Continuous positive airway pressure devices for the treatment of obstructive sleep apnoea-hypopnoea syndrome: a systematic review and economic analysis


CRD summary
This well-conducted review concluded that continuous positive airway pressure was an effective and cost-effective treatment for obstructive apnoea–hypopnoea syndrome compared with conservative/usual care and placebo in populations with moderate to severe daytime sleepiness. There may also be benefits in mild disease. This conclusion is likely to be reliable.

Authors' objectives
To determine the clinical effectiveness, safety and cost-effectiveness of continuous positive airway pressure devices for the treatment of obstructive apnoea–hypopnoea syndrome.

Searching
MEDLINE, EMBASE, CINAHL, Cochrane Library, Science Citation Index, ISI Proceedings Science & Technology, Zetoc Conferences, SIGLE, NHS EED, DARE, Index to Theses, Health Economic Evaluations Database, EconLit, EconPapers, Health Technology Assessment (HTA), Scottish Intercollegiate Guidelines Network (SIGN), National Guideline Clearinghouse, National Research Register, Health Services/Technology Assessment Text (HSTAT), Turning Research Into Practice database (trip), Health Evidence Bulletins Wales, Clinical Evidence and the National Library for Health (NLH) Guidelines Finder were searched without language restrictions.; Search dates (most recent January 2007) and strategy were reported. The contents pages of the nine relevant journals, conference proceedings of three societies and industry submissions were also searched.

Study selection
Randomised controlled trials (RCTs) in adults (16 years or older) with appropriately confirmed diagnosis predominantly of obstructive sleep apnoea (of any severity), were eligible for inclusion. Trials were required to compare fixed or autotitrating continuous positive airway pressure therapy to best supportive/usual care, placebo or dental devices. Trials had to be of parallel or crossover design.

Primary outcomes were: subjective sleepiness as assessed by the Epworth Sleepiness Scale (ESS); objective sleepiness as assessed by the Multiple Sleep Latency Test (MSLT), Maintenance of Wakefulness Test (MWT) or Osler test. A range of secondary outcomes were also assessed. Trials exclusively of participants with central nervous system dysfunction or heart failure were excluded.

The definitions used to select participants for inclusion in trials varied greatly; most had moderate or severe disease. Where reported, mean age ranged from 44 to 58 years, most participants were male, and where reported, most studies reported a mean body mass index of 30 or above. Treatment duration ranged from one to 52 weeks.

Studies were screened independently by two reviewers. Disagreements were resolved by consensus or recourse to a third reviewer.

Assessment of study quality
Study quality was assessed in terms of randomisation, allocation concealment, comparability at baseline, blinding, study design, comparator used, participants included, the analyses used and adjustments made, and loss to follow-up.

Study validity was assessed by one reviewer and checked by another. Discrepancies were resolved by consensus or referral to a third reviewer.

Data extraction
The mean difference and 95% confidence intervals were calculated for each outcome. Data for trials included in a previous review were extracted from the review (see Other Publications of Related Interest, Giles et al). Paired data
were extracted from crossover trials where available; if the measure of variance was not reported, the standard error was calculated from the t-statistic, p-value or confidence interval. Authors were contacted for additional data or to clarify uncertainties regarding data.

Data were extracted by one reviewer and checked by another. Disagreements were resolved by consensus or recourse to a third reviewer.

**Methods of synthesis**
Trials were combined in a narrative synthesis. Differences between trials were discussed in the text and trial details were tabulated. Where pooling was possible, the generic inverse variance method was used to calculate the mean difference and 95% confidence intervals where analyses contained crossover trials. Parallel data were transformed by calculating the standard error for the mean difference from the 95% confidence interval. When only parallel trials were pooled the weighted mean difference and 95% confidence intervals were calculated. All analyses presented were from a random-effects model. Heterogeneity was assessed using the I² statistic. Trials using placebo or best supportive/usual care as a comparator were pooled separately from trials using dental devices. Subgroup analyses were planned to investigate disease severity, daytime sleepiness, trial design, type of placebo and trial quality.

**Results of the review**
Forty eight trials met the inclusion criteria (n at least 2,294, some trials did not clearly report the number randomised; range 10 to 142). Eighteen trials reported an adequate method of randomisation and five trials reported adequate allocation concealment. Twenty two trials reported some level of blinding; only 18 trials using sham continuous positive airway pressure as the comparator were reported as double-blinded.

**Continuous positive airway pressure:** When compared to placebo or best supportive/usual care, continuous positive airway pressure produced a statistically significant benefit on the Epworth Sleepiness Scale (mean difference -2.7, 95% confidence interval (CI): -3.5 to -2.0; 23 RCTs, n=1,334 participants) and the Maintenance of Wakefulness Test/Osler test (mean difference 3.3, 95% CI: 1.3 to 5.3; five RCTs, n=287 participants), but not the Multiple Sleep Latency Test (seven RCTs, n=331). There was significant heterogeneity in the Epworth Sleepiness Scale analysis, which was reduced, but not eliminated, when trials were grouped by severity of daytime sleepiness.

**Dental devices:** When compared to dental devices, there was no significant benefit of continuous positive airway pressure on the Epworth Sleepiness Scale (six RCTs, n=337 participants) or the Maintenance of Wakefulness Test/Osler test (two RCTs, n=128 participants). No trials reported Multiple Sleep Latency Test.

Results for secondary outcomes and subgroup analyses are also presented.

**Cost information**
The incremental cost per quality adjusted life year gained of continuous positive airway pressure was below £20,000 for most scenarios. Continuous positive airway pressure was most likely to be more cost effective than dental devices and conservative management for a cost-effectiveness threshold of £20,000 per quality adjusted life year gained.

**Authors' conclusions**
Continuous positive airway pressure was an effective and cost-effective treatment for obstructive apnoea–hypopnoea syndrome compared with conservative/usual care and placebo in populations with moderate to severe daytime sleepiness. There may also be benefits in mild disease.

**CRD commentary**
The authors addressed a clear research question, supported by appropriate and well-defined inclusion criteria. The search was extensive, and foreign language papers and unpublished data were sought, reducing the potential for language and publication bias. Each stage of the review was conducted in duplicate, reducing the risk of error and bias. Appropriate quality criteria were used to assess trials. The results for each criterion were reported for each trial, and the impact on the results of the review investigated. The analysis used was appropriate, and heterogeneity was investigated. This was a well-conducted review and the conclusions are likely to be reliable.

**Implications of the review for practice and research**
Practice: The authors stated that dental devices may be a treatment option in moderate disease, but there is still uncertainty regarding this.

Research: The authors recommended further research to investigate: patients with mild obstructive apnoea–hypopnoea syndrome; dental devices compared to continuous positive airway pressure; the effect of continuous positive airway pressure on hypertension and cardiovascular events; the use of continuous positive airway pressure in the very young, elderly and women; and the side effects of continuous positive airway pressure. They also stated that research trials should be adequately powered to detect changes in cardiovascular events.

Funding
Health Technology Assessment Programme.

Bibliographic details

PubMedID
19103134

DOI
10.3310/hta13040

Original Paper URL

Other URL
Link to record in NHS EED: http://www.crd.york.ac.uk/crdweb/ShowRecord.asp?AccessionNumber=22009101154& UserID=0
Link to record in HTA database: http://www.crd.york.ac.uk/crdweb/ShowRecord.asp?AccessionNumber=32009100026& UserID=0

Additional Data URL
http://www.cochrane.org/reviews/en/ab001106.html

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Continuous Positive Airway Pressure /economics /instrumentation; Cost-Benefit Analysis; Dental Devices, Home Care /economics; Humans; Models, Economic; Pharyngeal Muscles /physiopathology; Quality-Adjusted Life Years; Randomized Controlled Trials as Topic; Sleep Apnea Syndromes /economics /physiopathology /therapy; Sleep Apnea, Obstructive /economics /physiopathology /therapy; Technology Assessment, Biomedical; Treatment Outcome

AccessionNumber
12009102369

Date bibliographic record published
31/03/2009

**Date abstract record published**
29/07/2009

**Record Status**
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.