In patients with acute pulmonary embolism (PE), is initial thrombolysis more effective than heparin for reducing the risk of recurrent PE and death?

METHODS

Data sources: Medline and EMBASE/Excerpta Medica (1980 to January 2003), Cochrane Library (Issue 1, 2003); and hand searches of reference lists of retrieved articles and abstracts of conference proceedings.

Study selection and assessment: published and unpublished randomised controlled trials (RCTs) with proper randomisation that compared thrombolytics with heparin for initial treatment of patients with objectively diagnosed symptomatic PE, and used objective methods to assess clinical outcomes. 2 independent reviewers assessed the methodological quality of individual trials based on allocation sequence and concealment, blinding, and follow up.

Outcomes: a composite of recurrent PE or death. Secondary outcomes were PE, death, major bleeding, non-major bleeding, and intracranial haemorrhage.

MAIN RESULTS

11 trials (n = 748) met the selection criteria. 3 RCTs used random number tables or programs for generating randomised allocation sequences, 5 had adequate concealment, 3 had blinding of patients and investigators, and none reported the number of patients lost to follow up. All studies included patients with symptomatic PE, and 5 trials also included patients with major PE (haemodynamic instability). Thrombolysis included urokinase, streptokinase, and tPA. Meta-analysis was done using a fixed effects model. Meta-analysis of 11 trials showed that thrombolysis increased the risk of non-major bleeding and intracranial haemorrhage.

CONCLUSIONS

No evidence exists that initial thrombolysis is better than heparin for reducing the risk of combined recurrent pulmonary embolism (PE) or death, major bleeding, or intracranial haemorrhage in unselected patients with acute PE. Thrombolysis increases the risk of non-major bleeding.

A modified version of this abstract appears in Evidence-Based Medicine.

Commentary

Healthcare professionals continue to seek out effective treatment choices for PE. Sample size and the crisis status of patients have limited many of the research studies to date. 3 previous meta-analyses have resulted in conflicting answers. The meta-analysis by Wan et al reviewed the available research over 3 decades and concluded that no current evidence exists of a benefit associated with using thrombolysis instead of heparin for PE. The 11 included studies did not use consistent selection criteria or outcome measures. Over the 3 decades during which the studies were published, thrombolytic agents and the types and formulations of anticoagulants have changed substantially. These factors make the meta-analysis difficult to interpret. Although the meta-analysis suggests a clear benefit for thrombolysis for patients at highest risk, the authors indicate that this finding deserves further investigation.

The authors acknowledged that the meta-analysis may have been underpowered to identify clinically important differences between the treatments. Meta-analysis using individual patient data might identify whether thrombolysis has a different effect depending on patient characteristics such as risk status or timing of treatment.

Nurses working in critical care settings would be most interested in this study. The results indicate that heparin is as effective as thrombolysis and less likely to cause non-major bleeding. However, more research needs to be done, with larger, adequately powered studies that use consistent methods and measurements.
Review: no evidence exists that thrombolysis is better than heparin for reducing the risk of recurrent pulmonary embolism and death

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