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The Role of Non-Pharmacological Intervention in Improving the Cognitive Disorder of Cancer Patient

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Abstract

Over the past few decades, cancer survival rates have improved significantly. This means that cancer patients have a longer life due to early diagnosis and advanced medical treatment. However, longer survival is often associated with cancer-induced side effects. Cognitive impairment is a common side effect that relates to the nature of cancer disease or related treatments including surgery, radiotherapy, and chemotherapy. Cognitive impairment associated with cancer can have negative effects on physical ability, social and occupational functioning as well as the daily life of patients after cancer and ultimately reduce their quality of life. Cognitive changes after cancer and their treatment also called chemotherapy or ambiguous chemical treatment has attracted more clinical attention. Studies show that 80% of cancer-related people live with cognitive impairments, and often have difficulty doing multitasking, short-term memory, word regulation, attention and focus, and working memory. The main causes and mechanisms in causing these cognitive changes are not clear, but they have predicted that they include direct Neuro-effects of treatment, oxidative damage, and genetic susceptibility, etc. Drug therapy options have many limitations for this clinical problem and non-pharmacological interventions for cancer-related cognitive impairment are largely unknown but one of the existing non-pharmacological treatments is cognitive rehabilitation programs that are an emerging area of research to manage cognitive changes associated with cancer treatment. The main purpose of this review article is to investigate the causes of cognitive impairment in cancer and its treatment and the diagnosis and affective symptoms in these disorders. We have also investigated non-pharmacological interventions to treat or reduce these cognitive disorders.

Keywords: Biofeedback; Cancer; Cognitive disorder; Exercise; Non-pharmacological

Introduction

Considering the large number of people who have survived after a cancer diagnosis, more attention is needed on the issues related to performance, quality of life, and social participation of these people in the society [1]. One of the main concerns of cancer patients is a cognitive dysfunction, which is usually expressed in a non-expert society as "brain chemistry", or "eerily chemotherapy" in the non-expert society [2]. This situation takes a range of symptoms such as short-term memory reduction, difficulty in thinking and concentration, multitasking work disorder, and other delicate cognitive changes [3]. In some studies, researchers have reported that cognitive changes associated with cancer treatment are often fixated over 1 year, while others have documented long-term changes over 20 years. Several studies have also shown that some patients had cognitive dysfunction before receiving any therapy [4-6].

Searching for effective interventions for cognitive changes associated with cancer and its treatment is very important for cancer survivors and oncology health care providers. Both drug and non-pharmacological interventions for managing cancer-related cognitive impairment are available in cancer survivors. Applied drug therapy approaches for cancer-related cognitive impairment include central nervous system propulsions, such as methylphenidate and modafinil, but the beneficial effects of central nervous system propulsions for cancer-related cognitive impairment are diverse among adult cancer survivors [7]. Although there are several new drug interventions to manage cancer-related cognitive impairment, most of them are in clinical stages and so far no guarantee has been given to the U.S. Food and Drug Administration for approval. In addition, it is noted that drug interventions for cancer-related cognitive impairment often have side effects such as negative effects on brain plasticity [8]. Therefore, non-pharmacological interventions are widely

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used to manage cognitive impairments associated with cancer.

In a network meta-analytic study, comprehensively evidence of direct and indirect comparison of 10 non-pharmacological interventions for the cancer-related cognitive disorder was expressed that generally non-pharmacological interventions such as stress reduction based on meditation/mindfulness, cognitive training, cognitive rehabilitation, and exercise interventions had more desirable effects These interventions were more effective in managing cognitive impairment sustention associated with cancer and statistically significant differences with other interventions such as meditation/mentality/reduction of mentality, stress, combined cognitive training with exercise, cognitive behavioral therapy, chigung, supportive treatments, yoga, and acupuncture [9,10,11]. In addition, another meta-analysis and the systematic study confirms that all non-pharmacological interventions for cancer-related cognitive impairment are safe and are significant without reporting side events [12].

Discussion

Many mechanisms have been suggested to explain the cause of cognitive dysfunction in cancer patients [3,13], including direct Neuro-effects of treatment (e.g., inhibition of hippocampus neurogenesis), genetic predisposition, oxidative damage, and impaired immune system regulation. Direct neurotoxicity of chemotherapy is one of the clear hypotheses for the cause of cognitive impairment in these settings. However, determining the most effective factor among the different factors of chemotherapy is very difficult. Since different categories of drugs are often used in combination, it is also difficult to separate the chemotherapy effects from other aspects of treatment such as radiotherapy and surgery [14]. However, we know that especially certain drugs (e.g., methotrexate and 5-fluoroasile) are neurologically seen in neural imaging that change the white matter [15-17]. Anemia is also a known side effect of chemotherapy and myeloid suppressor. It may cause cerebral hypoxia due to decreased hemoglobin concentration and may be associated with fatigue and cognitive dysfunction [18,19]. The field of psychology-immunology has clarified the mechanisms of cognitive change after cancer treatment. Surgical, radiotherapy, chemotherapy, biological therapy, and targeted treatment can cause systemic inflammation and cross the brain barrier and have harmful effects on the central nervous system [20]. On the other hand, it has been shown that pro-inflammatory cytokines in circulation cause impaired learning and memory in animals [21,22]. According to the studies, the use of pro-inflammatory cytokines in the brain increases the metabolism of key neurotransmitters, including noradrenaline, dopamine, and serotonin [22,23]. These neurotransmitters have importance for regulating memory, learning, sleep, and mood. Also, monitoring of immune cytokines in laboratory animals has shown that the hippocampus is disrupted in the long-term and thus disrupts memory [24,25]. After cytokines reach the brain, the immune cells (i.e., Microglya) are stimulated to produce other pre-inflammatory cytokines and intermediaries. This may explain why cognitive dysfunction is not limited to patients with brain tumors (primary or metastatic) or direct treatments in which they target the brain. Psychological and emotional stress can also affect the immune system [26]. According to this issue, some researchers believe that brain chemistry has physical components in some patients, such as when fibromyalgia and chronic fatigue syndrome may occur. This hypothesis stipulates that physical and mental distress caused by cancer treatment causes biological changes (such as acute changes in cytokines) that lead to epigenetic changes. These epigenetic changes may cause long-term hemostatic changes that are responsible for neurological changes in cancer-related cognitive dysfunction [27]. This evidence supports the International Report of Experts and The Workgroup's Knowledge of Cancer and shows a constant finding in the articles that subgroups of patients are more vulnerable to cognitive changes [28].

Cognitive rehabilitation

Cognitive rehabilitation includes several interventions with different goals. From an overall point of view, cognitive training typically involves a set of exercises to strengthen attention, focus, and memory skills [29,30]. These exercises can be done by a computer. Repetition and practice are very important for success in these interventions. Cognitive-behavioral training is more focused on adaptive strategies to compensate for deficiencies in different cognitive fields and may also focus on concurrent factors such as anxiety, depression, and fatigue. Many of the studies' designs include a combination of cognitive education and cognitive-behavioral training [31,32].

Exercise

Pieces of evidence in support of aerobic, resistance, and mindfulness exercises as potential interventions for cognitive changes associated with cancer treatment are emerging [33]. The main reasons for the success of physical activity and exercise are: (1) reduced of inflammatory markers that are associated with cancer and its treatment (2) increased levels of neural and brain factors caused by the brain and hippocampus volume [34]. The effect of exercise is known to deal with fatigue and sleep disorders [35] and has been shown to improve cognitive function in a variety of patient populations, including the elderly [36], Alzheimer's disease [37,38], Parkinson's patients [39] and patients with different types of cancer [35,40,41]. Also, systematic reviews of mixed training programs such as aerobic exercise and resistance training have shown a significant decrease in fatigue [3,42,43].

Complementary and alternative drug interventions

Evidence has shown that Tai Chi has positive effects on emotional well-being and also has short-term benefits [44,45,46] on the mobility of upper limb function [27,47,48]. No effect was observed from Tai Chi on BMI, bone mineral density, and muscle strength [46,49,50]. Needle stimulation, especially acupuncture at P6, may be useful for reducing chemotherapy-induced nausea and vomiting [36], and massage can also reduce anger and fatigue [48,51]. Another systematic study showed positive effects of acupuncture stimulation for pain and fatigue as well as a massage on anxiety and had benefits on fatigue and quality of life [52].

Biofeedback by using electroencephalography

The results of the experimental study on the possibility of using electroencephalographic biofeedback to reduce cognitive-mind complaints about survivors of breast cancer showed significant progress in perceived cognitive function [53]. This intervention involves using "Real-time display of brain electrical activity that is used as video or auditory information" and enables the participant to "change the activity of those brain waves [54]. This intervention is based on the assumption that brain neuroplastic can be used to restore brain function.

Conclusion

Understanding of effective interventions for cognitive

impairments associated with cancer can inform health care providers to provide optimized services to cancer patients, as health care providers play a fundamental role in identifying and managing complications and follow-ups of cancer such as cognitive deficits [36]. In general, non-pharmacological interventions for cognitive impairment management associated with cancer are safe, the most effective of them are meditation, cognitive training, cognitive rehabilitation, and exercise interventions. More than one intervention can have more positive effects on a specific symptom or problem, and these effects depend not only on the type of intervention but also on how and when to provide the intervention [55].

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