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Original Article

Propofol versus sevoflurane anesthesia in adults: a systematic review and meta-analysis

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Abstract: Objectives: We performed a systematic review and meta-analysis of relevant randomized controlled trials to assess the incidence of postoperative nausea and vomiting (PONV), intraoperative hypertension and hypotension of general anesthesia with propofol versus sevoflurane in adult patients. Methods: This meta-analysis was carried out at the Second Affiliated Hospital of Wenzhou Medical University, Wenzhou, Zhejiang, China in August 2014. Medline, PubMed, EMBASE, and Cochrane databases were searched for randomized controlled trials using combinations of the search terms sevoflurane, propofol, adults, and randomized controlled trial. Two authors independently appraised the quality of the reference research and extracted the data. Meta-analysis was performed using the Cochrane Collaboration's Review Manager 5.3. Results: A total of six studies (1,147 patients) met the inclusion criteria were analyzed. The results of the meta-analysis were expressed as risk ratio (RR), with their corresponding 95% confidence interval (CI). Propofol was associated with a similar rate of intraoperative hypertension (RR = 1.15, 95% CI = 0.88-1.49; *P* = 0.31) and a similar rate of intraoperative hypotension (RR = 0.84, 95% CI = 0.60-1.19; *P* = 0.33) compared to sevoflurane anesthesia groups, no statistical significance between the two anesthetic techniques. In addition, the results indicated that propofol anesthesia had significantly reduced the incidence of PONV (RR = 0.62, 95% CI = 0.46-0.83; *P* = 0.001). Conclusions: This meta-analysis provides evidence that propofol anesthesia was associated with a similar rate of intraoperative hypertension and hypotension compared to sevoflurane anesthesia, and results in a significant reduction of PONV in adults.

Keywords: Propofol, sevoflurane, anesthesia, meta-analysis

Introduction

Propofol remains one of the most widely used intravenous hypnotic for the induction and maintenance of general anesthesia because of its rapid onset time, short action duration, favorable induction of anesthesia characteristics, high patient satisfaction, and few postoperative side effects [1]. Sevoflurane may have similar efficacy for induction and maintenance of general anesthesia with propofol. Sevoflurane is a nonpungent inhaled anesthetic with a low blood gas solubility coefficient (0.69) [2] and minimal respiratory irritant characteristics that make it suitable for inhaled induction of anesthesia [3]. Furthermore, sevoflurane has the advantage of lacking of major side effects, providing better hemodynamic stability [4, 5], and better conditions for laryngeal mask airway (LMA) insertion [6-8].

Many clinical studies have compared propofol and sevoflurane anesthesia in adults. However, these studies have not always shown consistent results or a definite advantage of one technique over the other, and few of them enrolled sufficient numbers of patients to produce an adequate power to detect meaningful differences. Some trials were favoring propofol anesthesia but others indicating essentially no difference in general anesthesia between the two anesthetics. Thus, it remains unclear whether or not propofol anesthesia is better than sevoflurane. Moreover, a lack of systematic reviews have been undertaken to compare propofol-maintained anesthesia versus sevoflurane-maintained in adults. Clearly, newer systematic review and meta-analyses are required to resolve these differences, and definitive analyses can provide stronger rationales for the choice of anesthetic technique. Consequently, we performed a systematic review and meta-analysis of relevant randomized controlled trials (RCTs) to assess the incidence of postoperative nausea and vomiting (PONV), intraoperative hypertension and hypotension of general

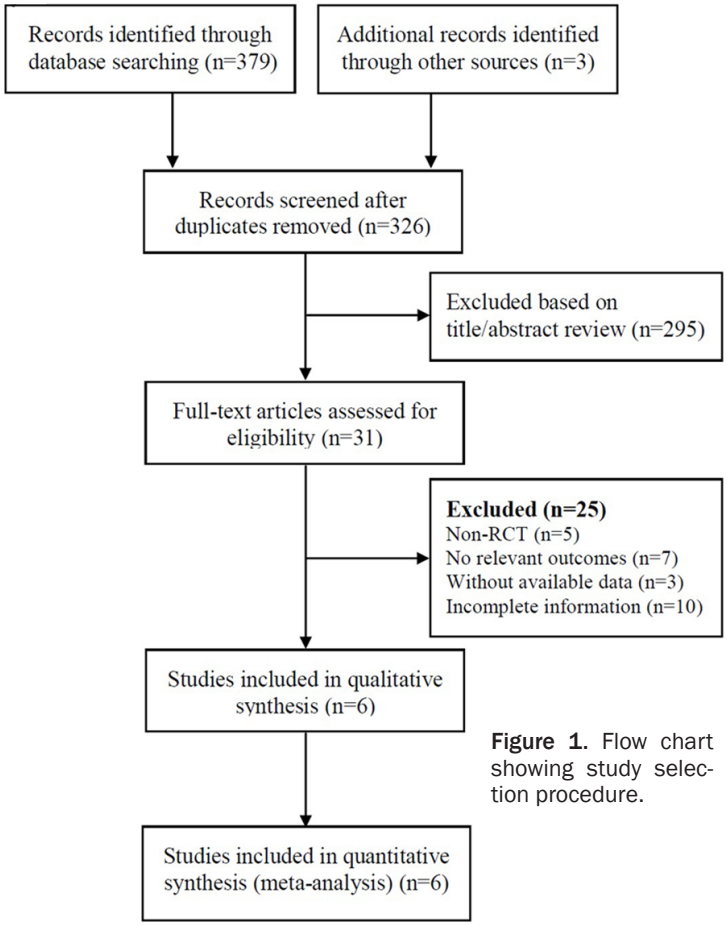

Figure 1. Flow chart showing study selection procedure.

anesthesia with propofol versus sevoflurane in adults.

Methods

Literature search strategy

This systematic review was carried out according to the methods recommended by the Cochrane Collaboration and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [9-11]. The meta-analysis was carried out at the Second Affiliated Hospital of Wenzhou Medical University, Wenzhou, Zhejiang, China in August 2014. We conducted a systematic literature search by using Medline, PubMed, EMBASE, and Cochrane databases, from their date of inception to August 2014, without language restriction. The following words were used as primary search items: sevoflurane, propofol, adults, and randomized controlled trial. The reference lists of all retrieved articles were also reviewed and searched for further identification of potentially relevant studies to identify all available evidence. Each publication was carefully examined, including the names of authors, to avoid duplication of data.

Selection criteria

Two independent reviewers (PS Q and XW Q) evaluated the search results and identified the eligible studies for possible inclusion using predefined selection criteria. Studies included in our meta-analysis had to meet the following criteria: (1) Research design (randomized controlled trials); (2) Trials contrasting the incidence of PONV, intraoperative hypertension and hypotension of general anesthesia with propofol versus sevoflurane in adult patients (age older than 18 years); (3) Outcomes included intraoperative hypertension, intraoperative hypotension, and PONV; (4) Having sufficiently effective data for extraction. Exclusion criteria for this analysis were as follows: (1) Case studies and review articles; (2) Studies lacking control groups; (3) Studies with no clearly reported outcomes of interest. Any disagreements in selection between the two authors were resolved by discussion or by consulting the second author (DX K).

Data extraction and quality assessment

Data were extracted independently by two authors (XW Q and LX J), and discrepancies were resolved by consensus including a second author (DX K). Details of the study population, the first author, the year of publication, interventions, and outcomes were extracted using a standardized electronic data extraction form. When data were missing or unclear in a paper, attempts were made to contact the authors for more information.

The overall quality of each study was assessed in accordance with the tool of “risk of bias” according to the Cochrane Handbook (version 5.1.0) [11]. Sequence generation, allocation concealment, blinding, incomplete data, selective reporting, and other sources of bias were assessed. Two reviewers, LX J and XW Q, inde-

Table 1. Characteristics of included studies

First author	Year	Country	Interventions		Patients, n	Men, n	Mean age	ASA
			P	S	P/S	P/S	P/S	
Citerio [17]	2012	Italy	10/8/6 mg×kg^{-1}×h^{-1}	0.75-1.25 MAC	138/273	70/139	54/55	ND
Lauta [16]	2010	Italy	10/8/6 mg×kg^{-1}×h^{-1}	0.7%-2%	153/149	62/75	53.1/58.1	I-III
Magni [15]	2007	Italy	10/8/6 mg×kg^{-1}×h^{-1}	1.5%-2%	80/82	31/33	52.3/53.4	I-III
Sneyd [14]	2005	UK	1-2 mg×mL^{-1} (TCI)	1.3%-1.8%	24/26	11/10	56/58	ND
Magni [13]	2005	Italy	10/8/6 mg×kg^{-1}×h^{-1}	1.5%-2%	60/60	31/33	52.3/53.4	I-III
Thwaites [5]	1997	USA	2.0-2.5 mg×kg^{-1}×h^{-1}	1.2%-2%	51/51	29/31	58/60	I-III

Abbreviations: P = propofol; S = sevoflurane; TCI = target controlled infusion; MAC = minimum alveolar concentration; 10/8/6 mg×kg^{-1}×h^{-1} = 10 mg×kg^{-1}×h^{-1} for 10 min, reduced to 8 mg×kg^{-1}×h^{-1} for 10 min, then reduced to 6 mg×kg^{-1}×h^{-1} for the remainder of the procedure; ASA = American Society of Anesthesiologists; ND, not derived.

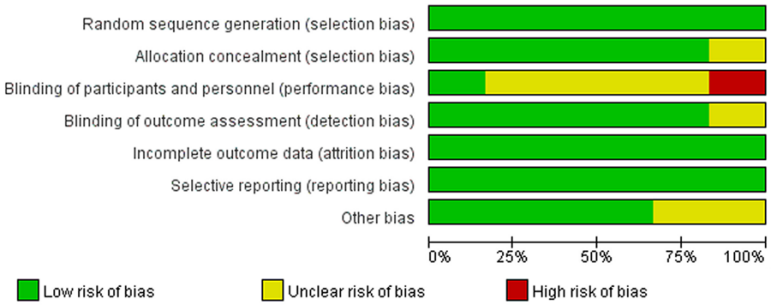

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

pendently assessed the methodologic quality. Disagreement between the two reviewers was settled by discussing with the second author (DX K).

Statistical analysis

We used the x^2 and I^2 tests to detect for heterogeneity across the different studies. For the x^2 statistic, a P value < 0.10 was considered statistically significant for heterogeneity. For the I^2 statistic, heterogeneity was interpreted as absent (I^2 = 0%-25%), low (I^2 = 25%-50%), moderate (I^2 = 50%-75%), or high (I^2 = 75%-100%). When heterogeneity was confirmed (P < 0.10, I^2 > 50%), the random-effect method was used. In the absence of statistically significant heterogeneity, the fixed-effect method was used to combine the results [12]. The results were presented as a risk ratio (RR) for dichotomous data with corresponding 95% confidence interval (CI). The nominal level of significance was set at 5%. All 95% CIs were two-sided. All statistical analyses were performed using Review Manager, version 5.3 software (The Cochrane Collaboration, Oxford, UK).

Results

Quantity of evidence

A total of six RCTs [5, 13-17] met the inclusion criteria, and were included in this study. Briefly, 382 records were identified by the database searches and screened for relevance. After excluding non-relevant studies and duplicates, 31 full text articles were assessed for eligibility, and further examination led to the exclusion of 25 studies from analysis. A diagram represents the flow of identification and inclusion of trials (**Figure 1**), as recommended by the PRISMA statement. The characteristics of the included RCTs are summarized in **Table 1**.

All the included studies were RCTs that were conducted in either a single centre or multiple centers. They mentioned the concealment of allocation clearly in the randomization process, and the randomization sequences were generated by computer-generated random numbers. An open-label design was commonly used in some studies. However, double-blinding was not a requirement, because adequate blinding was not felt to be possible in most studies. A risk of bias graph and summaries are shown in **Figures 2** and **3** illustrate our opinion about each item of bias risk for included RCTs, most of the items were at "low risk" based on Cochrane handbook (version 5.1.0) [11], suggesting a reasonable good quality of RCTs.

Intraoperative hypertension

The Forrest plot of the incidence of intraoperative hypertension is shown in **Figure 4**. Five

Figure 3. Risk of bias summary: review authors' judgements about each methodological quality item for each included study. "+", "-" or "?" reflected low risk of bias, high risk of bias and uncertain of bias respectively.

RCTs [13-17] with the data of intraoperative hypertension were included in the analysis. The heterogeneity test showed a random effect model was considered with a $P = 0.05$, and $I^2 = 57\%$. The result with an RR = 1.15 (95% CI 0.88 to 1.49; $P = 0.31$) indicated no statistically significant difference between propofol and sevoflurane groups.

Intraoperative hypotension

Figure 5 presents the incidence of intraoperative hypotension. There were five RCTs [13-17] included in the analysis. The heterogeneity test showed a random effect model was considered with $P = 0.001$ and $I^2 = 82\%$. The result with RR = 0.84 (95% CI = 0.60-1.19; $P = 0.33$) indicated no statistically significant difference between the two groups.

Postoperative nausea and vomiting (PONV)

The analysis result of the incidence of PONV is shown in **Figure 6**. Six RCTs [5, 13-17] with complete data of PONV were included in the analysis. The heterogeneity test showed a fixed effect model was considered with $P = 0.14$ and $I^2 = 40\%$. The result of the analyses indicated that propofol group was associated with lower rate of PONV (RR = 0.62, 95% CI = 0.46-0.83) than sevoflurane group, with a Z-statistic = 3.20 ($P = 0.001$).

Discussion

Currently, both propofol and sevoflurane are commonly used for the induction and maintenance of general anesthesia in adults [1, 18]. But limited data are available from studies to support a clear superiority for either anesthetic strategy [13, 16, 19]. To resolve this conflict, a pooled analysis of six RCTs including 1,147 patients was conducted in the meta-analysis. We performed this systematic review and meta-analysis by summarizing the existing RCTs of propofol *vs*. sevoflurane anesthesia in adults showed that propofol anesthesia was associated with a similar intraoperative hypertension rate, similar intraoperative hypotension rate, and a lower rate of PONV compared to sevoflurane anesthesia groups.

The hemodynamic stability of the two anesthetic techniques was evaluated in most of the primary studies and was frequently reported as the number of events of hypertension and hypotension. Although there is a known additive effect of propofol on mean arterial blood pressure [20, 21], we did not found any statistically significant difference between propofol and sevoflurane groups in our meta-analysis. However, these results should be interpreted with caution because the heterogeneity of the data was high, and higher heterogeneity implies greater variation in true effect sizes as a consequence of various confounding factors. In a multicenter prospective randomized trial, the authors found that no significant differences were observed in intraoperative hypertension or hypotension between the two anesthetic techniques, during the first 3 hours of the postoperative period [16]. While in the Sneyd *et al*. [14] and Jellish *et al*. [22] studies, propofol seemed to have less "hypotensive" compared with sevoflurane although no significant differ-

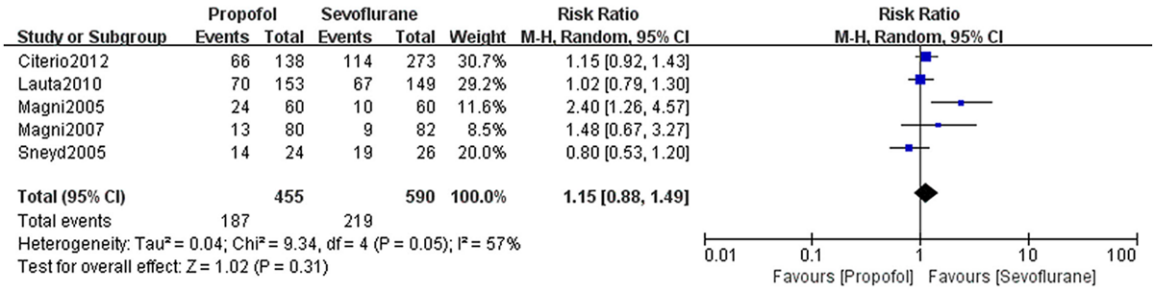

Figure 4. Forest plot of the incidence of intraoperative hypertension between propofol and sevoflurane anesthesia. RR = risk ratio; CI = confidence interval.

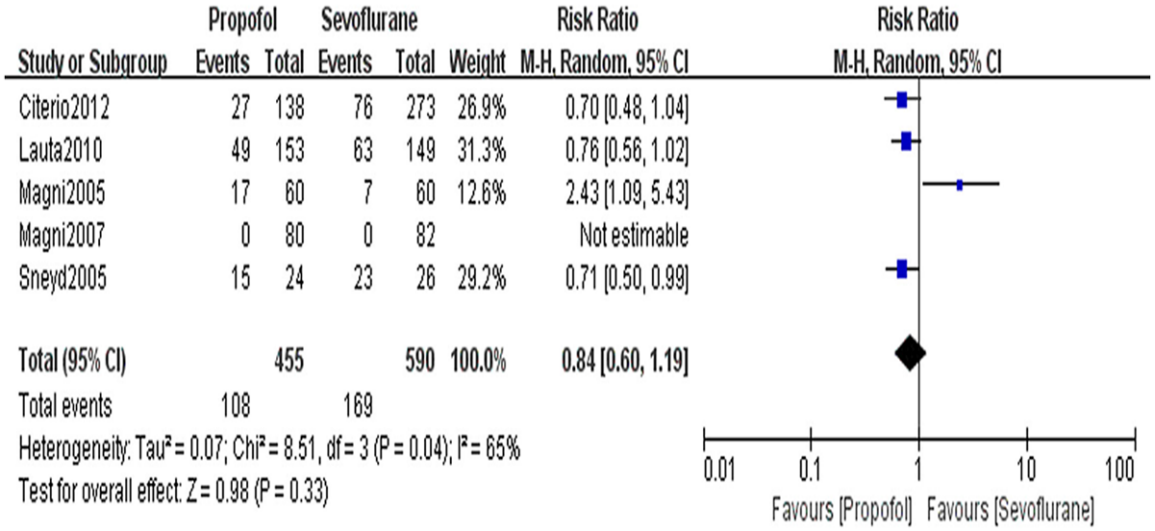

Figure 5. Forest plot of the incidence of intraoperative hypotension between propofol and sevoflurane anesthesia. RR = risk ratio; CI = confidence interval.

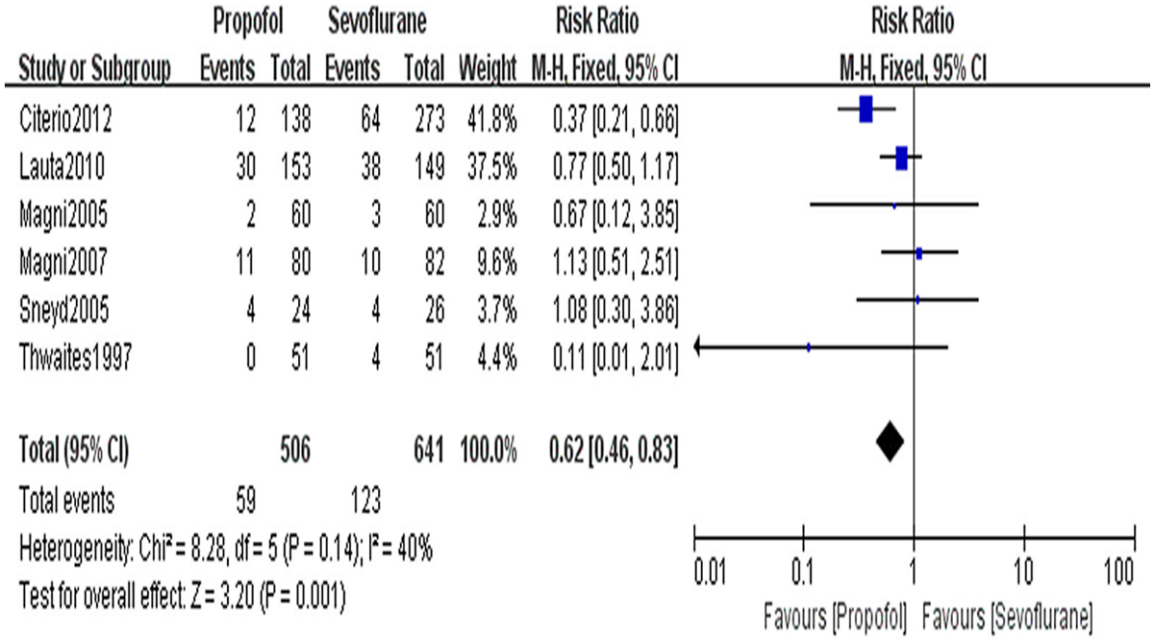

Figure 6. Forest plot of the incidence of PONV between propofol and sevoflurane anesthesia. PONV = postoperative nausea and vomiting; RR = risk ratio; CI = confidence interval.

ence was shown. The observed differences in hemodynamics in these studies may be related to the analgesic strategy used in some studies. Moreover, administration of a preemptive analgesia and more accurate postoperative control of pain may lead to different hemodynamic results [13].

PONV is probably the most common cause of morbidity following anaesthesia [23]. Many patients perceive PONV as highly unpleasant, and some even describe it as worse than postoperative pain [24]. PONV increases the cost of procedure because anti-emetic medication becomes necessary, or because discharge from hospital is delayed [25]. In our present meta-analysis, the cumulative incidence of PONV was significantly lower in propofol anesthesia groups when compared with sevoflurane anesthesia. The PONV reduction in our current meta-analysis is in agreement with results from previous meta-analyses [26, 27] and other studies [28-30]. Joo *et al*. [27] demonstrated in their meta-analysis that the incidence of PONV was significantly more frequent in the sevoflurane group ($P < 0.05$), patients were significantly more likely to have nausea with an odds ratio of 4.24 and/or vomiting with an odds ratio of 3.18 if they were in the sevoflurane group.

Our meta-analysis pooled all available data from published RCTs, which substantially reduced the type II error. However, this meta-analysis also has a number of limitations should be considered when interpreting these results. The small number of RCTs and sample size limited the ability to draw more solid conclusions. The inability to retrieve unpublished studies was also a drawback of this meta-analysis. We were not able to retrieve unpublished studies because of the absence of such a searching mechanism. Since there is a possibility of publication bias, studies that report significant findings are more likely to be published in indexed journals. Other factors, such as race differences of patients and different study protocols may confer limitations on this meta-analysis. Clearly, large-scale, multicenter, prospective studies would be warranted to account for these potential biasing factors and verify our results in this meta-analysis.

In conclusion, this meta-analysis provides evidence that propofol anesthesia was associated with a similar rate of intraoperative hypertension and hypotension compared to sevoflurane anesthesia, and results in a significant reduction of PONV in adults.

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Disclosure of conflict of interest

None.

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