A meta-analysis of the effects of atrial overdrive pacing on sleep apnea syndrome

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CRD summary
This review evaluated the effectiveness of atrial overdrive pacing in treating sleep apnoea and concluded that pacing appeared effective in reducing apnoeas and hypopnoeas and increasing minimum arterial oxygen saturation in patients with central sleep apnoea syndrome. Results for obstructive sleep apnoea syndrome were unclear. The conclusion may not be reliable due to small sample sizes and poor trial quality.

Authors' objectives
To compare the effectiveness of atrial overdrive pacing with nonpacing in patients with sleep apnoea syndrome (SAS).

Searching
PubMed, EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL) were searched from 1966 to January 2008. Bibliographies of retrieved articles and reference lists of reviews were searched. Search terms were reported. There were no language restrictions.

Study selection
Randomised control trials (RCTs) of more than five adult patients aged over 18 years were included if the patients had been diagnosed with SAS and atrial overdrive pacing was compared to nonpacing (defined as continuous positive airway pressure). Eligible outcomes were either the apnea hypopnoea index or minimum arterial oxygen saturation (SaO$_2$).

Eighty-five percent of patients included were male. Average age ranged from 60 to 74 years. Where reported, mean body mass index ranged from 27.7 to 32kg/m$^2$. Three studies indicated comorbid heart failure. Concomitant medication (where reported) included diuretics, β-blockers, ACE inhibitors, amiodarone, digitalis and calcium channel blockers. Treatment time varied from one night to one month. Most patients included suffered predominantly from obstructive rather than central sleep apnoea.

Two reviewers independently assessed whether articles were suitable for inclusion. It appeared that disagreements were resolved by consensus.

Assessment of study quality
Two reviewers independently assessed study quality in terms of randomisation, blinding and handling of withdrawals and dropouts. The Jadad scale was used to produce an overall quality score for each trial from zero to 5. Disagreements were resolved by consensus.

Data extraction
Two reviewers extracted information required to calculated mean differences (MD) and 95% confidence intervals (CIs) for the outcomes apnea hypopnoea index and minimum arterial oxygen saturation (SaO$_2$). Correlation coefficients (necessary to adapt standard meta-analysis approaches to crossover trials) were calculated for four of the eight studies used to estimate the apnea hypopnoea index outcome and for three of the seven studies used to estimate the minimum SaO$_2$ outcome; correlation coefficients were imputed for the remaining studies.

Methods of synthesis
Meta-analyses were performed using apnea hypopnoea index and minimum SaO$_2$ as outcomes. Heterogeneity was assessed using the I$^2$ statistic (25%=low, 50%=medium and 75%=high levels of heterogeneity). Where heterogeneity was identified, a random-effects (rather than fixed-effect) model was used and subgroup analyses were carried out to try to identify reasons for the heterogeneity. Analyses of crossover trials were performed using a paired analysis approach appropriate for the type of trial. Sensitivity analysis was performed using difference correlation coefficients and by assessment of effects of excluding trials on overall results.
Results of the review

Eight crossover trials were included in the review (n=129 patients, range 15 to 20). All trials received Jadad scores of either 1 or 2 (scale 0 to 5), which indicated poor study quality. Validity assessment by individual criteria were not reported.

Overall, there was a statistically significant mean difference in apnea hypopnoea index outcome (-5.40, 95% CI -9.82 to -0.98) that favoured overdrive pacing (based on eight trials), but no statistically significant mean difference between treatments that used the minimum SaO\textsubscript{2} measure (based on seven trials).

There was significant heterogeneity for the apnea hypopnoea index outcome ($I^2=67.7\%$). This disappeared when the eight trials were stratified into two subgroups according to the proportion of patients with obstructive rather than central sleep apnoea syndrome. For the two trials (n=31 patients) where most of the patients had central sleep apnoea syndrome, apnea hypopnoea index outcomes favoured overdrive pacing far more substantially (MD -17.08, 95% CI -23.25 to -10.91) than for the six trials (n=98 patients) where most patients had obstructive sleep apnoea syndrome (MD -2.94, 95% CI -5.33 to -0.54). In one trial where most patients had central sleep apnoea syndrome and minimum SaO\textsubscript{2} was assessed, outcomes favoured overdrive pacing (MD 4.00, 95% CI 2.48 to 5.52) over nonpacing; this was not the case for the six trials where most patients had obstructive sleep apnoea syndrome.

Four of eight correlations for apnea hypopnoea index pooled analysis and four of the seven correlations for the minimum SaO\textsubscript{2} pooled analysis were imputed as trial data did not allow them to be estimated. Sensitivity analysis performed to determine whether the assumptions made in these imputations affected the direction and statistical significance of either pooled outcome judged this not to be the case.

Authors' conclusions

Atrial overdrive pacing appeared to be effective in producing a reduction in apnea hypopnoea index and an increase in minimum SaO\textsubscript{2} in patients with central sleep apnoea syndrome; its role in treating obstructive sleep apnoea syndrome was unclear.

CRD commentary

The research question was clear and supported by relevant inclusion criteria. Inclusion criteria were clear enough to be reproducible. More than one database was searched, language bias was minimised and references of retrieved articles were searched for additional articles. It was unclear whether additional searches for unpublished papers were performed, which increased the risk of publication bias. Selection, quality assessment and data extraction stages of the review process were all carried out with sufficient attempts to minimise error and bias. The authors used what appeared to be the appropriate correction for pooling results from crossover trials.

Trials were generally of a small size. The acronyms OSA and OSAS appeared to have been used interchangeably and inconsistently. The overall quality score indicated the generally poor quality of included trials, but their individual assessment could not be verified. Because of these factors, the reliability of the conclusions is uncertain.

Implications of the review for practice and research

Practice: The authors did not state any implications for practice.

Research: The authors appeared to state that larger randomised control trials were needed to provide definitive evidence of the effect of cardiac overdrive pacing on obstructive sleep apnea syndrome.

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Bibliographic details

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