The acute effects of noninvasive ventilatory support during exercise on exercise endurance and dyspnea in patients with chronic obstructive pulmonary disease: a systematic review

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Authors' objectives
To determine the effectiveness of noninvasive ventilatory support (NIVS) on exertional dyspnoea and exercise endurance in patients with chronic obstructive pulmonary disease (COPD).

Searching
MEDLINE (from 1966 to 2001; search terms provided), the Cochrane Library (from 1993 to 2001), EMBASE (from 1974 to 2001) and CINAHL (from 1982 to 2000) were searched for articles in English, Dutch or German. The reference lists of identified studies and reviews were also searched, along with abstracts from the annual congresses of both the American Thoracic Society and the European Respiratory Society. Preliminary data from a study conducted by the authors of the review were also included.

Study selection
Study designs of evaluations included in the review
The inclusion criteria for study design were the presence of one or more intervention and control phases, and randomisation. All the included studies had a crossover design.

Specific interventions included in the review
Studies evaluating any form of NIVS were eligible for inclusion. The modes of NIVS used in the included studies were continuous positive airway pressure, pressure support and proportional assist ventilation. Studies employing supplementary oxygen as a cointervention were also included. Details on the type of ventilator used were not provided in the primary studies.

Participants included in the review
Studies of adult patients diagnosed with COPD, according to the definition of the European Respiratory Society, who were undergoing exercise training were eligible for inclusion. The participants evaluated in the included studies had a mean age of 64 years and a mean forced expiratory volume in 1 second of 0.97 L (35% expected).

Outcomes assessed in the review
Studies assessing acute effects on exercise endurance (during cycling or walking) and/or exertional dyspnoea (obtained from a score derived from the Borg-scale) were eligible for inclusion.

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 adapted the Delphi List to develop a 13-point quality scoring list to evaluate the adequacy of the following criteria: description of patient characteristics; randomisation procedure; blinding procedure; reliability and validity of outcome measurement instruments; control for cointerventions; description of the intervention; and description of withdrawals and drop-outs. Two reviewers independently assessed the validity of the included studies. Any disagreements were resolved by consulting a third reviewer.

Data extraction
One unblinded reviewer extracted data from the included studies. Data on the mean effect for the intervention and control groups and the standard deviation for the control group were extracted to derive the standardised mean
difference (Glass’ d) for each included study.

Methods of synthesis
How were the studies combined?
The results from the individual studies were combined using a fixed-effect meta-analysis. A pooled summary effect size (SES) with 95% confidence intervals (CIs) was calculated for exertional dyspnoea. Owing to variation in the mode of NIVS in the studies evaluating exercise endurance, pooled summary SESs and 95% CIs were derived assuming a best- and worse-case scenario. This involved pooling, separately, the highest and lowest effect sizes reported in each included study.

How were differences between studies investigated?
The homogeneity of the included studies was assessed statistically using chi-squared. In studies that evaluated exercise, post-hoc endurance subgroup analyses were performed according to the mode of NIVS.

Results of the review
Eight studies (n=104) were included in the analysis. Seven studies (n=65) met the inclusion criteria; preliminary data from the authors’ own study were also included (n=39).

Exertional dyspnoea.
Compared with the control phase, NIVS was associated with a statistically-significant reduction of 2 points on the Borg score for dyspnoea during exercise (SES 0.57, 95% CI: 0.04, 1.07, P=0.03), based on 22 patients with COPD in 4 studies. The results were statistically homogeneous across the individual studies (chi-squared 0.28; P not significant, value not reported).

Exercise endurance.
When assuming the best-case scenario, NIVS was associated with a statistically-significant improvement of 3.3 minutes in exercise endurance in comparison with the control phase (SES 0.58, 95% CI: 0.29, 0.87, P<0.001), based on 96 patients with COPD in 7 studies. The results were statistically homogeneous across the individual studies (chi-squared 3.95; P not significant). When assuming the worst-case scenario, NIVS was associated with a lower, but statistically-significant improvement of 1.7 minutes in exercise endurance in comparison with the control phase (SES 0.33, 95% CI: 0.05, 0.62; P<0.02). Again, the results were statistically homogeneous across the individual studies (chi-squared 2.3; P not significant). Post-hoc subgroup analyses according to the mode of NIVS only showed a statistically-significant improvement in exercise endurance with pressure support ventilation (SES 0.41, 95% CI: 0.06, 0.77, P=0.03), based on 62 patients in 3 studies.

The validity assessment revealed a strong agreement between reviewers (Cohen's Kappa 0.86). The methodological quality score assigned to the included studies ranged from 4 to 7 (maximum score of 13). The main weaknesses across the studies were no description of the randomisation procedure or blinding of the observer, no indication of the reliability or validity of the outcome measurement, and no information on withdrawals.

Authors’ conclusions
The authors concluded that the use of NIVS during exercise can potentially lead to an acute reduction in exertional dyspnoea and an improvement in endurance in patients with COPD.

CRD commentary
The review was guided by a clear question and explicit inclusion criteria. Several sources were searched for relevant studies to limit the potential for language and publication bias. However, the possibility of selection and observer bias in the study inclusion and data extraction processes cannot be ruled out. The methodological quality of the included studies was assessed systematically and was tailored to the subject area and study design. The details of the characteristics of the included studies were not reported adequately, and the quality criteria were not applied to the
included study that the reviews’ authors performed. This makes it difficult to assess whether the pooling of the studies was appropriate and free from selection bias, particularly given the small sample sizes and design of the included studies. The authors’ cautious conclusion and recommendations for further research is appropriate given the methodological weaknesses of the included studies and the apparent variation in effect depending on the mode of NIVS.

**Implications of the review for practice and research**

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

**Research:** The authors stated that further studies are required to assess the application of NIVS during exercise to improve the outcomes of patients with COPD. These studies should address the potential for differential effects of the different modes of NIVS and identify patients who are likely to benefit the most.

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