

## Review Article

# Synthesizing the best approach for the management of cancer related fatigue in children

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### ABSTRACT

Fatigue has been recognised as a symptom that affects 39%-90% of patients undergoing anti-cancer therapy. Fatigue is considered as the most frequently reported physical problem in children with cancer yet the most distressing symptoms of cancer therapy for children undergoing anti-cancer treatment. The effective diagnosis and treatment of fatigue will improve patient's quality of life. A thorough review of current literature is needed to understand the best approach for managing this problem. A review of several literature regarding cancer-related fatigue management from the last decade was conducted in 2012. As many as eight studies were identified as the qualified paper to summarise the best approach towards fatigue in pediatric cancer patient. Exercise, massage therapy, drug therapy and psychosocial therapy were synthesised as four different approaches that effectively applied to manage fatigue in children patients as a single modality. Fatigue-nursing intervention and the National Comprehensive Cancer Network (NCCN) Fatigue Practice Guidelines were multi-modality approaches that offer better option for the management of cancer-related fatigue in pediatric patients. The NCCN Fatigue Practice Guidelines seem to be the most effective approach for cancer-related fatigue management.

**Keywords:** Cancer, Fatigue, Children

### INTRODUCTION

Cancer treatments have been developed in an advanced level that leads to a lengthened patients' life expectancy but these treatments can result in some side effects.<sup>1,2</sup> These treatments may include chemotherapy, radiotherapy, bone marrow transplants and other procedures that may impact negative effects on patients' quality of life. Fatigue has been recognised as a symptom that affects 39%-90% of patients undergoing anti-cancer therapies such as chemotherapy, surgery, radiotherapy, hormonal therapy and biological therapy.<sup>3</sup> Fatigue is considered as the most distressing symptoms of cancer therapy for children undergoing anti-cancer treatment.<sup>4</sup> They added that the level of this symptom is increased

during treatment. In addition, this symptom is also recognised as the most frequently reported physical problem in children with cancer.<sup>1</sup>

Cancer-related fatigue is assumed as a complex phenomenon with no widely accepted definition.<sup>5</sup> A definitive explanation regarding cancer-related fatigue mentions that it is "a distressing, persistent, subjective sense of tiredness or exhaustion related to cancer treatment that is not proportional with recent activity and interferes with usual functioning".<sup>6</sup> Three subjective dimensions of fatigue recognized by scholars are lack of energy, unable to function and altered mood.<sup>7</sup>

There are several factors associated with cancer-related fatigue. Two of the possible causative factors are medical procedures and the hospital environment.<sup>4</sup> Another factor related to fatigue is the severity of the disease itself. Patients can experience anaemia, inflammation, pain, depression and sleep disturbance secondary to cancer, during and after treatment that may lead to fatigue.<sup>8</sup> If those conditions develop to fatigue, these will cause physical and mental problems.<sup>9</sup>

## METHODS

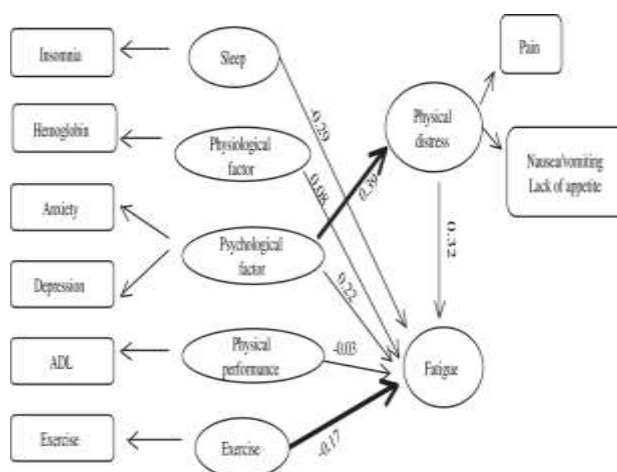
This paper reviews key literature regarding strategies for managing cancer-related fatigue in children with cancer. Relevant publications in English were identified through searches of MEDLINE and CINAHL from the year 2000 to 2012 for both anecdotal and empirical studies regarding fatigue using the keywords: fatigue, cancer and child. As many as eight studies were identified as the qualified paper to summarise the best approach towards fatigue in pediatric cancer patient. The paper begins with a framework of cancer-related fatigue as a complex problem recognised in the treatment of childhood cancer. Following this, key literature regarding approaches for managing the symptom and its effectiveness are reviewed. A current guideline regarding the management of this symptom will be provided thereafter. Finally, main argument regarding the best approach for managing this symptom will be summarised.

### The framework of cancer-related fatigue

The first research to identify cancer-related fatigue as a symptom that is often experienced by paediatric cancer patients was a study of adolescences with cancer conducted by.<sup>10</sup> Several more recent studies have identified the important factors related to this symptom and some studies resulted in the development of the conceptual framework of fatigue and instruments to evaluate cancer-related fatigue in children population.<sup>7,9</sup> The recent study about the developed framework of cancer-related fatigue was conducted by Seo, Oh, & Seo.<sup>11</sup> This study utilised a cross-sectional design and covariate structural analysis methods to verify the fitness of the hypotheses and the structural model of causality based on factors of fatigue in cancer patients. The relationships among those factors with cancer-related fatigue are provided in Figure 1 as shown below.

The framework indicates that psychological distress was found to have a significant direct effect on physical distress and affect fatigue indirectly while exercise showed a significant direct effect on fatigue.<sup>11</sup> These mean that patients with a higher level of psychological distress, such as, anxiety or depression, can result in a higher level of physical distress, which in turn result in fatigue and patients that did not exercise perceived more fatigue. The framework allows the oncology team better understand cancer-related fatigue and identify the presence of correctable correlated factors. As the

expected outcome, cancer-related fatigue would be better managed in the future.



**Figure 1: Path diagram of the cancer-related fatigue hypothetical model by Seo, Oh, & Seo (2009).**

Fatigue in cancer patients can be directly associated by sleep disorder, physiological factor, psychological factor, physical performance, and exercise as well as physical distress stimulated by psychological factor1: incidence of different types of asterion.

### Approaches for cancer-related fatigue management

It is generally accepted that the effective diagnosis and treatment of fatigue will improve patient's quality of life as well as health care professionals' quality of care.<sup>11</sup> Thus; it is considered important to review some literature of approaches or strategies to deal with cancer-related fatigue in children with cancer. Some vital literature indicated that several single strategies may work effectively to reduce symptom of cancer-related fatigue. However, a comprehensive analysis needs to be done to understand the best approach for this symptom management in children. This section reviews literature in six different approaches to manage cancer-related fatigue in children population including exercise, drug therapy, massage therapy, psychosocial therapy, fatigue-nursing comprehensive intervention and comprehensive management of fatigue based on the National Comprehensive Cancer Network.<sup>6</sup>

### Exercise

Studies regarding the implementation of exercise for reducing cancer-related fatigue symptom are varied. There are at least ten systematic reviews and meta-analyses conducted since 2004, but most of them were conducted in adults population.<sup>12, 13, 14, 15</sup> A systematic review to determine the effect of exercise on cancer-related fatigue in adults at any age, including young adults or adolescents, indicated that various types of exercise may give benefit to cancer patients in reducing cancer-related fatigue.<sup>16</sup> However, the optimal type,

intensity and timing of exercise intervention need to be studied further. While in children's population, a quasi-randomised control trial study on exercise conducted in children with acute lymphoblastic leukaemia (ALL) indicates that children who received the intervention showed a lower "general fatigue" score compared to children who did not receive exercise intervention.<sup>17</sup> The intervention was designed as 3 days a week activities, 30 minutes for each session, for 6 weeks. The same exercise video was used by all subjects in the intervention group, it was developed by an exercise specialist for the study. The content of the home-based aerobic exercise intervention included 3 sections: a warm-up (5 minutes), aerobic exercise (25 minutes), and cool down (5 minutes), which was developed according to the American College of Sports Medicine.<sup>17</sup>

### ***Drug therapy***

A systematic review was conducted to understand the effect of pharmacological intervention on cancer-related fatigue.<sup>18</sup> Based on this study, there is some evidence that pharmacological treatment for cancer-related fatigue using methylphenidate, which is a psycho-stimulant seems to be effective. The same study also found stronger evidence indicate that treatment using hematopoietic agent seems to be effective to reduce fatigue symptom caused by chemotherapy-induced anaemia.<sup>18</sup> Other medication, antidepressant and corticosteroid are also proven to be effective to minimise the burden of fatigue in cancer patients.<sup>19</sup>

Although many pharmacological agents showed a beneficial effect on cancer-related fatigue, limitation exists with regards to the side effects or adverse effects of the medication. For instance, the hematopoietic agents which are not recommended anymore because of the harmful long term side effects.<sup>20</sup> Thus, according to the same study, considering the bad sides of the intervention, the use of this intervention for children is very limited and should be avoided where possible.

### ***Massage therapy***

Massage therapy is one of complementary and alternative medicines (CAM) that is conducted in cancer patient with regard to minimise the burden of cancer-related fatigue. This intervention is highly reviewed as part of supported care for children with cancer.<sup>21</sup> Massage therapy is also one of three most preferred interventions by children undergoing chemotherapy and their parents for fatigue management beside rest and sleep.<sup>22</sup> Evidence from a randomised control trial involving 50 patients aged 1-19 years old indicated a significant reduction in anxiety in the intervention group receiving massage from professional therapist.<sup>23</sup> Results also indicated that children receiving massage showed shorter hospitalisation.

Most of studies investigating the effects of massage in fatigue management indicated that this intervention affects the immune system. Studies in adults found increased white blood cell count in the group following massage while in children population, a randomised control trial indicated increased of mean white blood cell count and mean neutrophils count in group of children following massage therapy for a month.<sup>21</sup> The only limitation of his intervention is that the underlying studies were mostly not blinded as it is difficult to blind participants from massage intervention. Other challenging things are a recommendation that this intervention should be given by a professional therapist and that there is no guideline available regarding the implementation of this instrument to children during and after anti-cancer treatment.

### ***Psychosocial therapy***

During the last two decades, the body of knowledge of the benefits of psychosocial intervention has grown significantly. Psychosocial interventions for reducing cancer-related fatigue include activities such as support interventions, education, stress management, coping strategy training, and behavioural interventions.<sup>24</sup> These interventions may be particularly useful for cancer patients whom exercise is contraindicated or as an adjunct to exercise intervention.<sup>25</sup> Several randomized, controlled clinical trials have examined a variety of psychosocial interventions in cancer survivors during and after treatment.<sup>12</sup> The results of those studies suggest that psychosocial support therapy affect lower levels of CRF among patients undergoing treatment and cancer survivors with different cancer diagnoses whether delivered individually or in a group setting, orally or written.

Things to be considered are that these interventions should be conducted by a health care professional, and repetition of action is usually needed to retain longer knowledge and behaviour regarding self-management of cancer-related fatigue.<sup>12</sup> Such intervention should also kept short and concise to maintain its effectiveness. In addition, implementation in paediatric population, parents are recommended to be involved during intervention as parents are considered the closest support system for the child.<sup>24</sup>

### ***A multi modality nursing intervention***

The nature of nursing is to provide care to patient by implementing a nursing process which consists of assessment, diagnosis, planning, intervention and implementation. In paediatric oncology nursing, an accurate assessment and effective nursing intervention may improve not only the quality of care but also quality of life of patients. To identify the effect of an effective nursing intervention in managing cancer related fatigue, a study involving 60 patients aged 7-12 years old and their parents was conducted.<sup>26</sup> Children and their parents were

randomised to experiment and control groups. The experiment group received a multi-modal intervention including health education regarding fatigue secondary to cancer treatment, counselling about activities that may reduce fatigue such as minimising day time sleep (naps) to optimise night time sleep. They were also given information on nutrition and energy conservation. Meanwhile, the control group received only a routine nursing care which is chemotherapy protocol administration.

The difference of this study with other previous studies is the involvement of a multi-modal strategy in managing cancer-related fatigue. This is considered worth more for patients as patients will benefit from more than one approach for their fatigue management.

Result indicated a statistically significant lower score of fatigue both in children and parent in the experiment group compared to fatigue score of children and parents in the control group.<sup>26</sup> Although the result is significant, the absence of fatigue value measurement at baseline becomes the limitation of the study. The absence of this value means there was a step in the nursing process that was missed out by the researcher which should be the integral part of the effective nursing care itself. Further study should include assessment at baseline to get a better comparison among groups.

#### ***National comprehensive cancer network (NCCN) fatigue practice guidelines***

The NCCN Fatigue Practice Guidelines are guidelines developed by experts in oncology by synthesized evidence regarding fatigue management.<sup>27</sup> The guidelines provide a definition of cancer-related fatigue, the standard of care for fatigue management and a step-by-step intervention.<sup>28</sup> The first step of the step-by-step intervention is a screening for fatigue. This is used to screen the presence and severity of fatigue. The severity of the fatigue is scored 0-10 and categorised as mild (fatigue score 1-3), moderate (fatigue score 4-6), and severe (fatigue score 7-10).

Following screening, health education related to fatigue will be given to patients with mild fatigue and primary evaluation will be conducted for moderate and severe fatigue patients.<sup>28</sup> (NCCN, 2007). The primary evaluation evaluates disease status and treatment, in depth fatigue assessment and assessment of primary factors that possibly induce fatigue in children. After a thorough assessment, patients will get interventions which are the combination of health education (psychosocial approach), cause-specific intervention such as intervention for pain, emotional distress, anaemia, insomnia, nutritional assessment, activity level, medication side effects, comorbidities, and/or non-pharmacologic intervention, and/or pharmacologic interventions.<sup>28</sup>

To date, the guidelines are revised and translated into practice in several different institutions and oncology centres. Despite the availability of the NCCN Fatigue Practice Guidelines for the assessment and management for cancer-related fatigue, assessment of cancer-related fatigue has not performed routinely at many institutions and oncology practice settings. Various patient-, provider-, and system-related barriers impede the translation of this guideline into practice.<sup>29</sup> Implementation of the guideline indicated significant immediate and sustained effects of the intervention on pain and fatigue barriers as well as knowledge. Measurable improvements in QOL were found in physical and psychological well-being.<sup>30</sup>

#### **CONCLUSION**

In conclusion, cancer-related fatigue remains a major problem in paediatric cancer patients. Exercise, massage therapy, psychosocial therapy and multi-modality interventions have been shown to be effective for management of fatigue in children with cancer. The use of pharmacological intervention seems to be minimised with concern of the long term side-effects of the medication. The NCCN Fatigue Practice Guidelines seem to be the most effective approach for cancer-related fatigue management although some challenges still exist in the translation of these guidelines into practice.

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