A comparison of fentanyl and sufentanil in patients undergoing coronary artery bypass graft surgery

Thomson I R, Harding G, Hudson R J

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
Fentanyl compared to sufentanil in patients undergoing coronary artery bypass graft (CABG) surgery.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population consisted of patients undergoing elective CABG surgery. The exclusion criteria were patients with: previous heart surgery; unstable angina requiring continuous electrocardiogram (ECG) monitoring or intravenous nitroglycerin; planned awake intubation; body weight more than 110kg; long-term use of sedative hypnotics, alcohol or drug abuse; previous reaction to any of the study drugs; mean arterial pressure more than 100mmHg; severe left ventricular dysfunction or left ventricular ejection fraction less than 0.3.

Setting
The study was set in secondary care. The economic study was carried out in Canada.

Dates to which data relate
No dates relating to the effectiveness evidence, resources used or prices used were reported.

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

Link between effectiveness and cost data
The cost data were collected prospectively for the same patient sample as that used in the effectiveness study.

Study sample
The authors did not report how patients were identified as potential participants in the study. No power calculations to determine sample size were reported. Patients undergoing elective CABG surgery were randomly assigned to the fentanyl or sufentanil group. The authors did not provide evidence to justify that the choice of the patient sample was appropriate for the clinical study question. Twenty-two patients were randomised: 11 in the fentanyl and 11 in the sufentanil group. No details were given about the subjects invited to participate who refused.
Study design
This study used a single-centre, prospective, randomised, double-blind controlled trial. The method of randomisation was not reported. Effectiveness and resource use data were collected from 1 minute after patients were preoxygenated before induction of anaesthesia until 2 minutes after placement of a stitch for aortic cannulation. Patients were interviewed about any intra-operative events immediately before discharge from hospital. One patient was excluded because of a protocol violation (not defined). The anaesthetist was not aware of the type of intra-operative opioid administered until after the operation was finished. The investigator operating the TCI system knew the identity of the opioid throughout the surgical procedure. The time to post operative extubation was recorded.

Analysis of effectiveness
It was not stated whether the clinical study was analysed on the basis of intention to treat or treatment completers only. The primary outcomes were serum opioid concentration, which was determined using commercially available radioimmunoassay kits, and haemodynamics, such as heart rate (HR), mean arterial pressure (MAP) and central venous pressure (CVP). The requirements for a volatile anaesthetic, isoflurane, were also recorded. The groups did not differ in terms of age, gender, weight, baseline haemodynamics, or preoperative use of beta-adrenergic blocking drugs.

Effectiveness results
The effectiveness results were as follows:

It was not necessary to increase the target opioid concentration in any patient.

The mean duration of the TCI of opioid did not differ between the two groups and was 1.64 (SD: 0.30) hours for fentanyl and 1.54 (SD: 0.56) hours for sufentanil.

95% confidence intervals were not reported.

The total opioid dose administered during the pre-cardiopulmonary bypass (CPB) period was fentanyl 20.6 micro g/kg (SD: 1.9) and sufentanil 1.59 micro g/kg (SD: 0.40).

Haemodynamic control did not differ between the two groups.

The mean isoflurane requirement (from intubation to aortic stitch) was 0.46% (SD: 0.21) for the fentanyl group and 0.56 (SD: 0.24) for the sufentanil group. The mean isoflurane requirement was not statistically different.

The use of other pharmacological interventions and duration of postoperative endotracheal intubation was the same between the fentanyl and sufentanil groups.

Two patients were excluded from the analysis of the duration of extubation. One patient from the fentanyl group developed postoperative respiratory failure requiring prolonged mechanical ventilation and one patient from the sufentanil group had a leg wound haematoma and was returned to the operating room.

No patients had recall of events during surgery.

Clinical conclusions
Fentanyl and sufentanil do not differ with respect to their ability to promote intraoperative haemodynamic control when they are used in a concentration ratio that reflects their EEG-suppressing potency.

Measure of benefits used in the economic analysis
The study indicated fentanyl and sufentanil were equivalent in terms of clinical effectiveness (haemodynamic control) suggesting cost minimisation analysis was appropriate. Therefore, no summary measure of health benefit was reported.
Direct costs
Hospital costs were valued using hospital prices. The evaluation only included opioid associated resource use during anaesthesia. The quantity and average cost of opioid use was reported separately. The date to which the price data refer was not reported. Discounting was not relevant because costs were measured over less than one year.

Statistical analysis of costs
Differences in mean costs were analysed using t-tests.

Indirect Costs
Indirect costs were not included in this evaluation.

Currency
Canadian dollars (Can$). No currency conversions or dates were reported.

Sensitivity analysis
No sensitivity analysis was carried out.

Estimated benefits used in the economic analysis
The reader is referred to the effectiveness results reported above.

Cost results
The study reported the cost of opioid use calculated using two methods: cost of the actual dose used and the cost based on the number of ampoules used. The cost based on the actual dose of fentanyl was Can$5.94 (SD: 1.01) and Can$14.16 (SD: 4.79) for sufentanil, (p<0.001). The cost based on the number of ampoules required to administer the dose was Can$6.12 (SD: 1.04) for fentanyl and Can$17.47 (SD: 4.65) for sufentanil, (p<0.001).

Synthesis of costs and benefits
Not relevant.

Authors' conclusions
The authors’ concluded that fentanyl and sufentanil were equivalent in terms of haemodynamic control and fentanyl was less expensive than sufentanil in terms of acquisition cost.

CRD COMMENTARY - Selection of comparators
The selection of comparators for the Canadian health care system seemed appropriate. However, sufentanil is not licensed for use in the UK. The results of this study can not be generalised to the UK setting because sufentanil is not an appropriate comparator reflecting routine UK clinical practice.

Validity of estimate of measure of effectiveness
The study used haemodynamic control of fentanyl and sufentanil, which seemed an appropriate measure to evaluate the short-term effectiveness in terms of achieving balanced anaesthesia. Features that enhanced the validity of the effectiveness estimate stem from the prospective, randomised and controlled study design and the comparability of patients at baseline. However, some aspects, such as the small sample size and absence of reporting of randomisation methods tend to limit these advantages.
Validity of estimate of measure of benefit
No summary measure of benefit was reported. The effect of fentanyl and sufentanil postoperatively was not reported. Relevant long-term effects and potential postoperative adverse effects associated with using fentanyl or sufentanil were not assessed.

Validity of estimate of costs
This study involved a cost-minimisation analysis but only reported the acquisition cost of these drugs and did not quantity further costs, such as the cost of volatile agent used to maintain anaesthesia or post-operative resources. The authors stated the observed difference in isoflurane use was clinically insignificant. The authors did not justify the small sample size used. However, they noted that a sample size of 85 patients per group would be needed to detect a statistically significant difference in the use of isoflurane. Additionally, the difference in isoflurane use may have had resource use implications but these were not quantified. The study did not state the perspective of the analysis, the time frame for the analysis, or the price year, and nor was any sensitivity analysis reported. The absence of these components from the evaluation limits the internal validity of the cost-minimisation analysis and the generalisability of the results of the evaluation.

Other issues
The investigators delivering the opioid were not masked to allocation. No information was provided about those members of the study population who did not participate. It is likely that the study sample was representative of the study population. However, the exclusion criteria used, and the small sample size indicate that the study sample and population may not have been representative of all patients eligible for elective CABG surgery.

CRD Commentary
This small (n=21 patients) randomised controlled trial appropriately and carefully reported the clinical evaluation of fentanyl and sufentanil.

Implications of the study
This study does not provide good, reliable economic evidence to inform the selection of an opioid for routine use in cardiac surgery and further, more robust evaluation is required. Furthermore, for this study to be relevant to UK practice sufentanil should be replaced with a more appropriate comparator. The authors recommended that further economic evaluations were required before final guidance can be issued regarding which opioid should be routinely used in cardiac surgery.

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