Saponins from Chinese buckeye seed reduce cerebral edema: metaanalysis of randomized controlled trials


CRD summary
This review assessed the effectiveness and safety of saponins from Chinese buckeye seed in the treatment of cerebral oedema in patients with stroke or cerebral trauma. The authors concluded that while saponins can reduce cerebral oedema, the poor quality of the available studies does not allow firm conclusions to be drawn. This conclusion appears reliable.

Authors' objectives
To evaluate the effectiveness and safety of saponins (escin) from Chinese buckeye (Aesculus wilsonii or Aesculus chinensis) seed in the treatment of cerebral oedema in patients with stroke or cerebral trauma.

Searching
The Cochrane Library (Issue 3, 2004), MEDLINE, EMBASE and the Chinese Biomedical Database were searched (all from inception to October 2004). The search term used was ‘escin’ and no language restrictions were applied. Other resources were searched manually.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion.

Specific interventions included in the review
Studies of the intravenous infusion of saponins from Chinese buckeye seed, with or without mannitol, were eligible for inclusion. The included studies used doses of 10 to 40 mg per day, administered for 5 to 28 days. Eligible control groups received placebo, no treatment, a non-specific treatment or mannitol. Of those studies included in the review, 34 trials compared the intervention with mannitol.

Participants included in the review
The participants were required to have stroke or cerebral trauma diagnosed by computed tomography or magnetic resonance imaging. Details of the participants in the included studies were not provided. The numbers of participants per study varied from 24 to 224 (mean 99).

Outcomes assessed in the review
Inclusion criteria for the outcomes were not specified. The main outcomes evaluated in the included studies were total effective rate (possibly a measure of effectiveness in reducing intracranial pressure), mortality and the incidence of impaired renal function.

How were decisions on the relevance of primary studies made?
Two reviewers independently selected papers for the review. Any disagreements were resolved by discussion.

Assessment of study quality
Validity was assessed using the Jadad scale, which evaluates randomisation, blinding and the handling of withdrawals or drop-outs. Allocation concealment was also assessed. The maximum validity score was 5. Studies scoring 1 to 2 points were considered low quality, while those scoring 3 to 5 were considered high quality. Two reviewers independently assessed validity. Any disagreements were resolved by discussion.
Data extraction
Two reviewers independently extracted the data. Any disagreements were resolved by discussion. For dichotomous outcomes, data on the numbers of events in each group were used to calculate the odds ratio (OR) and 95% confidence interval (CI).

Methods of synthesis

How were the studies combined?
The studies were combined by meta-analysis, using a fixed-effect model when heterogeneity was not significant and a random-effects model when significant heterogeneity was present. Potential publication bias was assessed using a funnel plot.

How were differences between studies investigated?
Statistical heterogeneity was investigated using the chi-squared test. For dichotomous outcomes, a sensitivity analysis was performed in which patients with incomplete or missing data were counted as treatment failures.

Results of the review
Forty-one RCTs involving 4,066 patients were included.

All of the included RCTs were low quality: none reported adequate randomisation, blinding, allocation concealment, intention-to-treat analysis or a priori sample size calculation. The funnel plot did not suggest significant publication bias. Sensitivity analyses for quality were not performed given the generally low quality of the trials.

Compared with control treatments, treatment with saponins significantly increased total effective rate (40 studies; OR 3.87, 95% CI: 3.25, 4.62) and reduced mortality (12 studies; OR 0.32, 95% CI: 0.19, 0.52) and the incidence of impaired renal function (18 studies; OR 0.22, 95% CI: 0.14, 0.35). Heterogeneity was not significant for these outcomes. Similar results were found in the 34 studies that compared saponins plus mannitol with mannitol alone. Ten studies reported adverse events; no serious adverse events were associated with saponin treatment. No placebo-controlled RCTs were found.

Authors’ conclusions
Saponins from Chinese buckeye seed can reduce cerebral oedema in patients with stroke or cerebral trauma. However, the evidence is not sufficient on account of the generally low methodological quality of the studies.

CRD commentary
The review addressed a clear question and had generally clear inclusion criteria. The authors searched a range of sources without language restrictions; however, the use of a single search term means that relevant studies could have been missed. No attempt to locate unpublished studies was reported, although potential publication bias was assessed. It appears that steps were taken to reduce the risk of bias and errors during the review process (selection and data extraction by two independent reviewers). The quality of the included RCTs was assessed using standard criteria. Details of the included studies were provided through a website that was only accessible to journal subscribers, so it is not possible to comment on this aspect of the review. The studies were combined by meta-analysis and statistical heterogeneity was assessed. The authors’ conclusion, that better quality trials (including placebo-controlled trials) are needed before firm conclusions can be drawn, appears reliable.

Implications of the review for practice and research
Practice: The authors stated that it is not appropriate to recommend saponins from Chinese buckeye seed for routine clinical use in patients with stroke or cerebral trauma.

Research: The authors stated that further large, double-blind, placebo-controlled trials are required to confirm the efficacy of Chinese buckeye seed saponins.
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