Meta-analysis of the effectiveness and safety of prophylactic use of nimodipine in patients with an aneurysmal subarachnoid haemorrhage


CRD summary
This review concluded that compared with placebo, nimodipine can improve clinical outcomes and reduce the occurrence of symptomatic cerebral vasospasm and delayed neurological function deficits as well as cerebral infarction. The authors’ conclusion reflects the evidence presented but should be interpreted with caution in view of limitations of reporting in several aspects in the review process and methods.

Authors' objectives
To assess the efficacy and safety of nimodipine in the prevention of cerebral vasospasm in patients with aneurysmal subarachnoid haemorrhage.

Searching
PubMed, EMBASE, The Cochrane Library, Stroke Trials Registry and National Science and Technology Library databases were searched from inception to November 2010 without language restrictions. Search terms were reported. Reference lists of relevant publications were screened.

Study selection
Randomised controlled trials (RCTs) that evaluated nimodipine versus placebo in the prevention of cerebral vasospasm in patients with aneurysmal subarachnoid haemorrhage were eligible for inclusion. Eligible studies had to report outcomes of death, delayed cerebral ischaemia and adverse effects.

All the included studies recruited patients with aneurysmal subarachnoid haemorrhage caused by a ruptured aneurysm. Most studies used oral administration of drugs. Some studies employed intravenous infusion or intravenous infusion followed by oral administration of drugs. Nimodipine dosage and treatment duration varied between the included studies. Where reported, patient age ranged from 15 to 79 years.

The authors did not state how many reviewers assessed studies for inclusion.

Assessment of study quality
Study quality was assessed using the five-point Jadad scale of randomisation, blinding, withdrawals and drop-outs. It appeared that allocation concealment was used as an additional criterion. The authors stated that studies that scored at least 3 were classed as high quality. The maximum possible quality score was unclear because of the inclusion of the additional criterion.

Two reviewers independently performed quality assessment. Uncertainties were resolved through discussion.

Data extraction
Data were extracted on event rates and used to calculate odds ratios (ORs) with 95% confidence intervals (CIs). Data were extracted on the basis of an intention-to-treat approach.

Two reviewers independently performed data extraction.

Methods of synthesis
The studies were combined in a meta-analysis. Pooled odds ratios with 95% CIs were calculated. The authors stated that statistical heterogeneity was evaluated but it was unclear which statistic was used. A random-effects model was used for the meta-analysis where there was significant heterogeneity and otherwise a fixed-effect model was employed. Stratification analyses were performed on the basis of cerebral vasospasm cases. Where the result was statistically significant, publication bias was assessed by calculating the fail safe number.
Results of the review
Eight RCTs were included in the review (1,514 participants, range 20 to 554). Quality scores for the included studies ranged from 6 to 8.

Compared with placebo, nimodipine was associated with a significant reduction in the rate of symptomatic cerebral vasospasm (OR 0.54, 95% CI 0.42 to 0.69; seven RCTs), delayed neurological function deficits (OR 0.62, 95% CI 0.50 to 0.78; seven RCTs) and cerebral infarction (OR 0.52, 95% CI 0.41 to 0.66; six RCTs) but with a significant increase in the rate of full recovery (OR 1.64, 95% CI 1.26 to 2.13; seven RCTs).

Stratification analyses of cerebral vasospasm cases showed that compared with placebo, nimodipine was associated with a significant reduction in the mortality rate (OR 0.26, 95% CI 0.09 to 0.71; three RCTs). There were no significant differences in the rate of recurrent haemorrhage and adverse reactions between the nimodipine and placebo groups.

Sensitivity analyses did not materially alter the results for most outcomes. There was no evidence of publication bias.

Authors' conclusions
Compared with placebo, nimodipine can improve clinical outcomes and reduce the occurrence of symptomatic cerebral vasospasm and delayed neurological function deficits as well as cerebral infarction.

CRD commentary
This review's inclusion criteria were clear. Several relevant databases were searched. Efforts were made to find published and unpublished studies without language restrictions, which minimised risks publication and language biases. Attempts were made to minimise reviewer bias and errors during data extraction and quality assessment. It was unclear whether study selection was performed in duplicate. Appropriate criteria were used to assess study quality, but the calculation of total quality score and quality scoring on each criterion were not reported. Statistical heterogeneity was assessed but it was unclear which statistic was used. Appropriate methods were used to pool the results.

The authors' conclusion reflects the evidence presented but should be interpreted with caution in view of limitations of reporting in several aspects in the review process and methods.

Implications of the review for practice and research
The authors did not state any implications for practice and research.

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