Systematic review of noninvasive positive pressure ventilation in severe stable COPD
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CRD summary
The authors concluded that bi-level non-invasive positive pressure ventilation may be a useful adjunct for a subset of patients with severe stable chronic obstructive pulmonary disease. Findings appeared to support the conclusions, but the assessment of multiple outcomes from generally small short-term studies meant that the evidence was limited and caution is advised.

Authors' objectives
To evaluate the effectiveness of bi-level non-invasive positive pressure ventilation (NIPPV) in patients with chronic respiratory failure (CRF) due to severe stable chronic obstructive pulmonary disease (COPD).

Searching
MEDLINE/Pre-MEDLINE/PubMed, EMBASE, CINAHL, Conference Papers Index, Online Computer Library Centre Inc., Papers First (Conference Papers), The Cochrane Library, American College of Physicians Journal Club, Biological Abstracts and Dissertation Abstracts were searched from 2001 to 2003. Search terms were reported. Reference lists of included studies were screened and six specified journals were handsearched from 2001 to 2003. Only English language articles were included.

Study selection
Randomised controlled trials (RCTs) and non-RCTs of within-patient crossover design that evaluated the effectiveness of bi-level NIPPV delivered via nasal, oronasal and/or total face mask in adults (aged 18 years or more) with chronic respiratory failure and chronic obstructive pulmonary disease were eligible for inclusion. Studies of patients with predominantly asthmatic and/or reversible airways obstruction were excluded. The primary review outcome was respiratory function assessed using specified measures. Secondary outcome measures were also specified.

Patients in the included studies were chronically dyspnoeic with severe chronic obstructive pulmonary disease. Most were male. The mean age was 66 years (range 44 to 74). The duration of follow-up ranged from five days to two years for the RCTs. For non-RCTs, study duration ranged from one to three days for short daytime studies and from six weeks to six months for nocturnal studies. All but two of the studies evaluated a Respironics BiPap NIPPV system; most studies used a nasal interface. Control treatments included spontaneous breathing, sham ventilation, long-term oxygen therapy (LTOT), exercise and other types of ventilation.

Two reviewers independently selected studies and resolved disagreements through consensus.

Assessment of study quality
Two reviewers independently assessed validity using criteria described by Estabrooks: treatment allocation; recruitment; inclusion and exclusion criteria; follow-up; control of confounders; description of intervention; data collection; measurement of outcomes and statistical analysis. Studies were classified as low, medium or high quality.

Data extraction
The authors stated neither how data were extracted for the review nor how many reviewers performed the data extraction. For each study, means and standard deviations were presented in tables.

Methods of synthesis
Clinical heterogeneity among studies was assessed. Where possible, random-effects models were used to calculate pooled weighted mean differences and 95% confidence intervals (CIs). RCTs were used to compare bi-level NIPPV with all controls. Subgroup analysis was used to compare bi-level NIPPV with all controls for RCTs with a duration of eight weeks or less and RCTs with duration of more than eight weeks. Non-RCTs were analysed separately using general inverse variance models to calculate mean differences for bilevel NIPPV versus all controls. Heterogeneity was
assessed using the $X^2$ and $I^2$ statistics. Where meta-analysis was not possible, studies were combined in a narrative synthesis.

**Results of the review**
Fifteen studies were included ($n=466$ enrolled, 351 randomised and 274 completed). These included six RCTs ($n=249$ randomised and 191 completed) and nine within-subject crossover studies (classified as the non-RCTs in the review, $n=102$ randomised, 83 completed). Sample size ranged from 10 to 47 for RCTs and from six to 14 for non-RCTs. Most studies were rated as high methodological quality. Four of the six RCTs used blinding of randomisation. All RCTs were single-blinded with respect to intervention. All of the cross-over studies (the non-RCTs) used randomisation and attempted to control for confounders statistically.

**Gas exchange**: For RCTs there was no statistically significant difference between bi-level NIPPV and control in arterial oxygen (six RCTs) or arterial carbon dioxide (six RCTs) tension. The non-RCTs found that bi-level NIPPV was associated with a statistically significant increase in arterial oxygen tension (mean difference 4.49 mmHg, 95% CI: 1.43 to 7.55, $p=0.004$; seven studies) and a significant reduction in arterial carbon dioxide tension (mean difference -3.52 mmHg, 95% CI: -5.93 to -1.11; eight studies) compared to control. Heterogeneity was evident.

**Muscle function/work of breathing**: Meta-analysis of two non-RCTs showed that bi-level NIPPV was associated with an increase in respiratory muscle strength. Heterogeneity was evident.

**Health-related outcomes**: Each of four RCTs showed that bi-level NIPPV was associated with a significant improvement in dyspnoea; one of two non-RCTs showed no change in dyspnoea. All three studies (two RCTs and one non-RCT) that assessed health-related quality of life reported significant improvements in at least one health-related quality of life measure.

Results for other outcomes were also reported.

**Authors’ conclusions**
Bi-level NIPPV may be a useful adjunct for a subset of patients with severe stable chronic obstructive pulmonary disease patients on maximal medical treatment.

**CRD commentary**
The review question was clearly stated and inclusion criteria specified for study design, participants, intervention and outcomes. Studies described as non-RCTs in the review appeared to be cross-over RCTs. Many relevant sources were searched, but it was unclear whether unpublished studies were eligible. No attempts were made to minimise language bias and only English-language studies were included. Appropriate methods were used to minimise reviewer error and bias during the selection of studies and validity assessment, but it was unclear whether similar methods were used for the extraction of data. Validity was assessed using specified criteria, but results were incompletely reported. No details of concomitant medical treatments were given, which made it difficult to determine the applicability of results and determine whether patients were indeed receiving maximal medical treatment. Appropriate methods were used for the meta-analyses and heterogeneity was assessed. Reporting many different primary and secondary outcome measures increased the probability of significant findings occurring by chance. Much of the evidence was based on a small number of patients in a few studies. Findings appeared to support the authors’ conclusions, but the assessment of multiple outcomes from generally small short-term studies meant that the evidence was limited and caution is advised.

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

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