Comparative meta-analysis of pharmacotherapy and behavior therapy for persistent insomnia

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Authors' objectives
To conduct a quantitative review of the literature to compare the short-term efficacy of pharmacotherapy and behavioural therapy in primary insomnia.

Searching
MEDLINE and PsycINFO were searched from 1966 to 2000 for publications in the English language, using the keywords ‘insomnia’ and ‘treatment’. Published studies were also identified from the bibliographies provided by the authors of two meta-analyses of insomnia (see Other Publications of Related Interest nos.1-2).

Study selection
Study designs of evaluations included in the review
Only studies in which within-subject measurements were obtained before and after treatment were included in the review.

Specific interventions included in the review
Studies of treatments considered most effective for insomnia were included in the review. These were benzodiazepines or benzodiazepine receptor agonists (e.g. zolpidem, zaleplon or zopiclone), and stimulus control or sleep restriction therapies.

Seven pharmacotherapies were presented; the mean length of treatment was approximately 2 weeks (standard deviation, SD=2). Flurazepam was used in three groups; quazepam, triazolam and zolpidem were each used in two groups; and lorazepam, midazolam and zopiclone were each used in one group.

Twelve of the behavioural studies included stimulus control therapy with or without sleep restriction; two studies used sleep restriction alone; and four combined stimulus control and sleep restriction. The mean number of behaviour therapy sessions was five (SD=2) over a mean period of approximately 5 weeks (SD=2).

Participants included in the review
Patients with primary insomnia, with a duration of at least one month and defined consistently with current definitions. Studies were excluded if they included patients with psychiatric and general medical conditions, or patients who were not withdrawn from hypnotic medications before entering the trial. Most studies involved multiple groups and included both sexes; 55% of the 445 participants in studies that reported gender were female. The mean age of the participants was 47.2 years (SD=11). The majority of the studies included participants who had diagnoses of mixed insomnia (trouble initiating and maintaining sleep) of at least 3 months’ duration.

Outcomes assessed in the review
Only studies that reported sleep continuity measures in minutes and were based on mean values before and after treatment, derived from prospective self-report sleep diaries, were included in the review. Three sleep continuity variables were evaluated: sleep latency, total sleep time and the number of awakenings. Additional information on the outcome of the two treatments on subjective sleep quality and wake time after sleep onset was presented, but this was taken from the literature; very few of the pharmacological studies included a measure of wake time after sleep onset.

How were decisions on the relevance of primary studies made?
All studies were reviewed by two of the authors to determine whether the inclusion and exclusion criteria were satisfied. However, it was not stated whether the reviewers were blinded to the source or results.
Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
All studies were coded by two of the authors, while a third author resolved any discrepancies between the ratings of each study. All values entered into the final database were verified by a research assistant. It was not stated whether the data extraction was performed blind. The studies were coded to extract major clinical variables, including demographics, the type and duration of treatments and the outcome variables.

Methods of synthesis
How were the studies combined?
The effect size (ES) was calculated for each individual study. These were then pooled, weighting the studies by sample size, to give an overall weighted ES for each outcome measure. Publication bias was not assessed.

How were differences between studies investigated?
Heterogeneity between the primary studies was assessed for the participant characteristics of age, gender and pre-treatment means of the five sleep outcome measures, and duration of treatment.

Results of the review
Twenty-one studies with a total of 470 participants satisfied the inclusion criteria: 7 studies (203 participants) evaluated only pharmacological therapies, 13 studies (232 participants) evaluated only behavioural interventions, and one study (35 participants) compared pharmacotherapy with behavioural therapy. The studies spanned the years from 1979 to 1999.

There were no differences in the patients' age, gender and pre-treatment means for sleep latency, number of awakenings, wake time after sleep onset, total sleep time and subjective sleep quality between the pharmacotherapy and behavioural treatment (p>0.05). As expected, the duration of behavioural treatment was significantly longer than pharmacotherapy (t=-4.38, d.f.=26.49, p<0.001). These comparisons indicated that the two treatment populations were similar.

Sleep latency was reduced by 30% with the pharmacological treatment, compared with 43% for the behavioural interventions (95% confidence interval, CI, for the difference between ESs: 0.17, 1.04). Both interventions reduced the number of awakenings each night by approximately one (95% CI for the difference between ESs: -1.24, 1.5). Wake time after sleep onset was reduced by 46% with pharmacotherapy and by 56% with behaviour therapy. Total sleep time was increased by 12% and 6% with pharmacotherapy and behaviour therapy, respectively (95% CI for the difference between ESs: -0.25, 1.01). Sleep quality was improved by 20% with pharmacotherapy and by 28% with behaviour therapy (95% CI for the difference between ESs: -1.70, 1.22). The mean ES for all five outcome variables was 0.87 for pharmacotherapy and 0.96 for behaviour therapy. Independent t-tests for unequal variances were calculated for the five individual sleep variables, in order to compare the weighted ESs for pharmacotherapy and behavioural therapy. Levine's test indicated that behavioural therapy had greater variability in weighted ESs for sleep latency than pharmacological studies (F=8.05, d.f.=20.6, p=0.01).

Authors' conclusions
Overall, behaviour therapy and pharmacotherapy produced similar short-term treatment outcomes in primary insomnia.

CRD commentary
The review question and the inclusion criteria were clearly stated. The search strategy was clear but limited: two databases and the bibliographies of two earlier meta-analyses were searched for English language publications. Relevant studies may, therefore, have been missed by this narrow search strategy, allowing the introduction of
selection bias. There was no attempt to identify unpublished or grey literature, and publication bias was not assessed.

The validity of the primary studies does not appear to have been assessed, which may have implications for the reliability of the findings of the review. The authors identified the following limitations of their review: patients undergoing behavioural interventions have more contact with their clinicians, and this greater access to clinician support may affect the efficacy of the intervention; patients were self-selected, therefore, it cannot be concluded that the treatments yield comparable gains across all patients; and subjective measures of outcome were used.

The tables of the primary data were adequate, and the synthesis of the data appears to have been appropriate. Heterogeneity was assessed for participant characteristics and treatment duration. The two treatment populations were similar; there were no differences in the participants' gender, age and pre-treatment means for sleep latency, number of awakenings, wake time after sleep onset, total sleep time, and subjective sleep quality between the groups (p>0.05).

The authors' conclusions should be interpreted with some caution given the potential for selection bias and the lack of a validity assessment.

**Implications of the review for practice and research**

**Practice:** The authors state that the present study demonstrates that behaviour therapy for persistent primary insomnia is as effective as pharmacotherapy in the short-term. In addition, that pharmacotherapies may be selected when immediate symptom reduction is the primary consideration, and behavioural treatment may be indicated when pharmacotherapies are contraindicated (e.g. because of potential drug interactions or a history of substance abuse). The authors also state that the difference in treatment cost is likely to be a major consideration since even the most expensive sedative hypnotics, in the short run, do not rival the costs of behaviour therapy. Finally, they state that in the instances when patients and clinicians do not wish to use hypnotics to treat persistent insomnia, practitioners should strongly consider referring patients for behaviour therapy, and that some should consider training in behavioural therapy.

**Research:** The authors state that more research is required before an overall cost-benefit analysis can be conducted.

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