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Fatigue in Oncology

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Abstract

Fatigue is one of the most common symptoms in Oncology but heavily underreported and under treated. Both patients and physicians may view cancer-related fatigue as something to be endured rather than a symptom amenable to differential diagnosis and treatment. Cancer-related fatigue can lead to severe cognitive, psychological and physiological symptoms which are amenable to specific medical interventions. As cancer-related fatigue becomes increasingly recognised, oncology team should promptly recognise and treat it. Modern medicine should make same progress in its management as they have achieved in pain control, nausea, and vomiting.

INTRODUCTION

In the modern world, cancer is one of the leading causes of morbidity and mortality. It places considerable mental, physical and emotional stress on patients and their loved ones. It requires them to make major adjustments in their lives and many other key areas such as social, financial, spousal and many other commitments as a human being. As a consequence, the demands on health care system and providers to satisfy the complex care needs of oncology patients have increased tremendously[1]. Of late, overall patient well-being has been recognized as one of the key indicators of health care quality and is now being used by many leading health care systems across the globe to monitor system efficiency, adequacy of existing programs and maintenance of accreditation and development of new marketing strategies[2]. The overall wellbeing can be affected by many external and internal factors such as fatigue, insomnia, pain etc[3].

Definition:Fatigue is one of the most common symptoms in Oncology, but is heavily underreported and under treated[4]. Today fatigue is the most debilitating symptom in patients with malignancy, either at diagnosis or after treatment[5]. Cancer-related fatigue results in some degree of cognitive, psychological and physiological consequences, which demands specific medical or non-medical interventions[6]. Cancer-related fatigue, whether due to disease or treatment, has become a prominent treatable symptom and eventually will make the same progress in its management as oncology has achieved in analgesia, depression, nausea and vomiting[7].

Because fatigue is a symptom of a number of different disorders, diseases, and lifestyle choices, diagnosis often is extremely difficult and challenging[8].

A consensus is emerging in the palliative oncology field that cancer-related fatigue is the most important but untreated symptom in modern oncology today. We have improved management options available for symptoms associated with cancer such as insomnia, pain, depression, nausea and vomiting but not for fatigue[9]. However, though the problem is real, it is rarely discussed and seldom treated. Both patients and physicians may view cancer-related fatigue as something to be endured rather than a symptom amenable to differential diagnosis and treatment[10]. Research currently underway should begin to change this perspective and offer effective approaches to treatment.

Factors causing fatigue in oncology: In modern medicine we do not know the exact mechanisms causing fatigue phenomenon. Hypothetical theories suggest relationship between fatigue and the consequences of the disease process itself. The finding that prevalence rates vary according to treatment site or moment of treatment, support the assumed importance of treatment related factors. A few somatic mechanisms for fatigue have been proposed, such as malnutrition resulting from anorexia, changes in metabolism, obstructions, vomiting, diarrhoea or swallowing difficulties[11]. Malnutrition may cause abnormal muscle function because of a lack or an imbalance of essential metabolites, and because of a loss of muscle mass[12].

Haylock and Hart mention the possibility that fatigue is caused by the accumulation of cell destruction end products and toxic metabolites inhibiting normal cell functioning[13]. Cancer patients, particularly when treated with chemotherapy, run a high risk of developing infections – and the fatigue that goes with it - because of immunosuppression.[14] Anaemia is frequently mentioned as a possible factor in fatigue in literature. However, a correlation between fatigue and the degree of anaemia is rarely found[15]. Oxidative stress, mediated by cancer or chemotherapeutic agents, is an underlying mechanism of the drug-induced toxicity. Non-targeted tissues, such as striated muscle, are severely affected by oxidative stress during chemotherapy, leading to toxicity and dysfunction[16]. Day-time tiredness can be induced by narcotics or drugs with a sedative effect such as anti-emetics, analgesics or sleeping-agents[17]. Tiredness can also result from insomnia, which is a common problem of cancer patients.[18] The National Comprehensive Cancer Network (NCCN) Fatigue Practice Guidelines Panel reviewed the available evidence and the consensus of doctors managing fatigue to produce guidelines for clinical practice. Five factors were identified as being associated with fatigue: anemia, pain, emotional stress, sleep disturbances and hypothyroidism[19].

ASSESSMENT OF FATIGUE

Assessment of fatigue in most clinical trials, are either single or multiple item tool depending on the objective. The single item assessment scales are very simple and can be captured in multiple assessments, but have strong issues with validity and reliability. Multiple item assessments carry 3-7 items in order to reduce error. It has greater content validity, but may be redundant[20]. It is a well-established fact now that, rather than constituting a single, discrete one-dimensional state, fatigue should be viewed as a continuous dimension, which is experienced as a subjective state and thus a “multidimensional experience that focuses not only on biochemical or pathophysiological causes but on spiritual, psychological, physical, sensory, motivational and behavioural aspect as well[21]. Fatigue, like any other human experience, is capable of expression in three major ways that is by physiological response, behavioural response and verbal description[22].

Previously fatigue has been measured by general symptom checklists such as the Symptom Distress Scale[23], Symptom Profile[24], the Rotterdam Symptom Checklist[25] or by Profile of Mood States (POMS).[26] Today more specific instruments have been used to assess fatigue in cancer patient populations. These can be divided in one dimensional or multidimensional instrument. The simplest one-dimensional measure of tiredness is the Rhoten Fatigue Scale (RFS), in which a visual analogue scale is combined with a numerical ten points rating scale, ranging from 'not tired, full of energy' to 'total exhaustion'[27].

The Fatigue Symptom Checklist (FSCL) is a multidimensional questionnaire; aiming to assess fatigue in a work situation.[28] This scale was used later on radiotherapy patients. The original FSCL contained 30 symptoms, divided into three subscales based on a factor analysis (1) general feelings of sleepiness, with items like 'feel tired in the legs' and 'want to lie down', (2) mental feelings of fatigue, with items like 'difficulty in thinking' and 'become nervous', and (3) specific bodily sensations, with items like 'headache' and 'dizziness'. Factor analysis on the Dutch version of the FSCL resulted in a three-factor solution with an item distribution, which differed from the original subscales. A physical fatigue scale, a mental fatigue scale and a malaise scale were distinguished[29]. Piper and colleagues set out to develop an instrument to measure the experience of fatigue of patients, the Piper Fatigue Self-report Scale (PFS)[30]. The total fatigue score is calculated on the basis of the scores from four subscales representing the temporal, intensity, affective and sensory dimensions of fatigue. Based on the results in a sample of breast and lung cancer patients who started their first week of radiation, the authors concluded that the PFS shows excellent reliability and moderate construct validity. However, a large percentage of patients had troubles filling in the questionnaire. Also, no mention was made whether the assumed dimensions of fatigue were reflected in the actual data of the patient population. In conclusion, most measures of fatigue in cancer are incorporated in instruments that measure broader aspects of patient functioning[31].

The 30-item Fatigue Symptom Checklist developed by Japanese Industrial Fatigue Research Committee to assess the characteristics of fatigue in manual and clerical workers included (1) general feelings of incongruity, (2) mental symptoms of fatigue and (3) bodily feelings of fatigue. A particular drawback of this instrument is the underlying assumption that the feeling of fatigue is unpleasant and that frequency and intensity are linearly related, together with concerns regarding validity, particularly in terms of the multicultural representatives of the chosen descriptors and the degree to which these might (or might not) reflect the feelings of fatigue associated with the cancer experience[32]. However, there are similarities in both the dimensions

identified, and items included, in this tool, and those in the more recent instruments developed for use with cancer patients, the Multidimensional Fatigue Inventory[33]and the Fatigue Assessment Questionnaire[34]. This can now be achieved with Mutidimensional Fatigue Inventory[35] (MFI) and the Fatigue Assessment Questionnaire (FAQ).[36] The former instrument, a 20-item self-report tool covers five dimensions of fatigue: general fatigue, physical fatigue, mental fatigue, reduced motivation and reduced activity, which have been supported through confirmatory factor analyses and has been tested for its psychometric properties in cancer patients receiving radiotherapy, patients with chronic fatigue syndrome, students of medicine and psychology, army recruits and junior doctors. Evidence for the existence of these dimensions in patients receiving other modes of treatment and at differing stages following diagnosis, treatment and recovery now needs to be collected[37]. The inductive approach adopted by both Glaus and Smets in developing a theoretical model through which to elaborate measuring instruments, is to be applauded and should be pursued more vigorously[38]. Characteristics of fatigue have so far been viewed as difficult to measure adequately and consequently neglected. Programmes of research are now producing results that appear to be consistent across different populations, and thus it is with some confidence that it can be assumed that a number of discrete dimensions of fatigue do exist in patients with cancer. A more comprehensive instrument, thoroughly tested for its psychometric properties, is not yet available.

FATIGUE AND CANCER TREATMENT

Smets et al. evaluated fatigue prospectively before and 9 months after RT in 139 patients, treated for various types of cancer. They did not find elevated levels of fatigue in disease-free patients at 9 months after treatment as compared to the general population. The authors pointed out that the pre-treatment level of fatigue best predicted chronic fatigue 9 months after therapy, explaining 29% of its variance.[39] Bower et al. examined fatigue in 1,957 breast cancer survivors who had undergone various types of treatment including radiation therapy. The authors did not find differences in the level of fatigue between patients and age-matched controls. However, about one-third of the breast cancer survivors reported more severe fatigue than the controls. Fatigue was associated with elevated levels of depression, pain, and sleep disturbance[40]. Vordermark et al. studied fatigue in 103 prostate-cancer patients at a median of 2.1 years after either definitive or postoperative radiation therapy. They found slightly higher fatigue levels in their study population as compared to published data for healthy controls. Fatigue was associated with fecal incontinence and urinary symptoms.[41] Knobel et al. studied fatigue in 92 Hodgkin's disease survivors at a mean of 10 years after therapy. All patients had received RT, which consisted of mantle field irradiation in 92% of the patients and of a mediastinal field in the remaining 8%; 68% had also received chemotherapy. Fatigue after RT was associated with pulmonary gas transfer impairment but not with cardiac- or thyroid dysfunction[42]. Loge et al. reported on fatigue in 557 Hodgkin's disease survivors at a median of 12 years after treatment. Of the patients, 85% had received radiation therapy alone or in combination with chemotherapy. As compared to 2,214 controls from the general population, Hodgkin's disease survivors had higher levels of fatigue. The authors reported that fatigue did not increase with the time elapsed since treatment. Two of the four above-cited controlled studies found higher fatigue levels in the cancer population than in control persons.[43] Nevertheless, even in the two ''negative studies'' subgroups of cancer, patients experienced high levels of fatigue, and fatigue was associated with reduced levels of quality of life, with physical distress including pain, with functional disability, and with impaired quality of sleep. It is known that fatigue is the commonest side-effect of chemotherapy and up to 82–96% of those receiving chemotherapy suffer from fatigue during their treatment[44]. In a review authors observed that patients with breast cancer who were treated with adjuvant chemotherapy or autologous bone marrow transplantation complained of significant levels or fatigue for months or even years after the completion of therapy. Conversely, this long-term effect is much less frequent in patients who undergo only loco-regional treatments[45].

Two investigations on the impact of fatigue on the quality of life of cancer patients were carried out by the Fatigue Coalition, a multidisciplinary group whose aim was to examine the importance of fatigue in patients and their caregivers, and to draw up guidelines on the diagnosis and treatment of the fatigue syndrome. Vogelzang et al. carried out a telephone investigation in 419 randomly selected patients who had received chemotherapy or radiotherapy, and also in their caregivers and oncologists. Fatigue was reported by 78% of the patients during the course of their disease or during treatment, and about one-third reported daily fatigue and difficulty in carrying out normal daily activities.[46]

CONCLUSION

Fatigue has significant impact on the overall quality of a cancer patient's life by influencing physical, psychological, and spiritual aspects. All randomized trials should include some sort of quality of life data as quality of life research should be the priority in modern day oncology practise. It is highly recommended that an integrated team of physicians, nurse practitioners and nurse clinicians should provide a comprehensive approach to the management of fatigue. More detailed research is required to give elucidate the factors that differentiate between patients for whom the fatigue is in part the result of psychological or behavioral factors, from those patients whose fatigue is mainly somatic in origin. This will help physicians to offer individualised treatment to patients as per their needs. At present, knowledge of fatigue as experienced by cancer patients is very limited. Much research will be required to classify the complex somatic and psychological mechanisms responsible for the development, maintenance and treatment of fatigue.

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