

# Pharmacologic Treatments for Fatigue Associated With Palliative Care

Marilyn Kirshbaum, RN, BSc, MSc, PhD, DipAdultOnc, FHEA

## Review Question

What is the best available evidence regarding pharmacologic treatments used to relieve nonspecific fatigue in people with advanced disease?

## Type of Review

A systematic review of randomized controlled trials (RCTs) was conducted. Meta-analysis was performed when two or more studies of the same substance could be analyzed in a subpopulation of participants (i.e., with the same illness).

## Relevance to Nursing

Fatigue is the most commonly reported symptom in individuals who have cancer and also is highly prevalent in populations with progressive life-threatening conditions. Fatigue presents a challenge for healthcare professionals because it can be nonspecific to treatment or illness, ongoing, subjective, and disabling to patients. In addition, the actual causes of fatigue are difficult to isolate, particularly in the person who is receiving palliative care because the symptom usually overlaps with concurrent disease-related problems such as malnutrition, sleep disturbances, pain, depression, asthenia, infections, and anemia. No consensus exists on the definition of fatigue or a standardized method of assessment. The working diagnosis used for the purpose of this review was “fatigue is a subjective feeling of tiredness, weakness or lack of energy” (Radbruch et al., 2008, p. 15).

In the context of palliative and advanced disease, fatigue can be viewed as an inevitable characteristic of the last

phase of life. However, several pharmacologic treatments have been studied in an attempt to reduce the severity of the symptom and thereby improve the overall quality of life. Knowledge of effective medical treatments will be of particular interest to nurses who care for patients who frequently experience debilitating fatigue.

## Characteristics of the Evidence

The review examined 22 RCTs of 11 medications used for the treatment of fatigue in people suffering from advanced disease of some kind, where the primary outcome was fatigue. Participants could be adults and of both genders, with incurable diseases such as advanced cancer, HIV/AIDS, lung and cardiac failure, or multiple sclerosis (MS). Interventions of any dose or frequency duration could be included, such as psychostimulants (amphetamines, modafinil, methylphenidate, pemoline), amantadine, corticosteroids (dexamethasone, prednisone), donepezil, and antidepressants (selective serotonin reuptake inhibitors). Megestrol was excluded because it has been included in a previous review for the treatment of cachexia. Interventions could be compared to no treatment, alternative treatment, or placebo. No mention of minimum follow-up time was required.

The review included 1,632 patients diagnosed with MS, HIV, hypergonadism, cancer of different origins, post-polio, or

chronic obstructive pulmonary disease (COPD). The drugs included in the review were amantadine (n = 6), pemoline (n = 3), methylphenidate (n = 3), dexamphetamine (n = 2), paroxetine (n = 2), acetyl-L-carnitine (n = 2), testosterone or dehydroepiandrosterone (n = 2), fluoxetine (n = 1), donepezil (n = 1), modafinil (n = 2), and acetylsalicylic acid (n = 1).

A wide range of outcome measures were used across studies: single-item scales, validated instruments (e.g., Clinical Global Impression Scale, Modified Fatigue Impact Scale, Chalder Fatigue Scale, Piper Fatigue Scale, Fatigue Severity Scale, Fatigue Symptom Checklist, Functional Assessment of Chronic Illness Therapy–Fatigue), patient or caregiver reports of fatigue, improvement of fatigue, asthenia, weakness, treatment-related burden, tiredness, and exhaustion. Seventeen trials had fewer than 100 participants, and sample sizes ranged from 10–479. All studies reviewed were RCTs, yet some did not include details of blinding procedures, so bias risk is inconclusive. The main threats were small sample sizes and heterogeneity of measurement instruments and health conditions.

## Summary of Key Evidence

- For MS, the evidence was weak and inconclusive regarding efficacy for amantadine, pemoline, and modafinil compared to placebo. Results from limited meta-analyses are as follows.

Marilyn Kirshbaum, RN, BSc, MSc, PhD, DipAdultOnc, FHEA, is a reader in nursing at the University of Huddersfield in the United Kingdom and a member of the Cochrane Nursing Care Field.

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