Cabergoline therapy and the risk of cardiac valve regurgitation in patients with hyperprolactinemia: a meta-analysis from clinical studies
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CRD summary
The authors concluded that patients with hyperprolactinaemia who were treated with cabergoline were at increased risk of tricuspid valve regurgitation. The authors’ conclusions appeared to be supported by the limited evidence, but lack of reporting of review methods and study quality mean that their reliability is uncertain.

Authors’ objectives
To determine if cabergoline therapy is associated with an increased risk of cardiac valve regurgitation in patients with hyperprolactinaemia.

Searching
PubMed (including MEDLINE) and ClinicalTrials.gov were searched from 2003 to October 2008 (2003 was the year in which the US Food and Drug Administration reported the registry of patients with pergolide-associated valvular heart disease). Some details of the search strategy were reported.

Study selection
Clinical studies that assessed cardiac valve regurgitation in patients with tumour or non-tumour hyperprolactinaemia who had received cabergoline were eligible for inclusion. Studies had to grade cardiac valve regurgitation using echocardiography following the American Society for Echocardiography guidelines. Single case reports were excluded.

The review assessed mild, mild plus moderate and mild plus moderate plus severe valve regurgitation of the tricuspid, aortic and mitral valves.

The primary studies mostly included patients with pituitary PRL (prolactin)-secreting adenomas; some patients had non-tumour hyperprolactinaemia. Control groups included patients with palpitations without heart disease or organic disease, healthy medical staff and patients matched for specified characteristics. The mean cumulative cabergoline dose ranged from 204mg to 443mg. Mean treatment duration ranged from 44.8 to 81 months.

The authors did not state how studies were selected for inclusion.

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

Data extraction
For each study the prevalence rate (PR) with the 95% confidence interval (CI) of each type and grade of valve regurgitation was calculated using the Katz method.

The authors did not state how many reviewers extracted data.

Methods of synthesis
Pooled PRs with 95% CI were calculated using a fixed-effect model; a random-effects DerSimonian and Laird model was used when heterogeneity was present even if it was not statistically significant. Heterogeneity was assessed using the Q statistic.

Results of the review
Six observational studies were included in the analyses (n=393 patients).

In patients who had received cabergoline, there was a statistically significant increase in mild plus moderate tricuspid
regurgitation (PR 1.40, 95% CI 1.17 to 1.67). No significant heterogeneity was found. The authors stated that none of the patients showed symptoms of cardiac valve disease.

There was no statistically significant increase associated with cabergoline in mild tricuspid regurgitation, or mitral or aortic valve regurgitation.

**Authors' conclusions**

Patients with hyperprolactinaemia who were treated with cabergoline were at increased risk of tricuspid valve regurgitation.

**CRD commentary**

The review question was clear and supported by appropriate inclusion criteria. The search was limited. No attempts were made to minimise publication bias and it was unclear whether attempts were made to reduce language bias. It was unclear whether methods to minimise reviewer error and bias were used in the selection of studies and extraction of data. Study validity was not assessed, which made it difficult to assess the reliability of results. Studies were pooled using meta-analysis. Heterogeneity was assessed. The authors’ conclusions appeared to be supported by limited evidence, but a restricted search and lack of reporting of review methods and study quality mean that their reliability is uncertain.

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

**Practice:** The authors recommended that all patients with hyperprolactinaemia who were candidates for or being treated with cabergoline should undergo echocardiography and have their cardiac valves monitored using echocardiography.

**Research:** The authors stated that larger longitudinal studies were required to determine the clinical significance of echocardiographic findings in patients with hyperprolactinaemia who received cabergoline.

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