

Prevention of Depression in Patients with Cancer: A Systematic Review

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Abstract--- *Depression and depressive symptoms are prevalent in patients with cancer. Depression is under-diagnosed and therefore the patients often receive inadequate treatment for their depression. The aim of this study was to identify ways to prevent depression in patients with cancer. This systematic review used the Preferred Reporting Items for Systematic Review (PRISMA) approach. Databases were used to identify suitable articles from Scopus, PubMed, Science Direct and Proquest. The articles were limited to being published between 2009 and 2020, written in English and full-text articles. The literature review used the keywords “anxiety, antidepressant, cancer, depression and preventive.” When searching the articles, “AND” was also used. The inclusion criteria in the search strategy consisted of: 1) adult humans ≥ 18 years of age diagnosed with cancer; 2) undergoing antidepressive treatment of any kind; 3) depression and/or depressive symptoms and 4) the study design was a randomized controlled trial. Studies were excluded if the studies had less than 30 samples as this means that they do not have enough strength to use to detect a significant relationship. Following this screening, 15 articles met the inclusion criteria. The studies were classified into 3 groups based on the type of intervention used. The interventions were pharmacotherapy, psychotherapy and other interventions such as exercise programs. Depression in patients with cancer can be prevented. Preventive treatment should start before or during the oncological treatment. Treating psychiatric conditions in patients with cancer may improve not only their quality of life and prognosis but also their survival.*

Keywords--- *Anxiety; Antidepressant; Cancer; Depression; Preventive*

I. INTRODUCTION

By 2030, depressive disorders are expected to be the leading cause of disability in high-income countries accompanied with a significant socio-economic burden [1]. There is a considerable overlap between depression and cancer with a high proportion suffering from both conditions [2]. Depression has shown to be treatable both with pharmacotherapy and psychotherapeutic interventions in adults with cancer [3], [4].

The prevalence of depression has been reported to be as high as 49% [5] and it has persistently been shown to be higher in cancer survivors more so than in the general population [6]. However, the reported prevalence in the studies varied greatly depending on the cancer type and severity, the method of depression assessment, and whether the patients were hospitalized or treated in an outpatient clinic [5], [7]. Overall depressive symptoms peak during adjuvant treatment and rebound after completing treatment. This is likely due to stressors such as the accumulated burden of disease or treatment and the

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diminishing social support. Rates of depression increase with recurrence, the progression of the cancer, and a peak in palliative care [5].

Depression in patients with cancer is both under-diagnosed and undertreated [8]. Depressive symptoms are associated with decreased health-related quality of life, treatment adherence and poor prognosis [9]. The overall mortality rate is higher in cancer patients with depressive symptoms and major depression disorder. Some studies have also reported a higher suicide rate among patients with cancer. Treating the psychiatric conditions of patients with cancer may improve not only their quality of life and prognosis, but also their survival [10]. To improve the anxiety and depression of patients with cancer, many interventions have been performed in this population such as music therapy and relaxation training [11].

Due to the lack of time, training and maybe also confidence, clinicians might not be able to identify the patients with cancer that are at risk of developing depression. Therefore, it might be beneficial to offer patients with cancer an intervention that could prevent depression as part of the routine cancer treatment. Patients with cancer are more vulnerable to depression in the first month after diagnosis and the estimated prevalence is highest during the acute phase of the cancer treatment[7]. The current systematic review aimed to identify the prevention of depression in patients with cancer.

II. METHODS

- Strategy in searching studies

Articles published in English were searched for on the Scopus (medical and nursing subject category), PubMed, Science Direct and ProQuest databases. The relevant articles were searched for from December 11th 2019 to February 18th 2020. The publication range was limited to 2009 - 2019. The articles used the keywords “anxiety, antidepressant, cancer, depression, preventive”. While searching for the articles, “AND” was also used.

- Study Selection

This systematic review used the Preferred Reporting Items for Systematic Review (PRISMA) approach. All of the studies found related to the prevention of depression in patients with cancer only. The search was focused on the titles, abstracts and keywords. The inclusion criteria for the studies were as follows: 1) adult humans ≥ 18 years of age diagnosed with cancer; 2) undergoing antidepressive treatment of any kind; 3) depression and/or depressive symptoms and 4) the study design was a randomized controlled trial. Studies were excluded if they had less than 30 samples, which meant that they do not have enough strength to detect a significant relationship. The publication was limited on 2009-2020.

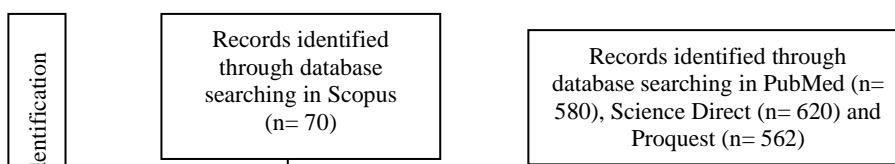


Figure 1 – Article selection process using the PRISMA approach

In the final quantitative synthesis, 15 articles published between 2009 and 2020 were included. The number of patients ranged from 40 to 465 who were predominantly female with an age range from 47 to 69 years old. The most common cancer form was breast cancer [8], [11]–[17]. Other studies included patients with head and neck cancer, lung cancer [18], colon cancer [19] and mixed cancer populations [9], [10], [20]. The majority of studies administered the intervention during active oncological treatment. Psychological assessments were conducted at baseline and were followed up at least once. This ranged from the time of discharge from hospital to more than one year after baseline.

Ethical issues when preparing the manuscript of the systematic reviews included the following: 1) avoiding redundant or duplicated publications; 2) avoiding plagiarism; 3) checking the transparency of the screening article, process analysis, and evaluation; 4) ensuring accuracy, and 5) flagging suspected plagiarism or fraudulent research.

III. RESULTS

- Pharmacological interventions

Three studies used a pharmacological intervention and were double-blinded, placebo-controlled trials [15], [21]. One study used 6 mg melatonin as an intervention for 12 weeks [15] and another study used a selective serotonin reuptake inhibitor (SSRI) – escitalopram – in equipotent doses with a 1 week run-in phase (half dose) followed by a 15 week and 27 week full-dose follow-up respectively [21]. Melatonin showed a lower incidence rate of depression compared to the placebo [15] and this was also the case with escitalopram [21]. The patients receiving celecoxib as a treatment for depression achieved greater reductions in their depression scores and higher response rates [22].

- Psychotherapeutic interventions

Seven out of 8 papers showed there to be a significant effect following their interventions. One psychologist delivered therapy and there was an improvement when a mixed linear model was applied in both lung and breast cancer groups [18]. The second used a combination of music therapy with progressive muscle relaxation training. This showed a significant improvement in the depression scores [11]. Mindfulness-based cognitive therapy significantly reduced psychological distress (both anxiety and depression) in patients with non-metastatic breast cancer [23]. Psychoeducational interventions have been proven to be successful at resolving psychological distress and improving the physical side effects [24]. A psychological intervention reported significantly lower mood disturbance, anxiety and depression, and it showed an improved global health status and physical, role and emotional functioning [25]. Behavioral activation treatment for depression (BATD) and problem-solving therapy interventions represent practical interventions that may improve psychological outcomes and the quality of life among depressed breast cancer patients [17]. No significant effect was found using telephone therapy [20].

- Other interventions

Four studies were performed with an intervention that was something other than pharmacological or psychological. Three studies used an exercise program as the intervention [12], [13], [19]. Only one exercise program showed a significant difference; it investigated a 10-week physical exercise rehabilitation program [13] and 2 18-week exercise programs that showed no effect on depression [12], [19]. The content of the 3 exercise programs did not differ greatly from one another. Other studies intervened using meditation [14] or a scalp cooling device [16], both of which found there to be no statistically significant effect.

IV. DISCUSSION

The present systematic review found that prophylactic interventions could prevent depression in patients with cancer. Celecoxib monotherapy is a potentially safe and effective treatment option for mild to moderate depression in patients with colorectal cancer who are undergoing concurrent chemotherapy [22]. Specifically in patients with breast cancer, it has been shown that depression represents a crucial factor in the acceptance of adjuvant chemotherapy [15]. Currently available antidepressants are useful at treating depression but they typically take approximately 4 weeks to achieve a clinical response and even longer treatment durations to achieve remission [15].

Regarding the psychotherapeutic studies, the combined music therapy and progressive muscle relaxation training study had a short follow-up period based on routine nursing care to reduce depression and anxiety. This is beneficial when it comes to reducing the days spent in hospital [11]. Psychological therapy showed an effect only when a mixed linear model was applied and no effect with the general linear model [18]. Psychoeducation improved the psychological distress level of the patients and their adjustment to cancer. Consequently, overall better health status and quality of life was found 2 weeks after the conclusion of the chemotherapy [24]. To prevent psychological distress and to improve the quality of life of these patients, the nurses could develop, lead and supervise supportive programs that provide education on symptom management in addition to encouraging the expression of emotions [25]. One study showed that a mindfulness-based cognitive therapy intervention substantially improved the patients' quality of life and spiritual well-being. It is of note that mindfulness-based cognitive therapy not only alleviated the negative psychological aspects experienced by the patients with cancer but it also increased the positive aspects of their lives. Spiritual well-being serves to buffer clinically important issues such as pain, fatigue, depression and the wish for a hastened death. Mindfulness, which cultivates a sense of wholeness and internal unity, may have the potential to elucidate the self-insights of patients with cancer regarding the meaning of life despite the presence of a life-threatening illness [23].

Since physical exercise programs have the potential to help the patients to regain physical fitness, this may exert a range of positive consequences that impact on the recovery and psychological well-being of the survivors. The potential impact of physical exercise programs has gained increasing attention in recent years [13]. Physical exercise rehabilitation programs lead to a decline in anxiety and depression and improved individual body image as well as increased physical fitness [19]. One study showed a significant decrease in depression and anxiety among breast cancer patients after they participated in an exercise intervention program. A further strengthening of the exercise program that may have contributed to its success is that it includes a lot of variation in terms of combining different elements and high patient participation [13].

There are methodological limitations in the current review. Firstly, there is potential bias in the actual process of searching, selecting and extracting the data. In an effort to eliminate this bias, the review authors independently selected and extracted the data. Likewise, the authors independently assessed the included studies for risk of bias. Secondly, we only included randomized controlled trials to ensure that the highest level of evidence was included.

V. CONCLUSION

The research systematic review examined 15 articles determined based on the inclusion criteria. The results show that preventive treatment should start before or during the oncological treatment selected. Treating the psychiatric conditions experienced by the patients with cancer may improve not only their quality of life and prognosis but also their survival. Future researchers are expected to make this systematic review study a reference when examining the prevention of depression to improve the quality of life of patients with cancer.

CONFLICT OF INTEREST

No conflicts of interest have been declared.

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APPENDIX

Table 1. Summary of the selected studies

Title/ Author	Type of cancer	Design	Sample	Variables	Results
A randomized clinical	Breast cancer	Clinical randomized	170 respondents	Depression, anxiety, and length of hospital stay	Music therapy and progressive muscle relaxation training can

Title/ Author	Type of cancer	Design	Sample	Variables	Results
controlled trial of music therapy and progressive muscle relaxation training in female breast cancer and patients after radical mastectomy: Results on depression, anxiety and length of hospital stay [11]		controlled trial			reduce depression, anxiety and the length of the hospital stay of female breast cancer patients after a radical mastectomy.
Effects of an 18-week exercise program started early during breast cancer treatment: a randomized controlled trial [12]	Breast cancer	Multi-centre controlled trial	204 respondents	Fatigue, quality of life, anxiety, and depression	Exercise early on in the treatment of breast cancer can be recommended to reduce anxiety and depression and increase quality of life.
Can a brief psychological intervention prevent anxiety or depressive disorders in cancer patients? A randomized controlled trial [20]	All cancers	Randomized controlled trial	465 respondents	Anxiety or depressive disorder	Psychological interventions can potentially prevent rather than treat depressive and anxiety disorders in a cancer setting.
Effects of a psychoeducational intervention in patients with breast cancer undergoing chemotherapy [24]	Breast cancer	A randomized controlled trial	40 respondents	Anxiety and depression	Psychoeducational interventions have been proven to be successfully at resolving psychological distress and improving the physical side effects.
Effects of a physical exercise rehabilitation group program on anxiety, depression, body image, and health-related quality of life among breast cancer patients [13]	Breast cancer	Randomized controlled trial	58 respondents	Anxiety, depression, body image and quality of life	There was a significant decrease in the depression and anxiety among breast cancer patients after participation in an exercise intervention program.
Prevention of depression with escitalopram in patients undergoing treatment for head and neck cancer [21]	Head and neck cancer	Randomized, double-blind, placebo-controlled clinical trial	148 respondents	Depression	Patients in the escitalopram group who had completed the study and Who were not depressed rated their overall quality of life as significantly better for 3 consecutive months after the cessation of drug use.
Effects of an exercise program in colon cancer patients undergoing chemotherapy [19]	Colon cancer	Multicenter randomized controlled trial	53 respondents	Fatigue, quality of life, anxiety and depression	Exercise programs are feasible, safe, and may have beneficial effects on physical fatigue, improving quality of life and decreasing anxiety and depression among colon cancer patients during chemotherapy.
Effects of meditation on anxiety, depression, fatigue, and quality of life of women undergoing radiation therapy for breast cancer [14]	Breast cancer	Randomized, non-program controlled and a parallel intervention clinical trial	102 respondents	Anxiety and depression, fatigue and quality of life	Meditation effectively reduces the depression level of breast cancer patients.
Effect of melatonin on depressive	Breast cancer	Randomized, double-	54 respondents	Depression, anxiety, and sleep disturbances	Melatonin significantly reduced the risk of depressive symptoms

Title/ Author	Type of cancer	Design	Sample	Variables	Results
symptoms and anxiety in patients undergoing breast cancer surgery: a randomized, double-blind, placebo-controlled trial [15]		blind, placebo-controlled trial			in women with breast cancer over a 3-month period after surgery.
A psychological intervention program for patients with breast cancer under chemotherapy and at a high risk of depression: a randomized clinical trial[25]	Breast cancer	Randomized clinical trial	60 respondents	Anxiety and depression, affective mood disturbance and quality of life	A physiological intervention reported significantly lower mood disturbance, anxiety, and depression. It also showed an improved global health status and physical, role and emotional functioning.
Efficacy and safety of celecoxib monotherapy for mild to moderate depression in patients with colorectal cancer: A randomized double-blind, placebo controlled trial [22]	Colorectal cancer	Randomized double-blind placebo controlled trial	81 respondents	Depressive symptoms	Celecoxib monotherapy as a potentially safe and effective treatment option for mild to moderate depression in patients with colorectal cancer undergoing concurrent chemotherapy.
Effect of a scalp cooling device on alopecia in women undergoing chemotherapy for breast cancer [16]	Breast cancer	Multicenter randomized clinical trial	182 respondents	Quality of life, anxiety and depression, body image	Women have reported decreases in their self-esteem, sexuality and body image related to chemotherapy-induced alopecia. The use of scalp cooling devices may help to alleviate some of this distress.
Effects of behavioral activation on the quality of life and emotional state of lung cancer and breast cancer patients during chemotherapy treatment [18]	Lung cancer and breast cancer	Randomized controlled trial	158 respondents	Anxiety and depression, quality of life and functional well-being	Behavioral activation was effective at improving quality of life (symptoms, emotional state and functioning) during adjuvant chemotherapy treatment.
Brief behavioral activation and problem solving therapy for depressed breast cancer patients: randomized trial [17]	Breast cancer	Randomized trial	80 respondents	Depression	Behavioral activation treatment for depression (BATD) and problem-solving therapy interventions represent the practical interventions that may improve the psychological outcomes and quality of life among depressed breast cancer patients.
Mindfulness-based cognitive therapy for psychological distress, fear of cancer recurrence, fatigue, spiritual well-being, and quality of life in patients with breast cancer: A randomized controlled trial[23]	Breast cancer	Randomized controlled trial	74 respondents	Psychological distress (anxiety and depression), fear of cancer recurrence, fatigue, spiritual well-being and quality of life	Mindfulness-based cognitive therapy significantly reduced the psychological distress (both anxiety and depression) in patients with non-metastatic breast cancer. Mindfulness-based cognitive therapy was proven to be effective at increasing their spiritual well-being and quality of life, and for reducing the fear of cancer recurrence and fatigue.