

Effects of Melatonin on Physical Fatigue and Other Symptoms in Patients With Advanced Cancer Receiving Palliative Care: A Double-Blind Placebo-Controlled Crossover Trial

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Abstract:

BACKGROUND: Patients with advanced cancer often experience fatigue and other symptoms that negatively impact their quality of life. The current trial investigated the effect of melatonin on fatigue and other symptoms in patients with advanced cancer. **METHODS:** Patients who were aged 18 years, had a histologically confirmed stage IV cancer (TNM Classification), and who reported feeling significantly tired were recruited from the palliative care unit at the study institution. The study was a double-blind, randomized, placebo-controlled crossover trial. Patients received 1 week of melatonin at a dose of 20 mg or a placebo orally each night, before crossing over and receiving the opposite treatment for 1 week. Between the 2 periods, a washout period of 2 days was implemented. Outcomes were measured using the Multidimensional Fatigue Inventory (MFI-20) and The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire. Physical fatigue from the MFI-20 was the primary outcome. The primary analysis was a complete complier analysis (ie, it included only those patients who had consumed at least 5 capsules per week and who had answered the MFI-20 on days 1, 7, 10, and 17). Sensitivity analysis using multiple imputations including all randomized patients and all patients completing the intervention were conducted. **RESULTS:** A total of 72 patients were randomized. Fifty patients completed the intervention and 44 patients were complete compliers. No significant differences between the placebo and melatonin periods were found for physical fatigue, secondary outcomes, or explorative outcomes. **CONCLUSIONS:** In the current study, oral melatonin at a dose of 20 mg was not found to improve fatigue or other symptoms in patients with advanced cancer.

Strengths:

- Double blinded RCT, with placebo crossover.
- exclusion of potential confounds such as anemia, hypercalcemia, low BP, warfarin, thyroid disease, steroids, methylphenidate, sleeping pills.
- Allocation concealment
- ITT analysis
- Validated fatigue scores

Weaknesses:

- Study power 70%
- Short treatment duration, applied to patient in terminal state of disease

Applicability:

Fatigue is a common and debilitating symptom in patients that profoundly affects quality of life. There is some evidence that melatonin levels in cancer patients may be deranged, thus it is reasonable to study whether melatonin supplementation may improve fatigue. Although this study failed to find any statistically significant difference between those receiving melatonin or placebo, the authors note that during the trial, the general condition of all patients deteriorated, and postulate that perhaps the effects of melatonin were negated by disease progression. They also end their paper by saying that perhaps patients treated in earlier stage of disease may show some response.