

Palliative Care Journal Watch

Multicentre, double-blind, randomised placebo-controlled clinical trial on the efficacy of methylphenidate on depressive symptoms in advanced cancer patients

Centeno, Carlos et al. *British Medical Journal* June 2012

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Abstract

Introduction: Methylphenidate is a psychostimulant that has been used to relieve depressive symptoms in advanced cancer patients. No studies compare its efficacy against placebo in this group of patients.

Objective: To explore the efficacy of methylphenidate compared with placebo in the relief of depressive symptoms in advanced cancer patients.

Material and methods: A multicentre, double-blind, randomised placebo-controlled clinical trial was undertaken comparing the efficacy of methylphenidate and placebo in depressive symptoms. Advanced stage cancer patients were eligible if they scored at least two points on the Two Question Screening Survey for depression. A reduction of at least two points on the Edmonton Symptom Assessment Scale for depression (0–10) was considered as a response.

Results: Sixty-nine patients were included (methylphenidate: n=31, placebo: n=38); median daily dose of methylphenidate was 25 mg. Fifty-eight patients (84%) who completed the first week of treatment were considered suitable for evaluation. In the intention to treat analysis, there were 14/31 (45%) responses with methylphenidate and 10/38 (26%) responses with placebo (difference: 19%; 95% CI: 4% to 39%; p=0.10). With the Hospital Anxiety and Depression Scale, 11/19 (58%) patients with methylphenidate and 10/24 (42%) with placebo improved from a score compatible with depression in the first 7 days (difference 16%; 95% CI 13% to 42%; p=0.29). The proportion of patients indicating adverse effects was similar for both cohorts (p=0.99).

Conclusion: Compared with the placebo, methylphenidate demonstrated a positive trend in the incidence of response for depressive symptoms in advanced cancer patients.

Strengths:

- First randomised, placebo-controlled RCT to look at effectiveness of methylphenidate for managing depressive symptoms in advanced cancer patients
- Used two different symptom scores/scales to assess for clinical response (ESAS and HADS).
- Study population very applicable to TPCU setting (terminally ill cancer patients)

Weaknesses:

- Small sample size of only 69 patients despite recruiting beyond 12 month period
- Limits applicability of study given exclusion criteria: excludes many sub-groups of patients including patients actively undergoing cancer treatment, patients already on antidepressants, and patients with previous history of MDE and suicide tendencies
- Average age 74 in Methylphenidate group and 70 in placebo group – can these results be generalized to all age groups or more applicable to elderly population?
- Recruitment settings somewhat unclear - article states that patients were recruited from “Home Palliative Care Units” and “Hospital Palliative Care Units”. Later on, states that some patients received care at home. What exactly is a “home palliative care unit”? Is that within home setting, a hospice? This is not entirely clear.
- All patients also received emotional support – study design did not elaborate on if and how they standardized the type of counselling provided to methylphenidate vs. placebo groups.

Relevance to Palliative Care:

This RCT was one of the first controlled studies to investigate in an area with paucity of data previously. Overall conclusion is that methylphenidate appears to be a well-tolerated medication that we could potentially consider in terminally ill patients who present with depression. But we must bear in mind that the positive trend seen in reducing depressive symptoms with Methylphenidate versus placebo was not statistically significant so one cannot make definite conclusions about the benefit of Methylphenidate from this trial alone. A larger RCT is required in this regard.