Living with Cancer-related Anaemia – What Is the Reality?

a report by
Jan Foubert

Past President, European Oncology Nursing Society and Dean, Faculty of Healthcare and Senior Lecturer, Nursing and Midwifery, Erasmushogeschool, Brussels

DOI: 10.17925/EOH.2007.0.1.120

Anaemia is defined as an imbalance between the production and destruction, or loss, of red blood cells (RBCs), leading to decreased RBC count, haemoglobin (Hb) content and oxygen-carrying capacity of the blood. It can be defined further by graded classification systems, Hb trigger values, tumour type and symptoms. Various classification systems are used to grade the severity of anaemia, from mild to life-threatening, on the basis of Hb concentrations (see Table 1). However, anaemia is more than an Hb level. It is a complex condition that impacts many body systems to produce a diverse range of symptoms that include effects on the central nervous, gastrointestinal, vascular and cardiorespiratory systems, as well as the genital tract (see Figure 1).1

Underdiagnosis of Anaemia in Cancer
Approximately 20–60% of cancer patients have anaemia at presentation2 and several factors may induce or exacerbate the condition, influencing incidence rates in specific patient groups. These factors include tumour type,3,4 disease stage,4,5 duration, intensity and type of treatment2,3,6–8 and patient age.9

Despite the high incidence of cancer-related anaemia, it is frequently underdiagnosed and undertreated.10 A survey of 284 oncologists treating 4,888 cancer patients throughout France, Germany, Italy, Spain and the UK revealed that 52% of patients (out of 3,067 patients with Hb data available) had Hb concentrations of ≤12g/dl. However, only 22% of this group were diagnosed as anaemic by their physician.10 This may reflect an under-appreciation of the seriousness of anaemia and its impact on the patient, as well as practical difficulties in diagnosing often vague, emotional and psychological symptoms.

Causes of Anaemia in Patients with Cancer
The causes of anaemia in patients with cancer fall into three distinct categories: anaemia that occurs as a result of the malignancy, anaemia attributed to the cancer therapy and anaemia caused as a result of other contributing factors, such as infections, nutritional deficiencies and underlying chronic disorders in addition to the cancer.11

Anaemia of Chronic Disease
Anaemia of chronic disease, in the absence of any treatment-related factors, is not fully understood, but it is represented by usually mild (>9g/dl) normochromic or hypochromic anaemia with a disproportionately low reticulocyte count relative to the severity of anaemia.11 Furthermore, RBC survival is shortened, possibly due to the action of immune and inflammatory cytokines activated by the presence of the tumour and an imbalance develops between RBC production and depletion, as a result of the inability of the bone marrow to produce RBCs at a rate sufficient to compensate for their reduced lifespan. This is thought to reflect the suppression of erythroid progenitor cells, impaired iron utilisation and inadequate production of endogenous erythropoietin (EPO) by the underlying malignancy.11,12 Other disease-related factors include direct bone-marrow involvement of the malignancy, haemolysis, blood loss associated with the tumour, renal insufficiency and hypersplenism.

Treatment-related Anaemia
The extent to which treatment for cancer can induce or exacerbate anaemia varies considerably according to the type of tumour and the treatment administered.2,4 Myelosuppressive, cytotoxic chemotherapy or radiotherapy, which involves large areas of bone marrow, will compromise bone marrow function such that the production and maturation of RBCs are reduced and anaemia follows.2,3,6,8 As the kidney is a primary site of endogenous EPO production, nephrototoxic drugs, including cisplatinum-based chemotherapy, may decrease the production of EPO via drug-induced renal tubular damage.12 Other possible treatment-related causes of anaemia include long-term damage to the stem cell pool or nutritional deficiencies as a result of radiotherapy and blood loss during extensive surgery.9

Cancer Anaemia and Fatigue
Fatigue is the most commonly reported clinical manifestation of anaemia in cancer patients,13,14 with 78% of patients experiencing symptoms.14 Fatigue is not relieved by sleep or rest and is not exacerbated by exertion. However, Hb concentration has been shown to have a considerable impact on the incidence of fatigue and subsequently on quality of life (QoL). In a study of 50 patients with solid tumours or haematological malignancies, those with Hb levels ≤12g/dl reported significantly more fatigue, worse physical and functional wellbeing and generally reduced QoL than those who had Hb >12g/dl.15 The relationship between Hb concentration and QoL changes was further defined in a retrospective analysis of data from two community studies that enrolled 4,382 anaemic cancer patients receiving chemotherapy.15 In these patients, the maximum QoL gain occurred in those whose Hb concentration was increased to ≥12g/dl (range 11–13g/dl).16

Patients rather than their physicians provide the best documentation of fatigue. Data from a survey of 419 cancer patients reiterated the negative impact and wide range of effects that fatigue has upon daily life (see Figure 2). More than 50% of patients reported that their ability to work, physical wellbeing, ability to enjoy life in the moment and emotional wellbeing were all somewhat or very much affected by fatigue.14 However, fatigue remains poorly understood and patients and oncologists differ in their perception of the importance of treating fatigue.15 When asked which factors affected their everyday life the most, 60% of patients ranked fatigue highest, followed by nausea (22%), depression (10%) and pain (6%).17 Interestingly, 41% of patients but
only 5% of oncologists felt that it was more important to reduce/relieve fatigue than pain (see Figure 3).14

Assessment of Cancer-related Anaemia and Fatigue
The assessment of cancer-related anaemia is based primarily on quantitative measures of haematocrit (Hct) or Hb, with considerably less emphasis placed on patient symptoms, changes in function or QoL. Furthermore, rather than long-term monitoring of patients’ symptoms alongside these quantitative indicators in order to establish trends, considerable reliance is placed on single measures. Anaemia is often, therefore, considered in a single dimension and the symptoms that most directly affect patients’ lives, such as fatigue, are not fully evaluated. However, cancer-related fatigue has now been accepted as a diagnosis in the 10th revision of the International Classification of Diseases and an algorithm has been proposed for its evaluation and management.18 Assessment of cancer-related fatigue has also been aided by the creation of a defined list of diagnostic criteria (see Table 2).19

A variety of tools is available to assess cancer-related fatigue. In the clinical setting, where there is limited time for detailed evaluation, assessment may be performed by asking simple questions such as “Are you experiencing any fatigue?” and “How severe has your fatigue been during the past week on a scale of one to 10?” However, multidimensional questionnaires provide further information on the patient’s symptoms and are more commonly used in the research setting.16,18 The Piper Fatigue Scale is an early example of a validated multidimensional instrument that uses a 41-item questionnaire to evaluate severity, distress and the impact of fatigue in patients receiving treatment.2 The algorithm has been proposed for its evaluation and management.18 Multidimensional fatigue assessment tools, although valuable in the research setting, are time-consuming and, consequently, may be used inconsistently. This highlights the need for the development of a more suitable assessment method that is compatible with the reality of healthcare assessment in European hospitals. An ideal assessment tool would consist of a minimum number of questions required to reach an accurate diagnosis and evaluation of fatigue. An accurate assessment of the level of fatigue would allow the healthcare professional to provide the patient with an explanation for their symptoms and to relate fatigue to disease, treatment or other concomitant conditions (e.g. anaemia, metabolic disturbances and pain).

Treatment of Cancer Anaemia and Fatigue
Historically, RBC transfusions have been the cornerstone of management for severe cancer-related anaemia, as they rapidly raise the RBC count and Hb concentration. However, the benefits of RBC transfusions are transient and potential risks include infection, haemolytic reactions and transfusion-related lung injury.2,20 Furthermore, a UK audit of 2,719 cancer patients receiving chemotherapy revealed that there is no general consensus between different clinical centres regarding the ‘transfusion trigger’ (the mean Hb concentration at which RBC transfusion is implemented), so treatment is not standardised.6

A valuable alternative to RBC transfusions is the use of the erythropoietic proteins, recombinant human erythropoietin (rHuEPO; epoetin alpha, epoetin beta) and darbepoetin alpha. These therapies mimic the role of endogenous EPO and thus aid in the management of anaemia. An abundance of data demonstrates that erythropoietic proteins increase Hb levels, improve QoL and reduce RBC transfusion requirements in anaemic cancer patients receiving or not receiving chemotherapy.21–25

In a randomised, double-blind study of 375 anaemic cancer patients receiving non-platinum chemotherapy, 359 of whom were analysed for efficacy, treatment with epoetin alpha 150IU/kg three times per week (TIW) for up to 28 weeks produced significantly greater increases in Hb concentration (p<0.001) and Hb response rate (an increase in Hb ≥2g/dl in the absence of RBC transfusion; p<0.001) than placebo.22 Significantly greater improvements in all primary cancer- and anaemia-specific QoL domains (p<0.01) including fatigue, as measured by the FACT-F subscale (p<0.004), were noted with epoetin alpha compared with placebo. There was also a statistically significant correlation between change in Hb level and all primary QoL parameters (range p=0.0002–0.0325), including fatigue (p=0.0002).22

Similarly, in a randomised trial in 343 anaemic patients receiving chemotherapy for haematological malignancies, treatment with epoetin beta 150IU/kg TIW for up to 16 weeks resulted in significantly higher Hb
Oncology-related Complications

Figure 2: Percentage of Cancer Patients (n=419) Reporting Aspects of Daily Routine That Were ‘Very Much’ or ‘Somewhat’ Affected by Fatigue

Table 2: Proposed Criteria for the Diagnosis of Cancer-related Fatigue

A. Six or more of the following symptoms have been present every day or nearly every day over a two-week period during the last month, and at least one of these symptoms is significant fatigue.

- Significant fatigue, diminished energy, increased need to rest, disproportionate to any recent change in activity level
- Complaints of generalised weakness or limb heaviness
- Diminished concentration or attention
- Decreased motivation or interest to engage in usual activities
- Insomnia or hypersomnia
- Experience of sleep as unrefreshing or non-restorative
- Perceived need to struggle to overcome inactivity
- Marked emotional reactivity (sadness, frustration or irritability) to feeling fatigued
- Difficulty completing daily tasks attributed to feeling fatigued
- Perceived problems with short-term memory
- Post-exertional malaise lasting several hours

B. The symptoms cause clinically significant distress or impairment in social, occupational or other important areas of functioning

C. There is evidence from the history, physical examination or laboratory findings that the symptoms are a consequence of cancer or cancer therapy

D. The symptoms are not primarily a consequence of co-morbid psychiatric disorders such as major depression, somatisation disorder, somatoform disorder or delirium

Source: Cella et al., 1998.13 The symptoms listed in A also relate to statements B, C and D. Reproduced with permission from the National Comprehensive Cancer Network.
GENEVA
SWITZERLAND
27-29 MARCH 2008

New ways of working: innovation in cancer nursing practice
Nouvelles méthodes de travail: innovation des pratiques de l’infirmérie en oncologie
Neue wege in der praxis: innovationen in der onkologiepflege

Conference Chair: Sara Fairfull

In partnership with the Swiss Oncology Nursing Society

Powered by
Oncology-related Complications

By accurately anticipating and assessing problems at all stages of treatment, the oncology nurse can be pivotal in reducing the adverse effects of cancer-related anaemia and fatigue. However, to achieve this, the training needs of oncology nurses must be addressed and education on anaemia and fatigue provided. The European Oncology Nursing Society (EONS), in conjunction with the limited liability company (GmbH) Amgen (Europe) have conducted a Learning Needs Assessment (LNA) study in 21 countries involving over 450 nurses. The main objective of this study was to identify the learning requirements of European oncology nurses relating to anaemia, neutropenia and mucositis. Results of this LNA study have been used to develop the Training Initiative in Thrombocytopenia, Anaemia and Neutropenia (TITAN) training programme, which is being piloted in Ireland, France and The Netherlands with results expected later this year. The delivery of accurate training programmes specifically tailored for European oncology nurses should improve the prevention, detection and management of haematological toxicities, including anaemia and fatigue, in cancer patients.

Conclusions

Although common in patients with cancer, anaemia is often underdiagnosed and undertreated. Fatigue, which is frequently associated with cancer-related anaemia, has a significant impact on patients’ everyday lives. However, cancer-related fatigue appears to be underappreciated by healthcare professionals. Indeed, many patients regard the treatment of fatigue as more important than the treatment of pain, in direct contrast with the opinions of many physicians. Accurate assessment of both anaemia and fatigue is essential if we wish to understand the reality of living with cancer-related anaemia and provide optimal treatment.

Oncology nurses are ideally placed to act as patient advocates and to play a key role in the identification and management of cancer-related anaemia, and to act as a patient advocate. Oncology nurses must proactively and accurately assess cancer-related anaemia and fatigue using appropriate tools and ensure that the information is documented and made available to the rest of the healthcare team. In addition, oncology nurses should: continuously assess and monitor patients; aim to identify signs and symptoms of anaemia early; realise that anaemia is not just a number; evaluate trends in blood profiles over time; implement strategies to prevent and/or reduce the incidence of anaemia; and use evidence-based models to identify patients at risk of developing anaemia.