Comparison of urokinase, alteplase, and reteplase for catheter-directed thrombolysis of deep venous thrombosis

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
Three thrombolytic agents used in the catheter-directed thrombolysis of patients with deep venous thrombosis (DVT) were examined. The three agents were the plasminogen activator urokinase (UK), alteplase (a tissue plasminogen activator, TPA) and reteplase (a recombinant plasminogen activator, RPA). The doses used were reported.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with DVT who were undergoing catheter-directed thrombolysis.

Setting
The setting was a hospital. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness and resource use data were gathered from August 1997 to June 2003. The price year was 2003.

Source of effectiveness data
The effectiveness evidence was derived from a single study.

Link between effectiveness and cost data
The costing was carried out retrospectively on the same sample of patients as that used in the effectiveness study.

Study sample
Power calculations, if performed, were not reported. The patients were identified from the radiology information systems database. UK patients were treated between August 1997 and May 1999 and between February and June 2003. TPA patients were treated between August 1999 and February 2003. RPA patients were treated between May 2001 and January 2003. Overall, 74 patients (27 men, 47 women) with 82 involved extremities were identified. The mean age of these patients was 49.6 (+/- 18.5) years.

Study design
This was a retrospective, comparative study with a historical control that was carried out at a single centre. It was not stated whether the patients were followed-up after hospital discharge. No patient was lost to the follow-up assessment. Fellowship-trained, full-time vascular interventional radiologists performed all thrombolytic procedures.

**Analysis of effectiveness**

All of the patients included in the initial study sample were accounted for in the analysis of effectiveness. The outcomes used were:

- the hourly infused dose,
- the total drug dose,
- the infusion time,
- the proportions of patients with complete, or complete or partial resolution of thrombus, and
- the proportions of patients with major, or major or minor complications.

Complete success was defined as cases in which there was less than 5% residual thrombus. Partial success was defined as cases in which short venous segments remained that demonstrated residual narrowing or occlusion.

Major complications were defined as death, intracranial haemorrhage, pulmonary embolism, bleeding requiring transfusion or surgery, unplanned hospitalisation, or prolonged hospitalisation. Minor complications were defined as adverse events requiring minimal therapy that did not prolong hospital stay.

At baseline, the study groups were comparable in terms of their gender, age, thrombus location, duration of symptoms, and use of additional interventional therapies.

**Effectiveness results**

No statistically significant differences were observed in any of the outcome measures.

The rate of complete resolution of thrombus was 71.1% with UK, 65.6% with TPA, and 50% with RPA. The rates of complete or partial resolution of thrombus were 97.4% (UK), 96.9% (TPA) and 100% (RPA), respectively.

The rate of major resolution of thrombus was 5.3% with UK, 3.1% with TPA, and 8.3% with RPA. The rates of major or minor resolution of thrombus were 10.5% (UK), 12.5% (TPA) and 16.7% (RPA), respectively.

**Clinical conclusions**

The effectiveness analysis showed that the three treatments were comparable in their efficacy, safety and infusion times.

**Measure of benefits used in the economic analysis**

No summary benefit measure was used since there was no statistically significant difference between the groups in terms of the outcome measures. In effect, a cost-minimisation analysis was carried out.

**Direct costs**

Discounting was not relevant because of the short timeframe of the analysis. The unit costs were presented separately from the quantities of resources used. The economic evaluation considered only the cost of the three thrombolytic agents. The cost/resource boundary of the authors' institution was adopted. Resource use was estimated on the basis of retrospectively collected data that came from the same sample of patients as that used in the effectiveness study. The costs came from contractual prices at the authors' institution in July 2003.
Statistical analysis of costs
The costs were presented as medians along with 25th and 75th percentiles. Statistical tests of the statistical significance of differences in drug costs were also conducted.

Indirect Costs
The indirect costs were not considered in the economic evaluation.

Currency
US dollars ($).

Sensitivity analysis
Sensitivity analyses were not carried out.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The median drug costs (25th - 75th percentiles) were $6,577 (3,144 - 14,212) with UK, $488 (255 - 666) with TPA, and $1,787 (1,296 - 2,006) with RPA. (UK versus TPA, p<0.001; UK versus RPA, p<0.01; RPA versus TPA, p<0.05).

Synthesis of costs and benefits
A synthesis of the costs and benefits was not relevant since a cost-minimisation analysis was carried out.

Authors’ conclusions
Urokinase (UK), tissue plasminogen activator (TPA) and recombinant plasminogen activator (RPA) were equally effective in the treatment of deep venous thrombosis (DVT). However, TPA and RPA were significantly cheaper than UK.

CRD COMMENTARY - Selection of comparators
The authors provided a justification for the choice of the comparators. UK represented the standard treatment until mid-1999, while TPA and RPA were more commonly used after 2000. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence came from a retrospective review of patients' charts. The use of a prospective trial would have been more appropriate. The retrospective design and the lack of random treatment allocation could have limited the internal validity of the study. The study groups were comparable at baseline, but the impact of confounding factors and selection bias cannot be ruled out. There was no evidence that the sample size was appropriate. No data on the length of follow-up was reported.

Validity of estimate of measure of benefit
No summary benefit measure was used in the analysis because a cost-minimisation analysis was conducted. Please refer to the comments in the 'Validity of estimate of measure of effectiveness' field (above).
Validity of estimate of costs
The cost analysis considered only drug acquisition prices, which were estimated from the authors' institution. The price year was reported, which aids reflation exercises in other settings. Similarly, the unit costs were provided. Statistical analyses of the costs were carried out, but the cost estimates were specific to the study setting. The authors noted that the pharmacoeconomic analysis was constrained by the possibility that the doses of UK used in the study were higher than those necessary to achieve successful thrombolysis.

Other issues
The authors stated that their findings were consistent with those from other published studies, although the success rates they found were higher. A possible explanation for such discrepancies was provided. The authors noted some limitations of their analysis. For example, the small sample size and the lack of a simultaneous assessment of the study groups.

Implications of the study
The study results supported the use of TPA and RPA for the treatment of DVT. The authors stressed that their findings should be corroborated in a prospective, randomised, multi-centre, clinical trial.

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Other publications of related interest

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