Melatonin modestly improves sleep efficiency in patients with neurocognitive disorders: a systematic review and meta-analysis

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Background

- In adults with neurocognitive disorders, sleep disorders are associated with an increased likelihood of institutionalization (1).
- Their caregivers are also affected by disruptions to sleep.
- Pharmacological interventions are generally discouraged, as they put this population at greater risk for falls and confusion.
- Melatonin is an alternative in common use, but the efficacy and long-term safety has yet to be established (2). Several melatonin receptor agonists (including ramelteon, prolonged-release melatonin, agomelatine and tasimelteon) also exist.

Knowledge Gaps

- New studies have emerged with melatonin receptor agonists, and new ones are under development or approval.
- Existing reviews have privileged Alzheimer and Parkinson disease at the expense of other neurocognitive disorders.
- In research on dementia caregiving, subjective caregiver burden remains unexplored quantitatively in meta-analytic research.

The goal is to synthesize RCTs of melatonin and melatonin-receptor agonists against placebo, other interventions, or usual care, for the treatment of sleep disturbances in adults with a neurocognitive disorder.

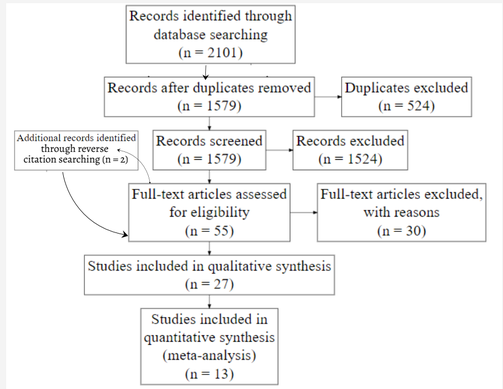
Method

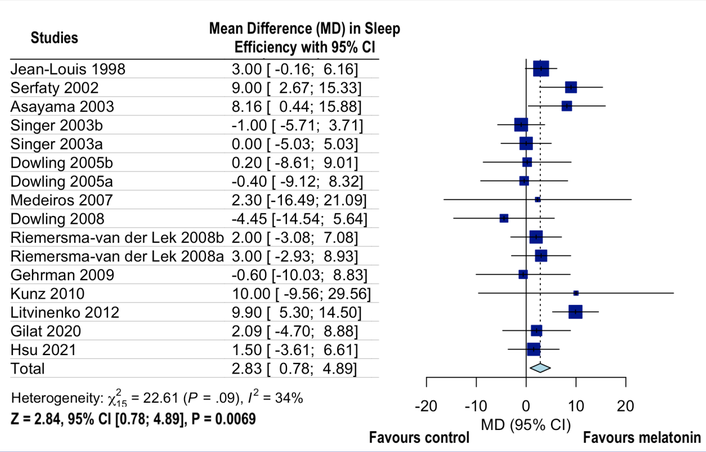
- We systematically searched for RCTs administering melatonin or melatonin receptor agonists adult participants with Alzheimer disease (AD), mild cognitive impairment (MCI), Parkinson disease (PD), Lewy body dementia (LBD), any aphasia (i.e., frontotemporal dementia and associated variants), Huntington's disease (HD), dementia due to multiple sclerosis (MS), or Creutzfeldt-Jakob disease (CJD).
- As control interventions, we accepted placebo, other medications, usual care, or no intervention.
- **In this meta-analysis, the primary outcome was sleep efficiency (SE) (percentage of total sleep time (TST) divided by time in bed).**
- The full project includes outcomes relating to patient and caregiver sleep quality, patient cognitive function, geriatric depression, and caregiver burden.
- We used the Cochrane Risk of Bias tool (RoB) and the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system to evaluate the quality of evidence.

Results

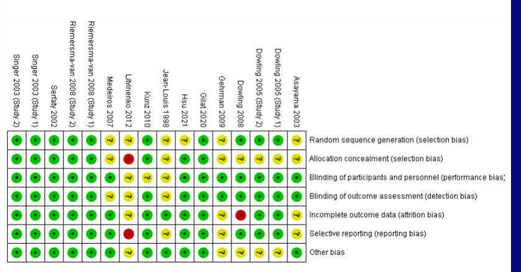
Thirteen articles (16 studies) were included. Mean differences in SE ranged from -4.45 to 10.00, with most estimates indicating a benefit to melatonin over placebo. The estimated average mean difference was 2.85 (95% CI: 0.88 to 4.81, Z = 2.84, p = 0.006).

PRISMA Flow Diagram

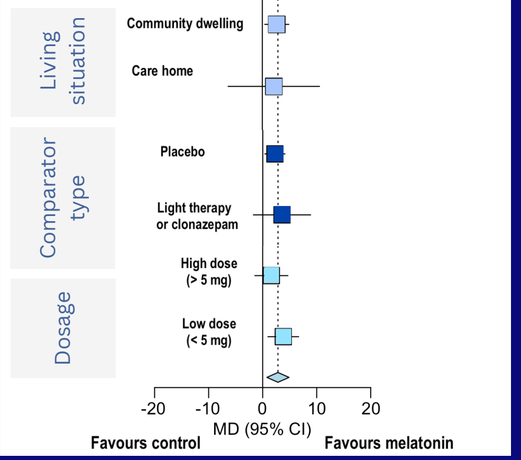




Risk of Bias (RoB) Assessment



Subgroup analyses



Discussion

Compared with placebo, bright light treatment, or clonazepam, **SE** significantly improved with melatonin administration.

In subgroup analyses, only low doses of melatonin (< 5 mg) yielded improvement to **SE** (MD = 3.81, 95% CI: 1.13 to 6.49, p = 0.005, I2 = 34%), and melatonin improved SE in patients with mild cognitive impairment, Parkinson's Disease, or multiple sclerosis (MD = 3.27, 95% CI: 0.11 to 6.43, p = 0.04, I2 = 41%), but not Alzheimer's disease.

We found the overall quality of evidence to be moderate according to GRADE. We conclude that melatonin may modestly improve sleep quality in patients with neurocognitive disorders by improving sleep efficiency—on average adding an extra 15 minutes of sleep to an 8-hour night—which may be clinically significant to patients and those who care for them.

References

1. Pollak CP. et al. Sleep problems in the community elderly as predictors of death and nursing home placement. J Community Health. 1990 Apr;15(2):123–35.
2. Besag FMC. et al. Adverse Events Associated with Melatonin for the Treatment of Primary or Secondary Sleep Disorders: A Systematic Review. CNS Drugs. 2019 Dec;33(12):1167–86.

Protocol on PROSPERO

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