Continuous positive airway pressure therapy for treating sleepiness in a diverse population with obstructive sleep apnea: results of a meta-analysis


CRD summary
This review of continuous positive airway pressure (CPAP) to treat sleepiness in adults with obstructive sleep apnoea was limited by the diverse nature of the available trials. The review findings indicate that CPAP appears effective in patients with severe sleep apnoea and significant sleepiness, but data are less reliable for less severely affected patients; in these patients CPAP is probably not effective.

Authors' objectives
To evaluate the use of continuous positive airway pressure (CPAP) in reducing sleepiness in adults with obstructive sleep apnoea.

Searching
MEDLINE (from 1966 to October 2001) and the Cochrane CENTRAL Register were searched; the search terms were reported. In addition, the reference lists of retrieved articles, previous meta-analyses and reviews were checked, and experts in the field were contacted. Only full-length original articles were included. The authors did not state whether any language restrictions were applied.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for the review. Both parallel-group and crossover design trials were included in the review. Across the studies, the follow-up was 2.2 to 24 weeks.

Specific interventions included in the review
Studies that compared CPAP therapy of at least one week with either no therapy or minimal therapy, or a true placebo, were eligible for the review. Studies in which CPAP devices were compared with oral appliances and auto-titrating devices were excluded. The duration of CPAP use in the included studies varied from a mean of 2.8 to 5.9 hours (not specified whether this was per day). The comparator treatments were conservative measures (e.g. weight loss, abstinence from alcohol and sedatives), placebo tablet or sham CPAP.

Participants included in the review
Studies of adults with obstructive sleep apnoea were eligible for the review. In all the included studies, the majority of participants were male (52 to 100%) and the mean age ranged from 44 to 54 years.

Outcomes assessed in the review
Studies that included a measure of sleepiness were eligible for inclusion. The subjective measure of sleepiness was the Epworth Sleepiness Scale (ESS) score. Objective measures of sleepiness were the Multiple Sleep Latency Test (MSLT) score and the Maintenance of Wakefulness Test (MWT) score. The measure of treatment effect in the review was the difference between the ESS, MSLT or MWT scores after CPAP and control.

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

Assessment of study quality
The included studies were assessed using the Jadad scale. Two reviewers independently assessed the quality of the studies.
**Data extraction**
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. The mean and standard deviation for the difference between the ESS, MSLT or MWT scores after CPAP and control were extracted.

**Methods of synthesis**
How were the studies combined?
The results of the primary studies were combined in a meta-analysis. Pooled estimates of effect were calculated using a random-effects (DerSimonian and Laird) model. The data were presented as forest plots. In the meta-analysis, the objective measures of sleepiness (MSLT and MWT) were combined. Additional analyses in which these were considered separately were conducted. Planned subgroup analyses were by study country, nature of control and study quality. Publication bias was investigated using funnel plots.

How were differences between studies investigated?
Statistical heterogeneity was assessed using the Q statistic (chi-squared distribution), while random-effects regression modelling was used to explore sources of heterogeneity. The significance of variables in explaining heterogeneity was investigated by individually incorporating them into a single covariate model. Predefined variables of interest were gender ratio, age, body mass index, apnoea-hypopnoea index, baseline ESS score, length of follow-up and CPAP compliance rate.

**Results of the review**
Twelve trials (all RCTs; n=745) were included in the review; 5 were crossover trials.

Effect on subjective measures (11 trials).

The pooled estimate of effect indicated a statistically significant beneficial effect of CPAP on sleepiness, as assessed by the reduction in ESS scores (weighted mean difference 2.87, 95% confidence interval: 1.48, 4.25). However, this analysis was subject to significant statistical heterogeneity and the pooled result cannot be considered reliable. Subgroup analyses found that heterogeneity could not be explained by differences in age, gender ratio, body mass index, study location, the mean number of hours of CPAP per study, or the nature of the control. When only the moderate- or good-quality trials were pooled the result was not statistically significant, but the level of statistical heterogeneity was not reported.

When trials of participants with severe sleep apnoea and significant sleepiness (6 trials) were analysed separately from those less severely affected (5 trials), the pooled reduction in mean ESS score was 4.75 (95% CI: 2.97, 6.53; statistically significant). This was different from the results from trials of participants less severely affected (5 trials; 1.10, 95% CI: 0.13, 2.32; not significant). The authors did not state if these two subanalyses were subject to statistical heterogeneity or not.

Effect on objective measures (8 trials).

The pooled estimate of effect indicated a statistically significant beneficial effect of CPAP on sleepiness, as assessed by the MSLT or MWT scores (weighted mean difference 0.93, 95% CI: 0.10, 1.76). This analysis was subject to some statistical heterogeneity, although this was not significant. Subgroup analyses of studies evaluating MSLT or MWT studies or by study quality did not alter the result.

Funnel plots did not indicate the presence of publication bias.

**Authors’ conclusions**
CPAP improves daytime sleepiness in patients with obstructive sleep apnoea. Patients with more severe apnoea and sleepiness benefit the most.
CRD commentary
This review addressed a well-defined question with clear inclusion criteria. The literature search, accessing a single electronic database, was rather limited. Although the authors’ assessment did not indicate publication bias, it was quite possible that studies were missed. The authors failed to report how the review was conducted, so it was impossible to know what efforts were made to minimise reviewer bias. The review was well reported in terms of the details of the primary studies and the quality assessment.

Given the nature of the primary studies, the use of a meta-analysis would appear appropriate. However, given the high degree of heterogeneity identified in the meta-analysis, the overall pooled estimate for ESS is unlikely to be reliable. This was not accurately reflected in the authors’ conclusions. The main result of the review appears to be that CPAP is effective in patients with severe sleep apnoea and significant sleepiness, and is much less effective, if effective at all, in less severely affected patients. This result, however, might also have been subject to statistical heterogeneity and may not be reliable.

Implications of the review for practice and research
The authors did not state any implications for practice or further research.

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Other publications of related interest
This additional published commentary may also be of interest. Rees PJ. Review: continuous positive airway pressure therapy improves subjective and objective sleepiness in obstructive sleep apnoea. Evid Based Med 2003;8:112.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.