Effect of nimodipine on outcome in patients with traumatic subarachnoid haemorrhage: a systematic review

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CRD summary
This review found no evidence of a beneficial effect of nimodipine over placebo in patients with traumatic subarachnoid haemorrhage following head injury. The authors' conclusions are in line with the evidence presented, but methodological weaknesses in the review suggest that the conclusions should be treated with caution.

Authors' objectives
To determine the effect of treatment with nimodipine on outcome in patients with traumatic subarachnoid haemorrhage.

Searching
The authors searched PubMed and EMBASE up to 2006 (week 10) for articles in English, French or German; the search terms were reported. The drug manufacturer (Bayer AG) and principal investigators or corresponding authors of identified studies were contacted for further information.

Study selection
Randomised controlled trials (RCTs) of nimodipine in patients with head injury were eligible for the review. All the included studies compared nimodipine (dose not stated) with placebo. The proportion of patients with confirmed traumatic subarachnoid haemorrhage varied between studies. The primary outcome of the review was occurrence of poor outcome (death, vegetative state or severe disability) 6 months after head injury, as measured by the Glasgow outcome scale. Mortality was a secondary outcome.

The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
One reviewer assessed validity using the Jadad scale, which awards scores of 0 to 5 based on randomisation (0 to 2 points), double-blinding (0 to 2 points), and withdrawals and drop-outs (0 to 1 point). Only trials scoring 1 or 2 for randomisation were included in the review.

Data extraction
For trials involving broader populations of patients with head injury, data were extracted only for the subgroup with traumatic subarachnoid haemorrhage. Data on the numbers of patients with poor outcome in each treatment group were extracted and used to derive an odds ratio (OR) and 95% confidence interval (CI) for each study. Data on mortality rates, based on intention-to-treat analysis, were also extracted. The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

Methods of synthesis
For the primary outcome, studies were pooled by meta-analysis using a random-effects model. Heterogeneity was assessed using the $\chi^2$ and $I^2$ statistics. Data on mortality rates were also pooled across studies. The authors did not state that they assessed publication bias.

Results of the review
Five RCTs of patients with head injury were included (1,074 participants with subarachnoid haemorrhage).

The Jadad scores ranged from 2 to 5.

There was no significant difference between the nimodipine and placebo groups for occurrence of poor outcome (pooled OR 0.88, 95% CI: 0.51, 1.54). Statistical heterogeneity was significant ($\chi^2=13.35$, $p=0.01$; $I^2=70\%$). Death rates
(based on 4 studies) did not differ between the groups (OR 0.95, 95% CI: 0.71, 1.26).

**Authors’ conclusions**
There is no evidence of a beneficial effect of nimodipine on outcome in patients with traumatic subarachnoid haemorrhage.

**CRD commentary**
This review addressed a clear question and had clear inclusion criteria. The authors searched two databases for studies in a restricted range of languages, which means that relevant studies could have been missed. Publication bias was not assessed and the authors noted that one included trial was not fully published, possibly because the results were disappointing; this suggests that publication bias could be an issue for this review. Validity was assessed using a standard scale. Validity was assessed by only one reviewer and the methods used to select studies and extract the data were not reported; this makes it difficult to assess the risk of reviewer error and bias affecting the review process.

Limited details of the included studies were reported, which makes it difficult to assess similarities and differences between them. The studies were pooled by meta-analysis for the primary outcome. Significant statistical heterogeneity was present, suggesting that the decision to pool the studies might not have been appropriate. The possible sources of heterogeneity were not explored. The authors’ conclusions are in line with the evidence presented, but the issues identified above suggest that they should be treated with caution.

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

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