CRD summary
This review, which evaluated the efficacy and safety of defibrase for acute cerebral infarction in China, concluded that defibrase may play a role in inhibiting the progression of stroke and prevent recurrence. Poor reporting of methods used in the analysis mean that it is not possible to assess the reliability of the review, thus the authors’ conclusion cannot be considered reliable.

Authors’ objectives
To assess the efficacy and safety of defibrase in the treatment of acute cerebral infarction in China.

Searching
The Chinese Hospital Knowledge Database (1994 to June 2005) and MEDLINE (1950 to June 2005) were searched for studies published in Chinese or English in major journals; the key terms were reported.

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 that compared defibrase with placebo, administered within 24 hours of symptom onset, were eligible for inclusion. It appears that both treatment groups had to use calcium-channel antagonists and dilatancy agents (excluding other fibrinogen agents, anticoagulants, thrombolysis agents or platelet aggregation inhibitors). In the included studies, treatment consisted of the administration of defibrase 10 to 15 U in 250 saline over 2 hours, followed by 5 U every other day for 2 or 4 occasions.

Participants included in the review
Studies of patients aged 35 to 75 years who had been diagnosed with acute cerebral infarction using criteria set up at the Fourth Cerebrovascular Diseases Conference in 1995 were eligible for inclusion. Myodynamia had to range from grade 0 to IV. Patients who were in a coma, suffered an epileptic seizure at stroke onset, had a blood glucose level less than 2 mmol/L or greater than 10 mmol/L, had previously suffered from intracranial haemorrhage, or suffered a stroke in the past 6 months, were not eligible.

Outcomes assessed in the review
Studies had to report the neurological deficit score (NDS), Barthel index, and numeration data including plasma fibrinogen level to be eligible for inclusion. The authors state the primary outcome measurement included NDS before treatment and at 2 weeks post-treatment, the Barthel Index at 3 months post-treatment, and plasma fibrinogen level before and after treatment.

How were decisions on the relevance of primary studies made?
Two reviewers independently selected studies for inclusion.

Assessment of study quality
The authors stated that two reviewers independently assessed validity, but details of this assessment were not reported. The authors of study reports were contacted to resolve any differences or ambiguity in the reviewers’ analysis of the original trial data. The reviewers stated that the data were then re-coded and merged into a single data set.

Data extraction
Two reviewers independently extracted the data. The authors of included studies were contacted to resolve any differences or ambiguity. Data were extracted to enable the calculation of a weighted mean difference (WMD) for each outcome before and after treatment.
Methods of synthesis
How were the studies combined?
The studies were combined by meta-analysis to give a pooled WMD, with 95% confidence interval (CI), for each outcome before and after treatment. The fixed-effect method was used if there was no evidence of statistical heterogeneity, and the random-effects method in the presence of statistical heterogeneity. The authors appear to have presented meta-analyses of treatment differences but the graphs were not labelled clearly.

How were differences between studies investigated?
Statistical heterogeneity was assessed using the chi-squared statistic, and the I-squared test was performed as part of the meta-analysis.

Results of the review
Fourteen double-blind RCTs (n=646) were included.

It appears that defibrase was associated with a significant decrease in the NDS at 2 weeks compared with control (WMD -2.2, 95% CI: -4.21, -0.18, p=0.03). There was evidence of significant heterogeneity (p=0.04; I-squared 44.8%).

It appears that defibrase was associated with a significant decrease in plasma fibrinogen level 2 days post-treatment (WMD -1.51, 95% CI: -1.88, -1.15, p<0.00001). There was evidence of significant heterogeneity (p<0.00001; I-squared 80.3%).

The Barthel index at 3 months post-treatment showed a WMD of 4.45 (95% CI: -0.13, 9.03, p=0.06).

Authors' conclusions
Defibrase may have an important role of anticoagulation and may inhibit the progression of stroke and prevent its recurrence.

CRD commentary
The review question was not well-defined and it was unclear whether an individual patient data (IPD) analysis or a systematic review of summary data was undertaken. It was also not clear whether only studies conducted in China were eligible, or whether the specificity of the intervention meant that only studies conducted in China met the inclusion criteria. It is therefore difficult to comment on the suitability of the search strategy. Methods were used to minimise reviewer error and bias in the study selection and data extraction processes, and the authors stated that a validity assessment was performed but did not specify the criteria used.

Based on the results reported there are some concerns with the analysis. Specifically, the authors presented a pooled WMD for each primary outcome before and post-treatment; however, the WMD is a summary estimate of the pooled mean differences between baseline and post-treatment of each study. Therefore, based on the results, it is possible that the authors have pooled actual means values at baseline and at post-treatment instead of calculating the mean difference between the two time points. In addition, the authors did not report any safety data, which was part of the review objective. Consequently, without being able to verify the data used in the analysis or the type of review (IPD or review of summary data), it is not possible to comment on the reliability of the evidence presented and the authors' conclusion cannot be considered reliable.

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

Research: The authors stated that long-term studies are needed, along with a stratified analysis of plasma fibrinogen and severity of disease, to determine the efficacy of defibrase.

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