Reteplase: a new thrombolytic for the treatment of acute myocardial infarction

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Authors' objectives
To summarize the published data on reteplase, the most recent thrombolytic agent approved by the Food and Drug Administration (FDA) for use in the management of acute myocardial infarction (AMI) in adults.

Searching
MEDLINE from January 1985 up to June 1997, as well as other pertinent literature (not specified).

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

Specific interventions included in the review
Reteplase, two 10-MU bolus doses in 30 minutes, compared to alteplase, 100 mg over 3 hours or 90 minutes; and reteplase in comparison with streptokinase, 1.5 MU over 60 minutes.

Participants included in the review
Adults with AMI.

Outcomes assessed in the review
Efficacy in terms of patency rates, as assessed by Thrombolysis in Myocardial Infarction (TIMI) grade flow at 90 minutes, reocclusion rates, ventricular function at discharge, other TIMI flow measures (at different time points) and mortality rates; and adverse effects.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
The authors do not report the method used to assess quality, or how the quality assessment was performed.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the authors performed the data extraction.

Methods of synthesis
How were the studies combined?
Narrative style, each study was discussed separately.

How were differences between studies investigated?
The authors do not state how differences between the studies were investigated.

Results of the review
Four RCTs in total: two multicentre trials comparing the patency rates between patients randomised to receive either reteplase or alteplase (n=632); one study to test for equivalency between reteplase and streptokinase (n=6,010); and one
trial to compare the mortality rates between patients receiving reteplase and those receiving alteplase (n=15,060).

In clinical trials, reteplase demonstrated more rapid and complete coronary patency compared with alteplase, without a significant increase in clinical adverse effects. However, the improvement in coronary artery patency with reteplase versus alteplase did not result in a reduction in mortality in one trial. The equivalence trial found that reteplase was at least as effective as streptokinase in preventing deaths in AMI patients.

Cost information
The cost of the 10-MU double bolus reteplase dosage regimen is comparable with that of the accelerated alteplase regimen, at approximately $2,750 per patient. The cost for reteplase and alteplase is significantly more expensive than streptokinase, which costs about $540 per patient.

Authors’ conclusions
Reteplase may have an advantage over alteplase due to a more rapid simpler dosing regimen, but the significance of this difference is yet to be determined. The difference in cost compared to streptokinase may affect how each institution decides to manage its use of thrombolytics.

CRD commentary
The review question was clear. The authors did not attempt to generate a summary estimate of effect across studies. Instead they described the results of primary studies in a narrative way. The review suffers from a lack of methodological details. Relevant publications may have been missed as only one electronic database (MEDLINE) was searched, only publications after 1985 were sought, and no attempt was made to search for unpublished data. There is no information on how decisions on the inclusion of primary studies were taken, nor on the quality of studies included and on the way data were extracted from primary studies, and there was no discussion of heterogeneity between studies. Study details presented in the paper were limited. Considering the above factors the findings from this review should be interpreted with caution.

Implications of the review for practice and research
Large, randomised trials involving two new genetically modified thrombolytic agents, TNK-tPA and novel Plasminogen Activator (nPA), are in progress to study their efficacy and potential adverse effects. The outcomes of these studies may influence the use of reteplase.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.