Which anaesthetic agents are cost-effective in day surgery? Literature review, national survey of practice and randomised controlled trial

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Executive summary

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The website also provides information about the HTA Programme and lists the membership of the various committees.
Background
The aim of the project was to provide robust evidence on the relative costs, patient benefits and acceptability of different anaesthetic agents, by assessing the relative cost-effectiveness of different anaesthetic agents in adult and paediatric patients undergoing day surgery.

Objectives
The objectives were to identify and value resource use, impact on patients and relative value for money associated with different anaesthetic agents in day surgery.

Methods
The study consisted of three parts:
- A literature review of clinical outcomes, patient-based outcomes and economic data.
- A national survey of 270 anaesthetists (October 2000) to determine anaesthetic practice in adult and paediatric day surgery.
- A prospective randomised controlled trial (RCT) to compare the cost-effectiveness of anaesthetic regimens (CESA). The trial was carried out at St. Mary’s Hospital, Manchester, and at Arrowe Park and Clatterbridge Hospitals, Wirral. The sample comprised adult general, orthopaedic and gynaecology patients, and paediatric general and ear, nose and throat (ENT) patients.

Results
Literature review
The large number of RCTs available that investigated clinical outcomes involved the use of various anaesthetic combinations and approaches. There were few good comparative studies of patient-based outcomes and economic evidence. No optimal regimen was identified for adults or children on the basis of clinical outcomes, patient acceptability or efficiency.

National survey
The national survey of anaesthetists (response rate 76%) indicated the following in adult urology, adult orthopaedic and paediatric general day-case surgery, respectively:
- use of premedication, 6%, 12% and 19%
- propofol as the preferred induction agent, 78%, 81% and 51%
- isoflurane as the preferred maintenance agent, 52%, 54% and 45%
- use of prophylactic anti-emetics, 32%, 41% and 24%
- use of a laryngeal mask airway, 86%, 83% and 85%.

CESA RCT
Recruitment to the CESA RCT was 73% (adult study) and 75% (paediatric study). Ninety-five adult patients and 25 paediatric patients were withdrawn, leaving 1063 adult patients (265 propofol/propofol, 267 propofol/isoflurane, 280 propofol/sevoflurane, 251 sevoflurane/sevoflurane) and 322 paediatric patients (159 propofol/halothane, 163 sevoflurane/sevoflurane) remaining in the study until discharge. Fifteen per cent of adults and 19% of children were lost to follow-up 7 days after discharge.

Interventions (comparators)
The anaesthetics in the adult treatment arm were:
- Total intravenous anaesthesia (TIVA): propofol induction, propofol maintenance.
- Intravenous/inhalational anaesthesia (mixed): propofol induction, isoflurane/nitrous oxide (N₂O) maintenance.
- Intravenous/inhalational anaesthesia (mixed): propofol induction, sevoflurane/N₂O maintenance.
- Total inhalational anaesthesia: sevoflurane/N₂O induction, sevoflurane/N₂O maintenance.

The anaesthetics in the paediatric treatment arm were:
- Intravenous/inhalational anaesthesia: propofol induction, halothane maintenance.
- Total inhalational anaesthesia: sevoflurane/N₂O induction, sevoflurane/N₂O maintenance.
Outcome measures
Postoperative nausea and vomiting (PONV) was the primary clinical outcome measure. The contingent valuation (CV) method was used to determine patient preferences for different anaesthetic agents at day 7. Prospective patient-based resource-use data were collected up to day 7 postdischarge, from the perspective of the NHS and the patients.

Results
Adult study
• More adults experienced PONV with sevoflurane/sevoflurane (29.9%) than with propofol/propofol (14.0%) \((p < 0.0001)\), propofol/sevoflurane (16.6%) \((p < 0.001)\) and propofol/isoflurane (18.2%) \((p < 0.003)\).
• The length of hospital stay and total costs were not statistically different between the four study arms, but variable costs were higher in the TIVA arm and lower in the propofol/isoflurane arm.
• Of those who received intravenous induction, 79% would prefer that method in the future to inhalational induction. Of those patients who received inhalational induction, 64% would prefer that method in the future. There were no differences in the CVs for induction or maintenance between the randomisation arms.
• Propofol/propofol was the most effective and most costly. Sevoflurane/sevoflurane was the least effective, and was more costly than the mixed arms. The incremental cost-effectiveness ratio (ICER) for propofol/propofol compared with propofol/sevoflurane is £296 to avoid one PONV incident. The ICER for propofol/sevoflurane compared with propofol/isoflurane is £333 to avoid one PONV incident.
• The use of the Dion algebraic approximation for volatile anaesthetic use resulted in a 6–27% underestimation. The impact of this was strongest in the sevoflurane/sevoflurane and propofol/sevoflurane arms due to the high acquisition costs of sevoflurane.
• Investigating the use of prophylactic intravenous ondansetron 4 mg suggested that propofol/propofol would remain the most costly and effective arm. However, if this agent was used in all arms except the propofol/propofol arm, propofol/sevoflurane became the most costly and effective regimen.
• The net benefit \((= \text{total cost} - (\text{CV[induction]} + \text{CV[maintenance]}))\) was positive in all arms and was positive for over 90% of patients. Sevoflurane/sevoflurane had a lower net benefit than did the other three arms.

Paediatric study
• More children experienced PONV with sevoflurane/sevoflurane (14.7%) than with propofol/halothane (5.7%) \((p < 0.01)\).
• The length of hospital stay was not different between the randomisation arms, but variable and total costs were higher in the sevoflurane/sevoflurane arm.
• Parents whose children had not had the mask (sevoflurane) before did not want it in the future. Parents whose children had not had the injection (propofol) before did not want it in the future. The CVs for PONV avoidance were not affected by the experience of PONV.
• Propofol/halothane was more effective and less costly than the sevoflurane/sevoflurane regimen.
• In a sensitivity analysis, when isoflurane was substituted for halothane, propofol/isoflurane was more effective and less costly than sevoflurane/sevoflurane. When sevoflurane was substituted for halothane, propofol/sevoflurane was more effective and more costly than sevoflurane/sevoflurane.
• Both arms had an overall positive net benefit, and these benefits were not statistically different. The net benefit was positive for over 90% of patients in both arms.

Conclusions
The main conclusions are:
• Sevoflurane/sevoflurane is not a cost-effective regimen for day surgery in adults or children. It is associated with higher rates of PONV than propofol followed by propofol, isoflurane or sevoflurane. It is more expensive than mixed anaesthesia regimens.
• In the adult study, there were no statistically significant differences in the incidence of PONV between the regimens that used propofol for induction. However, there were statistically significant differences in the variable costs of the regimens. The propofol/isoflurane regimen was associated with the lowest cost per episode of PONV avoided.

Implications for practice
• In both adults and children a propofol-containing regimen appears to confer anti-emetic protection over a sevoflurane/sevoflurane anaesthetic regimen, without increased costs, unless TIVA is used. In children, sevoflurane/sevoflurane is also associated with agitation in recovery.
The incidence of PONV was low despite the withholding of prophylactic anti-emetics, possibly due to the low opioid use in this study.

The reluctance to have an inhalation induction was reduced by experience of this technique.

Decisions around clinical practice in day surgery should not be based on inpatient evidence.

The current development of patient information on anaesthetics needs to incorporate patients’ views and preferences.

**Recommendations for further research**

Further research is needed in the following areas:

- the optimisation of perioperative analgesia
- routine perioperative PONV prophylaxis should be reviewed
- the risk factors for PONV
- the cost of volatile anaesthetics
- the role of patient preferences in anaesthesia.

**Publication**

The NHS R&D Health Technology Assessment (HTA) Programme was set up in 1993 to ensure that high-quality research information on the costs, effectiveness and broader impact of health technologies is produced in the most efficient way for those who use, manage and provide care in the NHS.

Initially, six HTA panels (pharmaceuticals, acute sector, primary and community care, diagnostics and imaging, population screening, methodology) helped to set the research priorities for the HTA Programme. However, during the past few years there have been a number of changes in and around NHS R&D, such as the establishment of the National Institute for Clinical Excellence (NICE) and the creation of three new research programmes: Service Delivery and Organisation (SDO); New and Emerging Applications of Technology (NEAT); and the Methodology Programme.

This has meant that the HTA panels can now focus more explicitly on health technologies (‘health technologies’ are broadly defined to include all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care) rather than settings of care. Therefore the panel structure has been redefined and replaced by three new panels: Pharmaceuticals; Therapeutic Procedures (including devices and operations); and Diagnostic Technologies and Screening.

The HTA Programme continues to commission both primary and secondary research. The HTA Commissioning Board, supported by the National Coordinating Centre for Health Technology Assessment (NCCHTA), will consider and advise the Programme Director on the best research projects to pursue in order to address the research priorities identified by the three HTA panels.

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