Risk of valvular heart disease associated with the use of dopamine agonists in Parkinson's disease: a systematic review

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CRD summary
This review assessed the frequency of cardiac valve regurgitation in patients with Parkinson's Disease treated with ergot-derived and non-ergot dopamine agonists, concluding that ergot-derived dopamine agonists (such as pergolide and cabergoline) increased their frequency. Given the variation across studies and shortcomings highlighted in the review process and reporting, the authors' conclusions should be interpreted with caution.

Authors' objectives
To assess the frequency of cardiac valve regurgitation following treatment with ergot-derived and non-ergot dopamine agonists in patients with Parkinson's disease.

Searching
MEDLINE, BioMed Central, Web of Science, the Cochrane Library and clinical trial registries were searched, without language restrictions, to December 2007. Search terms were reported. References of included studies were reviewed to identify additional studies.

Study selection
Case-control or observational studies with at least 10 Parkinson's disease patients, aged over 18 years, with Parkinson's disease of any duration, treated with dopamine agonists, were eligible for inclusion. Case reports of fibrosis, valvular heart disease or valvulopathy without a control group were excluded. Eligible studies assessed the incidence, odds or risk of fibrosis, valvular heart disease or cardiac valvulopathy, as confirmed by echocardiography. Included outcomes comprised: aortic valve regurgitation; mitral valve regurgitation; tricuspid valve regurgitation; or total valve regurgitation.

The ergot-derived dopamine agonist interventions in the included studies were pergolide (0.71 to 3.2 mg/day), cabergoline (3.6 to 4.0 mg/day), and bromocriptine (8.5 mg/day). The other dopamine agonist interventions in the included studies were ropinirole (8.4 to 14.3 mg/day) and pramipexole (1.7 to 3.0 mg/day). These were compared with a control group untreated with a dopamine agonist or treated with a different agonist.

The mean age of patients in the included studies ranged from 55.0 to 73.5 years, mean duration of Parkinson's disease (where stated) was 5.0 to 11.2 years, and the proportion of males was between 30 and 88%. In one study, 64% of patients were receiving treatment for restless legs syndrome rather than Parkinson's disease.

The 'author group' selected studies for inclusion in the review, but it was not stated how many reviewers this comprised or how disagreements were resolved.

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

Data extraction
Data for outcomes were extracted as percentages.

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

Methods of synthesis
A narrative synthesis was undertaken, supported by a table, with differences between studies discussed in the text.
Results of the review
A total of 14 studies were included in the review (n=2,639, range 72 to 725). The duration of treatment ranged from 11.2 to 82 months.

Significant increases in the frequency of cardiac valve regurgitation were reported for the ergot dopamine agonist group (11 studies; four with cabergoline and nine with pergolide), compared with non-ergot groups or controls. Two studies reported an association between the tenting area of the mitral valve and the dose of pergolide. No study detected an increased risk with non-ergot dopamine agonists compared with controls.

Authors’ conclusions
In patients with Parkinson's disease, an increased risk of cardiac valve regurgitation was associated with the use of ergot-derived dopamine agonists (pergolide and cabergoline) but not with non-ergot dopamine agonists.

CRD commentary
The review question was clear, but it was unclear whether inclusion criteria for study design and participants were adhered to. It was unclear whether randomised controlled trials were excluded from the review or that none were found. In one included study, the majority of participants had Restless Legs Syndrome, a condition that did not appear to meet the inclusion criteria for the review. The search was thorough but was restricted to publications in English. It appeared that non-English studies without an English abstract were excluded, so language bias may have been present. There was no apparent search for unpublished studies, so some studies may have been missed. The methods used for study selection and data extraction were not reported, making it unclear whether methods were used to reduce error and bias. There was no formal assessment of the validity of the included studies. Given the heterogeneity between the studies, the decision to employ a narrative synthesis was appropriate. The synthesis was poorly reported. It was unclear which studies represented better quality evidence. The review was funded by GlaxoSmithKline, the manufacturer of ropinirole (one of the drugs included in the review). In light of the between study heterogeneity, poor reporting of the review process and unclear synthesis, the authors' conclusions should be interpreted with caution.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.
Research: The authors stated that future research is required on: the natural history of heart disease in a large cohort of patients with Parkinson's disease; and whether Parkinson's disease patients are pre-disposed to degenerative cardiac valve regurgitation compared with age-matched controls.

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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.