BJA

British Journal of Anaesthesia, 0 (0): 1–12 (2017)

doi: 10.1093/bja/aex087
Review Article

REVIEW ARTICLE

Efficacy and safety of inhaled anaesthetic for postoperative sedation during mechanical ventilation in adult cardiac surgery patients: a systematic review and meta-analysis

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Abstract

The aim was to evaluate the efficacy and safety of volatile anaesthetic for postoperative sedation in adult cardiac surgery patients through a systematic review and meta-analysis. We retrieved randomized controlled trials from MEDLINE, EMBASE, CENTRAL, Web of Science, clinical trials registries, conference proceedings, and reference lists of included articles. Independent reviewers extracted data, including patient characteristics, type of intraoperative anaesthesia, inhaled anaesthetic used, comparator sedation, and outcomes of interest, using pre-piloted forms. We assessed risk of bias using the Cochrane Tool and evaluated the strength of the evidence using the GRADE approach. Eight studies enrolling 610 patients were included. Seven had a high and one a low risk of bias. The times to extubation after intensive care unit (ICU) admission and sedation discontinuation were, respectively, 76 [95% confidence interval (CI) −150 to − 2, I^2=79%] and 74 min (95% CI − 126 to − 23, I^2=96%) less in patients who were sedated using volatile anaesthetic. There was no difference in ICU or hospital length of stay. Patients who received volatile anaesthetic sedation had troponin concentrations that were 0.71 ng ml^{-1} (95% CI 0.23–1.2) lower than control patients. Reporting on other outcomes was varied and not suitable for meta-analysis. Volatile anaesthetic sedation may be associated with a shorter time to extubation after cardiac surgery but no change in ICU or hospital length of stay. It is associated with a significantly lower postoperative troponin concentration, but the impact of this on adverse cardiovascular outcomes is uncertain. Blinded randomized trials using intention-to-treat analysis are required. PROSPERO registry number: 2016:CRD42016033874. Available from http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42016033874.

Key words: anaesthetics, inhalation; cardiac surgical procedures; postoperative care

Editor's key points

- Volatile anaesthetics present the potential for an attractive risk–benefit profile in postsurgical sedation on the cardiac intensive care unit.
- In this meta-analysis, the authors reviewed the findings of eight clinical studies, comprising 610 subjects.
- They concluded that the available evidence indicates a shorter time to extubation after sedation using volatile agents, and a slightly lower troponin concetration, but no discernible difference in length of stay in the intensive care unit or the hospital.

Early extubation is a key component of 'fast-track' care after cardiac surgery and is associated with shorter intensive care unit (ICU) length of stay (LOS),[1 2] reduced costs, and improved efficiency.[1 2] I.V. sedative and analgesic medications are administered to facilitate tolerance of mechanical ventilation and alleviate postoperative pain and anxiety. However, these agents have shortcomings in the setting of a 'fast-track' approach, including prolonged mechanical ventilation, over-sedation, delirium, and haemodynamic instability.[3 4]

Volatile anaesthetics have an excellent safety record, and their pharmacokinetic and pharmacodynamic properties are ideally suited to the setting of the cardiac surgical ICU. They provide amnesia, and their low solubility in the blood allows for effective sedation and rapid recovery after discontinuation.[5] In addition, their elimination is independent of renal and hepatic function, which are often impaired in cardiac surgical patients,[5] and some evidence suggests possible cardioprotective properties.[6 7]

Since the development of the Anaesthetic Conserving Device (AnaConDa™; Sedana Medical, Uppsala, Sweden),[8] which allows for volatile anaesthetic administration through common ICU ventilators, their use in this setting has increased. Randomized controlled trials (RCTs) have demonstrated shorter time to extubation with volatile anaesthetic when compared with i.v. sedation,[9–13] and studies specific to the cardiac surgery population have found less myocardial damage.[14 15]

Evidence regarding the use of these agents is derived from small, single-centre studies that are underpowered to show an impact on ICU or hospital LOS, major adverse cardiovascular events, or mortality. To our knowledge, no systematic review on the effects of volatile anaesthetic usage for sedation exclusively in the cardiac surgical ICU setting has been published, although two reviews combining medical, surgical, and cardiac surgical ICU patients have been completed.[16 17] Given that cardiac surgery patients are a unique population with both underlying physiology and administrative considerations that are distinct from medical and surgical ICU patients, we undertook a systematic review and meta-analysis comparing volatile anaesthetic sedation with standard care in postoperative cardiac surgical patients, emphasizing their use in the context of a fast-track approach to cardiac surgical care.

Methods

We registered a protocol[18] developed *a priori* that adhered to the Methodological Expectations of Cochrane Intervention Reviews.[19] This protocol provided the framework for our review, which is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[20] Our review addresses the question: 'What is the efficacy and safety of inhaled anaesthetic for postoperative sedation during mechanical ventilation compared with i.v. sedation in adult patients who have undergone cardiac surgery?'

Criteria for study inclusion

We included RCTs comparing postoperative sedation with inhaled anaesthetic (desflurane, sevoflurane, isoflurane, enflurane, or xenon) with i.v. sedation in adult patients undergoing cardiac surgery. Sedation modality could be initiated in the operating room (OR) or ICU but needed to be continued for at least 2 h after surgery from the time of ICU admission. We used this cut-off based on the assumption that application of inhaled anaesthetic sedation for a shorter period would not allow adequate exposure to the intervention to assess its effects adequately and that requiring a longer duration would not be consistent with a 'fast-track' approach. Crossover studies were excluded. Our outcomes were time to extubation, ICU and hospital LOS, postoperative troponin elevation during the first 24 h after surgery, myocardial and cerebrovascular morbidity and mortality during the first 30 postoperative days (as defined in the trials), acute kidney injury (AKI), proportion of time within target range on a recognized sedation scale, inpatient costs, and the incidence of environmental pollution.[21 22]

Search method for identification of studies

Electronic searches

We searched Cochrane Central, MEDLINE, EMBASE and ISI Web of Science from inception to February 2016. The pretested SIGN filters (http://www.sign.ac.uk) for RCTs were used. No date, language, or journal restrictions were applied (see Supplementary Appendix 1 and 2 for MEDLINE and EMBASE searches).

Grey literature search

We hand-searched abstracts of major international conferences for the past 5 yr. We contacted Sedana Medical, the makers of the AnaConDa™ (Sedana Medical),[8] to obtain information about unpublished data and included reference lists published on their website. We searched Clinicaltrials.gov, International Standard Randomised Controlled Trial Number (ISRCTN) Register, Australian New Zealand Clinical Trials Registry (ANZCTR), and World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) for relevant trials and reviewed the reference lists of included studies for pertinent citations.

Data collection and analysis

Selection of studies

All references were screened by evaluation of title and abstract by two independent reviewers. If a reference was deemed potentially eligible by at least one reviewer, its full text report was retrieved. Two reviewers then independently assessed study eligibility using pre-piloted forms. We included studies that fulfilled all eligibility criteria. Agreement at each step was assessed using κ statistics.

Data extraction and management

Independent reviewers extracted data using pre-piloted forms. Data extracted included first author, title, year and type of publication, patient demographics, type of intraoperative anaesthesia, inhaled anaesthetic used for postoperative sedation, comparator sedation, and the outcomes of interest. Information pertaining to methodological quality was also collected.