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[Intervention Review]

Deliberate hypotension with propofol under anaesthesia for functional endoscopic sinus surgery (FESS)

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ABSTRACT

Background

Functional endoscopic sinus surgery (FESS) is a minimally invasive technique that is used to treat chronic sinusitis. Small bleeding areas can reduce operative visibility and result in destruction of surrounding structures. Deliberate hypotension (lowering the mean arterial blood pressure to between 50 and 65 mm Hg in normotensive patients) using a range of pharmacological agents during general anaesthesia reduces blood loss in many operations. This review was originally published in 2013 and updated in February 2016.

Objectives

We aimed to compare the use of propofol versus other techniques for achieving deliberate intraoperative hypotension during FESS procedures with regard to blood loss and operative conditions.

Search methods

We searched the following databases in the updated review: the Cochrane Central Register of Controlled Trials (CENTRAL; 2016, Issue 2), MEDLINE (1950 to February 2016), Embase (1980 to February 2016), LILACS (1982 to February 2016), and ISI Web of Science (1946 to February 2016). We also searched the reference lists of relevant articles and conference proceedings and contacted the authors of included trials.

Selection criteria

We sought all randomized controlled trials comparing propofol with other techniques for deliberate hypotension during FESS with regard to blood loss and operative conditions in both adults and children. Our primary outcome was total blood loss (TBL). Other outcomes included surgical field quality, operation time, mortality within 24 hours, complications, and failure to reach target blood pressure.

Data collection and analysis

We used standard methodological procedures expected by Cochrane. Two review authors independently extracted details of trial methodology and outcome data from the reports of all trials considered eligible for inclusion. We made all analyses on an intention-to-treat basis where possible. When I^2 was less than 40% and the P value from the χ^2 test was higher than 0.10, we pooled data using the fixed-effect model. Otherwise, we pooled data using the random-effects model.

Main results

We found no new studies. This updated review therefore includes four studies with 278 participants. Most analyses were based on data from few participants and low-quality evidence, so our results should be interpreted with caution. Deliberate hypotension with propofol did not decrease TBL (millilitres) when compared with inhalation anaesthetics in either children (1 study; 70 participants; very low-quality evidence), or adults (1 study; 88 participants; moderate-quality evidence). Propofol improved the quality of the surgical field by less than one category on a scale from 0 (no bleeding) to 5 (severe bleeding) (mean difference -0.64, 95% CI -0.91 to -0.37; 4 studies; 277 participants; low-quality evidence), but no difference in operation time was reported (3 studies; 214 participants; low-quality evidence). Failure to lower blood pressure to target was less common in the propofol group (risk ratio of failure with propofol 0.24, 95% CI 0.09 to 0.66; 1 study; 88 participants; moderate-quality evidence).

Authors' conclusions

Using propofol to achieve deliberate hypotension probably improves the surgical field, but the effect is small. Deliberate hypotension with propofol did not decrease TBL and the operation time. However, due to the very low quality of the evidence, this conclusion is not definitive. Randomized controlled trials with good-quality methodology and large sample size are required to investigate the effectiveness of deliberate hypotension with propofol for FESS.

PLAIN LANGUAGE SUMMARY

Induced hypotension with propofol under anaesthesia during endoscopic sinus surgery

Review question

Does the evidence support the use of propofol as an effective drug in reducing total blood loss and improving quality of the surgical field in people undergoing functional endoscopic sinus surgery (FESS) with induced hypotension, compared to inhalational (gas) anaesthetics and other drugs? This review updates the evidence published in 2013, and is current to February 2016.

Background

FESS is a minimally invasive technique used to treat patients with chronic sinusitis (inflammation of the mucous membrane in the air cavities within the facial bones, and fluid within the cavity for more than 12 weeks). The surgeon uses a miniature camera in the nose to get a close-up view of the sinuses. The main problem is that bleeding during the operation will obscure the view and cause the procedure to take longer, with an increased risk of damage to the surrounding structures (eyes and brain). One method for reducing bleeding under general anaesthesia is induced hypotension, which involves deliberately lowering the blood pressure to below normal in order to improve the surgical field. However, lowering the blood pressure carries its own risks including permanent brain damage, delayed awakening, blood clot in the brain, insufficient blood flow to the brain, and death. Propofol (an anaesthetic drug given intravenously) and volatile anaesthetic agents (given as inhaled gas) are alternative methods for reducing blood pressure during the anaesthetic period.

Study characteristics

We included four studies in our review (278 participants). The studies were conducted between 2003 and 2010. Although all four included studies were randomized, some elements of their methodology suggest a low to unclear risk of bias in all trials.

Key results

We found that propofol did not reduce measured overall blood loss in either children or adults (2 studies; 158 participants). Propofol might improve the quality of the surgical field a little (4 studies; 277 participants), but there was no difference in operation time (3 studies; 214 participants). Propofol was more reliable in achieving induced hypotension (1 study; 88 participants). No studies reported any adverse effects from induced hypotension with propofol.

Quality of the evidence

We found only four studies, which included a small total number of participants. The evidence from the studies were of moderate to very low quality, and therefore our results should be interpreted with caution. More studies are needed to confirm whether any important benefit is associated with the use of propofol.

SUMMARY OF FINDINGS

Summary of findings for the main comparison. Propofol versus inhalation anaesthetics for functional endoscopic sinus surgery (FESS)

Propofol versus inhalation anaesthetics for functional endoscopic sinus surgery (FESS)

Patient or population: patients undergoing FESS

Settings: operating rooms in Asia, Australia, and Europe

Intervention: propofol versus inhalation anaesthetics

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Control	Propofol versus inhalation anaesthetics				
Total blood loss - children	The mean total blood loss was 120 mL	The mean total blood loss was 20 lower (0.77 to 39.23 lower)		70 (1 study)	⊕⊕⊕⊕ very low ¹	
Total blood loss - adults	The median total blood loss was 170 mL	The median total blood loss was 100 mL (interquartile range 50 to 240 mL)		88 (1 study)	⊕⊕⊕⊕ moderate ²	
Quality of surgical field Scale from 0 to 5	The mean quality of surgical field in the control groups was 2.55	The mean quality of surgical field in the intervention groups was 0.64 lower (0.37 to 0.91 lower)		277 (4 studies)	⊕⊕⊕⊕ low ³	
Operation time	The mean operation time in the control groups was 91.51 min	The mean operation time in the intervention groups was 4.81 lower (11.82 lower to 2.21 higher)		214 (3 studies)	⊕⊕⊕⊕ low ⁴	
Failure of deliberate hypotension (%)	372 per 1000	89 per 1000 (33 to 246)	RR 0.24 (0.09 to 0.66)	88 (1 study)	⊕⊕⊕⊕ moderate ²	

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **RR:** risk ratio

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

- ¹Downgraded three levels due to concerns about random sequence generation, allocation concealment and very wide confidence interval for the difference.
- ²Downgraded one level due to concerns about random sequence generation.
- ³Downgraded two levels due to serious concerns about random sequence generation, and allocation concealment.
- ⁴Downgraded two levels due to serious concerns about random sequence generation, and allocation concealment.

BACKGROUND

Description of the condition

Chronic sinusitis is a common disease in any age group and may be defined as inflammation of the mucous membrane in the paranasal sinuses and fluid within the sinus cavity that lasts longer than 12 weeks. The primary treatments for chronic sinusitis are antibiotics and topical nasal steroids. Surgery is usually considered if these measures are unsuccessful (Dessouky 2015; Kennedy 2001; Rimmer 2014; Sharma 2014; Yanez 2003). The most common procedure is functional endoscopic sinus surgery (FESS). In this minimally invasive technique, the sinus air cells and openings into the nose (ostia) are opened under direct visualization through an endoscopic technique (Catalano 2004; Khalil 2006), thereby restoring sinus ventilation (Stammberger 1991). The use of FESS is now widely accepted (Dessouky 2015; Georgalas 2014; Khalil 2006), and the number of FESS procedures that are performed has grown (Dalziel 2003; Dalziel 2006; Danielsen 2003). Compared with other more traditional methods, endoscopic sinus surgery is associated with fewer complications and greater symptomatic improvement (Dalziel 2006; Dessouky 2015; Rimmer 2014; Sharma 2014), including less postoperative pain, no external scars, and more rapid recovery. Complications related to FESS include bleeding into the nose that obscures the surgical field, bleeding into adjacent structures (including around the eyes), damage to the structures around the eye, epiphora (excessive tear production), loss of vision, cerebrospinal fluid leak, damage to intracranial structures, and death (Georgalas 2014; Maniglia 1991; May 1994; Reinhart 1993; Rimmer 2014; Stankiewicz 2001). The main problem in practice is intraoperative bleeding, because even small areas of bleeding can reduce visibility during FESS, which can result in abandonment of the procedure or unintentional destruction of surrounding structures.

Description of the intervention

Deliberate hypotension can reduce blood loss in many situations, including orthopaedic surgery, maxillofacial surgery, and spine surgery (Choi 2008; Dutton 2004; Tobias 2002). The aim of any technique of deliberate hypotension during general anaesthesia is to lower the mean arterial blood pressure (MAP) to values between 50 and 65 mm Hg in patients with normal blood pressure, with the goal of significantly reducing blood loss (Cincikas 2003; Dutton 2012). Although the precise mechanism varies with the technique used, deliberate hypotension is usually the result of a reduction in cardiac output, blood pressure, or a combination of these factors (Aken 2000). Deliberate hypotension can reduce blood loss in FESS by between 80 and 141 mL (Cincikas 2003; Elsharnouby 2006). However, deliberate hypotension is not without potential complications, which include permanent cerebral damage, delayed awakening, cerebral thrombosis, brain ischaemias, and death (Aken 2000; Choi 2008).

Techniques for deliberate hypotension include controlling venous return (for example through positioning of the patient) and providing various pharmacological interventions including volatile anaesthetics (halothane, isoflurane, sevoflurane, desflurane), direct-acting vasodilator drugs (sodium nitroprusside, nitroglycerine, hydralazine), trimetaphan, alpha-adrenergic receptor blocking drugs (phenolamine, urapidil), selective alpha2-adrenergic agonist (dexmedetomidine), beta-adrenergic receptor blocking drugs (propranolol, esmolol), combined alpha- and beta-

adrenergic receptor blocking drugs (labetalol), calcium channel blockers (nicardipine), and prostaglandin E1 (Aken 2000; Dodds 2001; Morgan 2002; Shams 2013). Disadvantages are associated with each of these approaches. For example, the use of nitroprusside or nitroglycerine may require escalating doses because of tachyphylaxis (Aken 2000), nitroprusside in large doses can result in cyanide intoxication (Bendo 2001), and both require invasive monitoring of arterial blood pressure (Aken 2000). Volatile anaesthetics can prolong recovery and delay discharge (Aken 2000).

How the intervention might work

More recently, deliberate hypotension using the anaesthetic agent propofol has become popular. Propofol is commonly used during anaesthesia both as an induction agent and for maintenance of anaesthesia. It induces a state of general anaesthesia by facilitating inhibitory neurotransmission mediated by gamma-aminobutyric acid (GABA) (Fan 2015). Propofol has rapid onset and recovery times with a short half-life and duration of action (Darnobid 2015; Reves 2005). Disadvantages of propofol are that it is painful on injection and administration can decrease arterial blood pressure and cardiac output. Changes in blood pressure can be rapidly achieved in response to bolus doses or infusion, as required (Reves 2005).

Why it is important to do this review

For achieving deliberate hypotension, many studies have found that propofol seemed to be more effective in reducing blood loss than volatile anaesthetics (Aken 2000; Blackwell 1993; Dodds 2001; Eberhart 2003; Morgan 2002; Pavlin 1999). If propofol is superior to alternative agents in attaining deliberate hypotension for FESS, then this would be important information for the anaesthetist in choosing the more appropriate technique. If, on the other hand, any clear disadvantages are associated with propofol, this information would be equally important to the clinical practitioner.

OBJECTIVES

We aimed to compare the use of propofol versus other techniques for achieving deliberate intraoperative hypotension during FESS procedures with regard to blood loss and operative conditions.

METHODS

Criteria for considering studies for this review

Types of studies

We included all published and unpublished randomized controlled trials (RCTs).

Types of participants

We included participants of any age who received general anaesthesia for FESS.

Types of interventions

We compared propofol for deliberate hypotension (MAP lowered to values at or below 65 mm Hg) with other deliberate hypotension techniques.

Types of outcome measures

Primary outcomes

1. Total blood loss (blood loss during surgery measured as blood collected in the suction apparatus and by weight of the nasal swabs).

Secondary outcomes

1. Operator assessment of quality of surgical field: a 6-point scale (0 = no bleeding; 1 = slight bleeding and no suctioning of blood required; 2 = slight bleeding and occasional suctioning required; 3 = slight bleeding and frequent suctioning required (bleeding threatens surgical field a few seconds after suctioning is removed); 4 = moderate bleeding (frequent suctioning required, bleeding threatens surgical field directly after suction is removed); 5 = severe bleeding (constant suctioning required, bleeding appears faster than can be removed by suction, surgical field severely threatened) (Fromme 1986).
2. Operation time as assessed in minutes (from the start of the operation until the end).
3. Incidence of failed deliberate hypotension (defined as failure to reduce MAP to values below 65 mm Hg).
4. Mortality within 24 hours after surgery. Complications from the deliberate hypotension technique as reported in a trial (e.g. permanent cerebral damage, delayed awakening, cerebral thrombosis, brain ischaemia).
5. Need for reoperation.
6. Need for admission to intensive care or a high-dependency area postoperatively.

Search methods for identification of studies

Electronic searches

We searched the following databases for relevant trials in this updated review on 10 February 2016: the Cochrane Central Register of Controlled Trials (CENTRAL; 2016, Issue 2), MEDLINE SilverPlatter (1950 to February 2016), Embase SilverPlatter (1980 to February 2016), LILACS (1982 to February 2016), and ISI Web of Science (1946 to February 2016).

We developed a specific search strategy for each database. We based each search strategy on that developed for MEDLINE (Appendix 1) (please see Appendix 2 (CENTRAL), Appendix 3 (Embase), Appendix 4 (LILACS), and Appendix 5 (ISI Web of Science)).

Searching other resources

We searched the following for relevant trials on 10 February 2016.

1. Specialist journals (i.e. *Anesthesia and Analgesia*, *Anesthesiology*, *Anaesthesia*, *Acta Anaesthesiologica Scandinavica*, *British Journal of Anaesthesia*, *Canadian Journal of Anaesthesia*, *European Journal of Anaesthesia*, *Laryngoscope*, *American Journal of Otolaryngology*, *European Archives of Oto-Rhino-Laryngology*).
2. Conference proceedings and abstracts (American Society of Anesthesiologists (ASA), International Anaesthesia Research Society (IARS), European Society of Anaesthesiologists (ESA)).
3. Grey literature (such as SIGLE).

We contacted known trialists, experts, and medical or pharmaceutical companies for unpublished trials and checked the reference lists of relevant articles.

We did not apply any language restriction.

Data collection and analysis

Selection of studies

Two review authors (PB and SB) independently scanned the titles and abstracts of reports identified by electronic database searching and handsearching of journals. We obtained and assessed the full article of trials deemed possibly relevant according to the definitions provided in the criteria for considering studies for this review. We resolved any disagreements through discussion with the third review author (ML).

Data extraction and management

One review author (SB) summarized data from all included trials on a standardized data extraction form (Appendix 6), which a second review author (PB) checked. We resolved any disagreements through discussion. We recorded general details of the participants and deliberate hypotension techniques. We collected outcome measures as described for each study group. In studies with more than two groups, we avoided double counting of participants by following the guideline for analysis in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Assessment of risk of bias in included studies

Two review authors (PB and SB) assessed the methodological quality of each trial in accordance with the guidelines described by The Cochrane Collaboration in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Our assessment criteria were as follows.

1. Random sequence generation (selection bias): low, unclear, high risk.
2. Allocation concealment (selection bias): low, unclear, high risk.
3. Blinding (performance bias and detection bias): low, unclear, high risk.
4. Incomplete outcome data (attrition bias): low, unclear, high risk.
5. Selective reporting (reporting bias): low, unclear, high risk.

We independently evaluated and ranked the quality of each trial. We resolved any conflicts in assessment through discussion or, if necessary, by consulting a third review author (ML). For summary assessment of the risk of bias within and across studies, we followed the approach outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011), rating it as unclear, low, or high risk of bias.

Measures of treatment effect

For proportions (dichotomous outcomes: mortality, complications, incidence of failed deliberate hypotension, need for reoperation, need for postoperative admission to intensive care or a high-dependency area), we used risk ratio (RR). We analysed continuous data (blood loss during surgery, quality of surgical field, operation time) as mean differences (MDs) using the inverse variance method. We analysed continuous data that used different scales using standardized MDs when appropriate.

Unit of analysis issues

We encountered no unit of analysis issues.

Dealing with missing data

We attempted to contact the authors for the missing data. If the authors did not respond, we extracted the available data from the publication. If data were missing due to participant drop-out or losses to follow-up, we planned to conduct a primary analysis based on complete data and a sensitivity analysis with missing data imputed based on worst-case and best-case scenarios.

Assessment of heterogeneity

We assessed statistical heterogeneity using the I^2 statistic (Higgins 2011), and gave consideration to the appropriateness of pooling and meta-analysis. We explored heterogeneity and performed subgroup analyses when appropriate.

Assessment of reporting biases

We planned to assess reporting biases (such as publication bias) by using funnel plots if appropriate (Egger 1997).

Data synthesis

We analysed data and displayed them using the Review Manager software distributed by Cochrane (RevMan 5.3). We made all analyses on an intention-to-treat (ITT) basis where possible. When I^2 was less than 40% and the P value from the χ^2 test was higher than 0.10, we used a fixed-effect model for pooling data. Otherwise, we pooled data using a random-effects model (Egger 1997).

We have presented the key information for both primary and secondary outcomes in the 'Summary of findings' tables, which we created using GRADEpro software (GRADEpro 2008). We used the GRADE approach to assess the quality of the outcome (Higgins 2011), rating it as high, moderate, low, or very low. For assessments of the overall quality of evidence for each outcome that included pooled data from RCTs only, we downgraded the evidence from 'high quality' by one level for serious (or by two for very serious) study limitations (risk of bias), indirectness of evidence,

serious inconsistency, imprecision of effect estimates, or potential publication bias. We downgraded the quality of evidence from high if there were deficiencies in these domains. We included the following outcomes in the 'Summary of findings' table:

1. total blood loss;
2. quality of surgical field (scale from 0 to 5);
3. operation time;
4. failure of deliberate hypotension (%).

Subgroup analysis and investigation of heterogeneity

We intended to perform subgroup analysis in the presence of statistical heterogeneity (I^2 greater than 40%) or an indication of clinical heterogeneity, considering the following potential subgroups.

1. Age group: younger than 15 (children), 15 to 65 (adult), older than 65 years of age (elderly).
2. MAP level.
3. Anaesthetic technique (inhalation maintenance anaesthesia, intravenous maintenance anaesthesia).
4. Hypotensive drug combination.

Sensitivity analysis

We considered sensitivity analysis based on risk of bias and allocation of missing data. For the latter, we intended to investigate the influence on our estimate of overall effect of allocating missing data according to both a best-case (all missing data in the propofol group assumed to have a good outcome and in the comparator group to have a poor outcome) and a worst-case (the opposite) scenario.

RESULTS

Description of studies

Results of the search

(See Figure 1)

Figure 1. Study flow diagram.

After removal of duplicated citations, we identified 5085 citations from the database searches, journal searches, conference proceedings, and citation review in this update. In the first published version of this review (Boonmak 2013), we assessed nine full-text articles after screening by title and abstract, including four studies and excluding five. For this update, we obtained five full papers of potentially eligible studies. We excluded five of these articles for the reasons described in the [Characteristics of excluded studies](#) table. No trials are awaiting assessment. Four trials (278 participants) met our inclusion criteria.

Included studies

We included four trials in this review (Eberhart 2003; Ragab 2010; Tirelli 2004; Wormald 2005) (see [Characteristics of included studies](#)).

Two trials compared propofol infusion and remifentanyl versus isoflurane and alfentanil or fentanyl in adults (Eberhart 2003; Tirelli 2004).

Ragab 2010 compared propofol infusion and remifentanyl versus isoflurane, fentanyl, and esmolol in children.

Wormald 2005 compared propofol infusion and remifentanyl versus sevoflurane and fentanyl.

All four included trials reported surgical field grade as median, mean (standard deviation (SD)), and mean (standard error). We contacted the principal authors of two trials and received additional information by e-mail (Eberhart 2003; Wormald 2005).

Eberhart 2003 also reported blood loss, operation time, and failure of deliberate hypotension.

Wormald 2005 reported standard error, which we converted to standard deviation.

Excluded studies

We excluded a total of 10 studies (Ahn 2008; Ankichetty 2012; Arora 2013; Beule 2007; Chaaban 2013; Gomez-Rivera 2012; Miłośki 2013; Pavlin 1999; Sivaci 2004; Yoo 2010). We excluded five of these trials in our original review (Boonmak 2013), and in

this update excluded a further five trials because they did not directly compare the efficacy of propofol and an alternative treatment in maintaining deliberate intraoperative hypotension (see Characteristics of excluded studies).

Studies awaiting classification

There were no studies awaiting classification.

Ongoing studies

There were no ongoing studies.

Risk of bias in included studies

We assessed the risk of bias of included studies using the 'Risk of bias' tool developed by Cochrane (Higgins 2011). The risk of bias tool invites judgements on five items for each trial (see below). All review authors independently assessed risk of bias for each study. (Figure 2; Characteristics of included studies). We resolved any disagreements by discussion. No studies were of high methodological quality.

Figure 2. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding (performance bias and detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)
Eberhart 2003	?	+	+	+	+
Ragab 2010	?	?	+	+	+
Tirelli 2004	?	?	+	+	+
Wormald 2005	+	?	+	+	+

Allocation

Four studies reported unclear information on allocation concealment (Eberhart 2003; Ragab 2010; Tirelli 2004; Wormald 2005) (see Figure 3).

Figure 3. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

Blinding

Four trials had adequate blinding among participant, surgeon, and assessor (Eberhart 2003; Ragab 2010; Tirelli 2004; Wormald 2005).

Incomplete outcome data

All studies had complete outcome data.

Selective reporting

We found that all prespecified outcomes were reported in all four included trials. We noted no selective reporting of outcomes in any of the studies.

Other potential sources of bias

We remained mindful of the potential weakness of data for total blood loss (TBL) measurement. Two trials reported TBL (Eberhart 2003; Ragab 2010), although it is difficult to measure exact blood loss in both the surgical field and the pharynx. This outcome needs to be interpreted with caution. In addition, propofol dose, inhalation anaesthetic agents, and analgesic drug doses differed among trials, which may have biased the results of our analysis.

Effects of interventions

See: [Summary of findings for the main comparison Propofol versus inhalation anaesthetics for functional endoscopic sinus surgery \(FESS\)](#)

Primary outcomes

Total blood loss

Two trials including 158 participants reported this outcome (72% of the participants in this review) (Eberhart 2003; Ragab 2010). Eberhart 2003 enrolled 88 adults, and Ragab 2010 studied 70 children (Summary of findings for the main comparison). Concerns

about pooling the results of children and adults led us to report each age group separately.

In adults, Eberhart 2003 compared propofol with isoflurane and reported a median TBL of 100 mL (interquartile range 50 to 240 mL) in the propofol group versus a median TBL of 170 mL (interquartile range 100 to 270 mL) in the isoflurane group. This difference was not statistically significant ($P = 0.12$). We downgraded the evidence for the outcome to moderate quality due to unclear risk of selection bias.

In children, Ragab 2010 compared propofol with isoflurane and reported a mean (SD) TBL of 100 (39) mL in the propofol group versus 120 (43) mL in the isoflurane group. This difference was not statistically significant ($P = 0.084$). The outcome was downgraded to very low quality evidence due to unclear random sequence generation, allocation concealment, and very wide confidence interval for the difference.

Secondary outcomes

Quality of surgical field; mean scores

All four trials reported on this outcome using a 6-point scale, and all 277 participants were included in this outcome (Eberhart 2003; Ragab 2010; Tirelli 2004; Wormald 2005). Three trials compared propofol with isoflurane (Eberhart 2003; Ragab 2010; Tirelli 2004), and one trial compared propofol with sevoflurane (Wormald 2005). Only one trial enrolled children (Ragab 2010).

The mean score in the propofol group was 1.77 and in the control group 2.55. The difference in score of quality of surgical field with propofol was -0.64 compared with control (95% confidence interval (CI) -0.91 to -0.37; $P < 0.00001$; $I^2 = 68\%$; 4 studies; 277 participants; Summary of findings for the main comparison).

We noted some heterogeneity among trials, and therefore used a random-effects model. Subgroup analysis did not explain heterogeneity. It might be explained by a small 6-point scale. We downgraded the evidence for the outcome to low quality due to three studies having an unclear risk of random sequence and allocation concealment.

In adults, the mean score in the propofol group was 1.96 and in the control group 2.87. The difference in score of quality of surgical field with propofol was -0.75 compared with control (95% CI -1.10 to -0.40; $P < 0.0001$; $I^2 = 67\%$; 3 studies; 207 participants; low-quality evidence; [Analysis 1.1](#)). We downgraded the evidence for the outcome to low quality due to two studies having an unclear risk of selection bias.

In children, the mean score in the propofol group was 1.2 and in the isoflurane group 1.6. The difference in score of quality of surgical field with propofol was -0.40 compared with control (95% CI -0.64 to -0.16; $P = 0.001$; 1 study; 70 participants; [Analysis 1.1](#)). We downgraded the evidence for the outcome to low quality due to the study having an unclear risk of selection bias.

Operation time

Three trials including 214 participants reported this outcome (minutes) (77% of the participants in this review) ([Eberhart 2003](#); [Ragab 2010](#); [Wormald 2005](#)). The authors reported a mean operation time of 89.42 minutes in the propofol group versus 91.51 minutes in the control group. The difference in operation time with propofol was -4.81 compared with control (95% CI -11.82 to 2.21; $P = 0.18$; 3 studies; 214 participants; [Analysis 1.2](#)). We downgraded the evidence for the outcome to low quality due to two studies having an unclear risk of selection bias.

Failure of deliberate hypotension

Only one trial including 88 participants reported this outcome (32% of the participants in this review) ([Eberhart 2003](#)). The authors reported a failure rate of deliberate hypotension of 8.89% in the propofol group and 37.21% in the control group. The estimated risk ratio for failure of deliberate hypotension was 0.24 (95% CI 0.09 to 0.66; $P = 0.0056$). We downgraded the evidence for the outcome to moderate quality due to unclear random sequence generation.

Mortality within 24 hours after surgery

None of the included trials reported any mortality in either group.

Complications from the deliberate hypotension technique

None of the included trials reported any complications in either group.

Need for reoperation

None of the included trials reported any need for reoperation in either group.

Need for admission to intensive care or a high-dependency area postoperatively

None of the included trials reported any need for admission to intensive care in either group.

DISCUSSION

Summary of main results

Evidence from two studies contributing data to the primary outcome of this review suggests that deliberate hypotension with propofol may reduce the measured TBL in adults and children compared to a volatile agent ([Eberhart 2003](#); [Ragab 2010](#)), but the studies have insufficient power to confirm or refute this suggestion. A statistically significant improvement in the quality of the surgical field was observed with deliberate hypotension using propofol when compared with deliberate hypotension using inhalation anaesthetics (mean difference = 0.64 on a 6-point scale) with low-quality evidence ([Eberhart 2003](#); [Ragab 2010](#); [Tirelli 2004](#); [Wormald 2005](#)). This is a small improvement (less than one category), and it is unclear whether this difference is clinically important. Operation time did not differ between groups, with low-quality evidence ([Eberhart 2003](#); [Ragab 2010](#); [Wormald 2005](#)). A single study comparing propofol with isoflurane found fewer failures of deliberate hypotension with the use of propofol (risk ratio 0.24, 95% CI 0.09 to 0.66) with moderate-quality evidence ([Eberhart 2003](#)). No deaths were reported in any of the included studies.

Overall completeness and applicability of evidence

The main limitation of our findings is the small number of studies. This review includes findings from only four trials, and the evidence was insufficient to allow firm conclusions to be drawn for many of our outcome measures, particularly as these studies did not report on many of our clinical outcomes, including adverse effects. The overall applicability of the results of this review is limited because we have been unable to perform an adequate assessment of benefit to risk.

We were unable to perform any of our planned subgroup analyses, but of the two studies reporting our primary outcome, one enrolled children ([Ragab 2010](#)), and the other adults ([Eberhart 2003](#)). We were unable to perform sensitivity analysis by risk of bias or to determine the effect of allocating missing data because of insufficient data.

Even though this review suggests a slightly lower quality of the surgical field with inhalational agents compared with propofol, results may lack clinical significance because of the small difference. Some of the included studies had unclear random sequence generation and allocation concealment.

Despite the many drugs that have been used to induce deliberate hypotension during general anaesthesia, such as vasodilators, beta-adrenergic blockers, calcium channel blockers, dexmedetomidine, and opioids, only trials of propofol and inhalational anaesthetic agents have been reported with deliberate hypotension. Studies compared propofol with isoflurane (three studies), sevoflurane (five studies), and desflurane (one study). However, they did not keep mean arterial blood pressure below 65 mm Hg to achieve the definition of deliberate hypotension, so we added them to excluded studies.

Quality of the evidence

We found the evidence for most outcomes to be of moderate, low or very low quality, primarily due to risk of bias (for details see [Figure 2](#)). Two studies included a small number of participants, leading to imprecision of result.

The effect of propofol on quality of the surgical field may have been biased because all of the included trials used a combination of propofol and remifentanyl (an ultra-short-acting opioid) during the operation, and in the inhalation anaesthetics group, all participants received a longer-acting opioid (alfentanil or fentanyl). Propofol was therefore not the only difference in the therapeutic regimen, and these data should be properly interpreted as the effect of 'propofol with remifentanyl by infusion' compared with 'volatile anaesthesia plus intermittent fentanyl or alfentanil'. This is an important qualification to our findings, because remifentanyl has been shown to be effective in improving the surgical field. For example, one RCT showed that propofol and remifentanyl during deliberate hypotension improved the surgical field for tympanoplasty (Degoute 2001). This may be mediated through the effect of remifentanyl on lowering heart rate, cardiac output, and blood pressure. Remifentanyl can be rapidly titrated to produce the desired level of analgesia, which may contribute to the achievement of a target arterial blood pressure and may be at least in part responsible for the apparent success of propofol in this regard. The lack of standardized grading for surgical field among studies was a limitation, with studies using a 6-point scale surgical field, 10 cm visual analogue scale, and 11-point scale surgical field; reliability (inter-rater, intrarater) should be a concern.

Measurement of blood loss during FESS is difficult and may be inaccurate in these trials. Concealed blood loss (especially loss into the gut), although presumably similar across all groups, may be associated with underestimation of losses. In any case, only two trials reported this outcome.

Finally, although we could not find any difference in mortality or morbidity between the techniques examined in this review, this should not be taken to mean that we can exclude such consequences with any confidence. Adverse events are rare during FESS (for example the mortality rate has been reported to be 0.02% to 0.34% (Aken 2000)), and a much larger data set would be required to reliably confirm or refute any effects of using propofol instead of an inhalational agent. In general, reliable conclusions may therefore not be drawn from the four included studies.

Potential biases in the review process

We followed the standard approaches of the Cochrane review process and believe that no specific biases apply to this review other than those already discussed. However, we changed the grading of quality of surgical field from "good, fair, poor" in the protocol to 6-point scale surgical field in the review.

Agreements and disagreements with other studies or reviews

Two systematic reviews were published in 2013 (DeConde 2013; Kelly 2013), however they were not concerned with the effect of the deliberate hypotensive technique.

DeConde 2013 compared total intravenous anaesthesia with inhalation anaesthesia for FESS. They included seven studies, and reported lower blood loss and better surgical field quality during operation, however many of the participants did not receive deliberate hypotensive technique. DeConde et al, reported that evidence to support total intravenous anaesthesia was limited to a handful of inconsistently controlled and reported studies.

Kelly 2013 reviewed the evidence for the effect of total intravenous anaesthesia compared to inhalational anaesthesia on quality of the surgical field during FESS in adults. Kelly et al, included seven studies in their review (Ahn 2008; Ankichetty 2012; Beule 2007; Eberhart 2003; Tirelli 2004; Wormald 2005; Yoo 2010), three of which we included in this current review (Eberhart 2003; Tirelli 2004; Wormald 2005). Kelly et al, reported that they were unable to reach a firm conclusion on the effect of total intravenous anaesthesia on surgical field grading, despite several of the included studies reporting a benefit.

Two published narrative reviews compared surgical field and blood loss during FESS (Amoroch 2010; Baker 2010). Amoroch 2010 compared propofol general anaesthesia and inhalation anaesthesia. They concluded that propofol general anaesthesia improved the surgical field and reduced blood loss over inhalation anaesthesia. Baker 2010 compared propofol general anaesthesia and inhalation anaesthesia and concluded that propofol general anaesthesia improved the surgical field but did not reduce blood loss during FESS.

All four reviews included both normotensive and deliberate hypotensive techniques in their review, and so cannot be directly compared with this review; however, their outcomes did not in general conflict with our findings.

AUTHORS' CONCLUSIONS

Implications for practice

We found insufficient evidence to determine the effects of deliberate hypotension with propofol compared to inhalational agents for FESS surgery. We identified few existing studies, and those we did find were underpowered to show clinically important differences. However, the evidence suggests there may be advantages in both total measured blood loss and the quality of the surgical field with the use of propofol. This review is unlikely to change current practice, and experienced anaesthetists are unlikely to alter their preferred technique on the basis of these findings.

Implications for research

High-quality evidence is required to examine the effect of deliberate hypotension with propofol versus other techniques on surgical field quality, total blood loss, and complications. Larger studies with allocation concealment and blinding are needed to be able to draw any firm conclusions. Standard grading of surgical field quality and a reliability study should be done, and a similar approach taken to compare the total measured blood loss. Comparison studies of propofol with other antihypertensive drugs (vasodilators, beta-adrenergic blockers, calcium channel blockers, dexmedetomidine, magnesium, and opioids) for deliberate hypotension during general anaesthesia are required. The effect of opioids on blood loss during deliberate hypotension should be explored.

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CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Eberhart 2003

Methods	Randomization and treatment allocation method: yes Blinding of outcome assessment: yes Blinding of participants: yes Study period: not stated
Participants	Number: 88 participants (45 participants in propofol group vs 43 in isoflurane group)

Deliberate hypotension with propofol under anaesthesia for functional endoscopic sinus surgery (FESS) (Review)

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Eberhart 2003 (Continued)

Inclusion criteria: ASA grade I-II undergoing endoscopic surgery for chronic sinusitis

Exclusion criteria: not stated

Interventions	<p>Propofol group (propofol and remifentanyl continuous infusion keeping mean arterial pressure between 60 and 70 mm Hg)</p> <p>Isoflurane group (isoflurane and alfentanil keeping mean arterial pressure between 60 and 70 mm Hg)</p>
Outcomes	<p>Blood loss (volume of suctioned blood)</p> <p>Surgical conditions and dryness of the operation site (10-centimetre visual analogue scale and 6-point scale surgical field)</p> <p>Adverse events</p> <p>Operation time</p> <p>Failure deliberate hypotension</p>
Notes	<p>Additional information from Dr LH Eberhart</p> <p>Location: Germany</p> <p>Setting: operating room</p> <p>Source of funding: not stated</p> <p>Conflict of interest: not stated</p>

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit judgement
Allocation concealment (selection bias)	Low risk	Quote: "With the use of sealed envelopes the patients were allocated to one of the following two groups immediately before start of anesthesia"
Blinding (performance bias and detection bias) All outcomes	Low risk	Quote: "Several measures were made to keep the surgeon and the instrumenting nurse blind to the type of anesthesia. Isoflurane vapour and the display of end-tidal isoflurane concentrations on the anesthesia machine were covered. Perfusion syringes containing propofol and remifentanyl were connected to each patient but were also covered"
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing data
Selective reporting (reporting bias)	Low risk	Authors reported all prespecified outcomes

Ragab 2010

Methods	<p>Randomization and treatment allocation method: yes</p> <p>Blinding of outcome assessment: yes</p> <p>Blinding of participants: yes</p>
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Ragab 2010 (Continued)

Study period: not stated

Participants	<p>Number: 70 participants (35 participants in propofol/remifentanyl group vs 35 in isoflurane/fentanyl/esmolol group)</p> <p>Inclusion criteria: children undergoing endoscopic surgery for chronic sinusitis after failed maximal medical therapy after maxillary sinus aspirate or middle meatal culture and adenoidectomy</p> <p>Exclusion criteria: immunodeficiency, ciliary dyskinesia, cystic fibrosis, significant psychological problems, inability to comply with study protocol, systemic diseases affecting the nose, systemic diseases preventing participation in the study, and medical and/or surgical treatments influencing the study</p>
Interventions	<p>Propofol group (propofol and remifentanyl continuous infusion keeping mean arterial pressure 50 mm Hg)</p> <p>Isoflurane group (isoflurane, fentanyl, and esmolol keeping mean arterial pressure 50 mm Hg)</p>
Outcomes	<p>Blood loss (volume of suctioned blood)</p> <p>Surgical conditions and dryness of the operation site (10-centimetre visual analogue scale and 6-point scale surgical field)</p> <p>Operative time</p> <p>Heart rate and blood pressure</p> <p>Adverse events</p>
Notes	<p>Location: Egypt</p> <p>Setting: operating room in general hospital</p> <p>Source of funding: not stated</p> <p>Conflict of interest: no</p>

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "In order to maintain exactly equal treatment numbers in both groups, randomization was done using random blocks"
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding (performance bias and detection bias) All outcomes	Low risk	Quote: "At the time of randomization, neither the patients nor the investigators were aware of the group assignment"
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing data
Selective reporting (reporting bias)	Low risk	Authors reported all prespecified outcomes

Tirelli 2004

Methods	Randomization and treatment allocation method: unclear
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Tirelli 2004 (Continued)

	Blinding of outcome assessment: yes Blinding of participants: yes Study period: not stated
Participants	Number: 64 participants (37 in isoflurane group vs 27 in propofol group) Inclusion criteria: people who were undergoing endoscopic sinus surgery with ASA physical status I-II Exclusion criteria: not stated
Interventions	Propofol group (propofol infusion with remifentanyl) Isoflurane group (isoflurane and fentanyl) All participants were pre-medicated with atropine and midazolam Keep mean arterial pressure between 60 and 70 mm Hg
Outcomes	Surgical field grade Haemodynamic values during operation
Notes	Location: Italy Setting: operating room Source of funding: not stated Conflict of interest: not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit judgement
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding (performance bias and detection bias) All outcomes	Low risk	Quote: "... the surgeon, unaware of the drug used, evaluated the quality of the surgical field"
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing data
Selective reporting (reporting bias)	Low risk	Authors reported all prespecified outcomes

Wormald 2005

Methods	Randomization and treatment allocation method: unclear Blinding of outcome assessment: no Blinding of participants: yes Study period: not stated
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Wormald 2005 *(Continued)*

Participants	<p>Number: 56 participants (28 in sevoflurane group vs 28 in propofol group)</p> <p>Inclusion criteria: people over 18 years of age undergoing endoscopic sinus surgery with ASA physical status I-II</p> <p>Exclusion criteria: people receiving cardiovascular active drug and drug influencing blood coagulation</p>
Interventions	<p>Sevoflurane group (maintained with sevoflurane 0.8% to 1.8% and bolus doses of fentanyl up to 7 mcg/kg)</p> <p>Propofol group (target-controlled infusion 2 to 4 mcg/mL and remifentanyl infusion 0.2 to 0.3 mcg/kg/min)</p> <p>In both groups maintained mean arterial pressure between 55 and 70 mm Hg, pulse rate < 60 beats/min. Metoprolol (0.07 mg/kg) and clonidine (1 to 2 mg/kg) were added to control</p>
Outcomes	<p>Surgical grade (6-point scale surgical field)</p> <p>Surgical operating time</p> <p>Mean arterial pressure, heart rate</p>
Notes	<p>Location: Australia</p> <p>Setting: operating room</p> <p>Source of funding: not stated</p> <p>Conflict of interest: not stated</p>

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "... randomly assigned to each arm using a random number allocation method"
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding (performance bias and detection bias) All outcomes	Low risk	Quote: "Although it was not possible to blind the surgeon to the type of anaesthesia, the surgeon made a conscious effort not to try to ascertain which type of anaesthesia was administered. In most cases the syringe drivers for the propofol infusion were set up and present even when the patient was receiving inhalational anaesthesia"
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing data
Selective reporting (reporting bias)	Low risk	Authors reported all prespecified outcomes

ASA: American Society of Anesthesiologist's physical status classification

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Ahn 2008	Study group and control group did not receive deliberate hypotension
Ankichetty 2012	Study group and control group did not receive deliberate hypotension
Arora 2013	Study group and control group did not receive deliberate hypotension
Beule 2007	Study group and control group did not receive deliberate hypotension
Chaaban 2013	Study group and control group did not receive deliberate hypotension
Gomez-Rivera 2012	Study group and control group did not receive deliberate hypotension
Miłośński 2013	Study group and control group did not receive deliberate hypotension
Pavlin 1999	Study group and control group did not receive deliberate hypotension
Sivaci 2004	Study group and control group did not receive deliberate hypotension
Yoo 2010	Study group and control group did not receive deliberate hypotension

DATA AND ANALYSES

Comparison 1. Propofol versus inhalation anaesthetics

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Quality of surgical field (age group)	4	277	Mean Difference (IV, Random, 95% CI)	-0.64 [-0.91, -0.37]
1.1 Adult	3	207	Mean Difference (IV, Random, 95% CI)	-0.75 [-1.10, -0.40]
1.2 Children	1	70	Mean Difference (IV, Random, 95% CI)	-0.40 [-0.64, -0.16]
2 Operation time (minutes)	3	214	Mean Difference (IV, Fixed, 95% CI)	-4.81 [-11.82, 2.21]
2.1 Adult	2	144	Mean Difference (IV, Fixed, 95% CI)	3.89 [-9.64, 17.42]
2.2 Children	1	70	Mean Difference (IV, Fixed, 95% CI)	-8.0 [-16.20, 0.20]

Analysis 1.1. Comparison 1 Propofol versus inhalation anaesthetics, Outcome 1 Quality of surgical field (age group).

Study or subgroup	Propofol		inhalation anaesthetics		Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)			
1.1.1 Adult							
					-1 -0.5 0 0.5 1		
					Favours propofol		Favours inhalation

Analysis 1.2. Comparison 1 Propofol versus inhalation anaesthetics, Outcome 2 Operation time (minutes).

APPENDICES

Appendix 1. Search strategy for MEDLINE (Ovid SP)

1 exp Propofol/

Deliberate hypotension with propofol under anaesthesia for functional endoscopic sinus surgery (FESS) (Review)

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2 exp Hypotension/
 3 hypoten\$.mp.
 4 exp Anesthesia, General/
 5 Anesthesia-Inhalation/
 6 an?esthesia.mp.
 7 (propofol or diprivan or disoprofol or pofol) .mp.
 8 (1 or 2 or 3 or 4 or 5 or 6 or 7)
 9 exp Paranasal-Sinus-Diseases/
 10 exp Paranasal-Sinuses/
 11 Endoscopy/
 12 (surg\$ adj3 (paranas\$ or endoscop\$ or microscop\$)).mp.
 13 nasal.mp.
 14 (sinus\$ adj3 (maxillary or frontal or ethmoid or sphenoid)) .mp.
 15 exp Ethmoid-Sinus/
 16 exp Frontal-Sinus/
 17 exp Maxillary-Sinus/
 18 exp Sphenoid-Sinus/
 19 Paranasal-Sinus-Neoplasms/ or Sinusitis/
 20 (intranasal or paranasal or endonasal).mp.
 21 Nasal-Cavity/
 22 exp Otorhinolaryngologic-Surgical-Procedures/
 23 (surg\$ adj3 (paranas\$ or endoscop\$ or microscop\$)).mp. and (nasal or endonas\$ or intranas\$ or paranas\$).mp.
 24 (sinus\$ and (maxillary or frontal or ethmoid or sphenoid)).mp.
 25 rhin\$ not rhinoceros
 26 (9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25)
 27 (8 and 26)
 28 (randomized controlled trial.pt. or controlled clinical trial.pt. or randomized.ab. or placebo.ab. or clinical trials as topic.sh. or randomly.ab. or trial.ti.) not (animals not (humans and animals)).sh.
 29 (27 and 28)

Appendix 2. Search strategy for CENTRAL (Cochrane Library)

#1 MeSH descriptor Propofol explode all trees
 #2 MeSH descriptor Hypotension explode all trees
 #3 hypoten* in All Text
 #4 MeSH descriptor Anesthesia, General explode all trees
 #5 MeSH descriptor Anesthesia, Inhalation explode all trees
 #6 an?esthesia in All Text
 #7 (propofol in All Text or diprivan in All Text or disoprofol in All Text or pofol in All Text)
 #8 (#1 or #2 or #3 or #4 or #5 or #6 or #7)
 #9 MeSH descriptor Paranasal Sinus Diseases explode all trees
 #10 MeSH descriptor Paranasal Sinuses explode all trees
 #11 MeSH descriptor Endoscopy explode all trees
 #12 (surg* in All Text near/6 paranas* in All Text)
 #13 (surg* in All Text near/6 endoscop* in All Text)
 #14 (surg* in All Text near/6 microscop* in All Text)
 #15 nasal in All Text
 #16 (sphenoid in All Text and sinus* in All Text)
 #17 (ethmoid in All Text and sinus* in All Text)
 #18 (frontal in All Text and sinus* in All Text)
 #19 MeSH descriptor Ethmoid Sinus explode all trees
 #20 MeSH descriptor Frontal Sinus explode all trees
 #21 MeSH descriptor Maxillary Sinus explode all trees
 #22 MeSH descriptor Sphenoid Sinus explode all trees
 #23 MeSH descriptor Paranasal Sinus Neoplasms explode all trees
 #24 (ntranasal in All Text or paranasal in All Text or endonasal in All Text)
 #25 MeSH descriptor Nasal Cavity explode all trees
 #26 MeSH descriptor Otorhinolaryngologic Surgical Procedures explode all trees
 #27 (sinus* in All Text and (maxillary in All Text or frontal in All Text or ethmoid in All Text or sphenoid in All Text))
 #28 rhin* in All Text
 #29 (#9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28)
 #30 (#8 and #29)

Appendix 3. Search strategy for Embase (Ovid SP)

```

1 exp propofol/
2 exp hypotension/
3 general-anesthesia/
4 inhalation-anesthesia/
5 an?esthesia.mp.
6 hypoten$.mp.
7 (propofol or diprivan or disoprofol or pofol).mp.
8 (1 or 2 or 3 or 4 or 5 or 6 or 7)
9 paranasal-sinus-disease/
10 exp paranasal-sinus/
11 endoscopy/
12 exp ethmoid-sinus/
13 exp frontal-sinus/
14 exp maxillary-sinus/
15 exp sphenoid-sinus/
16 paranasal-sinus-tumor/
17 paranasal-sinusitis/
18 exp nose-cavity/
19 ear-nose-throat-surgery/
20 (surg$ adj3 (paranas$ or endoscop$ or microscop$)).mp.
21 nasal.mp.
22 (sinus$ adj3 (maxillary or frontal or ethmoid or sphenoid)).mp.
23 (intranasal or paranasal or endonasal).mp.
24 (surg$ (paranas$ or endoscop$ or microscop$)).mp. and (nasal or endonas$ or intranas$ or paranas$).mp.
25 (sinus$ and (maxillary or frontal or ethmoid or sphenoid)).mp.
26 (rhin$ not rhinoceros).mp.
27 (9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26)
28 (8 and 27)
29 ((RANDOMIZED-CONTROLLED-TRIAL/ or RANDOMIZATION/ or CONTROLLED-STUDY/ or MULTICENTER-STUDY/ or PHASE-3-CLINICAL-TRIAL/ or PHASE-4-CLINICAL-TRIAL/ or DOUBLE-BLIND-PROCEDURE/ or SINGLE-BLIND-PROCEDURE/) or ((RANDOM* or CROSS?OVER* or FACTORIAL* or PLACEBO* or VOLUNTEER*) or ((SINGL* or DOUBL* or TREBL* or TRIPL*) adj3 (BLIND* or MASK*))).ti,ab not (animals not (humans and animals)).sh.
30 (28 and 29)

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Appendix 4. Search strategy for LILACS (via BIREME interface)

("PROPOFOL" or "PROPOFOL/" or "HYPOTENSION" or "HYPOTENSION, CONTROLLED/" or "ANAESTHESIA" or "ANAESTHESIC" or "ANAETHESIA" or "ANAETHESIC" or "ANESTHESIA" or "ANESTHESIA AND ANALGESIA" or "ANESTHESIA, CLOSED-CIRCUIT/") and (rhinosinusal or paranasal or nasal or intranasal or endonasal or "NASAL CAVITY/" or "PARANASALE" or "PARANASALES" or "PARANASALS" or "ETHMOID SINUS" or "ETHMOID SINUS/" or "SPHENOID SINUS" or "SPHENOID SINUS/" or "SPHENOID SINUSITIS/" or "FRONTAL SINUS" or "FRONTAL SINUS/" or "FRONTAL SINUSITIS/" or "nasal" or "Endoscopy" or "sinus")

Appendix 5. Search strategy for ISI Web of Science

```

#1 TS=(propofol or diprivan or disoprofol or pofol)
#2 TS=hypoten*
#3 TS=an$esthesia
#4 #1 or #2 or #3
#5 TS=(paranasal or nasal or intranasal or endonasal)
#6 TS=(surg* SAME (paranas* or endoscop* or microscop*))
#7 TS=(sinus* SAME (maxillary or frontal or ethmoid or sphenoid))
#8 TS=Paranasal SAME TS=Sinus*
#9 TS=Nasal Cavity
#10 TS=rhin*
#11 #5 or #6 or #7 or #8 or #9 or #10
#12 TS=(random* or clinical or control*) SAME TS=trial*
#13 TS=(random* or clinical or control*) and TS=trial*
#14 TS=(random SAME allocat*)
#15 TS=random*
#16 TS=(singl* or doubl* or trebl* or tripl*) SAME
TS=(blind* or mask* or method*)

```

#17 TS=placebo*
#18 #17 OR #16 OR #15 OR #14 OR #13 OR #12
#19 #18 AND #11 AND #4

Appendix 6. Data extraction form

Data extraction form		Review
Study ID:	MEDLINE Journal ID:	Language:
Authors:		
Year of publication:	Country:	Type of study
Comment on study design		
Randomizations and allocation concealment	Adequate: e.g. numbered, sealed, opaque envelopes	
	Unclear	
	Inadequate	
	Not used	
Blinding of treatment	Adequate (patient, physician, assessor)	
	Unclear	
	Inadequate (patient, physician, assessor)	
Blinded outcome assessment	Adequate	
	Unclear	
	Inadequate	
Use of intention-to-treat analysis	Yes	
	No	
	No information	
PARTICIPANTS:		
Number of eligible participants		Number of males

(Continued)

Number enrolled in study		Number of females	
Age	< 15	15 to 65	> 65
Intervention:			
Propofol			
Other drug			
COMMENT ON TREATMENT:			
Withdrawals	Yes	No	Unclear
Outcome	Propofol		Other drug
Blood loss			
Visibility of operative field			
Operation time			
Failed deliberate hypotension			
Need for reoperation			
Need for admission ICU			
Others complication			
Changes in protocol:			
Contact with authors:			
Comment on this study:			

WHAT'S NEW

Date	Event	Description
10 February 2016	New search has been performed	We reran the search in February 2016. We included no new studies. We excluded five new studies. We updated the methods section to fully incorporate GRADE. We updated the plain language summary section to conform to the Plain Language Expectations for Authors of Cochrane Summaries
10 February 2016	New citation required but conclusions have not changed	The conclusion are unchanged

HISTORY

Protocol first published: Issue 3, 2007

Review first published: Issue 6, 2013

Date	Event	Description
7 April 2009	Amended	Converted to new review format.

CONTRIBUTIONS OF AUTHORS

Polpun Boonmak (PB), Suhattaya Boonmak (SB), Malinee Laopaiboon (ML)

Conceiving the review: PB, SB

Co-ordinating the review: PB, BS, ML

Undertaking manual searches: PB, SB

Screening search results: PB, SB

Organizing retrieval of papers: PB, SB

Screening retrieved papers against inclusion criteria: PB, SB

Appraising quality of papers: PB, SB

Abstracting data from papers: PB, SB

Writing to authors of papers for additional information: PB, SB

Providing additional data about papers: PB, SB

Obtaining and screening data on unpublished studies: PB, SB

Providing data management for the review: PB, SB, ML

Entering data into Review Manager ([RevMan 5.3](#)): PB, SB

Obtaining RevMan statistical data: PB, SB, ML

Performing other statistical analysis while not using RevMan: ML

Performing double entry of data: (data entered by person one: PB; data entered by person two: SB)

Interpreting data: ML

Making statistical inferences: ML

Writing the review: PB, SB, ML

Securing funding for the review: PB

Performing previous work that served as the foundation of the present study: PB, SB

Serving as guarantor for the review (one author): PB

Taking responsibility for reading and checking review before submission: PB, SB

DECLARATIONS OF INTEREST

Polpun Boonmak: none known.

Suhattaya Boonmak: none known.

Malinee Laopaiboon: received an honorarium from Thailand Research Fund, a nonprofit organization, in 2014.

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- Thai Cochrane Network, Thailand.

External sources

- The Thailand Research Fund, Thailand.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We made the following changes to the protocol ([Boonmak 2007](#)).

1. The quality of surgical field grading was changed from "good, fair, poor" to 6-point scale surgical field.
2. Principal author in this update (2016) is Polpun Boonmak.

INDEX TERMS

Medical Subject Headings (MeSH)

*Anesthetics, Intravenous; *Propofol; Blood Loss, Surgical [*prevention & control]; Endoscopy [*adverse effects] [methods]; Hypotension, Controlled [*methods]; Operative Time; Paranasal Sinuses [*surgery]; Randomized Controlled Trials as Topic

MeSH check words

Adult; Child; Humans