Melatonin in elderly patients with insomnia: a systematic review
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Authors' objectives
To determine the efficacy of melatonin in elderly insomniacs.

Searching
The Cochrane Controlled Trials Register and MEDLINE were searched from 1990 to 2000 using the terms 'melatonin', 'geriatrics' and '(frail)-elderly'. The references from identified articles were also reviewed.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) and meta-analyses were eligible for inclusion in the review. All the included RCTs were of a crossover design.

Specific interventions included in the review
Treatments with melatonin were eligible. The doses of melatonin ranged from 0.5 to 6 mg, with most doses given in a single dose 30 to 120 minutes before bedtime. Slow-release preparations and transbuccal preparations were included. The duration of treatment ranged from 4 days to 2 months.

Participants included in the review
Elderly insomniacs were eligible. The mean age of patients across the studies ranged from 65 to 79 years. The included patients were a highly selected group; the inclusion criteria varied considerably between studies, ranging from elderly people with a variety of chronic diseases to elderly patients without any co-morbidity, who fulfilled certain sleep disorder criteria.

Outcomes assessed in the review
The inclusion criteria were not defined a priori in terms of the outcomes. The following measures of sleep quality were assessed:

- sleep onset latency, i.e. the time elapsed between the participant's self-selected sleep time and sleep onset; wake after sleep onset, i.e. a summation of all the time awake during the sleep period; sleep efficiency, i.e. the percentage of time the participant was in bed following sleep onset, which was spent asleep; and total sleep time, i.e. the amount of sleep between sleep onset and sleep termination.

Actigraphy and polysomnography (consisting of electroencephalography, electromyogram, and electro-oculography) were used to measure the objective outcomes. Subjective sleep quality was assessed using visual analogue scales and sleep diaries.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the reviewers performed the selection.

Assessment of study quality
The studies were restricted to RCTs but no formal validity assessment was undertaken.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the reviewers performed the data extraction.
The following information were tabulated: author and year of publication; sample size; the mean age of the participants; details of the melatonin regimen; the duration of treatment; the methods used to assess the outcome; and the results.

**Methods of synthesis**

How were the studies combined?
A narrative synthesis was undertaken.

How were differences between studies investigated?
Differences between the studies were discussed in the text of the review in relation to the recruitment of participants, the correlation between low melatonin and sleep quality, clinical efficacy, and side-effects.

**Results of the review**

Six crossover RCTs (95 patients) were included in the review.

Methodological flaws in the individual studies included the following: concerns about the technical measurements (use of actigraphy in patients lying silently in bed without being asleep); a lack of control for lighting conditions; and the small sample size (range: 10 to 26 patients). Since, the participants were generally relatively fit elderly patients, the results may not generalise to frail geriatric patients.

Objective sleep quality.

Five of the 6 RCTs reported some positive effects. Sleep latency decreased in 4 studies. Sleep efficiency increased in 3 studies. Wake time during sleep decreased in 2 of the RCTs that assessed this outcome.

Subjective sleep quality.

Melatonin did not improve subjective sleep measures in the 2 studies that assessed this outcome.

Adverse reactions.

None of the studies reported an increase in adverse reactions with melatonin when compared with placebo. Only one RCT with 21 patients actually reported on adverse effects; this found no serious adverse effects.

**Authors' conclusions**

There was sufficient evidence that low doses of melatonin improved initial sleep quality in selected elderly insomniacs. However, there was insufficient evidence to warrant regular prescription of melatonin in elderly insomniacs, especially in the case of co-morbidity.

**CRD commentary**

The aims were stated and the inclusion criteria were defined in terms of the study design, intervention and participants. The inclusion criteria were not defined a priori in terms of the outcome, and no predetermined criteria were used to define insomnia. Two relevant literature sources were searched but it was not stated whether any language restrictions were applied. In addition, the methods used to select the studies were not described. The lack of an attempt to locate unpublished studies raises the possibility of publication bias. The eligible studies were restricted to RCTs but no other aspect of study quality was formally assessed, including quality issues relevant to crossover studies. The reader cannot tell how reliable the findings from the included studies are. Some relevant data were tabulated, but the methods used to extract the data were not described. A narrative synthesis was appropriate given the small sample size and differences between populations, but the results were not discussed in relation to study quality. The authors’ conclusion regarding the benefit of melatonin in selected elderly patients appears unduly confident given the above limitations, the short duration of most studies, and the small sample size of the included studies.
Implications of the review for practice and research

Practice: The authors state that further research is required before widespread use of melatonin in geriatric populations can be advocated.

Research: The authors state that larger RCTs, with less strict inclusion criteria, are necessary to yield evidence of effectiveness in geriatric populations. In particular, there is a need for large trials in which a combination of circadian rhythm regulators is tested. The authors also consider it would be worthwhile to investigate whether melatonin could have a role in reducing the amount of benzodiazepines used by elderly people.

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