Intrapleural streptokinase versus urokinase in the treatment of complicated parapneumonic effusions: a prospective, double-blind study

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
Two treatment strategies, intrapleural streptokinase (SK), and intrapleural urokinase (UK), involving the use of fibrinolytic therapy in the treatment of complicated parapneumonic effusions (CPE) and pleural empyema were compared.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Patients with complicated CPE (multiloculated pleural effusion confirmed by chest computed tomographic scanning (CT), ultrasound (US) or both, which was unresolved with the single thoracostomy) or empyema (with pus on thoracocentesis, or positive smear or pleural fluid cultures for bacteria and concomitant pneumonia).

Setting
Hospital. The economic study was carried out in Crete, Greece.

Dates to which data relate
The data for the effectiveness and resource use corresponded to patients admitted to the study institution between January 1990 and December 1995. The price date used was not reported.

Source of effectiveness data
Effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was undertaken only for the costs associated with drugs and was carried out, prospectively, on the same patient sample as that used in the effectiveness study.

Study sample
No power calculations were reported. A total of 50 patients was included in the analysis. Twenty-five patients were randomly included in the SK group and 25 in the UK group. The median age in the UK group was 51 (range: 17 - 89) versus 47 (range: 15 - 92) years in the SK group. One attending physician (who took the decision as to whether to continue fibrinolytic therapy or to proceed to thoracotomy), and a chest physician and a radiologist (who independently
evaluated the radiographic improvement) constituted the main operating team in the study.

**Study design**
This was a randomised double blind study carried out in a single centre. The mean duration of follow-up was 12 months (range: 6 - 30 months). No loss to follow-up was reported.

**Analysis of effectiveness**
The analysis was based on the intention to treat principle. The primary health outcome used was the response rate which was measured in terms of chest radiograph change, change in the mean daily fluid drainage and rate of treatment failure. The chest radiograph change measurement resulted from the comparison of the last chest radiograph obtained before starting treatment with either drug, and the chest radiograph taken at the end of treatment. From these radiographs, the dimension of the pleural effusion was estimated by measuring the two maximal diameters at right angles to each other. A score of 0 represented no change, 1 stood for less than one-third improvement, 2 for an improvement of magnitude between one and two thirds, and 3 for an improvement higher than two thirds. The mean daily fluid drainage after drug administration, as well as the volume of drainage for the first 24 hours after instillation, was compared to the drainage volume 24 hours before treatment. Side effects were also recorded. Haematological and biochemical parameters were shown to be comparable between groups. The median age of the groups, pH, glucose levels, lactate dehydrogenase (LDH) and white blood cell count levels were shown to be comparable between groups.

**Effectiveness results**
The mean volume drained during the first 24 hours after instillation was 380ml (+/- 99), as opposed to 47.6 (+/- 23) ml during the 24 hours previous to treatment, for the SK group, (p<0.001). The corresponding figures for the UK group were 420.8ml (+/- 110) and 55.5 (+/- 31) ml, (p<0.001), respectively. The mean daily pleural fluid drainage was reported to result in a significant increase for either drug relative to the drained volume 24 hours before initiation of treatment, (p<0.001). The overall improvements in the chest radiographic score were 2.5 (+/-0.7) and 2.7 (+/- 0.8), for the SK and UK groups, respectively, (p>0.05). There were two cases in each group in which an inadequate pleural fluid evacuation led to surgical intervention. Seven patients (28%) in the SK group experienced transient fever. No other adverse effects, or complications of tube thoracostomy were observed.

**Clinical conclusions**
The results suggest that early administration of UK is more effective.

**Measure of benefits used in the economic analysis**
No summary benefit measure was identified in the economic study, and only separate health outcomes were reported.

**Direct costs**
Costs were not discounted. The mean length of hospital stay (LOS) associated with each group was reported. The costs measured were only the (fibrinolytic) drug costs. The boundary adopted was the hospital. The estimation of quantities (LOS) and costs (drugs) was based on actual data. The quantities of resource use reported corresponded to patients admitted to the institution between January 1990 and December 1995. The price date used was not reported. The costs of antibiotics used during hospital stay were not included in the analysis, nor was the LOS translated into costs.

**Statistical analysis of costs**
Mean and standard deviation, for each treatment strategy, were reported.

**Indirect Costs**
Not considered.
Currency
US dollars ($).

Sensitivity analysis
No sensitivity analysis was performed.

Estimated benefits used in the economic analysis
Not applicable.

Cost results
The LOS for the SK group was 11.28 (+/- 2.44) days, whereas for the UK group 10.48 (+/- 2.53) LOS days were reported. The average total fibrinolytic drug cost was $180 (+/- 47) for SK and $320 (+/- 123) for UK.

Synthesis of costs and benefits
Costs and benefits were not combined.

Authors' conclusions
Intrapleural SK or UK is an effective adjunct in the management of parapneumonic effusions and may reduce the need for surgery. The authors reported to have found, in another study, that smaller doses of UK (50,000 IU) are also effective, and the cost of treatment is the same as that of SK. The authors stated that UK could be the treatment of choice in CPE and empyema given the potentially dangerous allergic reactions to SK and relatively small higher cost of UK.

CRD COMMENTARY - Selection of comparators
A justification was given for the choice of the comparator. SK was regarded as the recommended treatment of choice in the context in question. You, as a database user, should consider whether this is a widely used health technology in your own setting.

Validity of estimate of measure of effectiveness
The estimate of effectiveness is likely to be internally valid given the randomised design adopted in the study.

Validity of estimate of measure of benefit
Since no summary benefit measure was identified in the economic analysis, the study should be regarded as a cost-consequences study.

Validity of estimate of costs
The LOS was reported (as a resource utilisation item) separately from the costs associated with the drug use. The price date used was not reported. The study lacked a comprehensive cost analysis.

Other issues
Comparisons with other studies were carried out in terms of the effectiveness results (supporting the present study's findings). The issue of generalisability to other settings or countries was partially addressed by comparing the cost relationship in USA and Greece.

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