Comparison of hemodynamics, recovery profile, and early postoperative pain control and costs of remifentanil versus alfentanil-based total intravenous anaesthesia (TIVA)
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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 two combinations of drugs for total intravenous anaesthesia, remifentanil plus propofol (RP) versus alfentanil plus propofol (AP). In the anaesthesia procedures, either remifentanil (1 microg/kg) or alfentanil (20 microg/kg) was given over 60 seconds with a bolus syringe, followed by the infusion of either remifentanil (0.2 microg/kg per minute) or alfentanil (1 microg/kg per minute). Propofol was then given for hypnosis at a dose of 2 mg/kg, and was maintained at a dose starting at 150 microg/kg per minute.

Type of intervention
Anaesthesia.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients aged 28 to 70 years who were scheduled for lumbar discectomy procedures under general anaesthesia. Patients were excluded if they had significant arrhythmia, uncontrolled hypertension, or significant psychiatric, cardiovascular, renal or hepatic disease. Also excluded were patients with hypersensitivity to opioids or propofol, and chronic exposure to opioids, beta-blockers, alpha-adrenoceptors, anticonvulsants or benzodiazepines.

Setting
The clinical setting was a teaching hospital. The economic study was performed at the Gazi University School of Medicine, Ankara, Turkey.

Dates to which data relate
There was no information on when the effectiveness or resource use data were gathered. The price year was 2001.

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 of patients as that used in the effectiveness study.

Study sample
Power calculations were performed. These showed that a minimum sample of 20 patients in each group would have
been required to detect a difference in clinical outcomes with a power of 80% at the required level of significance.

Forty patients with ASA physical status I and II, who were scheduled for lumbar discectomy with general anaesthesia, were enrolled in the study. The patients were randomised into two groups receiving either RP (n=20) or AP (n=20). The study sample appears to have been appropriate for the clinical study question. No patient refused to participate or was excluded from the study. The mean age was 43.3 (+/- 10.7) years in the RP group and 48.5 (+/- 9.5) in the AP group. There were 14 men in the RP group and 13 men in the AP group.

**Study design**

This was a double-blind, randomised controlled trial that was performed in a single centre. In terms of follow-up, the outcomes were estimated during or immediately after the operation. A postoperative care unit (PACU) nurse was blinded to the patients' details for at least 1 hour in assessing postoperative nausea and vomiting, other side effects, the need for analgesic medication, and vital signs.

**Analysis of effectiveness**

Although the method of analysis (intention to treat or treatment completers only) was not stated, all of the patients initially included in the study were considered for the analysis of clinical effectiveness. The primary health outcomes assessed in the analysis were haemodynamics, recovery profiles and postoperative pain. The primary outcomes related to haemodynamics were heart rate, mean arterial pressure, partial oxygen saturation and respiratory rate. Recovery profiles were time to extubation, time to spontaneous eye opening, and response to verbal command (time). Postoperative pain was measured using a visual analogue scale (VAS) at 30 and 60 minutes after extubation. The number of patients with postoperative nausea and vomiting and the number requiring analgesics were also assessed. There was no statistically significant difference between the two groups in terms of age, gender, ASA physical status, weight, height, and duration of operation and anaesthesia.

**Effectiveness results**

There was no statistically significant difference between the two groups in heart rate in any of the periods considered, from induction of anaesthesia to 30 minutes after the operation.

The mean arterial pressure was significantly lower at 5, 15 and 30 minutes postoperatively for patients in the RP group than for those in the AP group, (p<0.05).

The respiratory rates and partial oxygen saturation values showed a significantly faster recovery in the RP group than in the AP group, (p<0.05).

There was no significant difference between the two groups for time to extubation, 6.3 (+/- 3.4) minutes for RP versus 6.1 (+/- 1.8) minutes for AP. Nor was there any significant difference in time to spontaneous eye opening, 7.4 (+/- 3.8) minutes for RP versus 7.4 (+/- 2.3) minutes for AP.

There was also no significant difference between the two groups for response to verbal command time, 7.9 (+/- 4.3) minutes for RP versus 7.5 (+/- 2.9) minutes for AP.

The RP group showed a significantly higher postoperative pain at 30 minutes and at 60 minutes. At 30 minutes, the VAS was 6.8 (+/- 2.4) for RP versus 3.9 (+/- 1.6) for AP, (p<0.05). At 60 minutes, the VAS was 6.6 (+/- 1.9) for RP versus 5.1 (+/- 1.9) for AP, (p<0.05).

The frequency of postoperative nausea and vomiting was similar in the two groups. However, a significantly higher number of patients required analgesics in the RP group (9) than in the AP group (0), (p<0.05).

**Clinical conclusions**

The authors concluded that both techniques provided reasonably rapid and reliable recovery from anaesthesia. However, while RP provided significantly better results in terms of haemodynamics (respiratory rate, in particular), it was characterised by higher postoperative pain and a higher number of patients requiring analgesics.
Measure of benefits used in the economic analysis
No summary benefit measure was used. A cost-consequences analysis was therefore carried out.

Direct costs
No discounting was applied, which was appropriate given the short time horizon of the costing analysis. The quantities of resource use and the unit costs were reported separately. The quantity/cost boundary was not explicitly reported, but it may have been that of the hospital. Only the costs of the drugs were considered in the analysis, because the staffing costs and operating room costs were assumed to be equivalent in the two groups. The quantities of resources used were estimated prospectively on the sample of patients included in the study. The unit costs were taken from the hospital pharmacy list and were based on the direct cost to the hospital from the manufacturer. There was no information on when the resource use data were gathered. The price year was 2001.

Statistical analysis of costs
Statistical analyses of the costs were performed using analysis of variance or Kruskal-Wallis tests.

Indirect Costs
The indirect costs were not included in the analysis.

Currency
US dollars ($). The original currency was Turkish Lira (TL), but the results were only reported in US dollars ($). The exchange rate at 1 April 2001 was $1 = TL 1,1150,000.

Sensitivity analysis
Sensitivity analyses were not performed.

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

Cost results
The total intraoperative cost per patient when drug wastage was not included was $30.42 (+/- 4.68) in the RP group versus $28.04 (+/- 3.89) in the AP group, (p non significant). When drug wastage was considered, the total intraoperative cost in the RP group ($33.41 +/- 4.53) was significantly higher than that in the AP group ($29.97 +/- 4.1), (p<0.05).

Synthesis of costs and benefits
Not relevant because a cost-consequences analysis was performed.

Authors' conclusions
The combination remifentanil-propofol (RP) was associated with higher intraoperative costs and early postoperative pain in comparison with alfentanil-propofol (AP), but it provided a quicker respiratory recovery.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear. The authors compared two new anaesthesia procedures in order to assess their relative costs and effectiveness. This was the first study that directly compared these two
anaesthetic techniques. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness analysis used a double-blind randomised clinical trial, hence enhancing the internal validity of the study. Appropriate statistical analyses were performed to compare the two groups at baseline and to estimate the significance of the differences in health outcomes. Power calculations were performed to assess the sample size necessary to detect differences in the main outcome measures. The exclusion criteria were described in detail and the initial sample of patients appears to have been appropriate for the study question.

Validity of estimate of measure of benefit
No summary benefit measure was used in the economic analysis.

Validity of estimate of costs
Only the costs of the drugs were included in the analysis. The authors stated that, given the similarity in recovery profiles and in times from discontinuation of anaesthesia to extubation, staffing costs and operative room costs were assumed equivalent between the two groups. The unit costs were reported separately from the resources used, and the source of the unit costs was given. Statistical analyses were performed to detect the significance of differences in the total costs, but sensitivity analyses were not carried out. However, the authors estimated the total costs with and without drug wastage, and found different conclusions. The perspective of the analysis was not reported but, given the source of the unit costs, it may have been that of the hospital.

Other issues
The authors compared the results of their finding in clinical outcomes with other published studies. They recognised that anaesthetic drug prices could vary widely between different areas and, therefore, the issue of generalisability was not addressed (no sensitivity analyses performed). The authors also underlined the fact that the total costs of the two anaesthesia procedures might have been influenced by the special infusion sets used in their department and the subsequent drug wastage. A reduction in drug wastage, which was higher in the RP group, might reduce the relative cost of this group in comparison with AP.

Implications of the study
RP was more costly than AP for total intravenous anaesthesia in this study. However, a different level of drug wastage and the potential reduction in the unit cost of remifentanil might alter this finding.

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