Comparison of Recovery Profile After Ambulatory Anesthesia with Propofol, Isoflurane, Sevoflurane and Desflurane: A Systematic Review

Anil Gupta, MD, FRCA, PhD*†, Tracey Stierer, MD*, Rhonda Zuckerman, MD*, Neal Sakima, MD*, Stephen D. Parker, MD*, and Lee A. Fleisher, MD*

From the *Department of Anesthesiology and Critical Care, and the Division of Ambulatory Surgery, Johns Hopkins Medical Institutions, Baltimore, Maryland and the †Division for Ambulatory Surgery, Department of Anesthesiology, University Hospital, Örebro, Sweden

In this systematic review we focused on postoperative recovery and complications using four different anesthetic techniques. The database MEDLINE was searched via PubMed (1966 to June 2002) using the search words "anesthesia" and with ambulatory surgical procedures limited to randomized controlled trials in adults (>19 yr), in the English language, and in humans. A second search strategy was used combining two of the words "propofol," "isoflurane," "sevoflurane," or "desflurane". Screening and data extraction produced 58 articles that were included in the final meta-analysis. No differences were found between propofol and isoflurane in early recovery. However, early recovery was faster with desflurane compared with propofol and isoflurane and with sevoflurane compared with isoflurane. A minor difference was found in home readiness between sevoflurane and isoflurane (5 min) but not among the other anesthetics. Nausea, vomiting, headache, and postdischarge nausea and vomiting incidence were in favor of propofol compared with isoflurane ($P < 0.05$). A larger number of patients in the inhaled anesthesia groups required antiemetics compared with the propofol group. We conclude that the differences in early recovery times among the different anesthetics were small and in favor of the inhaled anesthetics. The incidence of side effects, specifically postoperative nausea and vomiting, was less frequent with propofol.

(Anesth Analg 2004;98:632–41)

Ambulatory surgery has increased rapidly in the last 10 yr, and the availability of new minimally invasive surgical techniques has resulted in an increased emphasis on the expansion of day surgery. This has also been made possible by the safety of ambulatory surgery in sick patients and in those undergoing major surgery.

Together with the advancement in surgical techniques has been the availability of newer and better drugs with short onset and duration of effect, resulting in quick recovery and the possibility of earlier discharge from the day surgical unit. Specifically, the advantages of IV anesthesia using propofol over inhaled anesthesia have been intensively discussed as the subject of numerous studies with opposing results. The introduction of less-soluble inhaled anesthetics, desflurane and sevoflurane, has added a new dimension to recovery and fast-tracking (1–3) by allowing more rapid recovery and earlier discharge home. However, these anesthetics are associated with increased cost compared with older inhaled anesthetics and may be associated with an increased incidence of side effects and complications (4,5). Additionally, Dexter and Tinker (6) concluded that the theoretical advantages of one of these anesthetics, desflurane, did not translate into rapid recovery from anesthesia partly because patients received other drugs that may have tended to equalize differences between these anesthetics. The manner in which the anesthetic drugs are delivered, including the use of concomitant medications, may therefore influence the optimal choice of anesthetic used to achieve early discharge, and an understanding of the risks and benefits of the anesthetics could assist the practitioner to determine which anesthetic to use in clinical practice.

Supported, in part, by grants from the Olof Norlander Memorial Fund, Karolinska Hospital, Stockholm, Sweden.
Accepted for publication October 8, 2003.
Address correspondence and reprint requests to Anil Gupta, Department of Anesthesiology and Intensive Care, University Hospital, SE 701 85 Örebro, Sweden. Address email to anil_guptarca@hotmail.com.
DOI: 10.1213/01.ANE.0000103187.70627.57

0003-2999/04

Table 1. Characteristics of Studies Comparing Propofol and Isoflurane

Study	Type of surgery	Total number of patients	Induction anesthetic	Was N_2O used?	Early recovery	Intermediate recovery	Authors conclusion
Wilhelm (7)	Mixed	249	Propofol	No	No differences	NR	No differences
Ashworth (8)*	Mixed	60	Propofol	Yes	No differences	No differences	No advantage of propofol
Gupta (9)	Arthroscopy	50	Propofol	Yes	No differences	No differences	Psychomotor recovery earlier in isoflurane
Valanne (10)	Oro-dental surgery	50	Propofol	Yes	Propofol better	Propofol better	Propofol better
Nightingale (11)	Gynecological	50	Propofol	Yes/No	NR	NR	Psychomotor recovery earlier in propofol
Sung (12)	Breast	99	Propofol or thiopentone	Yes	NR	NR	Propofol better
Werner (13)	Dental	50	Propofol or methohexital	Yes	No difference	Psychomotor recovery earlier in isoflurane	Propofol better (less nausea/vomiting)
Korttila (14)	Gynecological	41	Propofol or thiopentone	Yes	Propofol better	Propofol better	Propofol better
Pollard (15)*	Oral	49	Propofol	Yes/No	NR	No differences	Both techniques suitable
Moffat (16)	Eye	40	Propofol or etomidate	Yes	Isoflurane better	NR	Isoflurane better
Larsen (17)	Arthroscopy	30	Propofol	No	NR	NR	Isoflurane better
Marshall (18)*	Dental and Gynecological	114	Propofol	Yes	No difference	NR	No difference between the agents
Visser (19)	Mixed	554	Propofol	Yes/No	NR	NR	Propofol better in many respects but expensive
Milligan (20)	Gynecological	60	Propofol	Yes	More rapid in propofol group	NR	Initial recovery quicker in propofol group
Collins (21)	Gynecological	30	Propofol	Yes/No	No difference	NR	Propofol has advantages
Lim (22)	Dental surgery	50	Propofol or thiopentone	Yes/No	NR	NR	Propofol better
Alhashemi (23)*	Knee surgery	62	Thiopentone or propofol	Yes/No	No difference	No difference	Isoflurane better and less expensive
Zuurmond (24)	Knee arthroscopy	40	Propofol	Yes	No difference	No difference	Propofol comparable to isoflurane

NR = not reported.
* Studies with more than two arms.

Meta-analysis has increasingly been used over the last 10 yr as one of several ways to assess the efficacy of newer drugs. The aim of this systematic review was to assess whether maintenance of anesthesia using propofol infusion, isoflurane, sevoflurane, or desflurane is associated with faster recovery and fewer side effects during ambulatory surgery in adults.

Methods

We searched MEDLINE (from 1966 to June 2002) via PubMed using the MeSH terms "ambulatory surgical procedure" or "outpatients." This was combined with the MeSH term "anesthesia" using the AND function. The results were limited to randomized controlled trials in humans, in the English language, and in the adult (>19 yr of age) patient population. We soon realized that we had missed a number of articles. Therefore, we did another search using the words "propofol," "sevoflurane," "desflurane," and "isoflurane" as text words, which produced more results. Finally, we searched the reference lists of the already published systematic reviews for any missing articles. A hand search was also done through the reference lists of included studies to further identify any articles that had been missed using earlier strategies.

The following criteria were used in identifying appropriate studies that could be included in the analysis. The studies had to be randomized with the specific primary end-point of assessment of "early" recovery, "intermediate" recovery, and side effects or complications. The results had to be presented as means (and a measure of variance but not range) or numbers (yes or no) for the study to be acceptable for meta-analysis.

Studies where the authors had compared inhaled anesthetics during "monitored anesthesia care" were excluded, as were studies in which halothane or enflurane was used for maintenance of anesthesia. Whenever an inhaled anesthetic was used for induction of anesthesia, the study (or the group that was induced by an inhaled anesthetic) was excluded. Finally, studies where the results were presented as graphs or histograms without digital data were also excluded. Because of the vast number of tests used for the assessment of psychomotor recovery in different studies, as well as their limited clinical significance, these tests were not included in our systematic review.

Table 2. Characteristics of Studies Comparing Propofol and Desflurane

Study	Type of surgery	Total number of patients	Induction anesthetic	Was N_2O used?	Early recovery	Intermediate recovery	Authors conclusion
Song (2)*	Gynecological	80	Propofol	Yes	Desflurane better	No difference	Desflurane better for fast-tracking
Tang (25)	Mixed	75	Propofol	Yes	Desflurane better	No difference	Faster recovery following desflurane
Ashworth (8)*	Mixed	60	Propofol	Yes	No difference	No difference	No clinical advantage of either
Hemelrijck (4)*	Laparoscopic	46†	Propofol	Yes/No	Desflurane better	No difference	Lower incidence of nausea after propofol
Rapp (26)*	Orthopedic	45†	Propofol	Yes/No	No difference	No difference	Desflurane comparable to propofol
Lebenbon-Mansour (27)*	Orthopedic	30†	Propofol	Yes/No	Desflurane better	No difference	Desflurane suitable for maintenance
Eriksson (28)*	Gynecological	59	Propofol	Yes	No difference	Favours propofol	Propofol better than desflurane alone
Raeder (29)	Laparoscopic	60	Propofol	No	Desflurane better	No difference	Advantages and disadvantages of both
Wrigley (30)*	Orthopedic	30†	Propofol	Yes/No	No difference	Psychomotor recovery better in desflurane	Desflurane suitable
Song (31)	Gynecological	104	Propofol	Yes	Propofol better	No difference	Desflurane associated with better postural control
Graham (32)*	Gynecological	28†	Propofol	Yes/No	Desflurane better	No difference	Desflurane provides rapid recovery
Larsen (33)*	Mixed	40	Propofol	Yes/No	Propofol better	Propofol better (cognitive functions)	Propofol better
Coloma (34)*	Gynecological	34	Propofol	Yes	Desflurane better	No difference	No difference in number of patients fast-tracked

* Studies with more than two arms; † groups with inhalation induction excluded.

Data extraction was done by two independent (primary) reviewers who were unaware of each other's results (AG and TS or NS and RZ). Data included aspects of patient characteristics, anesthesia, type of surgery, "early" recovery ("time to open eyes," "time to obey commands"), "intermediate" recovery ("time to transfer from Phase 1 to Phase II," "home readiness," and "home discharge"), minor complications in the PACU or within 24 h including "pain," "nausea or vomiting," "antiemetics" used, "dizziness/giddiness," "drowsiness/somnolence," "headache," "shivering," or "coughing". Because authors had used different terminology for recovery indices, we came to an agreement that the following terms would be treated as measuring the same end-point: time to open eyes and time to awakening; time to obey commands and time to orientation or squeezing fingers. Time to "emergence" was considered too abstract to be included, and this variable was therefore excluded from the analysis. A differentiation was made between "home readiness" (when the patient was ready to be sent home) and "home discharge" (when the patient was actually sent home). Data on post-discharge nausea and vomiting (PDNV) were excluded when authors did not differentiate between nausea and vomiting. Extracted data were compared for agreement between the primary reviewers by a secondary reviewer (SP). Any discrepancies were noted and discussed further to come to a consensus among all authors.

Data extracted from the relevant studies were entered into the program RevMan 4.1 (Review Manager, Cochrane Collaboration, UK) and analyzed. For dichotomous data, the relative risk (RR) with the corresponding 95% confidence intervals (CI) were calculated for each study, and the results were pooled together using the Mantel-Haenszel Method for combining trials. For continuous data, the weighted mean difference (WMD) and its corresponding standard error (SE) were calculated. The individual effect sizes were weighted according to the reciprocal of their variance. Subsequently, the inverse variance method was used to pool the WMD. The overall estimate of pooled effect was calculated. Heterogeneity was determined under the assumption (null hypothesis) that there are no differences in treatment effect between trials. For combined dichotomous data, a fixed effect model was used when there was no significant heterogeneity ($P > 0.05$), otherwise a random effect model was used. For continuous data, the weighted means

Table 3. Characteristics of Studies Comparing Propofol and Sevoflurane

Study	Type of surgery	Total number of patients	Induction anesthetic	Was N_2O used?	Early recovery	Intermediate recovery	Authors conclusion
Song (2)*	Gynecological	80	Propofol	Yes	Sevoflurane better	No difference	Sevoflurane better for fast-tracking
Tang (35)*	Mixed	69†	Propofol	Yes	No difference	Propofol better	Propofol better in most respects
Smith (36)*	Mixed	61†	Propofol	Yes	Sevoflurane better	Propofol better	Both drugs have advantages and disadvantages
Coloma (34)*	Gynecological	34	Propofol	Yes	Sevoflurane better	No difference	No difference in number of patients fast-tracked
Fredman (37)*	Mixed	98†	Propofol	Yes	No differences	No differences	Sevoflurane an acceptable alternative
Peduto (38)	General/ENT	60	Propofol	Yes	Sevoflurane better	Sevoflurane better	Faster emergence and recovery after propofol
Raeder (39)	Arthroscopy	169	Propofol	Yes	Sevoflurane better	No differences	More rapid recovery but higher PONV after sevoflurane
Smith (40)*	Mixed	142†	Propofol	Yes	No differences	No differences	Propofol better, but at a higher cost
Jellish (41)	Mixed	186	Propofol	Yes	Sevoflurane better	No differences	Sevoflurane compared favourably with propofol
Wandel (42)	Mixed	50	Propofol	Yes	Sevoflurane better	Sevoflurane better	Sevoflurane is a useful alternative to propofol
Larsen (33)*	Mixed	40	Propofol	Yes/No	Propofol better	Cognitive function better in propofol group	Propofol better (emergence and cognitive functions)

NR = not reported.
* Studies with more than two arms; † groups with inhalation induction excluded.

and their corresponding 95% CI were used. Results are presented as WMD and 95% CI for continuous data, and RR and 95% CI for dichotomous data. Whenever data were presented as mean and SE of mean, the latter was converted to standard deviation (SD) using the formula: $SD = \sqrt{N} \times SE$. The numbers-needed-to-harm (NNH) were calculated for those variables where a significant overall effect was seen ($P < 0.05$) by the reciprocal of the control event rate (CER) minus the experimental event rate (EER), mathematically: $1/(CER - EER)$. The NNH for each variable was the NNH when one anesthetic technique was compared with another. In case of antiemetics given, the NNH was calculated on the basis of the number of patients who received antiemetics in each group, when comparing two anesthetics.

Results

Literature Review

The MeSH term "anesthesia" revealed 127,165 articles, and "ambulatory surgical procedure" revealed 6017 articles. Combining these two terms and limiting the results to adults (>19 yr), in humans, and in English revealed 932 articles. The second search strategy using the text word "propofol" and combining it with "isoflurane" revealed 449 articles, with "sevoflurane" revealed 170 articles and with "desflurane" revealed 107 articles when limited to adults (>19 yr), in humans, and in English. Hand searching all these articles, and reviewing reference lists from previous publications including previously published systematic reviews revealed 42 articles that had extractable data. In a final search strategy, combining the MeSH terms "ambulatory surgical procedures" or "outpatient procedures" revealed 13,104 articles. The MeSH term "anesthetics, inhalation" revealed 30,538 articles. Combining these strategies using the AND function revealed 302 articles. Limiting these to adults (>19 yr), humans, and the English language revealed 180 articles. A hand search of these revealed 16 articles that could be finally included in the meta-analysis.

Propofol Versus Isoflurane

We found 18 studies (7–24) with data that could be extracted in the postoperative period (Table 1). No differences were found between propofol and isoflurane in early recovery or transfer from Phase I to Phase II, but there was significant heterogeneity between groups in all these variables (Table 5). However, home discharge was significantly earlier with propofol (15 min). There was a greater RR for postoperative complications including nausea (number needed to treat [NNT], 8), vomiting (NNT, 10), and headache (NNT, 22) in the isoflurane group (Table 5). The use of antiemetics (RR, 2.7) was also more common in the isoflurane group. The RR for postoperative

Table 4. Characteristics and Conclusions of Studies Included in the Meta-Analysis

Study	Comparison between	Number of patients	Type of surgery	Was N_2O used?	Early recovery	Intermediate recovery	Authors conclusions
Song (2)*	Sevoflurane vs Desflurane	80	Gynecological Laparoscopy	Yes	No differences	No differences	Similar
Coloma (34)*	Sevoflurane vs Desflurane	34	Gynecological Laparoscopy	Yes	No differences	No differences	Desflurane better
Larsen (33)*	Sevoflurane vs Desflurane	40	Elective surgery	Yes	No differences	NR	Cognitive function better in Desflurane
Nathanson (53)	Sevoflurane vs Desflurane	42	Gynecological Laparoscopy	Yes	Favours desflurane	No differences	Sevoflurane good alternative
Naidu-Sjösvärd (54)	Sevoflurane vs Desflurane	50	Arthroscopy	No	Favours desflurane	No differences	Sevoflurane acceptable alternative
Tarazi (55)	Sevoflurane vs Desflurane	60	Gynecological Laparoscopy	Yes	No differences	No differences	No significant differences
Ghouri (45)	Isoflurane vs Desflurane	38	Mixed	Yes	Favours desflurane	No differences	Desflurane better
Gupta (44)	Isoflurane vs Desflurane	50	Arthroscopy	Yes	NR	No differences	No difference
Rieker (46)	Isoflurane vs Desflurane	33	Elective surgery	Yes	No differences‡	No differences	Similar
Smith (47)	Isoflurane vs Sevoflurane	62	Elective surgery	Yes	NR	No differences	No differences
Sloan (48)	Isoflurane vs Sevoflurane	50	Amb Surg procedures	Yes	No differences	No differences	Sevoflurane better recovery profile
O'Hara (49)	Isoflurane vs Sevoflurane	47	Gynecological surgery	Yes	Favours sevoflurane	No differences	Sevoflurane better
Eriksson (50)	Isoflurane vs Sevoflurane	49	Gynecological Laparoscopy	Yes	No differences†	No differences†	Early recovery better in sevoflurane
Philip (51)	Isoflurane vs Sevoflurane	246	Amb Surg procedures	Yes	Favours sevoflurane	No differences	Sevoflurane better
Elcock (52)	Isoflurane vs Sevoflurane	180	Arthroscopy	Yes	NR	NR	No differences
Ashworth (8)*	Desflurane vs isoflurane	90	Ambulatory Surgery	Yes	No difference	No difference	No difference

NR = Not reported.
* Studies with more than two arms; † data reported as median (range) or ‡ mean.

nausea (PON) and postoperative vomiting (POV) after 24 h was significantly higher with isoflurane compared with propofol.

Propofol Versus Desflurane

There were 13 studies (2,5,8,25–34) with extractable data that were included in the meta-analysis (Table 2). Time to eye opening was significantly quicker with desflurane compared with propofol (1.3 min), as was the time to obey commands (1.3 min), with significant heterogeneity between the anesthetics (Table 5). No differences were found in home readiness or discharge between the anesthetics. The RR for postoperative complications including PON (NNT, 7) and POV (NNT, 10) was significantly greater with desflurane compared with propofol and the need for antiemetics was also increased with desflurane (RR, 3.9) (Table 5). No other differences were seen between the anesthetics.

Propofol Versus Sevoflurane

There were 11 studies including 821 patients with extractable data (2,33,35–43) (Table 3). No difference was found in the time to eye opening between sevoflurane and propofol, but time to obeying commands was quicker in the sevoflurane group (1.6 min), with significant heterogeneity between anesthetics (Table 5). No significant difference was found in the time to home-readiness between the anesthetics, but with significant heterogeneity. The time to home discharge was earlier with propofol compared with sevoflurane (10.3 min). The RR for postoperative complications including PON (NNT, 11) and POV (NNT, 16) was significantly greater with sevoflurane compared with propofol but with significant heterogeneity (Table 5). The need for antiemetics in the postoperative period was significantly increased with sevoflurane (RR, 4.9). There were no other significant differences between the anesthetics.

Isoflurane Versus Desflurane

Four studies compared isoflurane and desflurane in the ambulatory setting (8,44–46) and included 277 patients (Table 4). A statistically significant difference was found in "time to eye opening" ($P < 0.004$) and "time to obey commands" ($P < 0.01$) but in no other variable of recovery (Table 6). The WMD in early recovery between desflurane and isoflurane were modest (4–5 min) and in favor of desflurane. Sore throat was reported in only one study, and the incidence was more frequent in the desflurane compared with the isoflurane group ($P < 0.05$). No other differences were found between the anesthetics.

Table 5. Postoperative Recovery Profiles and Minor Complications Associated with Propofol Compared to the Inhaled Anesthetics

End-point	Propofol vs Isoflurane	Propofol vs Desflurane	Propofol vs Sevoflurane
Time to open eyes (min)	0.2 (−1.6 to 1.3)§	1.3 (0.4 to 2.2)§† (D)	0.9 (−2.2 to 0.5)§
Time to obey commands (min)	0.5 (−1.0 to 1.9)§	1.3 (0.4 to 2.3)§† (D)	1.6 (0.3 to 3.0)§* (S)
Time to Transfer from Phase 1 to Phase 2 (min)	4.3 (−5.4 to 14.1)§	NR	3.6 (−13.5 to 6.4)§
Time to home ready (min)	9.3 (−17 to 36)§	3.1 (−7.7 to 1.5)	5.6 (−3.4 to 14.5)§
Time to home discharge (min)	15 (8 to 23)† (P)	3.9 (−9.3 to 1.5)	10.3 (3.9 to 16.6)† (P)
Postoperative nausea (PON)	2.0 (1.6–2.5)† (P), NNH = 8	2.0 (1.4 to 2.8)† (P), NNH = 7	1.6 (1.2–2.0)† (P), NNH = 11
Postoperative vomiting (POV)	3.2 (1.3–7.5)† (P), NNH = 10	2.6 (1.4 to 4.8)† (P), NNH = 10	2.0 (1.3–3.0)† (P), NNH = 15
Postoperative drowsiness	NR	NR	0.9 (0.1–5.9)§
Postoperative dizziness	NR	NR	1.4 (0.8–2.3)
Postoperative shivering	0.8 (0.6–1.3)	1.5 (0.4–5.4)§	0.8 (0.5–1.3)
Postoperative headache	3.3 (1.1–9.6)* (P), NNH = 22	3.5 (0.6–19.8)	1.0 (0.2–7.1)
Antiemetics given	2.7 (1.7–4.2)† (P), NNH = 8.5	3.3 (1.8–6.0)† (P), NNH = 8	4.5 (1.5–14.0)† (P), NNH = 11
Post-discharge nausea (PDN)	1.8 (1.3–2.5)† (P), NNH = 8	1.2 (0.7–2.1)	1.3 (0.7–2.3)
Post-discharge vomiting (PDV)	2.5‡ (1.6–4.1) (P), NNH = 9	2.6 (0.1–62.7)	NR

All results are shown as weighted mean difference (WMD) or relative risk (mean and 95% confidence intervals).
* $P < 0.05$, † $P < 0.01$, ‡ $P < 0.001$.
Significant results are shown in favor of: S = sevoflurane, I = isoflurane, D = desflurane and P = propofol when significant.
§ Significant heterogeneity; NR = not reported (or reported in only one study); NNH = Numbers needed to harm for significant differences.

Isoflurane Versus Sevoflurane

Six studies could be included with relevant data examining a total of 634 patients undergoing a variety of ambulatory surgical procedures (47–52) (Table 4). Statistically significant differences were found in the "time to opening eyes," "time to obeying commands," "time to transfer from Phase 1 to Phase II recovery," "home readiness" ($P < 0.00001$), and "home discharge" ($P = 0.05$). The results of the latter are, however, based on only two studies. The WMD in all the recovery indices (early and intermediate recovery) between sevoflurane and isoflurane were small and in favor of sevoflurane (Table 6). Drowsiness was significantly more frequent with isoflurane compared with sevoflurane in the postoperative period ($P = 0.03$) but no other significant differences were found in the incidence of postoperative complications.

Sevoflurane Versus Desflurane

Six studies compared sevoflurane with desflurane with a total of 246 patients (2,33,34,53–55) (Table 4). The recovery variables "time to open eyes" ($P < 0.005$) and "time to obey commands" ($P < 0.00001$) were statistically significant, both in favor of desflurane. The WMD in early recovery between anesthetics were small (<1 min) and in favor of desflurane. The "time to transfer from Phase 1 to Phase II," however, was earlier with sevoflurane compared with desflurane ($P < 0.00001$) (WMD, 6 min) (Table 6). No other significant differences were found between the two anesthetic anesthetics in recovery indices.

IV Versus Inhaled Anesthetics

When data were combined into an inhaled group (isoflurane, desflurane, and sevoflurane) and compared with an IV group (propofol), the incidence of PON was 25.8% and 14.1% respectively (NNT, 8.6), POV was 14.1% and 5.2% respectively (NNT, 11.2), and the need for antiemetics was 16.6% and 5.1% respectively (NNT, 8.7). Similarly, the incidence of postdischarge nausea in the inhaled versus IV groups was 21.5% versus 13.5% (NNT, 12.5), and the incidence of postdischarge vomiting was 15.6% versus 5.9% (NNT, 10.3) respectively.

Discussion

In this systematic analysis of the literature, we found that early recovery, characterized by opening eyes and obeying commands, was statistically significantly different, but only marginally quicker, in desflurane and sevoflurane compared with isoflurane or propofol groups. Intermediate recovery characterized by home readiness was slightly earlier in the sevoflurane group compared with isoflurane group alone. Postoperative complications, specifically PON and POV, were significantly less frequent in the propofol group compared with isoflurane, sevoflurane, and desflurane groups.

No significant difference in early recovery was found when isoflurane or propofol was used for the maintenance of anesthesia. Although we found significant differences in early recovery between sevoflurane/desflurane compared with propofol/isoflurane in favor of the former, the magnitude of these differences was small (<5 min) and therefore of doubtful clinical relevance even in a busy ambulatory unit. The small differences between these anesthetics were seen following strict protocols and not allowing stepwise reduction in anesthetic concentration towards the end of surgery, which is normal clinical practice. Despite the low blood: gas partition coefficient of desflurane and sevoflurane with the theoretical advantage of rapid recovery from anesthesia, these anesthetics have provided only marginally better early recovery characteristics compared with propofol or isoflurane. One explanation for this could be that in most studies a combination of drugs is used. Therefore, residual effects of drugs used for premedication, opiates, and muscle relaxants may interact with the anesthetics to delay the onset of early recovery. Another reason for these minor differences could be that the depth of anesthesia at the end of the operation was unknown. Most studies have used clinical assessment of anesthetic depth based on hemodynamic responses to pain during anesthesia and therefore it is easy to err on maintaining patients deeply anesthetized, which in turn affects recovery. Indeed, recent studies using bispectral index (BIS) as a guide to anesthetic depth have shown that a large number of patients can be "fast-tracked" when anesthetic depth is monitored (4). Consequently, appropriate depth of anesthesia is an important factor in quick recovery after ambulatory surgery, a factor that has not been used to advantage in most published studies.

Our analysis demonstrated that sevoflurane was associated with an earlier home readiness (5 min) compared with isoflurane, with no differences among the other comparison of inhaled anesthetics or against propofol. However, propofol was associated with earlier (10–15 min) home discharge compared with sevoflurane/isoflurane. Similarly, sevoflurane was associated with a difference of 25 min in home discharge when compared with isoflurane. However, the latter findings were based on two studies with wide CI, and borderline statistical significance.

In interpreting differences in home readiness and discharge, it is critical to understand the factors influencing the interpretation of each outcome. "Home readiness" is the time when patients are ready to be discharged home as assessed by standardized methods such as the modified postanesthesia discharge scoring system, whereas "home discharge" is the actual time when the patient could leave the hospital. The latter is affected by many non-medical factors such as absence of an adult to accompany the patient home or waiting to meet the doctor before going home. Unfortunately, many authors have not made a distinction between these variables and it sometimes remains unclear which variable is actually being measured. Other factors such as duration and type of surgery and local hospital practices and routines may affect home discharge and may sometimes be more important than the choice of the anesthetic used. For instance, some hospitals use local anesthetics routinely into surgical wounds, which may reduce postoperative narcotic requirements, which in turn may affect discharge. Other hospitals require patients to empty their bladders before being considered home ready, which may also affect discharge times. Rapid early recovery may also be associated with a greater appreciation of pain in the early postoperative period, which increases postoperative analgesic requirement and thus delays recovery, a finding seen by Robinson et al. (56) in their meta-analysis of sevoflurane versus propofol. Recovery profiles can also be influenced by concomitant analgesics used preoperatively and the depth of anesthesia attained towards the end of the operation. For example, differences in recovery and home discharge have been found when using alfentanil or fentanyl as analgesics (57). Some authors have suggested that using BIS for depth of anesthesia monitoring may enhance recovery (4). However, using a standardized anesthetic regimen and strict discharge criteria, Ahmad et al. (58) showed that BIS monitoring does not have a significant effect on the ability to fast track outpatients. In addition, although more patients may be fast track eligible using desflurane or sevoflurane compared with propofol for maintenance of anesthesia (2), the number of patients who actually bypass the PACU is much smaller because of anesthetic-related factors such as residual sedation (34). All these confounding factors need to be considered when making a case for the use of a specific anesthetic for the maintenance of anesthesia in ambulatory surgical patients.

Postoperative nausea and vomiting (PONV) were significantly more common with inhaled anesthetics compared with propofol, and the use of antiemetics was also more common with inhaled anesthetics. The incidence of PDNV was also less frequent with propofol compared with isoflurane but not desflurane or sevoflurane. Tramer et al. (59) in a meta-analysis found that maintenance of anesthesia with propofol is an advantage compared with other anesthetics when the incidence of complications is in the range of 20%–60%, with NNT of <5. The incidence of PON was 25%–38% in our present analysis, which would support the use of propofol infusion. However, the efficacy of propofol for reducing PONV was small compared with the inhaled anesthetics, which may question the use of propofol alone without antiemetic prophylaxis in patients at risk. Other than headache, which occurred with more frequency with isoflurane compared with propofol, and drowsiness, which occurred with a significantly more frequency with isoflurane compared with sevoflurane, no other significant differences were found in the incidence of postoperative complications.

Table 6. Postoperative Recovery Profiles and Minor Complications Associated with Different Inhaled Anesthetic Regimens

End-point	Isoflurane vs Desflurane	Isoflurane vs Sevoflurane	Sevoflurane vs Desflurane
Time to open eyes (min)	NR	2.4 (1.8 to 2.9)† (S)	1.4 (−0.1 to 2.9)§
Time to obey commands (min)	4.6 (1.1 to 8.2)† (D)	2.4 (1.8 to 2.9)† (S)	2.7 (1.2 to 4.1)† (D)
Time to Transfer from Phase 1 to Phase 2 (min)	1.3 (−10 to 8)	8.2 (5.7 to 10.6)† (S)	6.4 (3.7 to 9.0)† (S)
Time to home ready (min)	6.4 (−8.7 to 21.5)	5.1 (2.8 to 7.4)† (S)	2.0 (−16 to 12)
Time to home discharge (min)	NR	25 (0.4 to 50)* (S)	2.1 (−18 to 13)
Postoperative nausea (PON)	1.7 (1.0–3.1)	1.2 (0.8–1.9)§	0.7 (0.4–1.2)
Postoperative vomiting (POV)	0.8 (0.3–1.6)	0.9 (0.6–1.4)	0.7 (0.2–1.8)
Postoperative drowsiness	NR	0.6 (0.4–1.0)* (S), NNH = 9.5	1.0 (0.6–1.6)
Postoperative dizziness	NR	0.8 (0.4–1.5)	NR
Postoperative shivering	NR	NR	NR
Postoperative headache	NR	NR	NR
Antiemetics given	NR	1.0 (0.7–1.4)	NR
Post-discharge nausea (PDN)	NR	0.4 (0.3–0.7)† (S), NNH = 7.2	0.8 (0.4–1.7)
Post-discharge vomiting (PDV)	NR	0.8 (0.4–1.6)	NR

All results are shown as weighted mean difference (WMD) or relative risk (mean and 95% confidence intervals).
* $P < 0.05$, † $P < 0.01$.
Significant differences are shown in favor of: S = sevoflurane, I = isoflurane and D = desflurane when significant. § Significant heterogeneity; NR = not reported (or reported in only one study), NNH = numbers needed to harm for significant differences.

There are a number of limitations in our meta-analysis. Although we conducted a thorough review of work published in the English language, there may be additional references not identified in our search strategies. Many authors did not state whether the patients studied were inpatients or outpatients. Whenever in doubt, we came to a consensus as to the study group. When authors had not specifically stated whether the data pertained to PON or POV, we decided to exclude these data from the analysis. This limits the number of patients studied, but we chose to report PDNV as distinct end-points. We included patients who were administered nitrous oxide was administered for maintenance in the IV anesthesia group because we believe that this is a common practice used in many studies. Excluding these studies would reduce the scope of this systematic review as well as limiting our findings to a very small and distinct population. Patients induced with inhaled anesthetic (e.g., desflurane and sevoflurane) were also excluded from our review, as this could affect the primary end-points. Finally, we only analyzed studies published in the English language, which can also be considered as a bias. Many authors publish "negative" findings in local (non-English language) journals (60), which would suggest that the differences found by us may be larger than the true differences among these anesthetics, which is further support that the overall differences between the inhaled anesthetics are probably very small.

In conclusion, the choice of anesthetic for maintenance of anesthesia should be guided by the training and experience of the individual physician, as well as the routines and equipment available in the hospital, because the specific anesthetic appears to play a minor role in outcome after ambulatory surgery.

We would like to thank the staff at the Welch Medical Library, Johns Hopkins Medical Institutions for the support in retrieving articles for the study. We would also like to thank the Olof Norlander Memorial Fund for financial support of this project.

References

1. Apfelbaum JL, Walawander CA, Grasela TH, et al. Eliminating intensive postoperative care in same-day surgery patients using short-acting anesthetics. Anesthesiology 2002;97:66–74.
2. Song D, Joshi GP, White PF. Fast-track eligibility after ambulatory anesthesia: a comparison of desflurane, sevoflurane, and propofol. Anesth Analg 1998;86:267–73.
3. Nathan N, Peyclit A, Lahrimi A, Feiss P. Comparison of sevoflurane and propofol for ambulatory anaesthesia in gynaecological surgery. Can J Anaesth 1998;45:1148–50.
4. Song D, van Vlymen J, White PF. Is the bispectral index useful in predicting fast-track eligibility after ambulatory anesthesia with propofol and desflurane? Anesth Analg 1998;87:1245–8.
5. Van Hemelrijck J, Smith I, White PF. Use of desflurane for outpatient anesthesia: a comparison with propofol and nitrous oxide. Anesthesiology 1991;75:197–203.
6. Dexter F, Tinker JH. Comparisons between desflurane and isoflurane or propofol on time to following commands and time to discharge: a metaanalysis. Anesthesiology 1995;83:77–82.
7. Wilhelm W, Grundmann U, Van Aken H, et al. A multicenter comparison of isoflurane and propofol as adjuncts to remifentanil-based anesthesia. J Clin Anesth 2000;12:129–35.
8. Ashworth J, Smith I. Comparison of desflurane with isoflurane or propofol in spontaneously breathing ambulatory patients. Anesth Analg 1998;87:312–8.
9. Gupta A, Kullander M, Ekberg K, Lennmarken C. Assessment of recovery following day-case arthroscopy: a comparison between propofol and isoflurane-based anaesthesia. Anaesthesia 1995;50:937–42.

10. Valanne J. Recovery and discharge of patients after long propofol infusion versus isoflurane anaesthesia for ambulatory surgery. Acta Anaesthesiol Scand 1992;36:530–3.
11. Nightingale JJ, Lewis IH. Recovery from day-case anaesthesia: comparison of total IV anaesthesia using propofol with an inhalation technique. Br J Anaesth 1992;68:356–9.
12. Sung YF, Reiss N, Tillette T. The differential cost of anesthesia and recovery with propofol-nitrous oxide anesthesia versus thiopental sodium-isoflurane-nitrous oxide anesthesia. J Clin Anesth 1991;3:391–4.
13. Werner ME, Bach DE, Newhouse RF. A comparison of propofol with methohexital and isoflurane in two general anesthetic techniques. J Oral Maxillofac Surg 1993;51:1076–9.
14. Korttila K, Ostman P, Faure E, et al. Randomized comparison of recovery after propofol-nitrous oxide versus thiopentone-isoflurane-nitrous oxide anaesthesia in patients undergoing ambulatory surgery. Acta Anaesthesiol Scand 1990;34:400–3.
15. Pollard BJ, Bryan A, Bennett D, et al. Recovery after oral surgery with halothane, enflurane, isoflurane or propofol anaesthesia. Br J Anaesth 1994;72:559–66.
16. Moffat A, Cullen PM. Comparison of two standard techniques of general anaesthesia for day-case cataract surgery. Br J Anaesth 1995;74:145–8.
17. Larsen LE, Gupta A, Ledin T, et al. Psychomotor recovery following propofol or isoflurane anaesthesia for day-care surgery. Acta Anaesthesiol Scand 1992;36:276–82.
18. Marshall CA, Jones RM, Bajorek PK, Cashman JN. Recovery characteristics using isoflurane or propofol for maintenance of anaesthesia: a double-blind controlled trial. Anaesthesia 1992;47:461–6.
19. Visser K, Hassink EA, Bonsel GJ, et al. Randomized controlled trial of total intravenous anesthesia with propofol versus inhalation anesthesia with isoflurane-nitrous oxide: postoperative nausea with vomiting and economic analysis. Anesthesiology 2001;95:616–26.
20. Milligan KR, O'Toole DP, Howe JP, et al. Recovery from outpatient anaesthesia: a comparison of incremental propofol and propofol-isoflurane. Br J Anaesth 1987;59:1111–4.
21. Collins SJ, Robinson AL, Holland HF. A comparison between total intravenous anaesthesia using a propofol/alfentanil mixture and an inhalational technique for laparoscopic gynaecological sterilization. Eur J Anaesthesiol 1996;13:33–7.
22. Lim BL, Low TC. Total intravenous anaesthesia versus inhalational anaesthesia for dental day surgery. Anaesth Intensive Care 1992;20:475–8.
23. Alhashemi JA, Miller DR, O'Brien HV, Hull KA. Cost-effectiveness of inhalational, balanced and total intravenous anaesthesia for ambulatory knee surgery. Can J Anaesth 1997;44:118–25.
24. Zuurmond WW, van Leeuwen L, Helmers JH. Recovery from propofol infusion as the main agent for outpatient arthroscopy: a comparison with isoflurane. Anaesthesia 1987;42:356–9.
25. Tang J, White PF, Wender RH, et al. Fast-track office-based anesthesia: a comparison of propofol versus desflurane with antiemetic prophylaxis in spontaneously breathing patients. Anesth Analg 2001;92:95–9.
26. Rapp SE, Conahan TJ, Pavlin DJ, et al. Comparison of desflurane with propofol in outpatients undergoing peripheral orthopedic surgery. Anesth Analg 1992;75:572–9.
27. Lebenbom-Mansour MH, Pandit SK, Kothary SP, et al. Desflurane versus propofol anesthesia: a comparative analysis in outpatients. Anesth Analg 1993;76:936–41.
28. Eriksson H, Korttila K. Recovery profile after desflurane with or without ondansetron compared with propofol in patients undergoing outpatient gynecological laparoscopy. Anesth Analg 1996;82:533–8.
29. Raeder JC, Mjaland O, Aasbo V, et al. Desflurane versus propofol maintenance for outpatient laparoscopic cholecystectomy. Acta Anaesthesiol Scand 1998;42:106–10.
30. Wrigley SR, Fairfield JE, Jones RM, Black AE. Induction and recovery characteristics of desflurane in day case patients: a comparison with propofol. Anaesthesia 1991;46:615–22.
31. Song D, Chung F, Wong J, Yogendran S. The assessment of postural stability after ambulatory anesthesia: a comparison of desflurane with propofol. Anesth Analg 2002;94:60–4.
32. Graham SG, Aitkenhead AR. A comparison between propofol and desflurane anaesthesia for minor gynaecological laparoscopic surgery. Anaesthesia 1993;48:471–5.
33. Larsen B, Seitz A, Larsen R. Recovery of cognitive function after remifentanil-propofol anesthesia: a comparison with desflurane and sevoflurane anesthesia. Anesth Analg 2000;90:168–74.
34. Coloma M, Zhou T, White PF, et al. Fast-tracking after outpatient laparoscopy: reasons for failure after propofol, sevoflurane, and desflurane anesthesia. Anesth Analg 2001;93:112–5.
35. Tang J, Chen L, White PF, et al. Recovery profile, costs, and patient satisfaction with propofol and sevoflurane for fast-track office-based anesthesia. Anesthesiology 1999;91:253–61.
36. Smith I, Thwaites AJ. Target-controlled propofol versus sevoflurane: a double-blind, randomised comparison in day-case anaesthesia. Anaesthesia 1999;54:745–52.
37. Fredman B, Nathanson MH, Smith I, et al. Sevoflurane for outpatient anesthesia: a comparison with propofol. Anesth Analg 1995;81:823–8.
38. Peduto VA, Peli S, Amicucci G, et al. Maintenance of and recovery from anaesthesia in elderly patients. A clinical comparison between sevoflurane and isoflurane. Minerva Anestesiol 1998;64(Suppl3):18–25.
39. Raeder J, Gupta A, Pedersen FM. Recovery characteristics of sevoflurane- or propofol-based anaesthesia for day-care surgery. Acta Anaesthesiol Scand 1997;41:988–94.
40. Smith I, Terhoeve PA, Hennart D, et al. A multicentre comparison of the costs of anaesthesia with sevoflurane or propofol. Br J Anaesth 1999;83:564–70.
41. Jellish WS, Lien CA, Fontenot HJ, Hall R. The comparative effects of sevoflurane versus propofol in the induction and maintenance of anesthesia in adult patients. Anesth Analg 1996;82:479–85.
42. Wandel C, Neff S, Bohrer H, et al. Recovery characteristics following anaesthesia with sevoflurane or propofol in adults undergoing outpatient surgery. Eur J Clin Pharmacol 1995;48:185–8.
43. Nathan N, Peyclit A, Lahrimi A, Feiss P. Comparison of sevoflurane and propofol for ambulatory anaesthesia in gynaecological surgery. Can J Anaesth 1998;45:1148–50.
44. Gupta A, Kullander M, Ekberg K, Lennmarken C. Anaesthesia for day-care arthroscopy: a comparison between desflurane and isoflurane. Anaesthesia 1996;51:56–62.
45. Ghouri AF, Bodner M, White PF. Recovery profile after desflurane-nitrous oxide versus isoflurane-nitrous oxide in outpatients. Anesthesiology 1991;74:419–24.
46. Rieker LB, Rieker MP. A comparison of the recovery times of desflurane and isoflurane in outpatient anesthesia. AANA J 1998;66:183–6.
47. Smith CE, Lever JS, Sawkar S, et al. Sevoflurane-N_2O versus propofol/isoflurane-N_2O during elective surgery using the laryngeal mask airway in adults. J Clin Anesth 2000;12:392–6.
48. Sloan MH, Conard PF, Karsunky PK, Gross JB. Sevoflurane versus isoflurane: induction and recovery characteristics with single-breath inhaled inductions of anesthesia. Anesth Analg 1996;82:528–32.
49. O'Hara DA, DeAngelis V, Lee H, Zedie N, et al. The effects of sevoflurane and isoflurane on recovery from outpatient surgery. Pharmacotherapy 1996;16:446–52.
50. Eriksson H, Haasio J, Korttila K. Recovery from sevoflurane and isoflurane anaesthesia after outpatient gynaecological laparoscopy. Acta Anaesthesiol Scand 1995;39:377–80.
51. Philip BK, Kallar SK, Bogetz MS, et al. A multicenter comparison of maintenance and recovery with sevoflurane or isoflurane for adult ambulatory anesthesia. Anesth Analg 1996;83:314–9.
52. Elcock DH, Sweeney BP. Sevoflurane versus isoflurane: a clinical comparison in day surgery. Anaesthesia 2002;57:52–6.

53. Nathanson MH, Fredman B, Smith I, White PF. Sevoflurane versus desflurane for outpatient anesthesia: a comparison of maintenance and recovery profiles. Anesth Analg 1995;81: 1186–90.
54. Naidu-Sjosvard K, Sjoberg F, Gupta A. Anaesthesia for video-arthroscopy of the knee: a comparison between desflurane and sevoflurane. Acta Anaesthesiol Scand 1998;42:464–71.
55. Tarazi EM, Philip BK. A comparison of recovery after sevoflurane or desflurane in ambulatory anesthesia. J Clin Anesth 1998;10:272–7.
56. Robinson BJ, Uhrich TD, Ebert TJ. A review of recovery from sevoflurane anaesthesia: comparisons with isoflurane and propofol including meta-analysis. Acta Anaesthesiol Scand 1999;43:185–90.
57. Gupta A, Vegfors M, Odensten M, Lennmarken C. Alfentanil or fentanyl during isoflurane-based anaesthesia for day-care knee arthroscopy? Acta Anaesthesiol Scand 1994;38:156–60.
58. Ahmad S, Yilmaz M, Marcus RJ, et al. Impact of bispectral index monitoring on fast tracking of gynecologic patients undergoing laparoscopic surgery. Anesthesiology 2003;98:849–52.
59. Tramer M, Moore A, McQuay H. Propofol anaesthesia and postoperative nausea and vomiting: quantitative systematic review of randomized controlled studies. Br J Anaesth 1997;78: 247–55.
60. Egger M, Zellweger-Zahner T, Schneider M, et al. Language bias in randomised controlled trials published in English and German. Lancet 1997;350:326–9.