Comparison of propofol/remifentanil and sevoflurane/remifentanil for maintenance of anaesthesia for elective intracranial surgery

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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
The use of sevoflurane (initial end tidal concentration 2%) and propofol (target 2 microg/mL) for the maintenance of anaesthesia during neurosurgical procedures. These were combined with remifentanil, a short-acting opioid (1 microg/kg followed by an infusion commencing at 0.5 microg/kg per minute, and reducing to 0.25 microg/kg per minute after craniotomy).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised unmedicated patients undergoing elective craniotomy at Derriford Hospital, Plymouth, UK.

Setting
The setting was secondary care. The economic study was carried out at Derriford Hospital, Plymouth, UK.

Dates to which data relate
The dates to which the effectiveness, resource and price data referred were not stated.

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

Link between effectiveness and cost data
The costing was undertaken retrospectively on the same patient sample as that used for the effectiveness study.

Study sample
The size of the study was determined by an a priori power calculation using data from a previous study. This suggested that the enrolment of 20 patients per group would determine a difference of 4 minutes in time to tracheal extubation with a power of 80% and a p-value of less than 0.05. Twenty-four patients were assigned to propofol anaesthesia (group P) and 26 to sevoflurane anaesthesia (group S).
Study design
This was a prospective, randomised, blind, single-centre study. Treatment allocations were generated using the random number function of Microsoft Excel Version 7.0 software and were concealed in individual opaque envelopes until shortly before the patient was anaesthetised.

Analysis of effectiveness
The analysis of effectiveness was conducted on an intention to treat basis. The primary outcomes were:

- the time of anaesthesia,
- brain condition,
- the number of hypertensive episodes,
- the number of hypotensive episodes,
- the number of patients who received labelotol,
- the number of patients who received ephedrine,
- postoperative nausea and vomiting (PONV), and
- the times to spontaneous respiration, eye opening, extubation and obeying commands.

There were no statistically significant differences between the two groups in terms of their age, gender, height, weight, body max index, operation (tumour/aneurysm/microvascular) and location (supratentorial/posterior fossa). A regression analysis was performed to explore the relationship between recovery time and hypotensive episodes.

Effectiveness results
Anaesthesia time was longer in group P, but the difference was not statistically significant, 200 minutes (range: 107 to 310) versus 164 minutes (range: 90 to 350), (p=0.082).

There were no statistically significant differences in brain condition between the two groups.

Arterial pressure before, during and after surgery was similar in the two groups.

Hypertensive episodes were seen in 7 patients in group P and 8 patients in group S. These patients experienced a median of 1 (range: 1 to 7) and 1 (range: 1 to 4) hypertensive episodes, respectively. The difference was not statistically significant, (p=0.374, chi-squared test).

Labetolol was given to 14 patients in group P (mean total dose 45 mg, standard deviation (SD)=33) and 19 in group S (mean total dose 76 mg, SD=58), (p=0.073).

Hydralazine was given to 2 patients in group P and 5 patients in group S.

Hypotensive episodes were seen in 15 patients (median 2, range: 1 to 4) in group P and 23 patients (median 3, range: 1 to 7) in group S, (p=0.053).

Ephedrine was given to 63% of patients in group P and 88% of group S. The total doses were 4.8 (2.2) mg in group P, and 9.8 (5.6) mg in group S, (p=0.02).

Time to spontaneous respiration was significantly shorter in group P than in group S, 7.0 minutes (range: 2.0 to 31.0) versus 10.0 minutes (range: 1.0 to 24.0), (p=0.02).

Time to eye-opening was 7.5 minutes (range: 3.0 to 30.0) in group P and 12.0 minutes (range: 3.0 to 33.0) in group S.
Time to extubation was 8.5 minutes (range: 3.0 to 40.0) in group P and 11.0 minutes (range: 3.0 to 33.0) in group S.

Time to obeying commands was 10.5 minutes (range: 3.0 to 40.0) in group P and 13.0 minutes (range: 4.0 to 48.0) in group S. These differences were not statistically significant.

**Clinical conclusions**
The study showed that both propofol/remifentanil and sevoflurane/remifentanil provided satisfactory anaesthesia for intracranial surgery.

**Measure of benefits used in the economic analysis**
The authors did not develop a summary benefit of measure for use in the economic analysis. In effect, a cost-consequences analysis was carried out.

**Direct costs**
The cost/boundary adopted for the costing appears to have been that of the hospital. Drugs for anaesthesia were the only area of expenditure included in the study. Discounting was not relevant because of the short follow-up period. No price year was reported.

**Statistical analysis of costs**
The costs were treated stochastically.

**Indirect Costs**
No indirect costs were included.

**Currency**
UK pounds sterling (£).

**Sensitivity analysis**
No areas of uncertainty were identified or investigated.

**Estimated benefits used in the economic analysis**
Given the cost-consequences approach adopted, the reader is referred to the 'Effectiveness Results' section.

**Cost results**
The acquisition cost of propofol was 3.83 per 20 mL ampoule for group S and 9.58 per 50 mL syringe for group P.

Remifentanil cost 5.98 per mg.

The cost of sevoflurane was calculated by the Rosenberg method, with an acquisition cost of 137.30 per 250 mL and a total flow of 1.5 L/minute.

The total hypnotic and analgesic drug costs of Group P were significantly higher than in group S, median cost 58.63 versus 39.03.

Group S required more vasoactive medication (labetolol, 2.94 per 100 mg; hydrazoline, 1.62 per 20 mg; ephedrine, 1 per 30 mg).
The combined hourly cost of hypnotic, analgesic and vasoactive medications was higher in group P than in group S. The median values were 19.31/hour for group P and 15.52/hour for group S, (p=0.016).

**Synthesis of costs and benefits**
The costs and benefits were not combined because of the cost-consequences approach adopted.

**Authors’ conclusions**
Both agents were appropriate for intracranial surgery. The combined hourly acquisition costs of hypnotic, analgesic and vasoactive drugs appeared to be lower in patients maintained with sevoflurane than with propofol.

**CRD COMMENTARY - Selection of comparators**
The rationale for the choice of the comparator was clear as it represented standard practice during neurosurgical procedures in the UK. You should decide whether this represents current practice in your own setting.

**Validity of estimate of measure of effectiveness**
Randomised controlled trials have become the accepted ‘gold’ standard for evaluating therapeutic efficacy. The primary outcomes were anaesthesia time, brain condition, numbers of hypertensive and hypotensive episodes, number of patients who received labetolol, number of patients who received ephedrine, PONV, and times to spontaneous respiration, eye opening, extubation and obeying commands. These are valid measures of effectiveness for the technology and patient domain examined. Appropriate statistical analyses were undertaken on the effectiveness data, and the effectiveness analysis appears to have been handled credibly. The sample size was determined by a power calculation. The results should, overall, have high validity.

**Validity of estimate of measure of benefit**
As a cost-consequences approach was adopted, the reader is referred to the commentary in the ‘Validity of estimate of measure of effectiveness’ field (above). The lack of a generic summary measure of benefit means that it would be difficult to make comparisons with other technologies necessary to help decision-makers in the allocation of resources. However, for the technology examined, it would not have been feasible to adopt measures such as the quality-adjusted life-year.

**Validity of estimate of costs**
The study perspective appears to have been that of the hospital. However, the costing study was limited to the costs of the drugs. Associated equipment and disposables costs were excluded; if these were not identical between the groups, difference in cost results should be treated with some caution. The resource quantities and the unit costs were reported separately. Neither the price year nor the source of the price data were reported, which will limit the transferability of the results to other settings.

**Other issues**
The authors made extensive and detailed comparisons of their findings with those of other studies. They acknowledged that the drug costs were very small in relation to the total cost of the neurosurgical procedure, thus cost-differences between sevoflurane and propofol should be interpreted cautiously as they ignore associated costs of equipment and disposables. The authors did not explicitly address the issue of generalisability of the results to other settings and the results could reflect the actual pattern of procedure for intracranial surgery in the UK. Caution will therefore be required when extrapolating the results to other settings.

**Implications of the study**
The study suggested that sevoflurane and propofol are both satisfactory agents for elective intracranial surgery.
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