A comparison of fentanyl, sufentanil, and remifentanil for fast-track cardiac anesthesia

Engoren M, Luther G, Fenn-Buderer N

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 fentanyl, sufentanil and remifentanil for fast-track cardiac anaesthesia was investigated. The patients in the fentanyl group received fentanyl 7 to 10 microg/kg for induction and additional doses of 1 to 2 microg/kg (as needed) for intense stimulus. The patients in the sufentanil group received sufentanil at doses of 1 to 4 microg/kg for induction and 0.1 to 0.3 microg/kg (as needed) for intense stimulus. The patients in the remifentanil group had anaesthesia induced with a remifentanil infusion of 0.5 to 1.0 microg/kg per minute (on the basis of ideal body weight), and anaesthesia maintained by titrating the infusion between 0.05 and 1.0 microg/kg per minute. Boluses of 0.5 to 1.0 microg/kg could be given (as needed) for intense stimulus. On arrival in the intensive care unit (ICU), the infusion was decreased to 0.025 to 0.2 microg/kg per minute and then discontinued 15 to 30 minutes later (after initial doses of ketorolac and morphine). All patients in the remifentanil group received fentanyl 250 microg as part of the induction.

Type of intervention
Other: Anaesthesia.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients undergoing cardiac surgery. Patients were excluded if they were having non-elective surgery, having combined carotid and cardiac surgery, or were mechanically ventilated before surgery. They were also excluded if they did not speak English, or were not capable of understanding instructions.

Setting
The setting was tertiary care. The economic study was carried out at St. Vincent Mercy Medical Centre, Toledo, USA.

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

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

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

Study sample
The a priori power calculation was based on 90% power, a 1.7% Type I error (to control for multiple comparisons.
among groups), and a standard deviation estimate of 202 minutes in time of mechanical ventilation from another study. The power calculation yielded a sample size of 90 patients. Ninety adult patients undergoing cardiac surgery were randomised to fentanyl-based (n=33), sufentanil-based (n=28), or remifentanil-based (n=29) anaesthesia. The patients in the fentanyl group had a median age of 58 years (interquartile range, IQR: 51 - 66) and 23 were males. The patients in the sufentanil group had a median age of 68 years (IQR: 60 - 74) and 17 were males. The patients in the remifentanil group had a median age of 66 years (IQR: 59 - 72) and 17 were males.

**Study design**
The study was a randomised controlled trial that was carried out in a single tertiary care setting in the USA. The patients were randomised to one of the three anaesthetics, as chosen by a computer-generated random number list that was designed to produce true randomisation rather than balanced groups. It would appear that the patients were followed up until they were discharged from hospital. Hence, no loss to follow-up was quoted.

**Analysis of effectiveness**
It was unclear whether the analysis of the clinical study was conducted on an intention to treat basis or for treatment completers only. The outcomes used in the analysis were:

- postoperative pain,
- time to extubation,
- time to discharge from the ICU,
- time to discharge from the hospital, and
- drug usage.

Postoperative pain was measured 30 minutes after the extubation and at 6:30am on the first postoperative day, with the patient being asked to rate his or her pain on the 101-point numeric rating pain scale (0, no pain; 100, pain as bad as could be). The patients in the fentanyl group were found to be younger than those in either of the sufentanil or remifentanil groups, (p=0.04). All the other preoperative demographics and types of surgery were similar. For primary outcomes of the continuous type, the groups were compared using a non-parametric Kruskal-Wallis test. If there was evidence for at least some group differences, (p<0.05), then a Bonferroni multiple comparisons procedure was used to examine which groups differed. The groups were compared using chi-squared or Fisher's exact tests for categorical type data. Spearman correlation coefficients were also used.

**Effectiveness results**
Patients who received sufentanil during surgery required less morphine (6 mg, IQR: 4 - 9) in the ICU than those who received fentanyl (8 mg, IQR: 8 - 12; p=0.02) or remifentanil (12 mg, IQR: 9 - 16; p<0.001).

Patients receiving remifentanil were more likely to require bolus doses of phenylephrine during surgery than patients in the other two groups (83% versus 55% for the fentanyl group and 43% for the sufentanil group; p<0.01). They were also more likely to receive bolus doses of nitroglycerine in the cardiovascular ICU (41% versus 21% for the fentanyl group and 14% for the sufentanil group; p<0.05).

The use of all other haemodynamic drugs was similar among the three groups.

No statistically significant differences were found between the three groups in extubation time, ICU stay and hospital stay.

**Clinical conclusions**
The study found no differences in the outcomes from fentanyl-, sufentanil- and remifentanil-based cardiac anaesthesia.
Measure of benefits used in the economic analysis
The authors did not derive a measure of health benefit. The analysis was, in effect, a cost-consequences analysis.

Direct costs
The resource quantities and the costs were reported separately for some components. The direct costs included in the analysis were those of the hospital. The hospital cost was calculated as the sum of each item and service used by the patient from preoperative preparation through to discharge or death. The costs were obtained from the hospital's internal accounting system. Discounting was not relevant since all the costs were incurred during a short time. The study reported the median costs. The price year was not reported.

Statistical analysis of costs
The costs were treated stochastically. The costs for the three different groups were compared using a non-parametric Kruskal-Wallis test, and were presented as the median value with IQR. Statistical significance was set at a p-value of less than 0.05.

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

Currency
US dollars ($).

Sensitivity analysis
No sensitivity analysis was performed.

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

Cost results
The opioid costs were highest, (p<0.001), in the remifentanil group ($78.35, IQR: 48.04 - 104.14) and lowest in the fentanyl group ($1.29, IQR: 1.29 - 1.29), and in between for the sufentanil group ($15, IQR: 15.00 - 15.00). The anaesthetic costs were also highest, (p<0.01), in the remifentanil group ($140.54, IQR: 113.54 - 179.29) and lowest in the fentanyl group ($43.33, IQR: 39.36 - 56.48), and in between for the sufentanil group ($51.41, IQR: 48.72 - 57.14).

However, the total direct variable costs were similar among all three groups, (p=0.3). The median costs were $6,286 (IQR: 4,546 - 7,819) for remifentanil, $7,841 (IQR: 4,957 - 9,482) for fentanyl and $5,943 (IQR: 4,394 - 8,658) for sufentanil.

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

Authors' conclusions
The study found no differences in the outcomes from fentanyl-, sufentanil- and remifentanil-based cardiac anaesthesia. The authors also concluded that these three anaesthetics had similar direct variable costs.
CRD COMMENTARY - Selection of comparators
The authors used fentanyl and sufentanil as the comparators, as they would appear to be common practice in their setting. You should decide if these two anaesthetics represent current practice in your own setting.

Validity of estimate of measure of effectiveness
The study was based on a randomised controlled trial. This was appropriate for the study question since well-conducted randomised controlled trials are considered the ‘gold’ standard study design when comparing health interventions. The study sample appears to have been representative of the study population. The patient groups were shown to be comparable in terms of preoperative demographics, although patients in the fentanyl group were slightly older. The types of surgery for the three different groups were similar. Appropriate statistical techniques, to detect any significant differences between the groups, were performed and the sample size was determined from a priori power calculations. Despite this, however, the authors pointed out that one of the limitations of their study was the low statistical power, which could account for the lack of significant differences found among the groups for some outcomes. The authors found that, for example, the actual standard deviation for extubation time was much larger than that estimated and used in the a priori power calculations.

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

Validity of estimate of costs
All the categories of cost relevant to the hospital perspective adopted were included in the analysis. The authors reported that the costs of items and services used by the patient from preoperative preparation through to discharge were included. However, it would have been useful if the authors had detailed, even briefly, the main costs included. Only some costs and quantities were reported separately, which will limit the generalisability of the authors’ results. The costs were obtained from the authors’ setting and appropriate statistical tests were undertaken to test for statistically significant differences between the groups. Discounting was unnecessary since all the costs were incurred during a short time. The dates to which the prices related were not reported, thus hampering any potential inflation exercises.

Other issues
The authors reported that few studies had compared remifentanil or sufentanil with fentanyl. The authors made appropriate comparisons of their findings with those from other studies that had found differing results. One found shorter times to extubation and shorter hospital stays for patients receiving remifentanil compared with patients receiving fentanyl. Another study found that sufentanil produced a quicker extubation than did fentanyl. According to the authors, these differences in results probably reflected differences in the process of care or criteria for discharge. The issue of generalisability to other settings was not addressed, although the authors warned that the costs used in their study might only be applicable in their own setting, and that some practices (e.g. the use of normothermic cardiopulmonary bypass) differed to the practices of other hospitals. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis. The authors reported no further limitations to their study.

Implications of the study
Based on the results of their study, the authors do not appear to recommend the use of either remifentanil or sufentanil because of their higher initial acquisition costs.

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