Vol.5 Issue2

Impact of Physical Inactivity on the Multifactorial Process of Developing Cancer-Related Cognitive Impairments

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Introduction

Many cancer survivors report cognitive impairment before, during and after medical treatment. It is well known that many factors other than chemotherapy take part in the development of these cancer- related cognitive impairments (CRCI), such as cancer-related fatigue, psychological as well as molecular factors. The purpose of this review is to describe the impact of physical inactivity in the genesis of these cognitive changes in cancer patients. References for this narrative review comes primarily from PubMed, Cochrane Library and Livivo databases. Itcontains literature search from October 2003 to April 2016. Our search was focused on available data for the

influence of physical inactivity on cognitive performance of cancer patients. Cancer patients have decreased levels of physical activity during treatment. It is suggested that lack of physical activity in general is associated with cognitive decline. At present, most available data comes from trials with heart failure patients as well as results from bed rest studies in space medicine. The development of CRCI is a multifactorial process with physical inactivity appearing to play an important role. However, the available data remains limited and future trials are needed toexamine the specific role of physical inactivity on CRCI.

Keywords: Bed rest; Cancer-related cognitive impairments;

Chemobrain; Cognition; Immobilization; Lack of exercise; Physical

Inactivity

Background of the Research

The development of CRCI is a multifactorial process. In addition to anticancer treatment numerous other factors such as depression, anxiety, patient-associated factors, molecular factors, tumor itself and cancer-related fatigue takes part in this process [3,10,27]. As a result of the above mentioned communalities between CRCI's genesis and influence of physical inactivity on cognitive performance in general, we also suggest that physical inactivity is another important causative factor of CRCI. However, data concerning influence of physical inactivity on cognitive performance are limited and are primarily from studies in patients with heart failure or from bed rest studies in space medicine [46-50]. Despite numerous clinical trials and some rodent research in the last years, the phenomenon of CRCI is not yet fully understood. Current data suggests that especially anthracyclinebased chemotherapeuticregimes have a negative effect on verbal memory performance and left precuneus connectivity [58]. Furthermore, the exact influence of hormone therapies is still unknown and therefore their exact role remains to be determined [3]. In addition, knowledge about the side effects of

antibody therapy on cognitive impairment is very weak [59]. Moreover, currently data on the influence of psychological factors on development of CRCI differs among studies [3,7,18]. Due to the large number of potential causative factors different treatment strategies exists to address CRCI. Time from active treatment seems to be one of the most important factors in the regression of CRCI as most patients' cognitive performance improves over the time [60]. Pharmacological treatment options are available but unfortunately are not well supported by clinical data [3,61]. Psychological intervention can also take place in treatment of mood disorders and cancerrelated fatigue [62,63]. In addition, other interventions such as skillfocused cognitive training seem to improve executive functions, memory functions, and speed of information processing.

Physical exercise intervention studies have also shown good efficacy in the management of CRCI [11,54-57,64,65]. Amongst several positive effects, improvement of verbal memory, attention and prefrontal lobe functions have been reported [55,56]. Physical exercise seems to also decrease level of proinflammatory cytokines like IL-6, IL-1 β and TNF- α as well as levels of inflammation in general in humans [52,57]. Moreover, physical exercise leads to improvement in selfperceived cognitive impairment and quality of life [53,54,57]. Although drawing similar conclusions, results from these studies must be critically interpreted due to methodological limitations and small sample sizes. Further randomized controlled studies with larger sample sizes are required to confirm and expand current preliminary findings. Conclusion The development of CRCI is a multifactorial process. In this narrative review, we provided the multifactorial genesis of CRCI and particularly the role of physical inactivity in this context. Existing data on changes of physical activity levels in cancer patients and its associated effects on CRCI remains limited. Future trials are encouraged to focus on these aspects to confirm and expand current findings. Importantly, the influence of physical inactivity on development of CRCI needs to be determined via randomized- controlled trials.