Induction with sevoflurane-remifentanil is comparable to propofol-fentanyl-rocuronium in PONV after laparoscopic surgery
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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
Induction with sevoflurane-remifentanil was compared to induction with propofol-fentanyl-rocuronium in terms of the frequency of moderate to severe postoperative nausea and vomiting (PONV) in the first 24 hr after laparoscopic surgery. Patients in the sevoflurane group (intervention) were given a vital capacity induction technique (sevoflurane 8%, N2O 2 L/minute, O2 1 L/minute) to obtain loss of consciousness, followed by a 30-second intravenous (i.v.) injection of remifentanil (1 to 1.5 microg/kg). One minute after remifentanil administration, tracheal intubation was attempted. Sevoflurane and additional boluses of remifentanil (0.5 microg/kg i.v.) were used to maintain anaesthesia until intubation was successful. Once the trachea was intubated, anaesthesia was maintained with N2O 1.3 L/minute, O2 0.7 L/minute, and sevoflurane as decided by the anaesthesiologist. Rocuronium (0.15 mg/kg i.v.) was used if muscle relaxation was inadequate with sevoflurane alone.

Type of intervention
Other: Anaesthesia.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients undergoing laparoscopic cholecystectomy or laparoscopic tubal ligation. The patients had to weigh less than or equal to 100 kg, have a body mass index of no more than 35 kg/m2, be older than 16 years of age, and be of an ASA physical status class of III or less. They also had to have an elective procedure booked for same day discharge. Patients were excluded if they had participated in another study with an experimental drug within the month prior to enrolment. Also excluded were patients who were pregnant or breastfeeding, those who had received medications with anti-emetic properties within 48 hours of surgery, and those who had contraindications to the anaesthetic techniques or the medications used in the study.

Setting
The setting was tertiary care (two academic hospitals). The economic study was carried out in Hamilton (ON), Canada.

Dates to which data relate
No dates for the data were reported.

Source of effectiveness data
The evidence for the final outcomes was derived from a single study.

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

**Study sample**
The sample size was calculated in the planning phase of the study to assure a power of 80%. After accounting for stratification by centre and surgical procedure and an anticipated 5% withdrawal rate, 78 patients per group were required. According to the authors' summary of the trial profile (which was slightly unclear), there were 653 potential participants in the clinic. Eighty-three patients were missed, 342 were ineligible and 55 refused to participate. Of the 179 patients who consented, 12 were cancelled by anaesthesia, 2 were cancelled by surgery and 5 withdrew consent. One hundred and fifty-nine patients were randomised during the study, but three subsequently withdrew: one patient had clinical signs strongly predictive of a difficult intubation, which was missed during the preoperative assessment clinic visit but detected prior to induction, one patient had severe nausea prior to induction, and one patient did not undergo the scheduled procedure. In total, 156 patients completed the study. Upon entry into the operating room, 77 patients were allocated to the sevoflurane group and 79 to the propofol group.

**Study design**
The study was a randomised controlled trial. A random numbers table was used to allocate the patients to the two groups. The duration of follow-up was the first 24 hours after surgery. There was no loss to follow-up. The anaesthesiologists and operating room nurses were not blinded to the induction technique used, but the patients themselves were not informed of the induction technique that they received. The surgical team was blinded to the induction technique. The postoperative data collectors and the data analysts were blinded to the intervention.

**Analysis of effectiveness**
The analysis was conducted on the basis of treatment completers only, as 3 patients withdrew post-randomisation. These individuals were not considered at analysis. The primary health outcome was the frequency of moderate to severe PONV over the first 24 hours after surgery. Severity of PONV was measured using a 10-cm visual analogue scale (VAS), with scores greater than 3 considered being moderate to severe. The secondary outcomes included:

- moderate to severe pain over the first 24 hours after surgery (measured using a 10-cm VAS),
- ease of intubation (measured using a six-item 12-point score),
- anaesthetic induction and emergence times,
- the time required to achieve fast-track criteria, and
- the amount of postoperative anti-emetics and analgesics used.

There were no statistically significant differences in the physical characteristics or the distribution of PONV risk factors between the two groups.

**Effectiveness results**
There was no statistically significant difference in the frequency of moderate to severe PONV over 24 hours between the sevoflurane group (53.2%) and the propofol group (36.7%).

An odds ratio, adjusted for the number of PONV risk factors, of 1.79 (95% confidence interval, CI: 0.92 - 3.38; \( p=0.12 \)) was reported.

No differences were seen between the two groups in their frequencies of postoperative pain, or in their intubating conditions, induction and emergence times, and time to achieve fast-track discharge criteria.

Patients in the sevoflurane group received more morphine (11 mg versus 8 mg; \( p<0.001 \)) in the post anaesthetic care unit.
No adverse events from anaesthesia were seen.

**Clinical conclusions**
There was no difference in PONV, pain, or anaesthetic or recovery times between the sevoflurane and propofol groups.

**Measure of benefits used in the economic analysis**
No summary measure of benefit was derived. The outcome indicator of effectiveness used was the frequency of moderate to severe PONV over the first 24 hours after surgery. This was derived directly from the effectiveness results. The outcomes were considered to be equal so, in effect, a cost-minimisation analysis was performed.

**Direct costs**
The perspective from which the analysis was conducted was not reported. The direct costs included were drug costs only. It is assumed that all other costs were excluded because they were common to both alternatives, although the authors did not explicitly state this. The costs and the quantities were not reported separately, and no information was provided on the source of the prices or the dates to which the costs related. Given the timeframe involved (24 hours), discounting was not necessary.

**Statistical analysis of costs**
Normally distributed, continuous data were expressed as means with standard deviations and were compared using a two-sided t-test. Non-normally distributed, continuous data were expressed as medians and were compared using the Wilcoxon rank sum test. It was unclear under which category the costs fell.

**Indirect Costs**
There was no attempt to measure the indirect costs associated with either group. Again, this probably reflects the authors' assumption that the indirect costs would be common to both alternatives.

**Currency**
Canadian dollars (Can$).

**Sensitivity analysis**
No sensitivity analysis was reported.

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

**Cost results**
The total drug cost was Can$56.81 in the sevoflurane group and Can$46.78 in the propofol group. The difference (Can$10.03) was not statistically significant, (p=0.045); p<0.001 was considered statistically significant because of the multiple comparisons.

**Synthesis of costs and benefits**
Not relevant.

**Authors' conclusions**
The study demonstrated no difference in postoperative nausea and vomiting (PONV), pain, anaesthetic or recovery times, or costs between the sevoflurane and propofol groups. Sevoflurane-remifentanil induction is a feasible technique for anaesthetic induction.

**CRD COMMENTARY - Selection of comparators**
Although no explicit justification was given for the comparator used, it would appear to provide the desired properties of a general anaesthetic with the additional advantage that separate muscle relaxants are not required. You should decide if this is relevant to your own setting.

**Validity of estimate of measure of effectiveness**
The analysis was based on a randomised controlled trial, which was appropriate for the study question. It was unclear whether the study sample was representative of the study population. The patient groups were shown to be comparable at analysis. Blinding was conducted where possible, and involved patients, surgeons, postoperative data collectors and data analysts. These facts help to maintain the internal validity by minimising the risk of introducing bias post-randomisation.

**Validity of estimate of measure of benefit**
The analysis of benefits was based upon the therapeutic equivalence of the treatment alternatives. Therefore, the economic analysis only included costs. The reader is referred to the comments in the 'Validity of estimate of measure of effectiveness' field (above).

**Validity of estimate of costs**
The perspective adopted in the study was not reported, so it was not possible to ascertain whether all the relevant costs were considered. Only the drug costs were included in the analysis, as all other costs were assumed to be common to both groups. Their exclusion is unlikely to have affected the authors' conclusions. The costs and the quantities were not reported separately. No statistical analysis of the quantities or prices was performed. The source from which the prices were taken was unclear, and the date to which the prices related was not reported.

**Other issues**
The authors made appropriate comparisons of their findings with those from other studies. However, the issue of generalisability to other settings was not addressed. The authors did not present their results selectively. The authors used a number of criteria to enrol patients, but such restrictions on inclusion to the study do not seem to have been reflected in their conclusions.

**Implications of the study**
The authors suggested that sevoflurane-remifentanil is a feasible technique for anaesthetic induction.

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**Bibliographic details**

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