Comparative analysis of costs of total intravenous anaesthesia with propofol and remifentanil vs. balanced anaesthesia with isoflurane and fentanyl

Epple J, Kubitz J, Schmidt H, Motsch J, Bottiger B W, Martin E, Bach A

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 total intravenous anaesthesia with remifentanil and propofol (TIVA-RP) before surgery. The anaesthetic regimen consisted of propofol (1.5 mg/kg) and remifentanil (1 ng/kg) administered to the patients over 3 minutes for the induction of anaesthesia, followed by a continuous infusion of propofol (0.05 - 0.1 mg/kg per minute) and remifentanil (0.15 - 0.3 ng/kg per minute) to maintain anaesthesia.

Type of intervention
Other (anaesthetic).

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised geriatric patients (aged over 65 years and with ASA physical status I, II or III) who were scheduled for elective cataract surgery under general anaesthesia.

Setting
The setting was tertiary care. The economic study appears to have been performed in Heidelberg, Germany.

Dates to which data relate
The dates to which the effectiveness and cost data related were not reported. The price year was not given.

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

Link between effectiveness and cost data
The costing was performed prospectively on the same sample population as that used for the effectiveness analysis.

Study sample
The authors reported that a minimum of 51 patients were required in each group to provide 80% power to detect a difference of at least 15 minutes in the time from the end of surgery until ready for discharge from the PACU (this was used as the primary end point in the effectiveness analysis). Geriatric patients scheduled for elective cataract surgery under general anaesthesia (aged over 65 years with ASA physical status I, II or III) were considered for the effectiveness analysis. Patients were excluded if they had a history of allergic reactions to one of the drugs used. The final study sample consisted of 124 patients (62 in each group). The authors stated that the study sample was
representative of the study population in term of the prevalence of systemic co-morbidity, although they did not provide any supporting evidence.

**Study design**
This was a prospective, randomised clinical trial (RCT), which appears to have been performed in a single centre. The patients were randomly allocated to the alternative anaesthesia procedures according to a computer-generated randomisation schedule. The patients were followed up from the moment they arrived in the operating room until 24 hours after anaesthesia. No loss to follow-up was reported. The authors reported that this was a single-blind study since the anaesthetist in charge of assessing some of the outcomes was not blinded to the anaesthetic technique.

**Analysis of effectiveness**
The basis of the clinical analysis was intention to treat. The primary health outcomes assessed in the effectiveness analysis for both anaesthetic procedures were:

- the mean time from the beginning of the anaesthetist's presence until anaesthesia induction was complete;
- the mean time from the start to the end of surgery;
- the mean time from the end of surgery until tracheal extubation, arrival in the PACU, and achievement of an Aldrete score of greater than 8;
- the mean recovery time (i.e. from end of surgery until PACU discharge readiness);
- the percentage of patients requiring related drug therapy;
- the incidence of postoperative shivering;
- the occurrence of adverse events;
- the percentage of patients who experienced a more pleasant recovery from anaesthesia than expected; and
- the percentage of completely satisfied patients (i.e. those who would choose the same anaesthesia regimen again).

A questionnaire was used on the first postoperative day to ask patients about postoperative complaints (nausea, vomiting, headache, wound pain, muscle pain, pain at the venous cannula location, sore throat, hoarseness, coughing, thirst and shivering) and satisfaction. The groups were shown to be similar in terms of their age, gender, ASA physical status, height and weight.

**Effectiveness results**
The mean time from the beginning of the anaesthetist's presence until anaesthesia induction was complete was 66.9 (standard deviation, SD=15.3) minutes in the TIVA-RP group, and 76.3 (SD=11.7) minutes in the BA-FI group, (p<0.001).

The mean time from the start to the end of surgery was 28.4 (SD=11.4) minutes in the TIVA-RP group, and 27.5 (SD=8.6) minutes in the BA-FI group, (p>0.05).

The mean time from the end of surgery until tracheal extubation was 4.6 (SD=3.2) minutes for the TIVA-RP group, and 11.1 (SD=4.9) minutes for the BA-FI group, (p<0.001).

The mean time from the end of surgery until arrival in the PACU was 7.2 (SD=3.1) minutes for the TIVA-RP group, and 14.9 (SD=4.4) minutes for the BA-FI group, (p<0.001).

The mean time from the end of surgery until an Aldrete score of greater than 8 was achieved was 13.1 (SD=13.7)
minutes for the TIVA-RP group, and 31.2 (SD=19.8) minutes for the BA-FI group, (p<0.001).

The mean recovery time was 77.3 (SD=31.0) minutes in the TIVA-RP group, and 93.9 (SD=47.6) minutes in the BA-FI group, (p<0.05).

In total, 52% of the TIVA-RP patients and 27% of the BA-FI patients needed cardiovascular medication after the anaesthetic procedure. None of the TIVA-RP patients required anti-emetic therapy, compared with 13% of the BA-FI patients. Sixteen per cent of the TIVA-RP patients and 8% of the BA-FI patients needed analgesics for postoperative pain (this difference was not statistically significant).

The incidence of postoperative shivering was significantly higher in the TIVA-RP group (10%) than in the BA-FI group (0%).

The response rate for the questionnaire used to assess the occurrence of adverse events and the patient's satisfaction was 97%.

The occurrence of adverse events was as follows:

- nausea occurred in 10% of the TIVA-RP patients and 34% of the BA-FI patients, (p=0.001);
- vomiting occurred in 3% of the TIVA-RP patients and 23% of the BA-FI patients, (p=0.002);
- coughing occurred in 45% of the TIVA-RP patients and 20% of the BA-FI patients, (p=0.003); and
- shivering occurred in 24% of the TIVA-RP patients and 2% of the BA-FI patients, (p<0.001).

A significantly higher proportion of TIVA-RP patients (56%) experienced a more pleasant recovery than expected in comparison with BA-FI patients (33%), (p=0.022).

The proportion of completely satisfied patients was 93.2% in the TIVA-RP group versus 65.6% in the BA-FI group, (p<0.001).

**Clinical conclusions**

While the mean times from the start to the end of surgery were not significantly different for TIVA-RP in comparison with BA-FI, TIVA-RP had advantages over BA-FI in terms of the recovery times. However, a higher percentage of patients receiving TIVA-RP needed cardiovascular medication and analgesics, and experienced coughing and shivering. On the other hand, a higher percentage of patients in the BA-FI group required anti-emetic therapy and experienced nausea and vomiting. The percentage of patients completely satisfied was significantly higher in the TIVA-RP group.

**Modelling**

The authors developed a model to simulate the patient flow through an operating suite in order to compare the cost-effectiveness of the two anaesthesia regimens under analysis. The type of model used was not reported. Two alternative scenarios were considered according to the operating suite work schedules. One had a given number of cases per day with an unlimited closing time, while in the other the closing time of the operating room was fixed. For the base-case analysis it was assumed that there were three operating theatres and one postanaesthetic recovery room (PACU).

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

The summary measure of benefit used in the economic analysis was the number of patients completely satisfied with the anaesthesia regimen. This was obtained from the questionnaire used in the effectiveness analysis. Therefore, the valuation was obtained directly from those patients included in the effectiveness analysis who answered the questionnaire.
Direct costs
Most of the resource quantities were reported separately from the costs. The direct costs considered in the economic analysis were those of the anaesthesia department. These were for the acquisition of drugs (including waste) and disposable material (e.g. perfusion syringes and cannulas), and for all anaesthesia staff involved (anaesthetists and anaesthesia nurses). The costs of the drugs and materials were obtained from the acquisition costs of the department in which the study was performed. The costs of isoflurane were derived from a published study. The staff costs were based on the clinical intern salaries. Therefore, the prices were estimated from actual data. Discounting was not performed, but it was irrelevant given that the costs were incurred in less than 2 years. The economic analysis reported the average costs. The dates to which resource use related were not reported, and the price year was not stated.

Statistical analysis of costs
The authors reported that the time intervals and expenses for drugs, materials, and staff were evaluated using Student t-tests (for comparison of mean values), F-tests (for SDs) and U-tests (for medians).

Indirect Costs
No indirect costs were reported.

Currency
Euros (Euro).

Sensitivity analysis
Sensitivity analyses were performed. Several input parameters were varied, such as the time intervals and the number of operating theatres in use (assuming that there was only one operating theatre instead of three). Therefore, the area of uncertainty investigated was variability in data, on one hand, and generalisability of the results on the other. Multi-way sensitivity analyses, which considered four alternative scenarios, appear to have been performed. The scenarios considered an operating room with a given number of cases per day and an unlimited closing time versus an operating room with a fixed closing time and unlimited cases per day, and a combination of three operating theatres and one PACU versus only one operating theatre and one PACU.

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

Cost results
The total cost per case was significantly lower in the TIVA-RP group than in the BA-FI group. The cost was Euro 164.15 (SD=27.70) per patient in the TIVA-RP group versus Euro 176.40 (SD=23.45) per patient in the BA-FI group, (p<0.001). Therefore, compared with the BA-FI group, the total cost of anaesthesia was reduced by Euro 12.25 per case in the TIVA-RP group.

Synthesis of costs and benefits
Cost-effectiveness ratios were calculated for both groups by dividing the total cost per patient by the fraction of completely satisfied patients (as assessed by the questionnaire). The cost-effectiveness ratio was significantly lower in the TIVA-RP group (Euro 176.13, SD=29.72) than in the BA-FI group (Euro 268.90, SD=35.75), (p<0.001).

Results from the sensitivity analyses showed that, independently of whether the closing time or the number of patients per day were fixed, and independently of whether there were three operating theatres or only one, more patients per day would be dealt with or less time would be required if TIVA-RP were used.
Authors' conclusions
The use of total intravenous anaesthesia with remifentanil and propofol (TIVA-RP) as a general anaesthetic regimen before cataract surgery had advantages over balanced anaesthesia with fentanyl and isoflurane (BA-FI), since it had lower total costs, higher patient satisfaction, and a more efficient operating theatre schedule.

CRD COMMENTARY - Selection of comparators
The authors justified their choice of the comparator. BA-FI was chosen since it was the most inexpensive current alternative for general anaesthesia in terms of drug costs, and it was also the standard method used in the authors' setting before the introduction of TIVA-RP. You should consider if BA-FI is a widely used anaesthetic procedure in your own setting.

Validity of estimate of measure of effectiveness
The study used a RCT. This was appropriate for the study question since it is the 'gold'-standard design, with the potential to provide a degree of assurance about the validity of the results obtained. The authors stated that the study sample was representative of the study population in terms of the prevalence of systemic co-morbidity, but they did not provide any evidence to support this. The patient groups were shown to be similar in terms of their age, gender, ASA physical status, height and weight.

Validity of estimate of measure of benefit
The summary measure of health benefit was obtained directly from the clinical study. The choice of the summary measure of health benefit used in the economic analysis was justified on the grounds that it had been used in another study (Tang et al., see Other Publications of Related Interest). A positive aspect of using this measure was that it was obtained directly from the patients' opinions through a questionnaire, and the rate of response to this questionnaire was high. However, the questionnaire was designed specifically for this study and had not been validated. This may have introduced uncertainty into the reliability of the conclusions. The methods of randomisation, sample selection, length and loss to follow-up were all reported, suggesting that the overall internal validity of the study is likely to be quite high.

Validity of estimate of costs
The perspective adopted was limited to the anaesthesia department. However, this perspective appears to have been adequate since the anaesthesia intervention is an intermediary intervention, in the sense that its aim is not to affect the final health of patients, but to avoid the patients experiencing pain during surgery. Most of the costs related to this perspective seem to have been considered for the economic analysis. Some costs (e.g. oxygen air, pulse oximeter probes, and anaesthetic circuit) were not included since they were common to both anaesthesia procedures. The costs related to facilities, administrative clerks, and so on, were also not included, and the authors stated that these costs would be lower for the TIVA-RP option. Most of the resource quantities were reported separately from the costs, and statistical analyses of the quantities reported were performed. These factors may enhance the reliability of the conclusions. Nevertheless, the dates to which the costs and resource use related, and the price year, were not reported. This hinders reflation exercises to other settings. Discounting was not reported, but was irrelevant since the costs were incurred in less than 2 years.

Other issues
The authors made appropriate comparisons of their findings with those from other studies in terms of recovery times, adverse effects and the cost analysis. The authors commented that the results cannot always be generalised to other settings since there are differences in drug, material and personnel costs across different hospitals, even in the same country. The study enrolled patients scheduled for elective cataract surgery under general anaesthesia, and this was reflected in the authors' conclusions.

Implications of the study
The results of this study showed that the use of TIVA-RP as a general anaesthetic regimen before elective cataract
surgery has advantages in terms of recovery times, use of operating theatre and lower costs.

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