

Journal Watch

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Full Reference: Bruera E, Valero V, Driver L, Shen L, Willey J, Zhang T, Palmer JL. Patient-Controlled Methylphenidate for Cancer Fatigue: A Double-Blind, Randomized, Placebo-Controlled Trial. *J Clin Oncol* 2006; 24(13): 2073-78.

Abstract:

Purpose: To evaluate the effectiveness of patient-controlled methylphenidate as compared with placebo in cancer patients with fatigue, as measured by the Functional Assessment for Chronic Illness Therapy-Fatigue (FACIT-F).

Patients and Methods: Patients with a fatigue score of at least 4 on a scale of 0 to 10 (0 = no fatigue, 10 = worst possible fatigue) and hemoglobin level of at least 10 g/dL were included. Patients were randomly assigned to receive 5 mg methylphenidate or placebo every 2 hours as needed (maximum of four capsules a day), for 7 days. Patients completed a daily diary including study drug record and fatigue intensity. A research nurse telephoned patients daily to assess toxicity and fatigue level. All patients were offered open-label methylphenidate for 4 weeks. FACIT-F and the Edmonton Symptom Assessment System (ESAS) were assessed at baseline, and days 8, 15 and 36. The FACIT-F fatigue subscore on day 8 was considered the primary end point.

Results: Of 112 patients randomly assigned, 52 patients in the methylphenidate and 53 in the placebo group were assessable for analysis. Fatigue intensity improved significantly on day 8 in both the methylphenidate and placebo groups. However, there was no significant difference in fatigue improvement by FACIT-F ($P = .31$) or ESAS ($P = .14$) between groups. In open-label phase, fatigue intensity maintained low as compared with baseline. No significant toxicities were observed.

Conclusion: Both methylphenidate and placebo resulted in significant symptom improvement. Methylphenidate was not significantly superior to placebo after 1 week of treatment. Longer study duration is justified. The role of daily telephone calls from a research nurse should be explored as a palliative care intervention.

Comments

Strengths/uniqueness: This is the first double-blinded randomized placebo-controlled trial studying the effect of methylphenidate on cancer fatigue. The authors used validated instruments for assessment of fatigue, including the Edmonton Symptom Assessment System (ESAS).

Weaknesses: The sample size was small and the analysis was not per intention to treat. Duration of the study was short (7 days). Low dosages of methylphenidate may have contributed to fewer adverse events and reduced effect on outcome. The study design may have contributed to the elevated placebo effect as noted by the authors.

Relevance to Palliative Care: this study highlights the need for further studies on the efficacy of methylphenidate in the treatment of cancer-related fatigue. Current evidence suggests that although methylphenidate significantly improves fatigue symptoms, there is no significant benefit of methylphenidate over placebo. However, future studies attempting to eliminate the placebo effect and using higher dosages of methylphenidate over longer periods are necessary to better assess the role of methylphenidate.