Meta-analysis of heart valve abnormalities in Parkinson's disease patients treated with dopamine agonists

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CRD summary
This review concluded that valvular heart disease occurs at a similar frequency in Parkinson's disease patients who are treated with two dopamine agonists, and around 26% of these patients show signs of moderate valvular disease. Overall, the review process is likely to have been susceptible to various biases, and the conclusions do not necessarily follow from the presented results.

Authors' objectives
This review explored the incidence and severity of heart valve disease in Parkinson's disease patients treated with dopamine agonists (DAs).

Searching
MEDLINE was searched to April 2007 for 'parkinson's disease' and 'heart valve', and variations of these as search terms. The reference lists of retrieved papers were also reviewed.

Study selection
Eligible studies reported on the incidence of heart valve disease in Parkinson's disease patients treated with DAs. Heart valve disease was described as restricted valvular disease (measured via tenting area or tenting distance), or valvular disease severity (graded in three steps: 0 = none, I = mild, II = moderate, III = severe). The authors did not specify eligible study design types. All included papers had to be published in peer-reviewed journals; no mention was made of any language restrictions.

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 did not state that they assessed validity.

Data extraction
Primary outcome data on the occurrence and severity of valvular heart disease were extracted. The authors used a 3-step severity scale and converted older 4-step measures. Risk ratios (RRs) were calculated based on a dichotomised severity scale, such that only moderate or severe cases were included.

The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

Methods of synthesis
The studies were pooled using a DerSimonian and Laird random-effects model for the meta-analysis. The results were grouped as Ergot-DAs (percolate or cabergoline) and non-Ergot DAs (ropinirole or pramipexole) for pooling.

Results of the review
This review included 7 cross-sectional studies (967 patients) of heart valve abnormalities in Parkinson's disease patients receiving DA treatment.

Based on analysis of all 7 studies (841 patients), patients treated with Ergot-DA were at a statistically significantly increased risk of moderate to severe valvular disease compared with patients receiving a control (RR 2.77, 95% confidence interval, CI: 1.72, 4.47, p<0.0001). No evidence of statistical heterogeneity was found ($I^2$=29.4%).
Subgroup analysis (4 studies, 413 patients) comparing Ergot-DA with non-Ergot-DA treatment found no increased risk of valvular disease for Ergot-DA-treated patients (RR 3.41, 95% CI: 0.83, 14.02, p=0.09). These studies were statistically significantly heterogeneous ($I^2=77.0\%$).

Patients treated with cabergoline were at a statistically significantly higher risk of valvular heart disease than those receiving pergolide (RR 1.73, 95% CI: 1.23, 2.44, p=0.002; 4 studies, 187 patients). No evidence of statistical heterogeneity was found ($I^2=5.1\%$).

Dose dependency of Ergot-DA treatment effects on valvular changes was not assessed statistically, owing to the variation in reported end points. Four out of 7 studies found some dose dependency for pergolide, and two out of four found similar effects in patients treated with cabergoline.

The authors also reported summary data on the overall incidence of valvular heart disease in Parkinson's disease patients treated with Ergot-DA.

**Authors' conclusions**

Valvular heart disease occurs at a similar frequency in patients with Parkinson's disease who are treated with either pergolide or cabergoline. Cross-sectional studies suggested that around 26% of Parkinson's disease patients treated with Ergot-DAs show signs of moderate valvular disease, while only 1% of patients show evidence of severe valvular changes.

**CRD commentary**

The review question was potentially ambiguous with the research appearing to largely address the extent to which DA treatment was associated with valvular disease in patients with Parkinson's disease. The inclusion criteria were not defined clearly and the search strategy might not have located all relevant studies. Searching only one database may allow publication and language biases to affect the review. Validity assessment was not mentioned, therefore the results of the primary studies and any resulting synthesis may not be reliable. Publication bias was not assessed and might have influenced the results. The reason why a random-effects model was chosen for the meta-analysis was not discussed; the use of random-effects rather than fixed-effect models can produce wider CIs and less precise effect estimates. Heterogeneity was identified as present for the Ergot-DA versus non-Ergot-DA comparison, suggesting that the result may be unreliable, but this was not investigated further. The authors’ conclusions do not appear to entirely reflect the results presented: from the forest plots the key findings appear to be that Ergot-DA treatment does result in a significantly greater risk of valvular disease, and cabergoline is associated with higher risk than pergolide. Overall, this review may have been susceptible to various biases, rendering the findings unreliable.

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

Practice: The authors stated that patients being treated with Ergot-DA should be closely monitored, both clinically and using echocardiographic techniques.

Research: The authors stated that longitudinal studies of Parkinson's disease patients receiving Ergot-DA treatment are urgently needed.

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