Pharmacologic Treatments for Fatigue Associated With Palliative Care

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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).

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 (amphetamine, 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.