Systematic review on the effects of volatile anesthetics on mortality in patients undergoing surgery

Christopher Uhlig, Thomas Bluth, Stefanie Deckert, Jochen Schmitt, Marcelo Gama de Abreu

Citation

Review question(s)
To evaluate the efficacy of volatile anesthetics compared to total intravenous anesthesia on mortality and postoperative pulmonary complications in patients undergoing general anesthesia for surgery

Searches
Systematic literature search in MEDLINE, EMBASE and the Cochrane Central Register of Randomised Controlled Trials (CENTRAL); hand search in reference lists of included papers, recent editorials and related reviews; contact with experts for further eligible trials

- http://www.thecochranelibrary.com/
- http://www.embase.com/
- No language restriction
- No publication status restriction
- Hand search of personnel files list of reviews

Link to search strategy
http://www.crd.york.ac.uk/PROSPEROFILES/8699_STRATEGY_20141114.pdf

Types of study to be included
Inclusion: Randomized Clinical Trials

Exclusion: Pseudo-randomized trials, controlled or non-randomized, Trials only published as abstracts

Condition or domain being studied
General anesthesia in patients undergoing surgery.

Participants/ population
Inclusion: Patients undergoing surgery, Age > 18 years

Exclusion: day case surgery

Intervention(s), exposure(s)
Patients receiving volatile anesthetics (sevoflurane, desflurane, isoflurane) for general anesthesia

Comparator(s)/ control
Inclusion: modern volatile anesthetics (sevoflurane, desflurane, isoflurane) vs. total intravenous anesthesia
Exclusion: halothan, enflurane, or non-halogenated agents (Xenon or nitrous oxide) as comparator

**Outcome(s)**

**Primary outcomes**
Hospital mortality (n, %) or 30-day mortality (n, %), longest available mortality (n, %)

**Secondary outcomes**
Postoperative pulmonary complications (PPCs) defined according to authors definition or:
- Hypoxemia
- ARDS
- Pulmonary infiltrate
- Pneumonia
- Pleural effusions
- Atelectasis
- Pneumothorax
- Bronchospasm
- Cardiopulmonary edema
- Aspiration pneumonitis

- Intensive Care Unit (ICU) length of stay (days) or ICU-free days
- Length of hospital stay
- Organ failure/extrapulmonary complications (including acute renal failure, hepatic failure, disseminated intravasal coagulation, extrapulmonary infection, gastrointestinal failure, myocardial infarction, coma)

**Data extraction, (selection and coding)**
Two reviewers (CU and TB) will independently assess trial eligibility based on titles, abstracts, full-text reports and further information from the investigators as needed; request protocol, case report forms and unedited databases from investigators of all eligible trials; data from each trial will be checked against reported results; queries have to be resolved with the corresponding principal investigator, trial data manager or statistician; discussion with all reviewers in cases of disagreement (CU, TB, JS, MGA).

**Risk of bias (quality) assessment**
Identification of bias (examination of concealment of treatment allocation, blinding of clinical outcome assessments and data analyses; examination of the proportion of patients lost to follow up and early stopping prior to enrolment of the target sample) according to Cochrane Handbook for Systematic Reviews of Interventions.

The GRADE approach will be used in order to summarize the quality of evidence

**Strategy for data synthesis**
Heterogeneity: Qualitative and statistical methods will be applied to assess the heterogeneity of the studies included. In case of obvious qualitative heterogeneity no meta-analysis will be performed. Statistical heterogeneity will be investigated using the computation of I-squared. An I-squared value of more than 75% is considered to represent considerable heterogeneity.

Quantitative synthesis: For binary outcomes (e.g. mortality) incidence rates will be calculated for each study. For
scores mean differences (MD) between treatment groups and proportions of patients with a clinically different change (RD) between groups will be calculated for each study. Depending on the conclusions from heterogeneity (i.e. I-squared) assessment, fixed or random effects meta-analysis will be conducted. Risk differences with corresponding 95% CI of rates of events and proportions of responders from included studies will be pooled with the appropriate statistical model (e.g. Peto Odds Ratio method or Mantel-Haensel estimator) and presented as forest plots.

Publication bias: Publication bias will be addressed visually using a funnel-plot, linear regression models for publication bias will be used additionally.

Analysis of subgroups or subsets
A subgroup analysis between cardiac surgery and non-cardiac surgery is planned.

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Subject indexing assigned by CRD

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**Stage of review at time of this submission**

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<td>Formal screening of search results against eligibility criteria</td>
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<td>Data extraction</td>
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