Meta-analysis of the long-term effect of nifedipine for pulmonary hypertension

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Authors' objectives
Assess the magnitude and consistency of the effect of nifedipine on reducing pulmonary artery pressure (PAP) in patients with pulmonary hypertensive disorders.

Searching
MEDLINE was searched from 1966 to 1995 using the keywords field for the combination 'nifedipine' and 'pulmonary hypertension'. Bibliographies of retrieved articles were also reviewed.

Study selection
Study designs of evaluations included in the review
Case series were included.

Specific interventions included in the review
Nifedipine (30 to more than 200 mg/day).

Participants included in the review
Patients with the following illnesses were included in the analysis:
pulmonary hypertension secondary to chronic obstructive pulmonary disease; primary pulmonary hypertension; clinically-stable cor pulmonale; primary pulmonary hypertension and New York Heart Association functional class 3 symptoms; primary pulmonary hypertension secondary to diffuse systemic sclerosis; crest syndrome; and mixed connective tissue disease.

Outcomes assessed in the review
Effect size in terms of the post-treatment and pre-treatment mean PAP.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection. The included studies had to meet the following inclusion criteria: have at least 5 patients; measure pre-therapy and post-therapy PAPs; have a long-term study component; and have nifedipine as the predominant drug in the trial.

Assessment of study quality
The authors do not state that they assessed validity.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the authors performed the data extraction.

Methods of synthesis
How were the studies combined?
Effect sizes found to be homogeneous were pooled to estimate the common effect. Each study contributed to the pooled estimate a weight that was proportional to its variance (square of the difference in standard errors between post-treatment and pre-treatment mean PAP values).

How were differences between studies investigated?
A chi-squared test for homogeneity was employed to determine the appropriateness of pooling. Trials that contributed the greatest variance were excluded from the meta-analysis; potential reasons for their divergence were explored.

**Results of the review**

Eight studies met the inclusion criteria (136 patients enrolled in acute phase; 59 patients enrolled in long-term phase; 47 patients completed long-term phase).

Six homogeneous trials were included in the meta-analysis. These trials indicated a significant decrease in PAP with nifedipine treatment (-7 mmHg, 95% confidence interval: -3, -11, p<0.01).

Two trials were excluded because of significant heterogeneity (chi-squared=31.4, p<0.01). These two trials exhibited differences in both the severity of initial PAPs and in the nifedipine dosages.

**Authors’ conclusions**

Nifedipine reduces PAP in patients with pulmonary hypertension, which is associated with an amelioration of clinical symptoms, although the lack of data infers that larger trials are needed to better define the drug's clinical value.

**CRD commentary**

The small number of included trials, each with relatively small sample sizes and therefore of low power, suggests that it would be unwise to consider the meta-analysis as strong evidence supporting the effectiveness of nifedipine. To the authors’ credit, they draw the reader’s attention to this statistical weakness in their conclusions. The authors are also to be commended for investigating heterogeneity before pooling the studies, and excluding those studies for which a valid reason for divergence of results could be found. It may have been useful if the paper had included more details of patient characteristics that could affect the global implications of the analysis, e.g. sex distribution, age and severity of illness. It is also unclear from the details presented whether the search strategy included studies of any language or was restricted to only those in English.

**Bibliographic details**


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**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.