

Journal Club

Phase III, Randomized, Double-blind, Placebo controlled study of long acting methylphenidate for cancer related fatigue: North Central Cancer Treatment Group and Mayo Clinic.

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Reference: Journal of Clinical Oncology – published online in advance of print, Authors: Amanda Morask, Amit Sood, Shaker Dakhil et al

Abstract:

Fatigue is one of the most common symptoms experienced by patients with cancer. This trial was developed to evaluate the efficacy of long-acting methylphenidate for improving cancer-related fatigue and to assess its toxicity. In total, 148 patients were enrolled. In the end, there was no evidence that methylphenidate, as compared with placebo, improved the primary end point of cancer-related fatigue in this patient population. Comparisons of secondary end points, including clinically significant changes in quality-of-life variables and cancer-related fatigue change from baseline, were similarly negative. However, a subset analysis suggested that patients with more severe fatigue and/or with more advanced disease did have some fatigue improvement with methylphenidate (eg, in patients with stage III or IV disease, the mean improvement in usual fatigue was 19.7 with methylphenidate v 2.1 with placebo; $P = .02$). There was a significant difference in self-reported toxicities (SED), with increased levels of nervousness and appetite loss in the methylphenidate arm.

Method: Patients were stratified according to stage of disease (0-IV), baseline fatigue score (4-7 v 8-10), and concurrent treatment. Adults with cancer were randomly assigned in a double-blinded manner to receive methylphenidate (target dose, 54 mg/d) or placebo for 4 weeks. The Brief Fatigue Inventory was the primary outcome measure, while secondary outcome measures included a Symptom Experience Diary (SED), the Short Form-36 (SF-36) Vitality Subscale, a linear analog self-assessment, the Pittsburgh Sleep Quality Index, and the Subject Global Impression of Change

Inclusion/Exclusion Criteria: Patients were included if they have a history of cancer related fatigue with severity of 4/10 (on 0-10 numerical scale) and duration of one month, at least. Other causes for fatigue such as hypothyroidism, insomnia, uncontrolled pain or anemia were grounds for exclusion from the study. Selected patients also were estimated to have a life expectancy of at least 6 months.

Primary Outcome measure: Brief fatigue inventory scores.

Secondary Outcome measure: weekly short form 36 vitality subscale, Pittsburgh sleep quality index and the subject global impression of change.

Conclusion: This clinical trial was unable to support the primary prestudy hypothesis that the chosen long-acting methylphenidate product would decrease cancer-related fatigue.

Study Strengths:

The sample size was large for this type of population.

Varied range of cancer types, stages and equal proportions of male and female participants were among the strength of this study.

Double blind, RCT

Secondary analysis based on disease stage helps to tease out specific groups which could possibly benefit from methylphenidate therapy.

Study Weaknesses:

74 patients allocated to each group but only 62 (treatment arm) and 63 (placebo arm) completed the study.

High rate of side effects in treatment group

Relevance to Palliative Care/ TCPU: This study had a majority of patients with later trajectory of the disease similar to our population of patients. Fatigue is a very common symptom in our patient population, and often recommended treatments (such as exercise) are not feasible for this population.

There is conflicting evidence from recent studies about the use of methylphenidate for cancer related fatigue. Overall there is a fair bit of evidence to support its use in later stage cancer patients with severe fatigue. Earlier stage disease does not seem to respond as well.