David C. Warltier, M.D., Ph.D., Editor

Anesthesiology 2003; 99:488–95

Does the Routine Prophylactic Use of Antiemetics Affect the Incidence of Postdischarge Nausea and Vomiting following Ambulatory Surgery?

A Systematic Review of Randomized Controlled Trials

Anil Gupta, M.D., F.R.C.A., Ph.D., Christopher L. Wu, M.D.,† Nabil Elkassabany, M.D.,* Courtney E. Krug, B.A., B.S.,‡ Stephen D. Parker, M.D.,† Lee A. Fleisher, M.D.§*

THE rapid increase in ambulatory surgery procedures performed over the past 10 yr has resulted in greater focus directed toward the control of postoperative nausea and vomiting (PONV), sometimes appropriately termed the "big, little problem."[1] The incidence of this complication is variable,[2] but PONV has emerged as one of the commonest complications following ambulatory surgery,[3] and the one that patients would most like to avoid.[4] Specifically, the postdischarge period has been poorly studied but is important from the patient's perspective.

Despite the increasing availability of newer and more expensive drugs for the prevention of PONV, some authors question the routine use of single-drug prophylaxis in low-risk patients.[5] The long-term (> 6 h) effect of antiemetics is even more uncertain in the ambulatory setting, because the focus of attention has previously been on the management of early PONV (in the day surgical unit). As many as 35–50% patients continue to have postdischarge nausea and vomiting (PDNV).[6,7] It is important to control this symptom after discharge, because resumption of normal activities may be delayed if PONV is prolonged[6] and ambulatory surgical patients are not under direct medical supervision after discharge.[7] In our experience, few centers routinely provide antiemetics for the control of PDNV at home. Numerous systematic reviews have now been published in the literature on PONV, but only one has focused on PONV after hospital discharge in ambulatory surgical patients.[8]

This systematic review was completed to address the question of whether the routine prophylactic use of antiemetics affects the incidence of PDNV following ambulatory surgery. We restricted our analysis to randomized, controlled studies published in the English literature.

Methods

Citation Search Strategy

The primary question for this systematic review was: Does prophylactic management of nausea and vomiting affect postdischarge outcome following ambulatory surgery? We searched MEDLINE (1966 through May 2002) *via* PubMed using the MeSH terms: *postoperative, nausea, vomiting*, and *postoperative nausea and vomiting*. The results were limited to studies in humans, the English language, and the adult patient population (> 19 yr old). Publication types were limited to clinical trials, controlled clinical trials, or multicenter studies. After obtaining a list of all the identified articles, a careful handsearch was done from the reference list of all relevant articles. The *related articles* search strategy of PubMed was also used to identify any missing articles. Finally, review articles or systematic reviews of PONV were searched to identify articles missing from the original list.

Inclusion Criteria

The following criteria were used to identify appropriate studies that could be included in the analysis: human studies in adults published in the English literature of patients undergoing ambulatory surgery. The studies also had to be controlled and randomized with the specific primary endpoint of assessing nausea or vomiting after discharge for at least 24 h after surgery.

Exclusion Criteria

Studies were excluded if they presented data for and included the first postoperative 24 h (*i.e.*, were not

* Postdoctoral Fellow, † Associate Professor, and ‡ Research Assistant, Department of Anesthesiology and Critical Care Medicine, Johns Hopkins Medical Institutions. § Professor of Medicine and Professor of Health Policy and Management, Department of Anesthesiology and Critical Care Medicine, Johns Hopkins Medical Institutions.

Received from the Department of Anesthesiology and Critical Care Medicine, Johns Hopkins Medical Institutions, Baltimore, Maryland. Submitted for publication July 15, 2002. Accepted for publication January 17, 2003. Dr. Gupta was supported by grants obtained from the Olof Norlander Memorial Fund, Karolinska Hospital, Stockholm, Sweden. Additional support was provided from institutional and/or departmental sources.

Address reprint requests to Dr. Fleisher: Department of Anesthesiology and Critical Care Medicine, Johns Hopkins Medical Institutions, 600 N. Wolfe Street, Carnegie 280, Baltimore, Maryland 21287. Address electronic mail to: lfleishe@jhmi.edu.

limited to the postdischarge period). If a study presented a nausea score or a visual analog scale for nausea without providing the number of patients with nausea, the data were not included in the analysis. Those studies in which the authors did not use the terms *ambulatory surgery* or *outpatient surgery* but instead used *major surgery* or *the patients were admitted to the ward* were also excluded from the analysis. Those studies in which direct comparisons were made between two drugs without a placebo group were also excluded.

Data Extraction

Data extraction was done independently by two primary reviewers (A.G., N.E.), who were unaware of each other's results. Data included aspects of patient characteristics, anesthesia, type of surgery, and incidence of PONV at 0–6 h (predischarge) and postdischarge. Extracted data were compared for agreement between the two primary reviewers by a third reviewer (C.L.W.). Any discrepancies were noted and discussed further to come to an agreement between all reviewers. Studies in which combinations of drugs were used for prophylaxis against PONV (> 1 antiemetic drug) were treated and analyzed together, irrespective of the type of antiemetic used (combination treatment).

Data Synthesis and Analysis

Only when data were extractable from more than one study was it subject to a meta-analysis. Dichotomous data extracted from the relevant studies were entered into the program RevMan 4.1 (Review Manager; Cochrane Collaboration, Oxford, U.K.) and analyzed. The relative risk with the corresponding 95% confidence intervals were calculated for each study, and the results were pooled together using the Mantel-Haenszel Method for combining trials. The overall estimate of pooled effect was calculated. Heterogeneity was determined under the assumption (null hypothesis) that there were no differences in treatment effect between trials. For combined data, a fixed effect model was used when there was no significant heterogeneity ($P > 0.05$). The numbers-needed-to-treat were calculated for those antiemetics in which a significant overall effect was seen ($P < 0.05$) by the reciprocal of the control event rate (CER) − experimental event rate (EER): 1/CER − EER. The chi-square test was used for calculating differences in the overall incidence of PONV or PDNV. A P value < 0.05 was considered to be statistically significant.

Results

Literature Review

The results from *outpatients* and *ambulatory surgical procedures* were combined using the OR function to yield 21,739 articles. The results from *nausea* and *vomiting* were combined to yield 38,561 articles. The term *postoperative* was combined with the above searches using the AND function to reveal 495 articles. As a last step, the LIMITED function was used to limit articles to humans, to the English language, and to the adult population (> 19 yr) and was restricted to clinical trials *or* controlled clinical trials *or* multicenter study using the function PUBLICATION TYPE, which yielded 189 articles. The abstracts of these 189 articles were read to see if they addressed the primary question. Forty-eight articles reported a primary aim of comparing drugs in the control of PONV. These 48 articles were further analyzed to see if any data were reported that could be extracted on *postdischarge nausea or vomiting* (PDNV). A hand-search was also done through the reference lists of these articles to find any "missing" articles. We realized that some articles were missed because authors had not used the term *outpatients* or *ambulatory surgical procedures* in their study, and that the MeSH term *ambulatory surgical procedure* was introduced as late as in 1998. Therefore, a second search was done without these MeSH terms to reveal a total of 1,315 articles, which were searched to see if they addressed the primary question. A final count of 22 articles was found in which the appropriate postdischarge data (nausea or vomiting) could be extracted (table 1).[9–30] The reasons for excluding the articles from the final list were: primary aim different from the assessment of PONV, lack of postdischarge data, studies in which data combined the immediate postoperative period and the 24-h postoperative period (not restricted to the postdischarge period) into a single data point, studies in which no comparison was made against a placebo, and studies in which nausea was reported as a visual analog scale or score rather than the number of patients with nausea.

Study Characteristics

Of the studies that met our inclusion/exclusion criteria, 19 reported the number of patients with postdischarge nausea (PDN), and 21 reported postdischarge vomiting (PDV) during the first 24 h. Primary admission because of persistent PONV was reported in five studies. No patients were readmitted because of PDNV in any study. The need for antiemetics after discharge to home was reported in only one study.[10]

Patient Characteristics

The demographic data of the population studied and the type of surgery in the 22 studies included in the meta-analysis are shown in table 1. Of the total 3,629 patients studied, 1,216 were given a placebo (33.5%) and 2,413 were given an active drug (66.5%). The mean age of the patients in the treatment group was 33.2 yr and in the placebo group, 34.1 yr ($P > 0.05$). The majority of patients studied were women (88.3%) undergoing gynecologic surgery.

Table 1. Studies Addressing PDNV Included in the Meta-analysis

Reference	Publication Year	Comparison	Total No. of Patients	No. of Females	Type of Surgery	Maintenance Agent	Postdischarge	
							Nausea (n)	Vomiting (n)
Patterson *et al.*[9]	1993	Prochlorperazine *vs.* placebo	52	52	Gynecologic surgery or breast biopsy	Isoflurane	2	6
Sun *et al.*[10]	1997	Ondansetron *vs.* placebo	75	35	Ear, nose, and throat	Desflurane	17	3
Coloma *et al.*[11]	2001	Dexamethasone *vs.* placebo	80	43	Anorectal	Propofol	8	NR
Wagley *et al.*[12]	1999	Ondansetron *vs.* placebo	50	25	Maxillofacial	Midazolam, fentanyl, methohexital	13	9
O'Donovan and Shaw[13]	1984	Droperidol *vs.* placebo	124	77	Dental surgery		11	6
Cholwill *et al.*[14]	1999	Ondansetron *vs.* cyclizine *vs.* placebo	175	175	Gynecologic laparoscopic surgery	Isoflurane	28	30
Wang *et al.*[15]	2000	Dexamethasone *vs.* placebo	81	81	Gynecologic laparoscopic surgery	Isoflurane	13	6
Malins *et al.*[16]	1994	Ondansetron *vs.* metoclopramide *vs.* placebo	150	150	Gynecologic laparoscopic surgery	Isoflurane	39	19
Paxton *et al.*[17]	1995	Ondansetron *vs.* metoclopramide *vs.* droperidol *vs.* placebo	118	118	Gynecologic laparoscopic surgery	Isoflurane	NR	15
Millar and Hall[18]	1987	Droperidol *vs.* placebo	144	144	Termination of pregnancy	Enflurane	8	0
Aasboe *et al.*[19]	1998	Betamethasone *vs.* placebo	78	73	Orthopedic + general surgery	Isoflurane	19	7
Scuderi *et al.*[20]	1999	Ondansetron *vs.* placebo	575	364	Mixed procedures	NR	NR	107
Bailey *et al.*[21]	1990	Scopolamine *vs.* placebo	138	138	Gynecologic laparoscopic surgery	Isoflurane	NR	10
Huang *et al.*[22]	2001	Dexamethasone *vs.* metoclopramide *vs.* placebo	115	115	Gynecologic laparoscopic surgery	Isoflurane	18	8
Wilson *et al.*[23]	2001	Metoclopramide *vs.* ondansetron *vs.* placebo	232	183	Laparoscopic cholecystectomy	Isoflurane	59	59
Tzeng *et al.*[24]	2000	Dexamethasone *vs.* droperidol *vs.* combination *vs.* placebo	151	151	Gynecologic (dilatation + curettage)	Propofol	19	12
Tang *et al.*[25]	1998	Ondansetron *vs.* placebo	164	164	Gynecologic laparoscopic surgery	Desflurane	94	46
Scuderi *et al.*[26]	2000	Combination *vs.* ondansetron *vs.* placebo	139	139	Gynecologic laparoscopic surgery	Sevoflurane	NR	28
Ahmed *et al.*[27]	2000	Ondansetron *vs.* combination *vs.* placebo	139	139	Gynecologic laparoscopic surgery	Isoflurane	41	13
McKenzie *et al.*[28]	1993	Ondansetron *vs.* placebo	544	544	Gynecologic surgery + laparoscopy	Isoflurane or enflurane	327	39
Wu *et al.*[29]	2000	Ondansetron *vs.* droperidol *vs.* combination *vs.* placebo	160	160	Gynecologic laparoscopy	Isoflurane	45	45
Tang *et al.*[30]	1996	Ondansetron *vs.* droperidol *vs.* placebo	161	161	Gynecologic laparoscopy	Desflurane	54	29

NR = not recorded; PDNV = postdischarge nausea and vomiting.

Table 2. Efficacy of Antiemetic Medication on PDN

	No. of Trials	Total No. of Patients Studied	Total No. of Patients with PDN	RR	95% CI	P Value	Heterogeneity (P Value)	NNT
Ondansetron *vs.* placebo								
1 mg	1	272	189	0.99	0.85–1.16	0.9	NA	
4 mg	10	1067	464	0.77	0.67–0.87	0.00009	0.36	12.9
8 mg	1	275	157	0.63	0.51–0.79	0.00004	NA	3.9
Droperidol *vs.* placebo								
<1 mg	3	278	49	1.02	0.63–1.65	0.9	0.28	
>1 mg	3	239	49	0.68	0.41–1.11	0.12	0.77	
Dexamethasone *vs.* placebo	4	316	45	0.55	0.31–0.97	0.04	0.99	12.2
Metoclopramide *vs.* placebo	3	323	87	0.76	0.53–1.09	0.14	0.99	
Cyclizine *vs.* placebo	1	70	19	0.92	0.42–1.99	0.8	NA	
Betamethasone *vs.* placebo	1	78	19	0.28	0.10–0.77	0.01	NA	3.7
Combination *vs.* placebo	3	219	47	0.32	0.19–0.54	0.00002	0.27	5.2

CI = confidence intervals; NA = not applicable; NNT = numbers needed to treat; PDN = postdischarge nausea; RR = relative risk.

Drug Characteristics

The following drugs were compared with placebo: droperidol < 1 mg (four studies) and > 1 mg (four studies); cyclizine 50 mg (one study); metoclopramide 10 mg (four studies); betamethasone 12 mg (one study); scopolamine 1.5 mg (one study); prochlorperazine 6 mg (one study); dexamethasone 4–10 mg (four studies); and ondansetron 1 mg (one study), 4 mg (13 studies), and 8 mg (one study). In addition, four studies compared combination treatment (2 or 3 drugs) against placebo. Meta-analysis was not performed when less than two 2 studies with extractable data could be identified.

Postdischarge Nausea

A total of 815 patients had PDN (32.6%). The number of patients who had PDN in the placebo and treatment groups was 276 (35.7%) and 539 (31.2%), respectively ($P < 0.05$). The overall incidence of postoperative nausea in these studies was 26.0% and 40.4% in the treatment and placebo groups, respectively ($P < 0.05$). When comparing different drugs with placebo in a meta-analysis of all studies with relevant data, ondansetron 4 mg, dexamethasone 4–10 mg, and combination treatment with more than one drug had a significantly lesser relative risk compared to placebo for PDN ($P < 0.05$) (table 2). The pooled data for the relative risk of PDN in the ondansetron 4 mg and combination treatment groups are shown in figures 1 and 2, respectively. No significant heterogeneity was observed between the studies. The overall incidence of PDN was significantly lower in the ondansetron 4 mg group (39.9%) than in the placebo group (48.1%) ($P < 0.05$). The number-needed-to-treat was large with all drugs except combination treatment, when single studies were excluded (table 2). In patients treated with ondansetron, the overall incidence of PDN in a subgroup of desflurane-anesthetized patients was 44.6% compared to 38.3% for isoflurane (not significant). The relative risks for desflurane and isoflurane were 0.75 (CI, 0.59–0.96) and 0.66 (CI, 0.47–0.92) compared to placebo.

Postdischarge Vomiting

A total of 497 patients had PDV (14.7%). In the placebo group, 19.6% of patients had PDV, whereas 12.1% of those in the treated group had PDV ($P < 0.05$). The overall incidence of postoperative vomiting was 14.6% and 26.5% in the treatment and placebo groups, respectively ($P < 0.05$). The relative risk for ondansetron 4 mg and combination treatment with two or more drugs was significantly lower than with placebo for PDV ($P <$

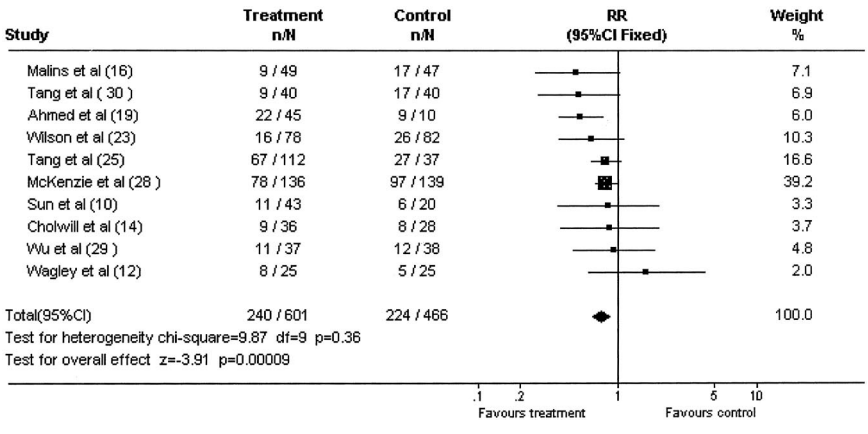

Fig. 1. Postdischarge nausea in the ondansetron 4 mg group *versus* the placebo group. CI = confidence interval, n = number of patients with nausea, N = total number of patients studied, RR = relative risk. Figures in parentheses are reference numbers to the authors quoted.

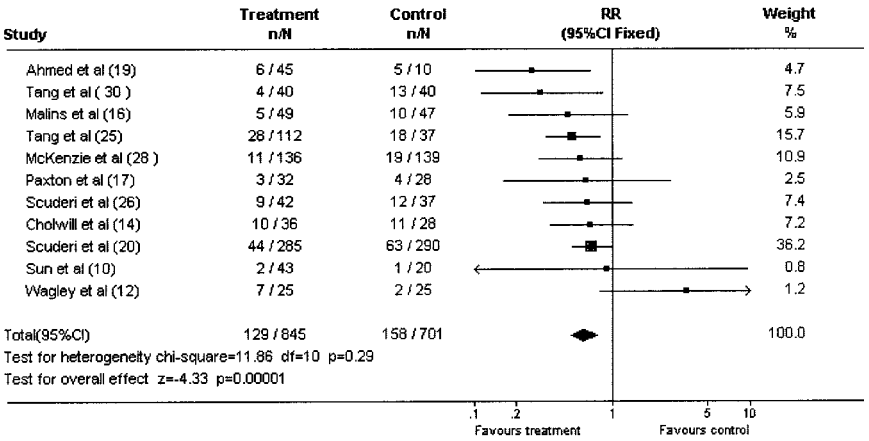

Fig. 2. Postdischarge vomiting in the ondansetron 4 mg group *versus* the placebo group. CI = confidence interval, n = number of patients with nausea, N = total number of patients studied, RR = relative risk. Figures in parentheses are reference numbers to the authors quoted.

0.05). The pooled data for the relative risk of PDV in the ondansetron 4 mg and combination treatment groups are shown in figures 3 and 4, respectively. No significant heterogeneity was observed between studies. The relative risk for PDV in patients treated with dexamethasone was 0.39 (CI, 0.14–1.05) (not significant). No drug had a significantly different relative risk as compared to placebo. The number needed to treat for ondansetron was 13.8 compared to 5.0 for combination therapy (table 3). The incidence of PDV in a subgroup of desflurane or isoflurane anesthetized patients, all of whom received ondansetron, was 17.4% and 22%, respectively (not significant). The relative risks for desflurane and isoflurane were 0.46 (CI, 0.30–0.71) and 0.55 (CI, 0.33–0.93) as compared to placebo.

Discussion

Numerous studies have examined the effects of various antiemetics on PONV in ambulatory surgical patients before hospital discharge. In our systematic review of all randomized controlled trials, we observed an overall beneficial effect with the use of either combination treatment or ondansetron 4 mg alone for the prevention of postdischarge nausea and vomiting. A similar beneficial effect was also seen with dexamethasone, which prevented nausea but not vomiting in the postdischarge period after ambulatory surgery.

Postdischarge Nausea and Vomiting

The overall incidence of PDN was found to be 32.6%, with significant differences between treatment and placebo groups. This is much higher than that reported earlier in one systematic review published recently (17%)[8] but is similar to that in another prospective randomized study in which the authors specifically addressed the issue of PDNV (30%).[6] Similarly, the incidence of PDV was 14.7%, with a significant difference between placebo and treatment groups, which is similar to that in the study by Carroll *et al.*[6] but is higher than that reported previously by Wu *et al.* (8%).[8] The authors of the latter study did not analyze randomized, controlled studies, which may explain their reported lower incidence of PDNV.

When studying the different drugs individually, however, no differences were found between placebo and treatment groups for droperidol (< 1 mg and > 1 mg) and metoclopramide (10 mg). However, both prophylactic ondansetron and dexamethasone in a dose of 4 mg can reduce the risk of PDNV. Similarly, combination management of PONV with more than one drug leads to a reduction in the relative risk for PDNV. The other drugs and different doses used with extractable data from less than two studies were not included in the meta-analysis.

Ondansetron has an elimination half-life of approximately 3.5 h in young, healthy volunteers,[31] which would not explain the long duration of action after a single intravenous dose administered perioperatively. The incidence of PDNV in the placebo group in the ondansetron trials was much higher than the average incidence of PDNV observed in all trials (48.1% *vs.* 35.7%, respectively), which is perplexing but may be attributable to a multitude of factors, including the num-

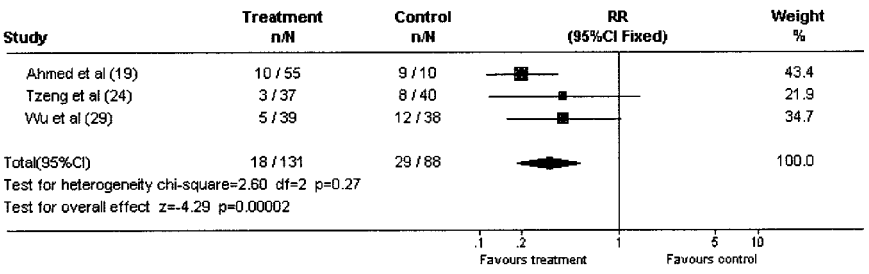

Fig. 3. Postdischarge nausea in the combination treatment group *versus* the placebo group. CI = confidence interval, n = number of patients with nausea, N = total number of patients studied, RR = relative risk. Figures in parentheses are reference numbers to the authors quoted.

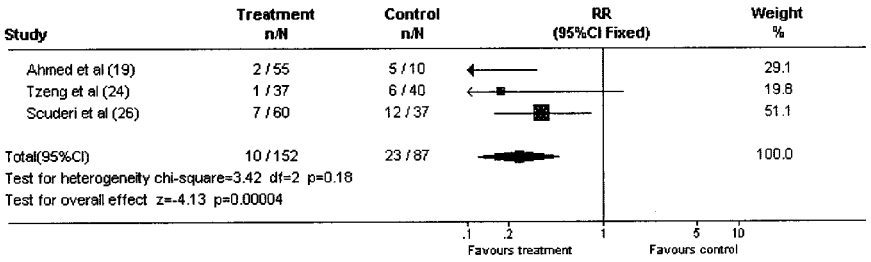

Fig. 4. Postdischarge vomiting in the combination treatment group *versus* the placebo group. CI = confidence interval, n = number of patients with nausea, N = total number of patients studied, RR = relative risk. Figures in parentheses are reference numbers to the authors quoted.

ber of women studied, number of patients that underwent laparoscopic gynecologic surgery, history of smoking, and past history of nausea and vomiting or motion sickness, all of which are known to affect the incidence of PONV. Furthermore, because of the overrepresentation of women in these studies (88%) undergoing operative procedures that are known to be highly emetogenic (*e.g.*, laparoscopic surgery), the use of inhalation agents for maintenance of anesthesia (instead of propofol infusion), and the use of opiates during and after surgery, it is important that the results not be extended to other groups of patients.

Dexamethasone reduced the incidence of PDNV, which was in agreement with the findings of Henzi *et al.*,[32] who showed that dexamethasone prevented both "late" nausea and vomiting. However, these authors included inpatients in their analysis and defined late PONV as that occurring from 0 to 24 h postoperatively (not restricted to the postdischarge period).

One unexpected finding in our analysis was that droperidol did not prove to be effective as a prophylactic against PDNV. In a large study conducted on ambulatory surgery patients, Hill *et al.*[33] found that droperidol 1.25 mg was effective and cheap and provided similar patient satisfaction compared with 4 mg ondansetron. The data in this study was confined to the postoperative period and did not include the postdischarge period. It is possible that droperidol might be effective for the prevention of "early" PONV but might not be equally effective in "late" (postdischarge) PONV.

A confounding factor in all these studies is the role of anesthetics in producing PONV. Although most of the studies in this review used propofol for induction of anesthesia, none used propofol as an infusion during anesthesia (in two studies, intermittent propofol injections were used for the maintenance of short-duration anesthesia). It is well known that propofol when used as an infusion can reduce PONV.[34] However, inhalational anesthetics are thought to be emetogenic probably only in the early postoperative period.[35] We observed no difference in the rates of PDNV between isoflurane and desflurane when controlling for nitrous oxide use, and the efficacy of ondansetron was similar between the two anesthetics, supporting the conclusion that the choice of anesthetic had minimal effect during this period.

The last and perhaps the most important factor, which has been repeatedly stressed in recent studies, is the role of combination therapy in the control of PONV and, probably, PDNV.[36] Because many factors induce PONV, it is increasingly believed that drugs acting at different receptors would reduce the risk for PONV. The major issue in drawing any definite conclusions from our findings is that the number-needed-to-treat for ondansetron 4 mg was high (> 12). In contrast, treatment with a combination of drugs produced a low number-needed-to-treat (5.2 and 5.3 in PDN and PDV, respectively). This would imply that combination management of PDNV has the greatest benefit for patients in the prevention of PONV, a fact supported by some other authors.[26,36]

Table 3. Efficacy of Antiemetic Medication on PDV

	No. of Trials	Total No. of Patients Studied	Total No. of Patients with PDV	RR	95% CI	P Value	Heterogeneity (P Value)	NNT
Ondansetron *vs.* placebo								
1 mg	1	272	26	0.39	0.17–0.89	0.02	NA	11.9
4 mg	11	1,546	287	0.63	0.51–0.78	0.00001	0.29	13.8
8 mg	1	275	21	0.11	0.03–0.45	0.002	NA	8.2
Droperidol *vs.* placebo								
<1 mg	3	278	25	0.56	0.27–1.16	0.12	0.69	
>1 mg	5	372	68	0.81	0.53–1.23	0.3	0.12	
Dexamethasone *vs.* placebo	3	236	18	0.39	0.14–1.05	0.06	0.94	
Metoclopramide *vs.* placebo	3	226	29	0.71	0.35–1.41	0.3	0.37	
Cyclizine *vs.* placebo	1	70	20	0.55	0.26–1.14	0.11	NA	
Scopolamine *vs.* placebo	1	138	10	1.46	0.43–4.94	0.5	NA	
Betamethasone *vs.* placebo	1	78	7	0.18	0.02–1.39	0.10	NA	
Combination *vs.* placebo	3	239	33	0.24	0.12–0.47	0.00004	0.18	5.0

CI = confidence intervals; NA = not applicable; NNT = numbers needed to treat; PDV = postdischarge vomiting; RR = relative risk.

Limitations

Although we were able to identify as many as 1,000 studies addressing the issue of PONV, a majority of these studies had been in inpatients. Many of the authors did not use the term *ambulatory surgery*; therefore, it was sometimes difficult to determine if the setting was ambulatory or not. Observation of patients in the hospital or in specific designated facilities outside the home environment for less than 24 h and subsequent discharge creates some problems, because this may not result in the same risk for PDNV as that associated with ambulatory surgery. Data extraction was not easy, because standard terminology is not often used. In some studies, the authors had provided data for the early postoperative period (0–2 h) and subsequently for the 0–24 h period. We deemed these studies unfit for the research question (PDNV) and consequently excluded them from the final analysis. Another problem was that some investigators provided the results as PONV and not separately as postoperative nausea or postoperative vomiting. We agreed to include these studies, but the data were assumed to refer to postoperative nausea and were excluded from the analysis from postoperative vomiting. When only single studies were available for a given drug or dose, we thought it inappropriate to perform a "meta-analysis"; consequently, these studies were eliminated, which further restricted our findings. A final problem was that the total number of patients studied in the postdischarge period was not specified by all authors. It was not always stated if there were dropouts from the initial number of patients recruited. Unless otherwise stated, we assumed that all patients initially randomized were also included in the postdischarge data (intention-to-treat). Our study also suffers from the same bias as reported in many others, in that we analyzed only published data in the English language. It has been reported that negative-outcome studies tend to be published non-English language journals,[37] which would mean that the number-needed-to-treat may be even higher than that found in our study.

Future Directions

The postdischarge period must be defined in a standardized fashion, and future studies should specifically focus on and properly examine this period of patient care. There is a need for prospective, randomized studies with a large number of patients, and a defined group of patients undergoing specific procedures. This could prevent "overtreatment" of low-risk patients, provide optimal management of the patients-at-risk, and, in the long run, prove to be cost-effective. Certain drugs that seem to be effective but inadequately studied (*e.g.*, betamethasone, ondansetron 8 mg, and prochlorperazine) must be better documented, specifically in the postdischarge period. The optimal time of administration of prophylactic antiemetics must be clearly defined, specifically in the context of ambulatory surgery. The emetogenic role of opioids and inhalation anesthetics should be confirmed in good prospective trials. Finally, the use of combination therapy for the prevention of PDNV should be further examined to confirm the results of the present meta-analysis.

Conclusions

In this systematic review of the literature, we found that prophylactic treatment of PDNV with ondansetron 4 mg or combination treatment with two drugs results in a significant decrease in the risk of PDNV when compared to placebo. The numbers-needed-to-treat was, however, 13 for ondansetron, which questions its routine use, especially in low-risk patients, to prevent PDNV. In contrast, the numbers-needed-to-treat for combination treatment was 5, which would favor this for prophylactic management of PDNV, particularly in high-risk patients.

The authors thank the staff at the Welch Medical Library, Johns Hopkins Medical Institutions, Baltimore, Maryland, for their constant support and help in getting the articles together. The authors also thank the Peri-operative Clinical Research Unit in the Department of Anesthesiology and Critical Care Medicine at Johns Hopkins University, Baltimore, Maryland, for their assistance.

References

1. Kapur PA: The big "little problem." Anesth Analg 1991; 73:243–5
2. Sadhasivam S, Saxena A, Kathirvel S, Kannan TR, Trikha A, Mohan V: The safety and efficacy of prophylactic ondansetron in patients undergoing modified radical mastectomy. Anesth Analg 1999; 89:1340–5
3. Jenkins K, Grady D, Wong J, Correa R, Armanious S, Chung F: Post-operative recovery: Day surgery patients' preferences. Br J Anaesth 2001; 86:272–4
4. Macario A, Weinger M, Carney S, Kim A: Which clinical anesthesia outcomes are important to avoid? The perspectives of patients. Anesth Analg 1999; 89:652–8
5. White PF, Watcha MF: Postoperative nausea and vomiting: Prophylaxis versus treatment. Anesth Analg 1999; 89:1337–9
6. Carroll NV, Miederhoff P, Cox FM, Hirsch JD: Postoperative nausea and vomiting after discharge from outpatient surgery centers. Anesth Analg 1995; 80:903–9
7. Gan TJ: Postoperative nausea and vomiting: Can it be eliminated? JAMA 2002; 13:287:1233–6
8. Wu CL, Berenholtz SM, Pronovost PJ, Fleisher LA: Systematic review and analysis of post-discharge symptoms after outpatient surgery. ANESTHESIOLOGY 2002; 96:994–1003
9. Patterson KW, Armstrong C, Timon D, O'Toole D, Keane PW: Buccal prochlorperazine as an antiemetic for day care surgery. Ir Med J 1993; 86:186–8
10. Sun R, Klein KW, White PF: The effect of timing of ondansetron administration in outpatients undergoing otolaryngologic surgery. Anesth Analg 1997; 84:331–6
11. Coloma M, Duffy LL, White PF, Kendall Tongier W, Huber PJ Jr: Dexamethasone facilitates discharge after outpatient anorectal surgery. Anesth Analg 2001; 92:85–8
12. Wagley C, Hackett C, Haug RH: The effect of preoperative ondansetron on the incidence of postoperative nausea and vomiting in patients undergoing outpatient dentoalveolar surgery and general anesthesia. J Oral Maxillofac Surg 1999; 57:1195–200
13. O'Donovan N, Shaw J: Nausea and vomiting in day-case dental anaesthesia: The use of low-dose droperidol. Anaesthesia 1984; 39:1172–6
14. Cholwill JM, Wright W, Hobbs GJ, Curran J: Comparison of ondansetron and cyclizine for prevention of nausea and vomiting after day-case gynaecological laparoscopy. Br J Anaesth 1999; 83:611–4
15. Wang JJ, Ho ST, Liu HS, Ho CM: Prophylactic antiemetic effect of dexamethasone in women undergoing ambulatory laparoscopic surgery. Br J Anaesth 2000; 84:459–62
16. Malins AF, Field JM, Nesling PM, Cooper GM: Nausea and vomiting after gynaecological laparoscopy: Comparison of premedication with oral ondansetron, metoclopramide and placebo. Br J Anaesth 1994; 72:231–3

17. Paxton LD, McKay AC, Mirakhur RK: Prevention of nausea and vomiting after day case gynaecological laparoscopy: A comparison of ondansetron, droperidol, metoclopramide and placebo. Anaesthesia 1995; 50:403–6

18. Millar JM, Hall PJ: Nausea and vomiting after prostaglandins in day case termination of pregnancy: The efficacy of low dose droperidol. Anaesthesia 1987; 42:613–8

19. Aasboe V, Raeder JC, Groegaard B: Betamethasone reduces postoperative pain and nausea after ambulatory surgery. Anesth Analg 1998; 87:319–23

20. Scuderi PE, James RL, Harris L, Mims GR III: Antiemetic prophylaxis does not improve outcomes after outpatient surgery when compared to symptomatic treatment. ANESTHESIOLOGY 1999; 90:360–71

21. Bailey PL, Streisand JB, Pace NL, Bubbers SJ, East KA, Mulder S, Stanley TH: Transdermal scopolamine reduces nausea and vomiting after outpatient laparoscopy. ANESTHESIOLOGY 1990; 72:977–80

22. Huang JC, Shieh JP, Tang CS, Tzeng JI, Chu KS, Wang JJ: Low-dose dexamethasone effectively prevents postoperative nausea and vomiting after ambulatory laparoscopic surgery. Can J Anaesth 2001; 48:973–7

23. Wilson EB, Bass CS, Abrameit W, Roberson R, Smith RW: Metoclopramide versus ondansetron in prophylaxis of nausea and vomiting for laparoscopic cholecystectomy. Am J Surg 2001; 181:138–41

24. Tzeng JI, Tswei TS, Tang CS, Ho ST, Wang JJ: Dexamethasone alone does not prevent postoperative nausea and vomiting in women undergoing dilatation and curettage: A comparison with droperidol and saline. Acta Anaesthesiol Sin 2000; 38:137–42

25. Tang J, Wang B, White PF, Watcha MF, Qi J, Wender RH: The effect of timing of ondansetron administration on its efficacy, cost-effectiveness, and cost-benefit as a prophylactic antiemetic in the ambulatory setting. Anesth Analg 1998; 86:274–82

26. Scuderi PE, James RL, Harris L, Mims GR III: Multimodal antiemetic management prevents early postoperative vomiting after outpatient laparoscopy. Anesth Analg 2000; 91:1408–14

27. Ahmed AB, Hobbs GJ, Curran JP: Randomized, placebo-controlled trial of combination antiemetic prophylaxis for day-case gynaecological laparoscopic surgery. Br J Anaesth 2000; 85:678–82

28. McKenzie R, Kovac A, O'Connor T, Duncalf D, Angel J, Gratz I, Tolpin E, McLeskey C, Joslyn A: Comparison of ondansetron versus placebo to prevent postoperative nausea and vomiting in women undergoing ambulatory gynecologic surgery. ANESTHESIOLOGY 1993; 78:21–8

29. Wu O, Belo SE, Koutsoukos G: Additive anti-emetic efficacy of prophylactic ondansetron with droperidol in out-patient gynecological laparoscopy. Can J Anaesth 2000; 47:529–36

30. Tang J, Watcha MF, White PF: A comparison of costs and efficacy of ondansetron and droperidol as prophylactic antiemetic therapy for elective outpatient gynecologic procedures. Anesth Analg 1996; 83:304–13

31. Pritchard JF, Bryson JC, Kernodle AE, Benedetti TL, Powell JR: Age and gender effects on ondansetron pharmacokinetics: Evaluation of healthy aged volunteers. Clin Pharmacol Ther 1992; 51:51–5

32. Henzi I, Walder B, Tramer MR: Dexamethasone for the prevention of postoperative nausea and vomiting: A quantitative systematic review. Anesth Analg 2000; 90:186–94

33. Hill RP, Lubarsky DA, Phillips-Bute B, Fortney JT, Creed MR, Glass PSA, Gan TJ: Cost-effectiveness of prophylactic antiemetic therapy with ondansetron, droperidol, or placebo. ANESTHESIOLOGY 2000; 92:958–67

34. 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

35. Apfel CC, Kranke P, Katz MH, Goepfert C, Papenfuss T, Rauch S, Heineck R, Greim CA, Roewer N: Volatile anaesthetics may be the main cause of early but not delayed postoperative vomiting: a randomized controlled trial of factorial design. Br J Anaesth 2002; 88:659–68

36. Hammas B, Thorn SE, Wattwil M: Superior prolonged antiemetic prophylaxis with a four-drug multimodal regimen: Comparison with propofol or placebo. Acta Anaesthesiol Scand 2002; 46:232–7

37. Egger M, Zellweger-Zahner T, Schneider M, Junker C, Lengeler C, Antes G: Language bias in randomised controlled trials published in English and German. Lancet 1997; 350:326–9