Indications for fibrinolytic therapy in suspected acute myocardial infarction: collaborative overview of early mortality and major morbidity results from all randomised trials of more than 1000 patients

Fibrinolytic Therapy Trialists' (FTT) Collaborative Group

Authors' objectives
To measure the effects on morbidity and mortality of treatment with fibrinolytic therapy (FT), on patients with suspected acute myocardial infarction (AMI) in randomised trials of more than 1,000 patients.

Searching
The authors do not state which sources were searched, or how they were searched.

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

Specific interventions included in the review
FT: streptokinase, anistreplase, tissue plasminogen activator (alteplase or duteplase) and urokinase.

Participants included in the review
Patients with suspected MI; 58,600 patients randomised equally to treatment and control groups.

Outcomes assessed in the review
Proportional and absolute mortality at 35 days. Proportional and absolute number of strokes and non-cerebral bleeding events.

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
Individual patient data obtained from studies were checked and reanalysed.

Trials were included if randomisation was carried out in a manner that precluded prior knowledge of the next treatment; only those that did not include other confounding treatments and had sample sizes of at least 1,000 patients were included. The authors do not state how the papers were assessed for validity, or how many of the authors performed the validity assessment.

Data extraction
The required tabular data were calculated from original patient data in 7 studies, and obtained from the authors for the remaining 2 studies.

Methods of synthesis
How were the studies combined?
The overall effect of FT and the effects in subgroups were estimated using Peto's method of meta-analysis (see Other Publications of Related Interest).
How were differences between studies investigated?
Effects were analysed in 8 subgroups, as defined by entry ECG, hours from onset of symptoms, age, sex, systolic blood-pressure, heart rate, history of AMI and presence of diabetes. Tests for heterogeneity were carried out.

Results of the review
Nine RCTs involving 58,600 patients were included.

Mortality Outcomes.
Overall: fibrinolytic 9.6%, control 11.5%.

This is an 18% (standard deviation-squared, SD2) proportional reduction in 35-day mortality (95% confidence interval: 13, 23), which represents the avoidance of about 18 deaths per 1,000 patients allotted treatment.

Mortality rates were higher on the day of randomisation with an excess of 5 deaths per 1,000 patients allotted treatment.

There were significant trends towards greater proportional and absolute mortality reductions among patients treated earlier after symptom onset: 26% in patients presenting in less than 3 hours, 18% in patients presenting in 4 to 6 hours and 14% in patients presenting at 7 to 12 hours.

Older patients are at higher absolute risk of death from AMI, but absolute mortality reductions appear similar among older and younger patients.

The benefit of FT is highest amongst patients with bundle-branch block or ST elevation. Patients with ST depression or other ECG abnormalities showed no conclusive evidence of benefit.

Strokes and non-cerebral bleeding.

FT was associated with a small but significant number of extra strokes occurring within the first day, i.e. 3.9 (SD 0.8) per 1,000 patients, and also an extra 7.3(SD 0.7) nonfatal major bleeds per 1,000 patients.

Authors' conclusions
This overview of the 9 largest fibrinolytic trials demonstrates that treatment is beneficial for a wide range of patients with suspected AMI, many of whom are still not routinely given FT. Moreover, it has helped to characterise the early excess of deaths and strokes associated with FT, and to show that this is outweighed by a much larger benefit in the proceeding weeks.

CRD commentary
A detailed review of the largest trials in this area, which when combined allow the drawing of conclusions previously in doubt; in particular, the area of patient benefits and how soon treatment must be delivered to be effective. The absence of information on treatment regime differences does not allow generalisations regarding the 'best' form of treatment, only that FT is generally advantageous. The absence of information also requires the reader to gather further information prior to making a definitive decision regarding the delivery of care to patients with suspected AMI.

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Other publications of related interest

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Record Status
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.