Comparison of the time to extubation after use of remifentanil or sufentanil in combination with propofol as anesthesia in adults undergoing nonemergency intracranial surgery: a prospective, randomized, double-blind trial


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 remifentanil as total intravenous anaesthesia was studied. Patients were given 1 microg/kg remifentanil to induce anaesthesia, and anaesthesia maintained with a continuous remifentanil infusion of 0.25 microg/kg per minute. The remifentanil pump was left running until completion of the surgical dressing. A comparator group of patients were given the same treatment, except that sufentanil was used for anaesthesia instead of remifentanil. Patients were given 25 microg/kg, administered over 1 minute using a regular syringe pump, and anaesthesia maintained with a continual sufentanil infusion of 0.0025 microg/kg per minute. The sufentanil pump was stopped immediately after the placement of the last skin suture.

Both patient groups were given a target-controlled infusion of propofol using an electric syringe. It started 1 minute after opioid administration at an initial target blood concentration of 3 microg/mL; the target was decreased to 2.5 microg/mL to maintain anaesthesia. One hour before the anticipated end of surgery both groups were given propacetamol, 2 g intravenously. The patients had assisted ventilation until they recovered spontaneous breathing and were extubated when seven criteria were satisfied.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients aged between 18 and 75 years scheduled to have a supratentorial neurological procedure with a maximum duration of 8 hours, and who had immediate postoperative extubation planned. The patients had to fall into American Society of Anesthesiologists physical status class 1 - 3. They were excluded if they had altered consciousness, preoperative renal or hepatic dysfunction, severe chronic respiratory disease, or were expected to need postoperative sedation or mechanical ventilation.

Setting
The treatment was provided by a secondary care provider in an inpatient setting. The economic study was carried out in France.

Dates to which data relate
The dates to which the effectiveness and cost evidence referred were not given. The price year was not reported.
The costing was carried out prospectively on the same patients that provided the effectiveness evidence.

**Study sample**
The authors reported that 60 patients would be needed if the study was to have 90% power to detect a difference in extubation time of 15 minutes. All patients meeting the inclusion criteria were eligible. Sixty-four patients were enrolled initially in the study and 4 were excluded after randomisation (2 due to illness and 2 for administrative reasons). This meant that 29 patients received remifentanil and 31 sufentanil.

**Study design**
This was a randomised controlled trial that was conducted at a single centre. On the afternoon of the day preceding surgery, sealed envelopes were used to randomise patients between the two groups. The anaesthetist was blinded as to which group the patients belonged to, but the pharmacist administering the syringes containing remifentanil or sufentanil was not blinded. There was no follow-up after the patients left hospital.

**Analysis of effectiveness**
The primary outcome measured was the time to extubation. Other outcomes were haemodynamic stability (measured by mean arterial blood pressure and heart rate), postoperative morphine requirements and postoperative nausea and vomiting. The analysis was conducted on an intention to treat basis.

**Effectiveness results**
One patient in the sufentanil group was not extubated after 6 hours, their data being censored at 6 hours for drawing the Kaplan-Meier curves. It was unclear what the eventual outcome was for this patient.

There was no significant difference between the two patient groups in terms of extubation times. The median time to extubation was 10 minutes (interquartile range, IQR: 5 to 19) in the remifentanil group and 16 minutes (IQR: 10 to 30) in the sufentanil group, (p not significant).

Apart from the period just before scalp incision, the mean arterial blood pressure was significantly lower in the remifentanil group throughout the procedure, (p<0.05).

A significantly smaller proportion of patients in the sufentanil group received morphine (22.6% versus 44.8%; p=0.01).

Mean morphine doses over 6 hours postoperatively were 1.3 mg (standard deviation, SD=2.7) in the sufentanil group and 4.0 mg (SD=5.3) in the remifentanil group, (p=0.016).

The incidence of postoperative nausea and vomiting was similar in the two groups.

**Clinical conclusions**
In terms of the primary health outcome, time to extubation, there was no significant difference between the two kinds of anaesthesia. However, the greater use of morphine in the remifentanil group showed that these patients suffered from greater postoperative pain.

**Measure of benefits used in the economic analysis**
The authors did not derive a summary measure of health benefit. They carried out a cost-consequences analysis. See 'Analysis of Effectiveness' for the clinical outcomes measured. There was no need to discount the benefits as they occurred within one year.

**Direct costs**
The study reported the direct costs to the hospital. The costs included were those for remifentanil, sufentanil and propofol. The resource use data were obtained from the hospital, whereas the unit cost was obtained from local pharmacy acquisition costs. The unit costs of remifentanil and sufentanil were given. The doses (per patient) of remifentanil, sufentanil and propofol were also given. The costs of adverse effects were not dealt with. The costs were not discounted as they were incurred within one year. The price year was not reported.

**Statistical analysis of costs**
The mean and SDs of quantities of drugs used per patient were given.

**Indirect Costs**
Productivity costs were not considered.

**Currency**
Euros (EUR).

**Sensitivity analysis**
Uncertainty was not examined.

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

**Cost results**
The average cost per patient for anaesthetic drugs was EUR 51.9 in the remifentanil group and EUR 50.2 in the sufentanil group, (p not significant).

The average cost of propofol per patient was EUR 42.5 in the remifentanil group and EUR 46.5 in the sufentanil group, (p not significant).

The average cost of opioid per patient was EUR 9.4 in the remifentanil group and EUR 3.7 in the sufentanil group.

**Synthesis of costs and benefits**
The costs and benefits were not combined.

**Authors’ conclusions**
Although the cost per patient was higher for remifentanil than for sufentanil, the lower propofol cost meant that it did not lead to higher anaesthesia costs. The time to extubation did not differ between the two groups.

**CRD COMMENTARY - Selection of comparators**
The justification for comparing the two opioids in this study was that they were both commonly used for intracranial surgery. Remifentanil is noteworthy for allowing a rapid emergence from anaesthesia, but is more expensive in the authors' setting than sufentanil. You should decide if these represent valid comparators in your own setting.

**Validity of estimate of measure of effectiveness**
The analysis was based on a randomised controlled trial and power calculations were performed to ensure an adequate sample size. Thus, the study methodology ensured an adequate degree of validity. The authors described the
demographic and medical characteristics of the two patient groups in the study sample. These showed that apart from age, in which the remifentanil group was significantly younger than the sufentanil group, the two groups were comparable. The authors stated that making an adjustment for age did not affect the results. The reader is able to gain an adequate impression of the patient characteristics of the study sample. The patients were enrolled sequentially and so will have been representative of the study population attending that hospital.

**Validity of estimate of measure of benefit**
The authors did not derive a summary measure of health benefit. In effect, a cost-consequences analysis was performed.

**Validity of estimate of costs**
From the study perspective adopted (i.e. that of the hospital), only one category of costs, anaesthetic drug costs, were included. Therefore, capital equipment costs, all labour costs, energy costs and non anaesthetic drug costs were not studied. It was unclear how these omissions would have affected the authors' conclusions. The morphine intake was higher in the remifentanil group, thus the inclusion of morphine costs would have increased the relative cost per patient in that group although it is not possible to determine by how much. The patient who was not extubated after 6 hours was in the sufentanil group, thereby increasing relative costs in that group. The resource quantities and the unit costs were taken from the authors' setting. No price year was given and it was not clear over what time period the study took place, which makes it difficult to evaluate the cost data. As has already been stated, many costs were not included but, for some of those that were, the unit costs and the resource quantities were reported separately.

**Other issues**
The authors compared their findings with those from other studies, most of which were in agreement with the authors' conclusions about extubation time. The authors stated that patients over 75 years old were not included in their study, so their results may not be generalisable to that category of patients. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis. The authors raised the question of whether the time to extubation should be regarded as the primary consideration when evaluating anaesthesia for this category of patients since it is not clear whether it is related to patient health. The authors stated that the usefulness of rapid postoperative neurological examination, which is a consequence of rapid extubation, was not obvious. It would seem more useful to evaluate the patients' well-being immediately after the surgery and also their longer term health outcomes. The authors acknowledged two other limitations to their study. One was the greater age of the sufentanil patients; the other was that the authors could not confirm that equipotent dosages of the two opioids were used since blood opioid concentrations were not measured.

**Implications of the study**
The authors state that their study showed no significant difference between the two kinds of anaesthesia in terms of the time to extubation and the costs. Future research should examine the effects on the costs of lower remifentanil dosages in patients with a lower body weight. However, drawbacks in the current cost analysis mean that future research should take the total costs of treating patients into account and not merely the anaesthetic costs. It would also be interesting to assess the effects of the two kinds of anaesthesia on patients postoperatively (as mentioned in the above commentary).

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**Bibliographic details**