The impact of continuous positive airway pressure on blood pressure in patients with obstructive sleep apnea syndrome: evidence from a meta-analysis of placebo-controlled randomized trials


CRD summary
This review evaluated the effects of continuous positive airway pressure (CPAP) on ambulatory blood-pressure in patients with obstructive sleep apnoea syndrome. CPAP was associated with lower 24-hour mean arterial blood-pressure especially in patients with severe forms of the disease or in those using the CPAP device more effectively at night. This review was well-conducted and its conclusions appear reliable.

Authors' objectives
To evaluate the effects of continuous positive airway pressure (CPAP) on ambulatory blood-pressure in patients with obstructive sleep apnoea syndrome (OSAS).

Searching
MEDLINE, EMBASE, and the Cochrane Controlled Trials Register were searched up to August 2006; the search terms were reported. No language restrictions were applied. The bibliographies of all retrieved articles were checked to identify additional studies.

Study selection
Study designs of evaluations included in the review
Crossover or parallel-design randomised controlled trials (RCTs) were eligible for inclusion.

Specific interventions included in the review
Studies evaluating CPAP versus placebo in patients with OSAS were eligible for inclusion. Effective nightly use of CPAP varied from 3.3 hours to up to 6.7 hours per night. Patients in the placebo group received either sham CPAP or oral tablets.

Participants included in the review
To be eligible, studies had to include patients with OSAS. The mean age ranged from 45.5 to 57 years, the mean body mass index (BMI) from 29 to 36, and the apnoea-hypopnoea index from 12.9 to 66.1. The percentage of patients with hypertension in the included studies varied between 0 and 100. Drop-out rates ranged from 0 to 53%.

Outcomes assessed in the review
Studies were eligible for inclusion if they reported 24-hour ambulatory mean blood-pressure (MBP). Secondary outcomes were changes in 24-hour ambulatory systolic blood-pressure (SBP), 24-hour diastolic blood-pressure (DBP), and night-time and daytime MBP, SBP and DBP.

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 authors did not state how the papers were assessed for validity, or how many reviewers performed the validity assessment.

Data extraction
Two independent reviewers performed the data extraction, with any disagreements being resolved by consensus. For parallel-design RCTs, data were extracted to compute the mean difference of the change from baseline to follow-up between CPAP and placebo. For crossover trials, the mean difference between the ends of the CPAP and placebo periods was calculated.

**Methods of synthesis**

**How were the studies combined?**

Mean differences and the corresponding 95% confidence intervals (CIs) were calculated using a fixed-effect model and the DerSimonian and Laird random-effects model. Publication bias was visually explored by a funnel plot and tested by the Begg and Mazumdar test and Egger's test.

**How were differences between studies investigated?**

Statistical heterogeneity was visually evaluated by a forest plot and formally tested by the Cochran Q test and the I-squared statistic. I-squared values of less than 25% indicated low heterogeneity, values between 25% and 50% moderate heterogeneity, and above 50% high heterogeneity.

The severity of OSAS, age, gender, BMI, the percentage of hypertensive patients, the arousal index, the degree of sleep hypoxemia, the Epworth Sleepiness Scale, the hours of nightly CPAP use, and the total study duration were evaluated as potential sources of heterogeneity by random-effects meta-regression analyses. The effect of study design or type of control treatment on the overall estimate was evaluated. One-way sensitivity analysis was performed to assess the effect of individual studies on the pooled effect estimate.

**Results of the review**

Twelve RCTs (n=572) were included.

The use of CPAP was associated with a significantly lower 24-hour MBP (1.69 mmHg, 95% CI: -2.69, -0.69) as compared with the control treatment. There was no statistical heterogeneity for this outcome (I-squared 41%; p=0.07). The lowest 24-hour MBP values with CPAP were found among patients with a severe degrees of OSAS (2 trials, n=65).

Compared with placebo, CPAP was associated with a statistically significant reduction of all secondary outcomes, apart from night-time DBP. There was evidence of statistical heterogeneity for daytime MBP (I-squared 54%, p=0.02).

Meta-regression analyses showed a significant inverse relationship between the 24-hour MBP and the apnoea-hypopnoea index, the arousal index and the effective nightly use of CPAP. None of the other pre-specified variables modified the effect of CPAP on the primary outcome. The pooled results remained unchanged on sensitivity analyses. The funnel plot was not perfectly symmetrical, but formal statistical analysis by the Begg and Mazumdar test and Egger's test seemed to exclude publication bias.

**Authors' conclusions**

In patients with OSAS, the use of CPAP is associated with a significant reduction in the 24-hour ambulatory MBP, and is apparently more effective among patients with a more severe degree of the disease and in those who use the CPAP device more effectively at night.
authors stated that there was no significant statistical heterogeneity for the main outcomes; this supports the authors’ decision to pool the studies in a meta-analysis. The authors’ conclusions appear supported by the data presented and are likely to be reliable.

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

Research: The authors stated that a meta-analysis of individual patient data is needed to evaluate the relevance of OSAS duration before inclusion, and history of hypertension, in relation to the effects of CPAP on ambulatory blood-pressure.

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