Use of Volatile Anesthetics During Cardiopulmonary Bypass: A Systematic Review of Adverse Events

Caetano Nigro Neto, MD, PhD, Giovanni Landoni, MD, Luigi Cassarà, Francesco De Simone, CPT, Alberto Zangrillo, MD, and Maria Angela Tardelli, MD, PhD

Objectives: **Recently, evidence of reduction in mortality due to the use of volatile agents during cardiac surgery led to an increase in their use during cardiopulmonary bypass (CPB). Because this technique could be beneficial to patients, but might present several hazards to new users, the authors decided to perform a systematic review of the main problems and complications.**

Design: **Systematic literature review.**

Setting: **Hospital.**

Participants: **Adults undergoing cardiac surgery with use of volatile anesthetic agents during CPB.**

Intervention: **Several databases were searched for pertinent studies to identify all reports on the adverse events of using volatile agents during CPB and all randomized controlled trials using volatile agents during CPB.**

Measurements and Main Results: **Six nonrandomized trials reporting adverse events or complications with the use of volatile agents during CPB for cardiac surgery were identified: 2 reporting low transfer of isoflurane to the blood with diffusion membrane oxygenators; 2 reporting iatrogenic causes of damage after spilling liquid isoflurane onto the surface of the membrane oxygenators while filling the vaporizer; and 2 suggesting that the use of volatile agents during CPB increased the pollution of the room and the risk of occupational exposure of the operating room staff. On the other hand, no adverse event was reported in 19 studies that randomized 1,195 patients to receive isoflurane, desflurane, or sevoflurane during CPB.**

Conclusion: **It is mandatory for industry to provide safe and easy-to-use devices to administer volatile agents during CPB with the standard membrane oxygenators.**

KEY WORDS: volatile anesthetic, cardiopulmonary bypass, anesthesia, cardiac surgery, safety, desflurane, isoflurane, sevoflurane

THE USE OF VOLATILE anesthetic agents during cardiopulmonary bypass (CPB) was described for the first time in 1974.[1] Originally, volatile agents were vaporized and administered, mixed with oxygen, in the early-generation bubble oxygenators.[2–4] Today, most cardiac surgery interventions are performed with standard membrane oxygenators.

Recently, evidence of reduction in mortality due to the use of volatile agents during cardiac surgery [5–8] led to an increase in their use during CPB, mainly because the cardioprotective properties might be related to the modalities of its administration.[9]

Despite all the newest CPB machines having appropriate connections for volatile anesthetic vaporizers, clinicians still need to adapt anesthetic vaporizers to the bypass circuit as well as the scavenging systems to not pollute the room.

Because the administration of volatile agents through CPB could be beneficial to patients, but might present several hazards to new users, the authors, using a systematic search of the literature, decided to summarize the main risks to alert new users to possible problems that could happen.

METHODS

BioMed Central, PubMed, Embase, and the Cochrane Central Register of Clinical Trials were searched for pertinent studies (updated October 1, 2012) by two investigators. The full search strategy (Appendix 1 and Appendix 2) was performed to identify (a) all randomized controlled trials (RCTs) that used volatile agents in adult patients during CPB and (b) all reports on the adverse events of using volatile agents during CPB. Further searches involved conference proceedings from congresses in the field. The references of retrieved articles carefully were checked. No language restriction was enforced.

References obtained from database and literature searches were at first independently examined at the title/abstract level by 2 investigators. Divergences were settled by consensus with the supervision of a third investigator. Eventually, if potentially pertinent, the references were retrieved as complete articles.

Any RCT performed in patients undergoing cardiac surgery with the use of volatile anesthetic agents during CPB was identified. Furthermore, the authors identified as potentially relevant those studies presenting at least one of these characteristics: (a) description of a technique or a device that allows delivery of volatile anesthetics during CPB; (b) awareness or risk of awareness during CPB in patients receiving volatile agents; (c) pollution of the room during CPB with the use of volatile agents; (d) adverse events to the patients or damage to a component of the CPB machine due to the use of volatile agents; and (e) malfunction of the vaporizer system adapted to the CPB machine. Two investigators selected the studies for the final analysis, independently assessing their compliance to the selection criteria. Divergences were resolved by consensus.

Author(s), year of publication, study design, number of patients related with volatile agents during CPB, patients' population, clinical setting, and adverse events during CPB (awareness, pollution of the room, damage to the CPB machine compounds, and malfunction of the adapted vaporizer system) were extracted independently by 2 investigators.

Awareness was investigated to alert the new users that diffusion membrane oxygenator might reduce the transfer of volatile agents lowering anesthetics blood levels during CPB, resulting in superficial levels of anesthesia.

Pollution of the room was investigated, because vaporizing anesthetic gases via the CPB circuit might result in increased concentrations of waste gases in the room with a higher risk for occupational exposure. Damage to CPB compounds was investigated, because bottled volatile agents spilled directly onto a membrane oxygenator could result in cracks in the polycarbonate shell or venous reservoir.

From the Department of Anesthesia and Intensive Care, Dante Pazzanese Institute of Cardiology and San Raffaele Scientific Institute, Milan, Italy.

Address reprint requests to Giovanni Landoni, MD, Anesthesia and Intensive Care Department, San Raffaele Scientific Institute, Via Olgettina 60, 20132 Milan, Italy. E-mail: landoni.giovanni@hsr.it

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RESULTS

The flowchart of selected papers (Fig 1) describes the 19 RCTs[9–28] comparing volatile agents administered only or also during CPB versus a total intravenous anesthesia (TIVA) (Fig 1A), and the 6 studies[28–33] describing adverse events or complications related to the use of volatile agents during CPB (Fig 1B).

The 19 RCTs that compared volatile agents versus TIVA during CPB are detailed in Table 1. In these studies, 1,195 patients received a volatile agent during CPB without reporting any adverse event. In summary, 384 patients received desflurane, 604 patients received sevoflurane, and 207 patients received isoflurane.

Table 2 shows the 6 manuscripts that mentioned adverse events or complications related to the use of volatile agents during CPB for cardiac surgery. Two reports[28,29] observed a low transfer of isoflurane to the blood with diffusion membrane oxygenators. Two studies[30,31] reported iatrogenic damage after spilling the liquid isoflurane onto the surface of the membrane oxygenators while filling the vaporizer. Two studies[32,33] indicated that the use of volatile agents during CPB increased the pollution of the room and the risk of occupational exposure for the operating room staff.

Interestingly, no study reported on the physical chemical effect, referring to molecular changes that could occur in the internal surface of the oxygenator due to exposure of vaporized volatile anesthetic agents, and no study reported malfunction of the adapted vaporizer system.

Table 3 describes some problems administering volatile agents during CPB and tips to minimize them, based on the respective studies that reported problems related to this technique.[30–33]

DISCUSSION

The most important result of this systematic review was confirmation that new users of volatile agents during CPB should be alerted to possible adverse events associated with the use of this technique.

Assuming that continued administration of inhaled agents during CPB leads to better outcomes for the patient (avoids awareness, organ protection), provided that these agents are administered safely (occupational hazard for the operating room personnel), the authors reviewed existing literature on the topic and identified 19 RCTs comparing volatile agents to TIVA and 6 articles describing adverse events related to using volatile agents during CPB.

Currently, there are 2 groups of hollow-fiber membrane oxygenators used in practice. The first type includes hollow-fiber membranes, for which the basic compound is microporous polypropylene (PPL), which has been used widely for standard CPB; these offer excellent oxygen exchange and carbon dioxide removal up to 6 hours. The second type is diffusion, plasma-resistant oxygenators, for which the basic membrane compound is poly-(4-methyl-1-pentene) (PMP), which has been used increasingly for extracorporeal life support or extracorporeal membrane oxygenation (ECMO) that could be used for more than 6 hours, even for days.[34] Two studies showed[28,29] that diffusion membrane oxygenators increased the risk of intraoperative awareness during CPB by lowering the transfer of isoflurane to the blood; the authors concluded that

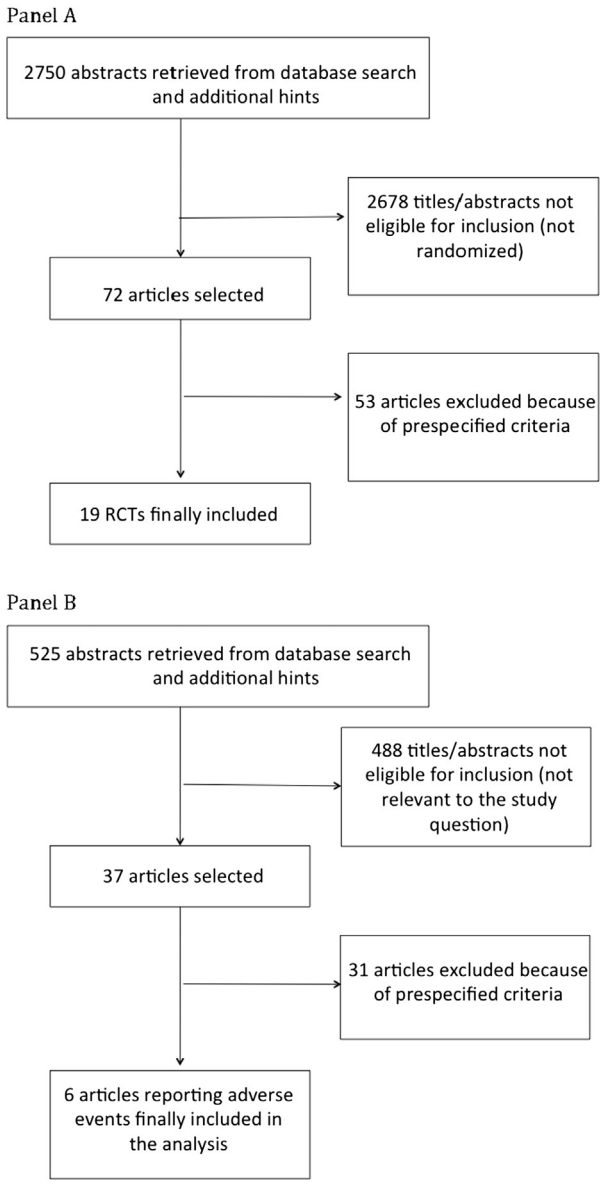

Fig 1. Flow chart of the search process to identify all randomized controlled trials comparing volatile agents during cardiopulmonary bypass versus total intravenous anesthesia (A), and all manuscripts describing adverse events with the use of volatile agents during CPB (B).

isoflurane should be avoided to maintain deep levels of anesthesia. Other authors[35] described the pharmacokinetics of isoflurane with different membrane oxygenators tested in vitro and evaluated its elimination from blood. They demonstrated that polypropylene oxygenators had better uptake and elimination of isoflurane compared with polydimethylsiloxane oxygenators. Until now, there are no data from industry that show that the newest diffusion membrane oxygenators in use have a better uptake and elimination of volatile agents than the early generation. The authors agree that isoflurane has a track record of more than 35 years of successful use in cardiac surgery and that recall is quite rare, but care must be taken vaporizing it in polydimethylsiloxane oxygenators. To date, no data on