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Multidimensional fatigue and its correlates in hospitalised advanced cancer patients

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ABSTRACT

Although fatigue is a multidimensional concept, multidimensional fatigue is rarely investigated in hospitalised cancer patients. We determined the levels and correlates of multidimensional fatigue in 100 advanced cancer patients admitted for symptom control. Fatigue dimensions were general fatigue (GF), physical fatigue (PF), reduced activity (RA), reduced motivation (RM) and mental fatigue (MF). Investigated correlates were tumour load, prior anti-tumour treatment, medication use, haemoglobin levels, serum biochemical variables, physical symptoms and mood. Median GF, PF and RA scores were very high; median RM and MF scores were moderate, and differed from the GF, PF and RA scores. Multiple regression analyses showed that symptoms and mood correlated with all fatigue dimensions. Each fatigue dimension had different relationships with other factors. Hospitalised advanced cancer patients differ in fatigue levels depending on the fatigue dimension, and each fatigue dimension has different correlates. The results confirm that fatigue should be regarded as a multidimensional concept.

1. Introduction

Levels of five fatigue dimensions and a prospective analysis of correlates of fatigue in hospitalised advanced cancer patients are presented. Clinical research on fatigue in advanced cancer patients is important, because fatigue is an essential determinant of quality of life, health status and symptom burden.[1–5] Fatigue is nominated by patients as the most important factor influencing daily functioning.[6] Furthermore, fatigue is prevalent: fatigue in excess of the 95th percentile of a healthy control group was present in 78% of cancer patients receiving specialist inpatient palliative care.[3] In a recent systematic review (46 studies, including 26,223 advanced cancer patients), the prevalence of fatigue was 64% in studies concerning the last 1–2 weeks of life and 75% in other studies.[7] While there is little debate about the importance of fatigue as a determinant of ill-being, adequate methods of managing fatigue are lacking, also because the aetiology of fatigue in advanced cancer is unknown. This study aims to provide knowledge of potential determinants of fatigue, which may help physicians make informed treatment decisions.

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The multidimensional conceptualisation of fatigue is widely accepted[8–10]; fatigue manifests itself in multiple, reasonably independent[11] dimensions, e.g. physical, cognitive, motivational, or in terms of reduced activities. Nevertheless, fatigue is seldom investigated as a multidimensional construct in hospitalised advanced cancer patients. In palliative care research fatigue is labelled differently in different studies: tiredness, weakness and asthenia are used as synonyms. This complicates the generalisability of results even more in the often heterogenic palliative care populations. In a recent study, Munch and colleagues investigated correlates of multidimensional fatigue in advanced cancer. They found that anxiety and especially depression were related to fatigue dimensions, but the strength of the relationships varied from dimension to dimension. The authors suggested that the different dimensions of fatigue in their study measure different aspects of fatigue.[12] In an earlier study, Shun and colleagues also found relationships between anxiety and depression and fatigue. In other studies, more possible correlates of fatigue were identified. Symptoms and symptom distress were identified as significant correlates in a number of studies examining advanced cancer patients receiving anti-tumour treatment.[13–16] Jacobson and colleagues found that greater declines in haemoglobin levels were related to increases in fatigue duration and disruptiveness.[17] Opioids and other centrally functioning medication,[12] and (prior) anti-tumour therapy were also identified as a factor influencing fatigue.[13,18] Lastly, a positive response of fatigue was found on the administration of corticosteroids.[19] Additional likely correlates of fatigue include stage of disease, tumour load, markers for liver and renal function, anti-emetics, anti-convulsants and weight loss.

In this prospective study, fatigue is conceptualised as a multidimensional construct. Differences in levels and distributions of fatigue dimensions were determined, and relationships between all the above-mentioned medical and psychological variables and the fatigue dimensions were explored. The patients studied in this work were all admitted for symptom control. Therefore, it was hypothesised that they would exhibit high levels of physical fatigue and reduced activity. It was also hypothesised that due to the independence of the fatigue dimensions, each fatigue dimension will result in a different predictive model of correlates.

2. Patients and methods

2.1. Patients

One hundred patients with advanced cancer admitted to the palliative care unit (PCU) of the Erasmus MC Daniel den Hoed Cancer Centre were included. All patients were admitted for symptom control. Of the 263 patients who were asked to participate in the study, 100 did not fulfil the inclusion criteria: 62 patients appeared to have received immuno- or chemotherapy within 4 weeks prior to PCU admission, 34 patients could not be interviewed due to cognitive impairment, 4 patients had life expectancies of less than 14 days, and 2 patients had insufficient command of the Dutch language. Two patients were cognitively impaired and had life expectancies of less than 14 days. Of the remaining patients, 33 patients refused participation, and 30 patients could not be included due to other reasons.

2.2. Data collection

Data were collected within 48 h after admission by trained oncology nurses. Socio-demographic data and data on anti-tumour therapies and medication use were collected from the medical records. All other data were obtained by interview using the instruments listed below. Ethical clearance was provided by the Medical Ethical Committee of the Erasmus Medical Centre.

2.3. Measures

The multidimensional fatigue inventory (MFI)[11] was used for the measurement of multidimensional fatigue. The MFI consists of 20 statements of which patients are requested to indicate agreement on a five-point scale. The MFI measures five dimensions of fatigue: general fatigue (GF), physical fatigue (PF), reduced activity (RA), reduced motivation (RM) and mental fatigue (MF). Scores range from 4 to 20 (higher values indicate more fatigue). The Hospital Anxiety and Depression Scale[20] (HADS), a 14-item questionnaire with four-point rating scales, was used to measure anxiety and depression. Scores range from 0 to 20 (higher scores denote more distress); patients with 'probable' anxiety and/or depressive disorder are identified with scores $\geqslant 11$. Physical symptoms were measured with the symptom subscale of the European Organization for Research and Treatment of Cancer QLQ C-30.[21] Patients indicate on four-point rating scales to what extent they suffer from dyspnoea, pain, need for rest, sleeping difficulties, weakness, lack of appetite, nausea, vomiting, diarrhoea and fatigue (range 1–4; higher values indicate higher symptom levels). Data on itch and hiccups were additionally collected using visual analogue scales. Symptom load was calculated by counting the number of these 12 physical symptoms present in each patient (symptom intensity >0; see Table 1). The fatigue-related items from the EORTC QLQ C-30 (need for rest, weakness and fatigue) were not used in the analyses on correlates of fatigue, because they measure the same construct as the outcome variable. Functional status was measured with the Palliative Performance Scale (PPS[22]) with which staff members assigned a performance percentage score (higher percentages indicate better performance). Tumour load was defined as the number of organs involved and serum LDH level. Prior anti-tumour treatment variables were the number of chemotherapy lines, one or more instances of prior chemotherapy, one or more instances of prior radiotherapy, and one or more instances of prior immunotherapy. Haemoglobin levels and serum biochemical variables were obtained through blood samples. All medication was coded given (1) or not (0), except opiates, for which the daily dose used was expressed as dose in oral morphine equivalents before coding it into three range categories: no morphine, below the median dose value and above the median dose value.

2.4. Statistical methods

Differences between fatigue dimensions were tested with Friedman's χ^2 test. Initial bivariate relationships were tested with Pearson correlations, Oneway analyses of variance and