-reactively.[19] It has been shown to reduce stress, anxiety, depression and improve sleep.[20-22] Breathing is both an involuntary and voluntary physiology process that controlled by the brain stem and motor cortex. Mindful breathing is the anchor of mindful practices because human breathe every second of everyday. The advantages of this intervention include easy to understand, can be practise at any time and at anywhere, without cost, and has instant impact. A single session of 5-minute mindful breathing had been shown to reduce distress significantly in patients with cancer; while a single session of 20-minute mindful breathing significantly reduced dyspnea in patients with chronic lung disease and lung cancer.[23,24]

In the current study, we aim to determine the efficacy of single session 30-minute mindful breathing in reducing fatigue symptom among patients with haematological cancer. A longer duration of mindful breathing is designed in view of fatigue is a complex multidimensional symptom that it's specific underlying mechanism still remained unclear.[25]

Executive Summary:

Fatigue is the most prevalent symptom of haematological cancer, as well as the commonest side-effect of haematological cancer treatment. It may persist for years or remained for life in patients who successfully achieved haematological cancer remission. The presence of fatigue significantly impaired patients' quality of life, daily activities, employment, social relationships and mood. In the current study, we aim to determine the efficacy of single session 30-minute mindful breathing in reducing fatigue symptom among patients with haematological cancer. A total of 138 samples are needed based on calculation. Eligible patients are randomly assigned into control group that receives standard care versus intervention group that receives standard care plus a single session of 30-minute mindful breathing. The study outcomes at 0-

minute include fatigue severity according to visual analogue scale (VAS) and score of Functional Assessment of Chronic Illness Therapy (FACIT) Fatigue Scale Version 4; while the outcomes at 30-minute include fatigue severity according to VAS, score of FACIT Fatigue Scale Version 4, as well as satisfaction and willingness to practise this intervention. We hypotheses a single session of 30-minute mindful breathing significantly reduces the fatigue symptom among patients with haematological cancer. Patients are also satisfied and willing to practise this manoeuvre in their daily life. The output of this study will benefit the society and nation because reducing fatigue symptom help to improve patients' quality of life, employment, social activities and mood. Besides, it also helps to reduce the needs of hospital admission, length of hospital stay and utilisation of healthcare resources to handle fatigue.

Objectives:

Primary:

1. To determine the efficacy of single session 30-minute mindful breathing in reducing fatigue symptom among patients with haematological cancer.
2. To determine the satisfaction and willingness of patients with haematological cancer to practice 30-minute mindful breathing in their daily life.

Secondary:

1. To compare the efficacy of single session 30-minute mindful breathing in reducing fatigue symptoms among patients with active haematological cancer versus those with haematological cancer in remission.

Location of Research:

Hemato-oncology unit and palliative unit of University Malaya Medical Center (UMMC), Kuala Lumpur, Malaysia

Methodology:

Study design:

This is a parallel-group, non-blinded, randomised control study that will be conducted at the hemato-oncology unit and palliative unit of University Malaya Medical Center (UMMC), Kuala Lumpur, Malaysia from 1st August 2019 to 31st July 2021. The medical ethic approval will be obtained from the medical ethic committee of UNIMAS and UMMC. Written informed consent will be obtained from all the subjects. The study will be conducted according to the Declaration of Helsinski.

The inclusion criteria:

1. Patients age 18 years and above,
2. Histopathological diagnosis of haematological cancer according to World Health Organisation classification,
3. Fatigue score ≥ 4 based on the Edmonton Symptom Assessment System (ESAS).

The exclusion criteria:

1. Impaired conscious level, cognitive impairment or psychiatric illness that would prevent the patient from giving informed consent or participating fully,

2. Current or history of cancer of other system,
3. Haemoglobin level of less than 8g/l.

Sample size:

A plan sample size of 138 patients (69 patients per arm) is powered to detect the effect size difference between two arms of 1.99 standard deviation units (change of fatigue score of 0.91), with two-tailed type I error rate of 0.05 and 80% power.[26]

Procedure:

Recruitment:

The demographic and clinical data of the eligible patients which include age, gender, ethnicity, religion, occupation, education level, marital status, body mass index, type of haematological cancer, current status of cancer, types of cancer treatment, duration of cancer, blood parameters and other co-morbidities will be obtained from patients' electronic case record. Missing information will be obtained by direct face-face interview with the patients or relatives.

Patients are randomly assigned into 2 groups based on computer generated sequence. Patients in the control group will receive the standard care by the primary physician; while patients in the intervention group will receive the standard care by the primary physician plus a single session of 30-minute mindful breathing guided by investigators or research assistants that trained in delivering mindful breathing. The instruction of 30-minute mindful breathing is as described in Table 1.

Outcomes measurement:

The study outcomes will be assessed at 0-minute (before intervention - T0) and 30-minute (after intervention – T30). The outcomes at T0 include fatigue severity according to visual analogue scale (VAS) of 0 – 100 and score of Functional Assessment of Chronic Illness Therapy (FACIT) Fatigue Scale Version 4; while the outcomes at T30 include fatigue severity according to VAS, score of FACIT Fatigue Scale Version 4, as well as dichotomous answer of satisfaction and willingness to practise 30-minute mindful breathing in daily life.

Statistical analysis:

Results for continuous variables will be expressed as mean ± standard deviation (SD), median or inter-quartile range depending on normality of the variable distribution; while results for categorical variables will be expressed as percentages. Between groups difference for continuous data will be compared by using independent t-test or Mann-Whitney U test, as applicable; while between group difference for categorical data will be compared by using Chi-Square test or Fisher-Exact test, as applicable. A 2-sided p value of less than 0.05 is considered as significant in this study. Statistical analyses will be performed by using the software package, Statistical Package for the Social Sciences (SPSS for windows version 25.0, SPSS Inc, Chicago, IL, USA).

New Findings:

1. A single session of 30-minute mindful breathing significantly reduce the fatigue symptom among patients with haematological cancer.

2. Patients with haematological cancer are satisfied with 30-minute mindful breathing and willing to practise this manoeuvre in their daily life.

3. A single session of 30-minute mindful breathing is equally effective in reducing fatigue

symptom among patients with active haematological cancer and those with haematological cancer in remission.

Potential Applications:

1. 30-minute mindful breathing may become the standard of care for patients with fatigue symptom due to haematological cancer.
2. 30-minute mindful breathing can be another alternative of symptomatic relief for patients with haematological cancer related fatigue but contraindicated for exercise due to anaemia, thrombocytopenia, active infection, bone lesion or risk of falls.
3. 30-minute mindful breathing can be another alternative of symptomatic relief for patients with haematological cancer related fatigue but unable to attend regular outpatient psychological interventions due to tiredness, financial constraint or logistic issue.
4. 30-minute mindful breathing can reduce the use of pharmacological treatment in patients with haematological cancer related fatigue, therefore reduce patients medical expense and avoid potential side-effects.
5. The synergistic effect of 30-minute mindful breathing added to other non-pharmacological treatment such as exercise and psychological interventions can further enhance fatigue symptom reduction.

Impacts of research:

1. 30-minute mindful breathing significantly reduce the fatigue symptom among patients with haematological cancer, therefore:

a. Improves the quality of life of these patients,

b. Improve the mood and mental health of these patients,

c. Enables patients to return to employment, as well as social and recreational activities,

d. Reduces the need of hospital admission, length of hospital stay and utilisation of healthcare resources.

2. 30-minute mindful breathing can reduce the use of pharmacological treatment for fatigue, therefore:

a. Reduce the medical cost to purchase the drug.

b. Reduce the medical cost to handle the side-effect of the drug.

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