A comparison of the cost-effectiveness of remifentanil versus fentanyl as an adjuvant to general anesthesia for outpatient gynecologic surgery

Beers R A, Calimlim J R, Uddoh E, Esposito B F, Camporesi E M

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 versus fentanyl as an adjuvant to general anaesthesia for outpatient gynaecologic surgery.

Remifentanil was given as an opioid adjuvant to general anaesthesia at a dosage of 0.5 microg/kg per minute. The remifentanil infusion was decreased to 0.2 microg/kg per minute immediately after confirmation of endotracheal tube position. Fentanyl, 25 microg intravenous and 75 microg intramuscular, was administered for postoperative analgesia. After the last skin suture was placed, the remifentanil infusion was discontinued.

In the comparator group, 3 microg/kg fentanyl was administered at least 3 minutes before anaesthesia. Unlike the remifentanil group, no additional opioid analgesics were given for postoperative analgesia after completion of the procedure. All other aspects of treatment were the same for both two treatment options.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised individuals aged at least 18 years, with ASA physical status I-III, who were undergoing outpatient laparoscopy or hysteroscopy. Patients with a history of substance abuse within the last year were excluded, as were those taking opioid analgesics within the last 6 weeks. Also excluded were those who were unable to communicate effectively in English, those whose weight exceeded 150% of their ideal body weight, and those who were allergic to any of the study protocol medications.

Setting
The setting was secondary care. The economic study was carried out in Syracuse, USA.

Dates to which data relate
The study did not report the dates when the effectiveness data and resource use data were gathered.

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

Link between effectiveness and cost data
The same patients provided the cost data and the effectiveness data. It was unclear whether the costing was carried out
prospectively or retrospectively.

**Study sample**
The sample size necessary to provide at least 80% power to detect a 20-minute difference in postanaesthesia care unit (PACU) discharge, and a 40-minute difference in home discharge, was calculated. The sample size needed for each group was 16. No details of the sample selection process were described. A total of 34 patients were randomly assigned to either the remifentanil group (study group, n=16) or the fentanyl group (control group, n=18).

**Study design**
This was a prospective, randomised double-blinded trial that was carried out in a single centre. The patients were followed up 24 hours after hospital discharge. A blinded nurse observer evaluated each patient’s experience during and after the operation, and after home discharge.

**Analysis of effectiveness**
The analysis was conducted on an intention to treat basis. The primary health outcomes were:

- intraoperative adverse events,
- postoperative sequelae,
- recovery times,
- patient and provider satisfaction, and
- perioperative drug dosage.

The outcomes used to assess the patients during the operations were:

- average bispectral (BIS) index value,
- end-tidal sevoflurane,
- sevoflurane down-titrations,
- sevoflurane up-titrations,
- intraoperative hypotension,
- intraoperative signs of light anaesthesia, and
- intraoperative adverse events.

The outcomes used to assess postoperative recovery were:

- postoperative hypotension,
- postoperative sequelae,
- first rescue antiemetic treatment,
- second rescue antiemetic treatment,
- nausea visual analogue scale (VAS) score on arrival at the PACU,
nausea VAS score in the PACU,
nausea VAS score on discharge from the PACU,
nausea VAS score at second stage recovery,
time to first analgesic request, and
postoperative fentanyl requirements.

The times for the following were also used to assess postoperative recovery:
follows verbal commands,
first analgesic request,
PACU discharge,
first antiemetic request,
first intake by mouth,
home discharge, and
first "felt like myself".

The anaesthesiologist and the blinded nurse observer completed a brief survey on each patient and the patients were surveyed 24 hours after discharge. The groups were generally comparable at baseline apart from the mean weight. This was higher in the remifentanil group (70.2 kg) than in the fentanyl group (62.1 kg), (p=0.015).

**Effectiveness results**
The BIS index was significantly higher (55 versus 45) and the end-tidal sevoflurane concentration smaller (0.6 versus 1.3) in the remifentanil group, (p<0.05).

Downward titrations of the sevoflurane dose were more frequent in the fentanyl group (1.65 versus 0.2), while upward titrations were more frequent in the remifentanil group (2.35 versus 0.45; p<0.05).

The incidence of intraoperative adverse events was similar between the two groups.

Intraoperative signs of light anaesthesia were greater in the fentanyl group, (4 versus 0; p=0.045)

After the operation, patients in the remifentanil group experienced more sequelae (14 versus 10; p=0.041) and nausea requiring first-line antiemetic treatment (8 versus 2; p=0.013). In the second stage recovery unit, the mean nausea VAS scores were also higher (0.6 versus 0.2; p=0.017).

There was no statistically significant difference between the two groups in pain VAS scores, postoperative fentanyl consumption, time to the first analgesic request, times to reach recovery milestones, and in the results of the patients, nurse and anaesthesiologist satisfaction survey.

**Clinical conclusions**
For the particular category of patients studied (i.e. those undergoing outpatient gynaecologic laparoscopy or hysteroscopy), there was no improvement in clinical outcomes resulting from the use of remifentanil rather than fentanyl as an adjuvant to general anaesthesia.
Measure of benefits used in the economic analysis
No summary measure of benefits was produced. In effect, the authors carried out a cost-consequences analysis.

Direct costs
No discounting was carried out since the costs were incurred during less than one year. The quantities and the costs were not analysed separately, although the dosage and costs of sevoflurane, remifentanil and fentanyl were given. The cost/resource boundary was not reported. The drug costs of sevoflurane, remifentanil, fentanyl, antiemetic treatment, per-os analgesics, and other protocol drugs were measured. No other costs were measured as it was assumed they would be the same in both treatment groups. The drug costs were obtained from the pharmacy acquisition costs in the hospital. They did not include the added cost of the equipment and supplies used to administer the drug. No dates were given and no price year was reported.

Statistical analysis of costs
The cost data between groups were compared using Student’s t-test, (p<0.05).

Indirect Costs
No indirect costs were given.

Currency
US dollars ($).

Sensitivity analysis
No sensitivity analysis was carried out.

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

Cost results
There were statistically significant differences between groups in the cost of sevoflurane and in the total cost of antiemetic treatment, (p<0.05). Sevoflurane cost less in the remifentanil group ($5.01 versus $9.08), while antiemetic treatment cost more in the remifentanil group($4.20 versus $0.93).

The total drug costs per patient were $65.78 in the remifentanil group and $48.04 in the fentanyl group, (p<0.05).

Synthesis of costs and benefits
The costs and benefits were not combined as the study was, in effect, a cost-consequences analysis.

Authors' conclusions
Remifentanil was not cost-effective compared with fentanyl. There was no improvement in clinical outcomes with remifentanil, but there was added expense.

CRD COMMENTARY - Selection of comparators
Fentanyl was chosen as the comparator since it is the most common opioid used as an adjuvant to general anaesthesia for outpatient gynaecological laparoscopy or hysteroscopy. You should decide if this is a widely used health technology in your own setting.
Validity of estimate of measure of effectiveness
The effectiveness data were derived from a single study. The study design, a randomised controlled trial, was appropriate for the purpose. The study sample appears to have been representative of the study population and, apart from the higher weight in the remifentanil group, the patients were comparable at baseline. The analysis of effectiveness was handled credibly.

Validity of estimate of measure of benefit
The authors did not derive a summary measure of health benefit.

Validity of estimate of costs
The economic perspective adopted was unclear, but it is likely to have been that of the hospital. The authors assumed that the only cost-difference was due to the different anaesthetics and other drugs. They did not include any other costs, assuming that they were similar. It would have been interesting to have seen whether the other costs were truly identical in the two groups. Also, the costs of administering the drugs were not included. Although some drug dosages were given separately from the costs, there was no systematic reporting of the costs separately from the quantities, which makes comparisons with other settings more difficult. The resource use quantities were taken from a single study, and there were no statistical or sensitivity analyses of the quantities. The prices were taken from the authors' setting, and there were no statistical or sensitivity analyses of the prices. The price year and the dates of the cost evidence were not reported, which will prevent future reflation exercises.

Other issues
The authors made appropriate comparisons of their results with the findings from other studies, finding similar results. However, the issue of the generalisability to other settings was not addressed. The authors did not present their results selectively and, for the effectiveness evidence, their conclusions reflected the scope of the analysis. The authors did not directly consider how their findings might be generalised to other settings. However, they stated that their conclusion may not be extended to other patient categories and procedures.

Implications of the study
The authors did not make any recommendations for practice. They indicated that remifentanil must be used selectively in the ambulatory setting to have potential cost-effectiveness.

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