Pharmacologic Treatment Options for Cancer-Related Fatigue:
Current State of Clinical Research

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Fatigue is a highly distressing symptom of cancer associated with significant psychological morbidity and reduced quality of life. Cancer-related fatigue (CRF) has been underreported, underdiagnosed, and undertreated. Fatigue and depression may coexist in patients with cancer, and considerable overlap of symptoms often occurs. This has led researchers to examine the role of psychotropic medications to treat fatigue. Psychostimulants, wakefulness-promoting agents, antidepressants, and cholinesterase inhibitors have been studied for CRF treatment. Methylphenidate has been studied most and is effective and well tolerated despite common side effects. Some preliminary data support using modafinil for patients with CRF. Antidepressant studies have shown mixed results. Paroxetine shows benefit for fatigue, primarily when it is a symptom of clinical depression. Bupropion sustained release may have psychostimulant-like effects and, therefore, may be beneficial in treating fatigue. Donepezil, a cholinesterase inhibitor, has shown benefit only in open-label trials. Randomized, placebo-controlled trials with specific agents are needed to further assess the efficacy and tolerability of psychotropic medications in CRF treatment.

Fatigue is a highly prevalent and distressing symptom of cancer, associated with reduced quality of life and considerable psychological and functional morbidity (Cella, Peterman, Passik, Jacobsen, & Breitbart, 1998; Curt et al., 2000; Hwang, Chang, Rue, & Kasimis, 2003; Vogelzang et al., 1997). Cancer-related fatigue (CRF) is typically underreported, underdiagnosed, and undertreated (Mock et al., 2000). Patients perceive fatigue as the most distressing symptom associated with cancer and its treatment, more distressing than pain, nausea, and vomiting (Vogelzang et al.). The purpose of this article is to provide an update and a critical review of the literature on the pharmacologic treatment options for CRF.

The reported prevalence of CRF ranges from 4%–91% depending on the population of patients with cancer studied and the methods of assessment (Lawrence, Kupelnick, Miller, Devine, & Lau, 2004). Fatigue is present at the time of diagnosis in about 50% of patients with cancer and occurs in up to 75% of patients with bone metastases; about 60%–96% of patients with cancer experience fatigue during cancer treatment (Flechtner & Bottomley, 2003). Chemotherapy, radiation therapy, biologic, and hormonal therapies exacerbate fatigue. Women with early-stage breast cancer have reported a 4% rate of fatigue before chemotherapy; that number increased to 28% after four cycles of chemotherapy (Jacobson et al., 1999). A study of men with localized prostate cancer showed that the fatigue rates increased from 8% before radiation treatment to 25%

At a Glance

- Psychostimulants, wakefulness-promoting agents, antidepressants, and cholinesterase inhibitors are the main psychotropic medications that have been studied in the treatment of cancer-related fatigue (CRF).
- Psychostimulant use has been studied and shows promise for CRF treatment.
- Randomized, placebo-controlled trials are needed to further assess the efficacy and tolerability of various medications in CRF treatment.

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