

## Relief from cancer chemotherapy side effects with pharmacologic vitamin C

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### Abstract

Fatigue is a common, often debilitating, side effect of cancer chemotherapy. Pharmacologic vitamin C has been used as an alternative treatment for the disease itself but its effects on fatigue have not often been documented. Here we report on the case of a woman with recurrent breast cancer, undergoing weekly chemotherapy, with lethargy as a major symptom. Vitamin C (50 g/session) was administered twice weekly and quality of life and multidimensional fatigue symptomology questionnaires were undertaken. Dramatic decreases in fatigue and insomnia were observed, as well as increased cognitive functioning. There were no adverse side effects of i.v. vitamin C.

Fatigue is the most common symptom reported by cancer patients and can affect quality of life more than pain.<sup>1,2</sup> Fatigue can be expressed at physical, emotional and mental levels, and questionnaires that cover these multidimensional aspects have been developed for use with cancer patients.<sup>3</sup>

The use of i.v. vitamin C in cancer is relatively common, but there is controversy as to any proven benefits. Vitamin C has numerous functions, including a co-factor role in collagen, carnitine, neurotransmitter and neuropeptide hormone synthesis and in the regulation of epigenetics and gene transcription.<sup>4</sup> Many of these functions could potentially influence quality of life and fatigue.<sup>5</sup>

### Case report

Here we report the case of a 45-year-old female diagnosed in May 2009 with invasive ductal carcinoma of the left breast (grade 2, ER+, PR+, HER2-). She immediately underwent wide local excision (no lymphovascular invasion evident) and radiation therapy to the breast. Tamoxifen was terminated after 4 days due to intolerance. Axillary lymph node recurrence occurred in Feb 2013 followed by axillary lymph node clearance (4/22 lymph nodes with extra nodal disease).

In March 2013 a CT scan of chest, abdomen and pelvis showed no evidence of distal metastatic disease. Two cycles of fortnightly chemotherapy with doxorubicin and cyclophosphamide were initiated in April and May, and in June once weekly paclitaxel was initiated for 12 weeks. Lethargy was a major symptom of chemotherapy.

Prior medical history included gastric bypass in 2004 for weight reduction and a hysterectomy in 2005 for adenomyosis. At that time the patient was tired and lethargic and blood tests indicated low iron and B12 levels. In 2007 a toxic nodule on the thyroid was diagnosed and in 2012 a total thyroidectomy was carried out for a multinodular goitre.

A buccal swab was analysed for selected single nucleotide polymorphisms by the Department of Genetics, La Trobe University (Melbourne, Australia). Profiling of specific inflammatory, immune, antioxidant and detoxification genes indicated a number of adverse gene polymorphisms in this patient (Table 1).

Of particular interest for this case are the CYP1B1 (cytochrome P450 1B1) and NQO1 (nicotinamide quinone oxidoreductase 1) polymorphisms. CYP1B1 is located mainly in breast, endometrium and ovaries and is involved in oestrogen metabolism. Increased activity due to the indicated homozygous polymorphism, leads to enhanced activation of pro-carcinogens.<sup>6</sup> NQO1 has strong antioxidant capacity and has been described as an anti-cancer enzyme. The heterozygous polymorphism indicates extremely reduced enzyme activity.<sup>7</sup> It is possible that these deleterious gene polymorphisms contributed to the development of breast cancer in this patient.

**Table 1. Selected genes involved in inflammation, immune systems, cell antioxidant defence and detoxification**

Gene product	Dysfunction	Polymorphism	Heterozygous	Homozygous
<b>CRP-1</b>	Increased risk of inflammation	0169171C>T	X	
<b>CRP-2</b>	Increased risk of inflammation	0143294G>A	X	
<b>CAT</b>	Increased risk of oxidative stress	262C>T	X	
<b>CYP1B1</b>	Increased levels of reactive toxins	Val432Leu		X
<b>GSTP1</b>	Decreased capacity to clear toxins and reactive oxygen species	313A>G	X	
<b>NQO1</b>	Highly decreased antioxidant capacity	690C>T	X	
<b>HO-1</b>	Increased risk of oxidative stress and inflammation	-413A>T	X	

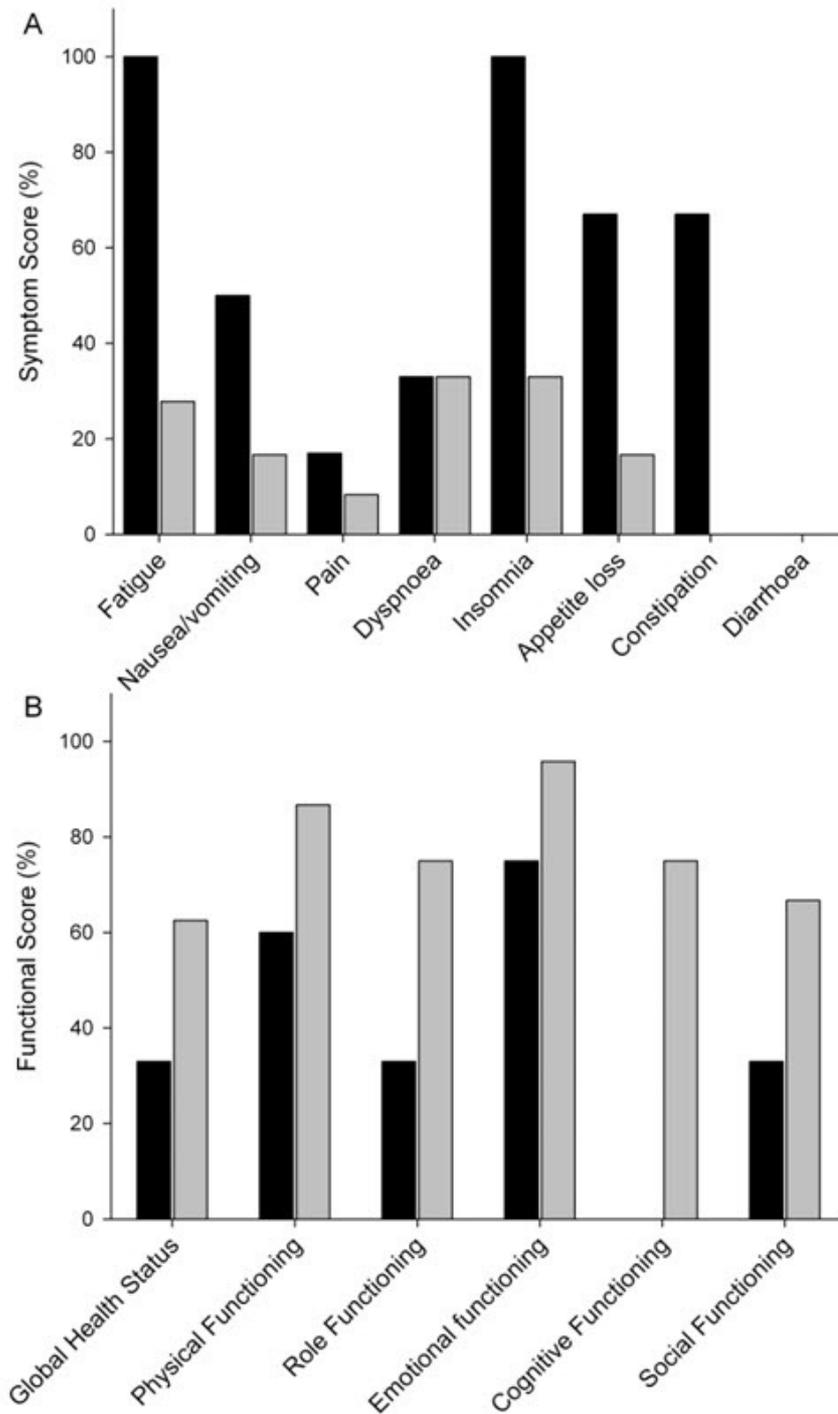
To investigate the effects of pharmacologic vitamin C on quality of life and fatigue due to chemotherapy, intravenous vitamin C (50 g/session, AscorL500, McCuff Pharmaceuticals, Santa Ana, USA) was initiated twice weekly, 2 days either side of each chemotherapy session (doxorubicin/cyclophosphamide in May and paclitaxel in June of 2013). Quality of life (EORTC QLQ-C30)<sup>8</sup> and fatigue (MFSI-SF)<sup>9</sup> questionnaires were undertaken before and after 4 weeks of vitamin C intervention.

The quality of life questionnaire showed dramatic decreases in fatigue, pain, appetite loss, nausea/vomiting and insomnia following vitamin C administration (Figure 1A). Increases in physical, emotional, cognitive and social functioning were also observed, as well as a doubling of the patient's "global health status" (Figure 1B).

The multidimensional fatigue symptomology questionnaire showed decreases in general, physical, emotional and mental fatigue, as well as increased vigour, following vitamin C administration (Figure 2).

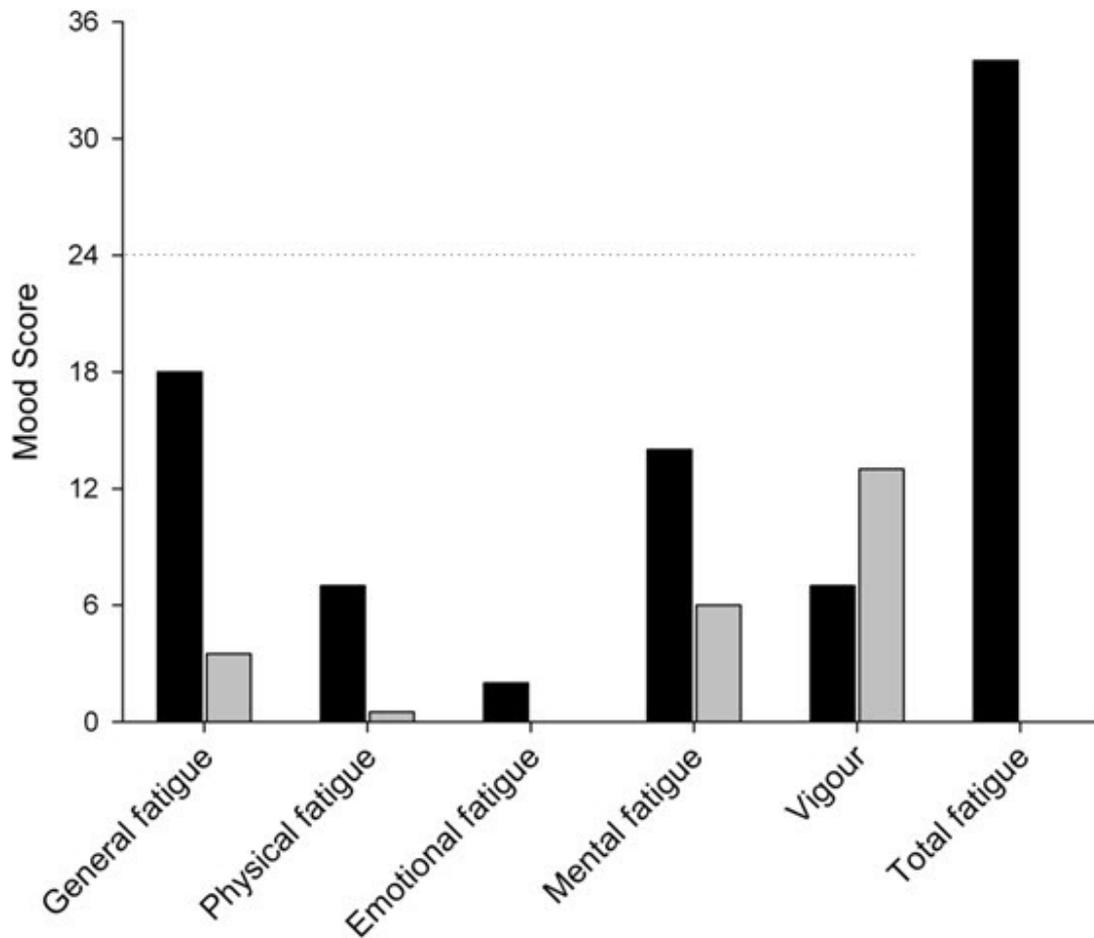
Final assessments were made after 4 weeks of vitamin C administration, but positive effects were noticed following the first administration. No adverse side effects of the vitamin C administration were observed by the patient or her GP.

**Figure 1. Patient’s health-related quality of life scores before (black bars) and after (grey bars) i.v. vitamin C administration**



**Note:** All of the scales range in score from 0 (no bar)–100, with a high score representing a higher response level, i.e. a high score for a symptom scale (A) represents a high level of symptomology/problems, whereas a high score for the global health status scale (B) represents a high quality of life and a high score for a functional scale (B) represents a high/healthy level of functioning.

**Figure 2. Patient's multidimensional fatigue scores before (black) and after (grey) i.v. vitamin C administration**



Note: All of the single-item measures range in score from 0 (not at all = no bar) to 24 (extremely). Total fatigue represents the sum of general, physical, emotional and mental fatigue scores minus the vigour score.

## Discussion

Research has shown that fatigue has a constant presence following chemotherapy and also increases incrementally with consecutive cycles of chemotherapy.<sup>2</sup> A retrospective, multicentre, epidemiological cohort study has indicated that intravenous vitamin C administration improves quality of life, including fatigue, in breast cancer patients during chemo-/radiotherapy and aftercare.<sup>10</sup>

Our case report supports the findings of Vollbracht et al<sup>10</sup> and extends these by further investigating the effects of intravenous vitamin C on the multidimensional aspects of fatigue. Following pharmacologic vitamin C administration there were dramatic decreases in chemotherapy-related fatigue and other symptoms, as well as increased functioning and overall health.

It is not possible to rule out a placebo effect, particularly as this effect tends to be more prevalent with measures of subjective symptoms.<sup>11</sup> However, based on the

varied functions of vitamin C in the body,<sup>4</sup> it is plausible that vitamin C contributed to some of the observed quality of life effects and similar findings have recently been reported.<sup>12</sup>

Overall, our report has shown that pharmacologic vitamin C may be considered for patients experiencing side effects from chemotherapy. Furthermore, based on our prospective findings and others<sup>12</sup> and the retrospective findings of Vollbracht et al,<sup>10</sup> a double-blind placebo-control study of the efficacy of intravenous vitamin C on chemotherapy-related quality of life and fatigue appears warranted.

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