

**Bon Secours Richmond
Pharmacy & Therapeutics Committees
Antiemetic Prophylaxis and Treatment of Postoperative and Opioid-Induced Nausea and Vomiting
7/2005**

Recommendations:

- Droperidol is recommended as a first-line agent for the prevention of opioid-induced nausea and vomiting.
- Surgical patients should be assessed and stratified for their risk of postoperative nausea and vomiting (PONV). The patients score should be noted in the anesthesia notes or on the anesthesia record.

Prophylaxis For Patients At Risk For PONV		
Risk Factors for PONV: female, history of PONV/motion sickness, opioid therapy, non-smoker		
<u>Number of Risk Factors</u>	<u>Risk Classification</u>	<u>Incidence of PONV</u>
0-1	Low	10-21%
2-3	Moderate	39-60%
3-4	High	61-79%
Recommended Prophylaxis:		
<u>Low Risk</u>	<u>Moderate Risk</u>	<u>High Risk</u>
<p>NONE <u>OR</u> One of the following agents:</p> <p>Dexamethasone 8-10mg IV Droperidol 0.625mg IV 5HT3 receptor antagonist</p>	<p><u>Monotherapy:</u> use one of the agents listed under “Low Risk”</p> <p><u>Combination therapy:</u> Dexamethasone 8-10mg IV <u>plus</u> one of the following agents: Droperidol 0.625mg IV <u>OR</u> 5HT3 receptor antagonist</p>	<p>Dexamethasone 8-10mg IV <u>plus</u> Droperidol 0.625mg IV <u>plus</u> 5HT3 receptor antagonist</p> <p>NOTE: Use 3 or more agents from different classes in high risk patients</p>
<p><u>First line agents</u> (dexamethasone, droperidol, 5HT3 antagonist) reduce incidence of PONV by approximately 26%. When first line agents are combined the same % reduced is produced by each additional agent administered. N Engl J Med. 2004 Jun 10;350(24):2441-51</p> <p>For <u>alternative agents</u> choose one of the following: Prochlorperazine 10mg IV, Promethazine 12.5mg-25mg IV, Metoclopramide 10 mg IV, or Scopolamine patch 1.5 mg apply evening before or 4 hours before end of surgery.</p>		
PACU Treatment of Patients With PONV Based on Initial Prophylaxis		
Initial Prophylaxis None	Initial Prophylaxis 5HT3 receptor antagonist	Initial Prophylaxis Combination (5HT3 receptor antagonist + 2 other 1 st line agents)
Droperidol 0.625 mg IV or 5 HT3 antagonist IV or alternative agent +/- Dexamathasone 8-10 mg IV	Droperidol 0.625 mg IV or alternative agent +/- Dexamethasone 8-10 mg IV	Repeat one or more first line agents (except dexamethasone) +/- alternative agent
Using an agent from another class is more 1.4-1.7 times effective for treatment of PONV than repeating the previously administered agent if nausea and vomiting occurs in PACU.		

Table 3. Estimated Incidence of Postoperative Nausea and Vomiting as a Function of Baseline Risk, on the Basis of the Assumption That Each Intervention Reduces the Relative Risk by 26 Percent.

Baseline Risk (No Intervention)*	Estimated Incidence of Postoperative Nausea and Vomiting			
	One Intervention	Two Interventions	Three Interventions	Four Interventions
	<i>percent</i>			
10%	7	5	4	3
20%	15	11	8	6
40%	29	22	16	12
60%	44	33	24	18
80%	59	44	32	24

* The baseline risk levels of 10 percent, 20 percent, 40 percent, 60 percent, and 80 percent reflect the presence of 0, 1, 2, 3, and 4 risk factors, respectively, according to a simplified risk score.¹⁷

- Preprinted physician order forms will be updated to include the following for opioid-induced nausea and vomiting.
 - At each episode of nausea or vomiting try drug below before 5HT3 antagonist (granisetron)
 - Droperidol 0.625 mg IV q 4 hours prn nausea or vomiting
 - Prochlorperazine 10 mg IV q 4 hours prn nausea or vomiting
 - Promethazine 12.5 mg IV q 4 hours prn nausea or vomiting
 - Metoclopramide 10 mg IV q 4 hours prn nausea or vomiting
 - If no response from ordered drug above
 - Granisetron 0.1 mg IV q 4 hours prn nausea or vomiting
- A single injection of dexamethasone 8-10 mg is recommended at induction of anesthesia for surgical patients to prevent PONV and opioid induced nausea and vomiting. It is as effective as multiple doses of droperidol in patients using PCA.
- The PCA order form will be updated to include medications for prevention and treatment of nausea and vomiting.
 - Dexamethasone 10 mg IV x 1 before start of PCA, if not administered perioperatively.
 - At each episode of nausea or vomiting try drug below before 5HT3 antagonist (granisetron)
 - Droperidol 0.625 mg IV q 4 hours prn nausea or vomiting
 - Prochlorperazine 10 mg IV q 4 hours prn nausea or vomiting
 - Promethazine 12.5 mg IV q 4 hours prn nausea or vomiting
 - Metoclopramide 10 mg IV q 4 hours prn nausea or vomiting
 - If no response from ordered drug above
 - Granisetron 0.1 mg IV q4 hours prn nausea or vomiting

Cost per Dose of Selected Antiemetics	
Dexamethasone 10 mg Inj.	\$1.23
Droperidol 2.5 mg Inj.	\$1.17
Kytril 0.1 mg Inj.	\$9.32
Prochlorperazine 10mg Inj	\$1.89
Promethazine 25 mg Inj	\$0.93
Zofran 4 mg Inj.	\$16.61

Annualize Cost for Equivalent Number of Doses				
	MRMC	RCH	SMH	Total
Kytril 0.1 mg	\$105,046	\$4,170	\$382,182	\$491,399
Zofran 4 mg	\$143,669	\$5,704	\$522,704	\$672,079

Using best possible purchase price for both agents

Findings:

- The most effective drugs for prevention of PONV and opioid induced nausea and vomiting are dexamethasone, droperidol, and 5HT3 antagonists; NNT is approximately 5 for these agents.
- Metoclopramide does not display a dose-response curve; 10 mg IV is the best documented dose in adults; it is approximately half as effective as droperidol, 5HT3 antagonists, and dexamethasone. The NNT is 9 to prevent early and late vomiting. It does not have significant anti nausea effects. Br J Anaesth. 1999 Nov;83(5):761-71.
- The combinations of dexamethasone with droperidol or a 5HT3 antagonist are equally effective for PONV.
- Droperidol does not display a dose response curve when used for PONV; 0.625 mg is the recommended dose.
- Droperidol in low doses, less than 0.625 mg, is effective for opioid induced pruritus.
- A single dose of dexamethasone 8-12 mg is as effective as multiple doses of droperidol for prophylaxis of opioid induced nausea and vomiting (PCA) for post surgical patients. Anesth Analg. 2004 Apr;98(4):1066-71. Dexamethasone decreases early (0-6 hours) and late PONV (0-24 hours) and has a biological half-life of 36-72 hours.
- Using an agent from another class is 1.4-1.7 times more effective for treatment of PONV than repeating the previously administered medication, if nausea and/or vomiting occurs in PACU. J Clin Anesth. 2005 Feb;17(1):62-5.
- In patients who do not achieve adequate control of postoperative nausea and vomiting following a single prophylactic dose of ondansetron 4 mg IV, administration of a second IV dose of 4 mg postoperatively does not provide additional control of nausea and vomiting. (Zofran package insert)
- Treatment of Postoperative Nausea and Vomiting in Adult Patients who received no prophylactic regimen per the package insert: NNT 5.5 for Zofran 4 mg, NNT 5.5 Kytril 0.1 mg.

Background:

Opioid-induced nausea and vomiting:

- The incidence of nausea and vomiting associated with various opioids has been reported as follows: morphine (18.3-28%), buprenorphine (8.3-22.7%), codeine (16.2-29.7%), and oxycodone (10-40%).¹
- Nausea affects 40-70% of cancer patients receiving opioids for pain control.²
- Route of administration of the opioids agent can contribute to the occurrence of nausea and vomiting- IM has lower emetic potential than IV (however, IV has higher potency than IM).³ Oral antiemetics should be reserved for patients with nausea without vomiting or for prophylaxis.
- Female patients are more likely to experience opioid-induced nausea and vomiting.³
- Opiates induce nausea and vomiting by the following mechanisms:
 - Direct activation of the chemoreceptor trigger zone (CTZ) in the area postrema of the medulla, with action conveyed to the vomiting center;
 - Increased sensitivity of vestibular function and indirect stimulation of the CTZ, with action conveyed to the vomiting center;
 - Decreased stomach motility, prolongation of gastric emptying time, and increased possibility of esophageal reflux.

Anatomic location and receptor site of clinical emetic stimuli in humans²:

Anatomic Site	Clinical Stimuli	Receptors Activated	Most Common Antiemetic therapy
Area postrema	Medications (dopamine agonists, digoxin, opiates , nicotine, cytotoxics); metabolic (uremia, DKA, hypoxemia, ↑Ca); bacterial toxins; radiation	dopaminergic, serotonergic, histaminergic, muscarinic, vasopressinergic	Antidopaminergics; ? 5HT ₃ antagonists
Labyrinths	Motion sickness; Meniere disease; labyrinthine tumors or infections	histaminergic, muscarinic	Antihistamines; anticholinergics
Peripheral afferents	Gastric irritants; nasogastric stimuli; chemotherapy; abdominal irradiation	serotonergic	5HT ₃ antagonists
Cerebral cortex Somatic pain	Noxious odors; visions; tastes	Poorly characterized	

Common antiemetics and their receptor and site of action⁴:

Antiemetic class	Antiemetic agent/s	Receptor type	Site of Action
Benzamides	Metoclopramide (Reglan [®])	dopamine	GI and CNS
Phenothiazines	Prochlorperazine (Compazine [®]), Promethazine (Phenergan [®])	dopamine	GI and CNS
Butyrophenones	Haloperidol (Haldol [®]), Droperidol (Inapsine [®])	dopamine	GI and CNS
Antihistamines	Diphenhydramine (Benadryl [®]), Meclizine (Antivert [®])	histamine	CNS
Anticholinergics	Scopolamine	acetylcholine	CNS
Serotonin antagonists	Granisetron (Kytril [®]), Ondansetron (Zofran [®])	serotonin	GI and CNS
Cannabinoids	Dronabinol (Marinol [®])	unknown	CNS
Corticosteroids	Dexamethasone (Decadron [®])	unknown	GI

Literature Review:

Prophylaxis:

Overview

- A quantitative review of studies reviewing antiemetics for the prevention of nausea and vomiting induced by morphine for post-op pain yielded the following results⁵:
 - Three drugs were effective for prophylaxis with respect to PONV: dexamethasone (OR 0.23, 95% CI 0.15-0.35) from 6 studies, droperidol (OR 0.27, 95%CI 0.21-0.34) from 11 studies, and metoclopramide (OR 0.48, 95% CI 0.3-0.75) from 5 studies.
 - Dexamethasone was the most effective agent and was shown to decrease the incidence of nausea and vomiting from 56-80% to 16-50% with a dose of 1.25-10mg.
 - 5HT3 antagonists showed no significant difference in relief of nausea and vomiting, but patient numbers were small and further studies were recommended.

Metoclopramide

- The antiemetic effect of metoclopramide and ondansetron used in conjunction with intrathecal morphine was studied in 73 patients undergoing orthopedic surgery. Patients were randomized to receive metoclopramide 20mg q 6 hours x 3 doses; ondansetron 8mg q12 hours x 2 doses; or saline x 3 doses. The incidences of nausea and vomiting over a 24 hour period were 60% and 56% in the saline group; 52% and 48% in the metoclopramide group; and 52% and 40% in the

ondansetron group. It was concluded that metoclopramide and ondansetron were no better than saline in the prevention of post-operative emesis induced by intrathecal morphine.⁶

- The effect of metoclopramide on the incidence of nausea and vomiting in patients receiving morphine or meperidine in the emergency department was studied in 122 patients. Patients were randomized to receive either metoclopramide 10mg or saline as an IV bolus immediately following the morphine or meperidine. Only 7 patients total experienced nausea and vomiting. Because of the low incidence of nausea and vomiting in this patient population, it was concluded that prophylactic metoclopramide should not be used. Also, the frequency of other side effects was higher in the metoclopramide group (7.9% vs 3.4% in the saline group).⁷
- In a best evidence topic report, 405 studies were evaluated to answer the following question: In patients treated with opioids is metoclopramide better than nothing in reducing nausea and vomiting? Only one study was relevant for inclusion (see bullet above). It was concluded that there was insufficient evidence to support prophylactic metoclopramide in patients taking opioids.⁸

Droperidol

- The antiemetic effect of droperidol mixed with morphine (in patient-controlled analgesia- PCA (5 mcg per mg, 15 mcg per mg, 50 mcg per mg, droperidol to morphine respectively) was shown to be antiemetic at the two higher doses with an increased incidence of sedation at the highest dose.⁹

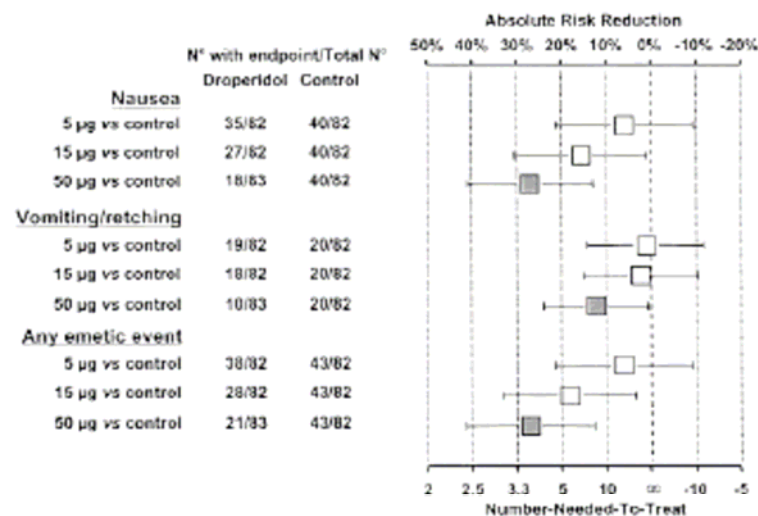


Figure 2. Antiemetic efficacy of three droperidol patient-controlled analgesia regimens (5, 15, and 50 µg/mg of morphine) compared with no treatment (control). Horizontal bars are 95% confidence intervals.

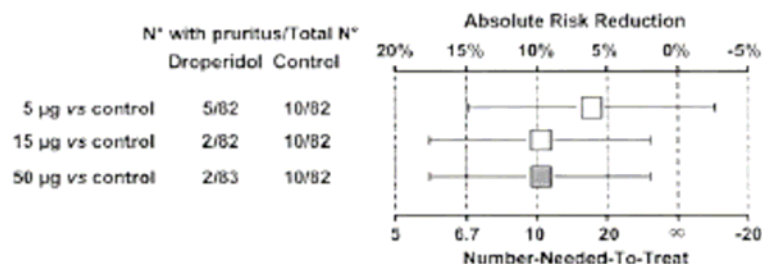


Figure 3. Pruritus with three droperidol patient-controlled analgesia regimens (5, 15, and 50 µg/mg of morphine) compared with no treatment (control). Horizontal bars are 95% confidence intervals.

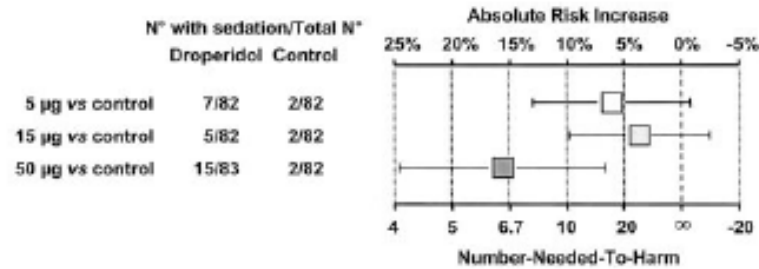


Figure 4. Sedation (score 2 = drowsy and disoriented or 3 = asleep but rousable) with three droperidol PCA regimens (5, 15, and 50 µg/mg of morphine) compared with no treatment (control). Horizontal bars are 95% confidence intervals.

- A second study comparing the effects of high-dose ondansetron vs droperidol mixed with morphine PCA in patients undergoing hysterectomy showed no significant difference in the antiemetic effect of either agent. At the high dose of ondansetron (4mg induction and 0.32mg per 1mg of morphine), the course of therapy was expensive with no clinical benefit over the droperidol group (1.25mg induction and 0.1mg per 1mg morphine).¹⁰ 80% of patients in each group never vomited and equivalent doses of rescue agent was administered. The droperidol group used significantly less morphine at 4, 8 and 12 hours with equivalent pain relief.

5HT3 Antagonists

- See first bullet under metoclopramide above.
- 70 women undergoing hysterectomy under epidural anesthesia were randomized to receive either 4mg of ondansetron or saline following surgery. One minute later all of the patients received morphine through the epidural catheter. The incidence of nausea and vomiting was significantly reduced by 22% in the ondansetron group vs 52% in the saline group. Rescue medications were required in 12% of the ondansetron patients and 39% of the saline patients.¹¹

Scopolamine

- In a prospective pilot study, 9 of 13 cancer patients experienced rapid relief of their opioid-induced nausea when they used a scopolamine patch alone. Further trials with larger number of patients are needed to establish whether transdermal scopolamine is useful for opioid-induced nausea.¹²

Dexamethasone

Anesth Analg. 2004 Apr;98(4):1066-71

A dose ranging study of dexamethasone for preventing patient-controlled analgesia-related nausea and vomiting: a comparison of droperidol with saline.

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We designed this study to determine the minimum dose of dexamethasone for preventing nausea and vomiting associated with the use of morphine by patient-controlled analgesia (PCA). Two hundred forty female patients were randomly assigned to receive dexamethasone 2, 4, 8, or 12 mg IV immediately before induction of anesthesia. Droperidol (0.1 mg/mL with morphine 1 mg/mL in PCA pump) and saline were used as controls. The complete response (no postoperative nausea and vomiting and no need for rescue antiemetic for a 24-h postoperative period) rates for dexamethasone 8 mg (72.2%) and 12 mg (78.9%) were significantly more than

for saline (42.9%) ($P < 0.05$). Patients who received dexamethasone 12 or 8 mg also reported higher patient satisfaction than those who received saline ($P < 0.05$). These results were as effective as adding droperidol 0.1 mg/mL to the morphine PCA without causing drowsiness, restlessness, or arrhythmias. Smaller doses of dexamethasone (4 or 2 mg) were not effective for this purpose. The results suggest that dexamethasone 8 mg IV is the minimum effective dose for the reduction of PCA morphine-related nausea and vomiting. **IMPLICATIONS:** Morphine administration by patient-controlled analgesia (PCA) is often associated with nausea and vomiting. In this double-blind study, the minimum effective dose of dexamethasone for reducing this complication was 8 mg. This was as effective as adding droperidol 0.1 mg/mL to the morphine PCA without causing drowsiness, restlessness or arrhythmias.

Table 3. Complete Response (no PONV, no Rescue Antimetic), Requirement for Rescue Antimetics, Pain Score and Patient Satisfaction in the First 24 h Postoperatively

	Groups					
	Dexamethasone 12 mg ($n = 38$)	Dexamethasone 8 mg ($n = 36$)	Dexamethasone 4 mg ($n = 38$)	Dexamethasone 2 mg ($n = 36$)	Droperidol 0.1 mg.ml ⁻¹ ($n = 37$)	Saline ($n = 35$)
Complete response	30 (78.9)*‡	26 (72.2)*‡	22 (57.9)†	15 (41.7)†	30 (81.1)*	15 (42.9)
Rescue antiemetics	5 (13.2)*‡	6 (16.7)*‡	12 (31.6)†	17 (47.2)†	4 (10.8)*	16 (45.7)
Morphine consumption	37.3 ± 15.5	38.6 ± 14.6	35.8 ± 12.2	32.4 ± 16.3	36.5 ± 15.8	31.2 ± 16.7
Satisfaction score	7.5 ± 1.6*‡	7.4 ± 1.5*‡	6.9 ± 1.4	6.6 ± 1.3†	7.7 ± 1.6*	6.1 ± 2.3
Satisfaction score ≥ 8	24 (63.2)*‡	22 (61.1)*‡	17 (44.7)†	12 (33.3)†	26 (70.3)*	12 (34.3)

Values are mean ± sd or number (percentage).

$P < 0.05$ compared with *saline group, †droperidol group, and ‡dexamethasone 2 mg group.

Complete response = no postoperative nausea and vomiting, no rescue emetic.

Anaesthesia. 2002 Jul;57(7):705-9.

The effect of dexamethasone upon patient-controlled analgesia-related nausea and vomiting.

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Ninety female patients were enrolled in this randomised, double-blind, placebo

-controlled study to compare the anti-emetic effect of intravenous dexamethasone 8 mg with saline control in preventing patient-controlled analgesia-related nausea and vomiting following major orthopaedic surgery. The prophylactic administration of dexamethasone 8 mg significantly reduced the overall incidence of patient-controlled analgesia-related nausea and vomiting ($p < 0.001$) and the need for rescue anti-emetics ($p < 0.01$). Furthermore, patients who received dexamethasone showed a higher incidence of complete responses (no vomiting or need for rescue anti-emetic for a 24-h postoperative period) than those who received saline ($p < 0.05$). We conclude that dexamethasone 8 mg may be valuable for preventing patient-controlled analgesia-related nausea and vomiting in women undergoing major orthopaedic surgery.

Treatment:

5HT3 Antagonists

- In a study by Rung et al., 121 patients who experienced postsurgical nausea and vomiting were randomized to receive a single dose of ondansetron (0.1mg, 4mg, or 16mg IV) or placebo. Patients treated with 4mg and 16mg doses of ondansetron experienced significantly less emesis and received fewer doses of rescue antiemetics. Adverse effects were similar across all groups. It was concluded that IV ondansetron is effective for postsurgical opioid-induced nausea and vomiting.¹³
- In a study by Sussman et.al., 520 patients with nonsurgical pain (primarily back or neck pain) developed nausea or vomiting after opioid administration and were randomized to receive a single dose of 1 of 3 treatments: placebo (n=94), ondansetron 8mg (n=215), or ondansetron 16mg (n=211). Ondansetron showed a significant improvement in both nausea and vomiting over placebo.¹⁴
- Cancer patients who were receiving a full opioid agonist for pain were randomized to receive one of three treatments: oral ondansetron 24mg daily, metoclopramide 10mg three times a day, or placebo. Study medication was started only if the patient experienced nausea and/or vomiting following opioid administration. The study was ended early because of difficulty recruiting patients meeting these criteria. In the 92 patients studied, ondansetron and metoclopramide were no more effective than placebo in the control of opioid induced emesis in cancer patients.¹⁵

Summary:

- For prevention of opioid-induced nausea and vomiting, droperidol, dexamethasone, and ondansetron have been shown to be effective. Droperidol and ondansetron were equally effective; however, droperidol was less expensive than ondansetron, \$1.17 versus \$16.61. Decadron cost \$1.23 per 10 mg. Further evidence is necessary to support the use of metoclopramide or scopolamine in the prevention of opioid-induced nausea and vomiting.
- For treatment of opioid-induced nausea and vomiting, ondansetron is effective in surgical and nonsurgical pain when compared with placebo. Further studies are needed to determine if ondansetron and metoclopramide are effective for the control of opioid-induced emesis in cancer patients.

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Meta-analysis

J Clin Anesth. 2005 Feb;17(1):62-5.

The effectiveness of rescue antiemetics after failure of prophylaxis with ondansetron or droperidol: a preliminary report.

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STUDY OBJECTIVES: To compare the effectiveness of treating established postoperative nausea and vomiting (PONV) with an antiemetic acting at a different receptor with that of treating PONV with the antiemetic used for prophylaxis.

DESIGN: Analysis of data collected in a previously published randomized, double-blind, placebo-controlled study.

SETTING: Outpatient surgical procedures from 50 institutions in North America. **PATIENTS:** Patients (N = 2061)

undergoing outpatient surgical procedures planned to last no more than 2 hours. **INTERVENTIONS:** Patients were

randomized to receive ondansetron 4 mg, droperidol 1.25, droperidol 0.625 mg, or placebo. In the postoperative anesthesia care unit, patients who developed PONV received rescue antiemetics at the discretion of the attending anesthesiologist. The following antiemetics were used for rescue: ondansetron 4 mg, droperidol 0.625 to 1.25 mg, metoclopramide 10 mg, promethazine 6.25 to 25 mg, and dimenhydrinate 25 to 50 mg. **MEASUREMENTS:** The complete response rate (no nausea, no emesis, and no need for further rescue) after administration of the rescue antiemetic in patients with established PONV

was calculated. The complete response rate after administration of each of the different rescue antiemetics was compared with that after administration of the same antiemetic used for PONV prophylaxis. **MAIN RESULTS:** In patients who failed prophylaxis with ondansetron 4 mg, the complete response rate was significantly higher (P = .02) after rescue with promethazine 6.25 to 25 mg (78%) than after rescue with ondansetron 4 mg (46%). In patients who failed prophylaxis with droperidol 0.625 and 1.25 mg, the complete response rate was significantly higher after rescue with promethazine 6.25 to 25 mg (77%; P = .02) and dimenhydrinate 25 to 50 mg (78%; P = .04) than after rescue with droperidol 0.625 to 1.25 mg (56%).

CONCLUSION: In patients who failed prophylaxis with ondansetron or droperidol, promethazine was significantly more effective than the agent used for prophylaxis for the treatment of PONV. In patients who failed prophylaxis with droperidol, dimenhydrinate was also more effective than droperidol for the treatment of established PONV in the postoperative anesthesia care unit.

Anesthesiology. 2004 Dec;101(6):1454-63.

Is low-dose haloperidol a useful antiemetic?: A meta-analysis of published and unpublished randomized trials.

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The antiemetic efficacy of haloperidol was studied using data from 15 published (1962-1988) and 8 unpublished randomized trials; 1,397 adults received haloperidol, and 1,071 were controls. Settings were postoperative nausea or vomiting (1,994 patients), gastroenterology (261), chemotherapy (189), and radiation therapy (24). The relative benefit to prevent postoperative nausea or vomiting during 24 h with 0.5-4 mg haloperidol compared with placebo was 1.26-1.51 (number needed to treat, 3.2-5.1), without evidence of dose responsiveness; 0.25 mg was not antiemetic. With 1 mg haloperidol, the relative benefit to stop postoperative nausea or vomiting during 2-4 h compared with placebo was 1.53 (95% confidence interval, 1.17-2.00; number needed to treat, 6); with 2 mg, the relative benefit was 1.73 (1.11-2.68; number needed to treat, 4). In gastroenterology, 2 mg haloperidol was more effective than 1 mg. For chemotherapy and radiation therapy, no conclusions could be drawn. With 4 mg, one patient had extrapyramidal symptoms. With 5 mg, sedation was increased, with a relative risk of 2.09 (95% confidence interval, 1.73-2.52; number needed to treat, 4.4). There were no reports on cardiac toxicity. Postoperatively and in gastroenterology, haloperidol is antiemetic, with minimal toxicity. For other clinical settings and for children, valid data are unavailable.

Can J Anaesth. 2004 Apr;51(4):311-9.

The efficacy of the 5-HT₃ receptor antagonists combined with droperidol for PONV prophylaxis is similar to their combination with dexamethasone. A meta-analysis of randomized controlled trials.

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PURPOSE: The aim of this quantitative systematic review is to compare the efficacy and side effects of combining one of the 5-HT₃ receptor antagonists (5-HT₃) with droperidol or dexamethasone for postoperative nausea and vomiting (PONV) prophylaxis. **METHODS:** We performed a systematic search (Medline, Embase, and the Cochrane Library) for randomized

controlled trials that compared the antiemetic efficacy of combining one of the 5-HT₃ with droperidol or dexamethasone vs 5-HT₃ alone. Relevant endpoints were prevention of early (0 to 6 hr), and overall (0 to 24 hr) PONV, and side effects. The articles that could meet the inclusion criteria were scored for inclusion and methodological validity using the three-item, five-point, Oxford-scale. Relative risk and numbers needed-to-treat with 95% confidence intervals were calculated for each combination vs 5-HT₃ alone. The two combinations were then indirectly compared. A random effects model was used.

RESULTS: We considered 41 trials for analysis but subsequently excluded eight. Thirty-three trials with data from 3,447 patients were analyzed. Except for early nausea with the 5-HT₃ plus droperidol, both combinations were significantly more effective than 5-HT₃ in preventing early and overall PONV. There was no difference in antiemetic efficacy between the two combinations. The incidence of commonly reported side effects was also similar in the two combination groups.

CONCLUSION: We conclude that there is no statistically significant difference in antiemetic efficacy or side effects profile

when one of the 5-HT is combined with either droperidol or dexamethasone and that both combination regimens are significantly more effective than 5-HT alone.

Anesth Analg. 2002 Jul;95(1):133-43, table of contents.

The efficacy and safety of transdermal scopolamine for the prevention of postoperative nausea and vomiting: a quantitative systematic review.

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The role of scopolamine administered via transdermal therapeutic systems in the prevention of postoperative vomiting, nausea, and nausea and vomiting is unclear. We performed a systematic search for full reports of randomized comparisons of transdermal scopolamine with inactive control. Dichotomous data were extracted. In the meta-analysis, relative risks and numbers-needed-to-treat/harm were calculated with 95% confidence intervals (CI). In 23 trials, 979 patients received transdermal scopolamine, and 984 patients received placebo. Sensitivity analyses were performed using restricted data for truncated control event rates (40%-80%) and for large trials. With these data, the relative risks for postoperative vomiting (five reports), nausea (five reports), nausea and vomiting (eight reports), and rescue treatment (three reports) were 0.69 (95% CI, 0.58-0.82), 0.69 (95% CI, 0.54-0.87), 0.76 (95% CI, 0.66-0.88), and 0.68 (95% CI, 0.54-0.85), respectively. This means that of 100 patients who receive transdermal scopolamine, approximately 17 will not experience postoperative vomiting who would have done so had they all received a placebo. However, 18 of 100 patients will have visual disturbances, eight will report dry mouth, two will report dizziness, one will be classified as being agitated, and 1-13 patients who are prescribed transdermal scopolamine will not use it correctly. The timing of application does not alter efficacy. IMPLICATIONS: Of 100 patients who receive transdermal scopolamine, approximately 17 will not vomit in the postoperative period who would have done so had they all received a placebo. However, 18 of 100 patients will have visual disturbances, and eight will report dry mouth. Incorrect use further limits its efficacy.

Acta Anaesthesiol Scand. 2002 Mar;46(3):238-44.

Comment in: [Can J Anaesth. 2003 Jan;50\(1\):11-2](#), [Can J Anaesth. 2003 Jan;50\(1\):12-3](#).

Dimenhydrinate for prophylaxis of postoperative nausea and vomiting: a meta-analysis of randomized controlled trials.

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BACKGROUND: Diphenhydramine and its theoclate salt dimenhydrinate are traditional antiemetics still in use. However, so far the quantitative effect of dimenhydrinate in the prophylaxis of postoperative nausea and vomiting (PONV) has not been evaluated systematically. METHODS: Results from randomized controlled trials investigating the efficacy of dimenhydrinate vs. a control to prevent PONV were included in a meta-analysis. Studies were systematically searched through MEDLINE, EMBASE, the Cochrane-Library, manually screening of reference lists of matching review articles and current issues of locally available peer-reviewed anesthesia journals, up to June 2001. The numbers of patients with complete absence of PONV within 6 h and within 48 h after surgery were extracted as the main end point. Pooled relative benefits (RB) and numbers-needed-to-treat (NNT) with their corresponding 95% confidence intervals (CI) were calculated using a random effects model. This quantitative systematic review was performed following the recommendations of the QUORUM statement. In all, 18 trials with 3045 patients were included in the analysis: 1658 patients received a placebo (control) and 1387 patients received dimenhydrinate. RESULTS: The RB to stay completely free of PONV was 1.2 (95% CI: 1.1-1.4) for the early period (NNT = 8; 95% CI: 5-25) and 1.5 (1.3-1.8) for the overall investigated period (NNT = 5; 95% CI: 3-9). CONCLUSION: Dimenhydrinate is a traditional and inexpensive antiemetic with an efficacy that might be considered as clinically relevant. Although in use for a long time, the dose-response, precise estimation of side-effects, optimal time of administration and the benefit of repetitive doses still remain unclear.

Acta Anaesthesiol Scand. 2001 Jul;45(6):659-70.

Comment in: [Acta Anaesthesiol Scand. 2001 Jul;45\(6\):657-8](#).

The influence of a dominating centre on a quantitative systematic review of granisetron for preventing postoperative nausea and vomiting.

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BACKGROUND: We performed a meta-analysis on granisetron in the prevention of postoperative nausea and vomiting (PONV) and further investigated whether total results and the dose-response characteristics may be significantly affected by a single centre. METHODS: Systematically searched randomised controlled trials (RCT) using granisetron for the prevention of PONV after general anaesthesia were included in the analysis. The pooled relative risks (RR) and numbers needed to treat (NNT) with their corresponding 95%-confidence intervals (CI) were calculated. For all centres, one dominating centre and other centres pooled, comparisons were performed according to all doses, low dose (≤ 20 microg/kg) and high dose (> 20 microg/kg) granisetron. RESULTS: A total of 27 RCT with 2938 patients were included in the analysis. RR (CI) to suffer from PONV with granisetron when all comparisons were considered was 0.46 (0.39-0.54), 0.7 (0.6-0.81) and 0.34 (0.28-0.41) for all doses, low and high dose, respectively. RR of the dominating centre (1867 patients) were significantly better

compared to the remaining centres (1071 patients), with 0.41 (0.34-0.49) and 0.60 (0.49-0.73), respectively. In the dominating centre low dose granisetron was ineffective with a RR of 0.84 (0.68-1.04), while high dose granisetron led to a strong decrease with a RR of 0.30 (0.26-0.36). In contrast, the RR of other centres pooled for low and high dose granisetron were comparable with 0.62 (0.49-0.79) and 0.56 (0.42-0.75), respectively. CONCLUSIONS: Overall results and dose-response characteristics of meta-analyses may be significantly altered by one dominating centre. Further, if data of a dominating centre do not appear to be valid for other centres, it may seem advisable to either exclude them from the analysis or to perform sub-group analyses so that results without the data from the dominating centre are available.

Yakugaku Zasshi. 2001 Feb;121(2):179-85.

Evaluation of the effective drugs for the prevention of nausea and vomiting induced by morphine used for postoperative pain: a quantitative systematic review.

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Department of Hospital Pharmacy, Kitasato University East Hospital, 2-1-1 Asamizodai, Sagami-hara 228-8520, Japan. Postoperative nausea and vomiting (PONV) with morphine therapy develops in more than 60% of patients after surgery, markedly reducing patient QOL. The prophylactic effect of several antiemetics has already been studied, but evaluations, and even those using the same drug, are not uniform. The present research involved a meta-analysis of randomized controlled trials on prophylactic drug therapy for PONV in patients receiving morphine for the treatment of postoperative pain. The efficacy of the prophylactic administration of the drugs was examined. As a result, meta-analysis of five drugs was possible and the evidence of efficacy was shown for three drugs ranked in order of an increasing odds ratio (OR) and confidence interval (CI): dexamethasone (OR: 0.23, 95% CI: 0.15-0.35, $p < 0.00001$), droperidol (OR: 0.27, 95% CI: 0.21-0.34, $p < 0.00001$), and metoclopramide (OR: 0.48, 95% CI: 0.30-0.75, $p < 0.001$). These results suggest that the three drugs are effective in prophylactic treatment for PONV. Of them, dexamethasone used as a prophylactic drug for PONV provided the best results. Dexamethasone was shown to reduce the incidence of PONV from 66-80% to 16-50% with a dose of 1.25 to 10 mg and to be suitable as a first drug of choice.

Eur J Anaesthesiol. 2001 Jun;18(6):346-57.

Pharmacological control of opioid-induced pruritus: a quantitative systematic review of randomized trials.

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BACKGROUND AND OBJECTIVE: Numerous drugs have been used to prevent or to treat opioid-induced pruritus in the surgical setting. Their relative efficacy is not well understood. METHODS: The methods employed involved the systematic search (MEDLINE, EMBASE, Cochrane library, bibliographies, without language restriction, up to June 2000) for full reports of randomized comparisons of any intervention which is thought to be anti-pruritic (active) compared with placebo or no treatment (control) in surgical (including labour) patients receiving opioids. The number of patients who had no pruritus were analysed using relative risk and number-needed-to-treat with 95% confidence interval. RESULTS: Twenty-two trials (1477 patients) were analysed. Two trials (66 patients), both with low-dose propofol, were on treatment of established pruritus; propofol had no anti-pruritic effect compared with Intralipid. In prophylaxis trials, the average incidence of pruritus with control was 59% (range, 10% to 100%). Most mu-receptor antagonists were efficacious: intravenous naloxone 0.25-2.4 microg kg⁻¹ h⁻¹, relative risk 2.31 (95% confidence interval, 1.5 to 3.54), number-needed-to-treat to prevent pruritus compared with control 3.5; oral naltrexone 9 mg, relative risk 2.80 (1.35-5.80), number-needed-to-treat 1.7; naltrexone 6 mg was less effective and 3 mg did not work; different intravenous and epidural nalbuphine regimens, relative risk 1.71 (1.12-2.62), number-needed-to-treat 4.2. Intravenous nalmefene 0.5 or 1 mg was not anti-pruritic. Intravenous (but not epidural) droperidol 2.5 mg was efficacious, relative risk, 1.71 (1.28-2.29), number-needed-to-treat 4.9. There was a lack of evidence for any anti-pruritic efficacy with prophylactic propofol, epidural or intrathecal epinephrine, epidural clonidine, epidural prednisone, intravenous ondansetron, or intramuscular hydroxyzine. CONCLUSION: Naloxone, naltrexone, nalbuphine and droperidol are efficacious in the prevention of opioid-induced pruritus; minimal effective doses remain unknown. There is a lack of valid data on the efficacy of interventions for the treatment of established pruritus.

BMC Anesthesiol. 2001;1(1):2.

Treatment of established postoperative nausea and vomiting: a quantitative systematic review.

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BACKGROUND: The relative efficacy of antiemetics for the treatment of postoperative nausea and vomiting (PONV) is poorly understood. METHODS: Systematic search (MEDLINE, Embase, Cochrane Library, bibliographies, any language, to 8.2000) for randomised comparisons of antiemetics with any comparator for the treatment of established PONV.

Dichotomous data on prevention of further nausea and vomiting, and on side effects were combined using a fixed effect model. RESULTS: In seven trials (1,267 patients), 11 different antiemetics were tested without placebos; these data were not further analysed. Eighteen trials (3,809) had placebo controls. Dolasetron 12.5-100 mg, granisetron 0.1-3 mg, tropisetron 0.5-5 mg, and ondansetron 1-8 mg prevented further vomiting with little evidence of dose-responsiveness; with all regimens, absolute risk reductions compared with placebo were 20%-30%. The anti-nausea effect was less pronounced. Headache was

dose-dependent. Results on propofol were contradictory. The NK1 antagonist GR205171, isopropyl alcohol vapor, metoclopramide, domperidone, and midazolam were tested in one trial each with a limited number of patients.

CONCLUSIONS: Of 100 vomiting surgical patients receiving a 5-HT₃ receptor antagonist, 20 to 30 will stop vomiting who would not have done so had they received a placebo; less will profit from the anti-nausea effect. There is a lack of evidence for a clinically relevant dose-response; minimal effective doses may be used. There is a discrepancy between the plethora of trials on prevention of PONV and the paucity of trials on treatment of established symptoms. Valid data on the therapeutic efficacy of classic antiemetics, which have been used for decades, are needed.

Anesth Analg. 2000 Jan;90(1):186-94.

Dexamethasone for the prevention of postoperative nausea and vomiting: a quantitative systematic review.

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The role of dexamethasone in the prevention of postoperative nausea and vomiting (PONV) is unclear. We reviewed efficacy and safety data of dexamethasone for prevention of PONV. A systematic search (MEDLINE, EMBASE, Cochrane Library, hand searching, bibliographies, all languages, up to April 1999) was done for full reports of randomized comparisons of dexamethasone with other antiemetics or placebo in surgical patients. Relevant end points were prevention of early PONV (0 to 6 h postoperatively), late PONV (0 to 24 h), and adverse effects. Data from 1,946 patients from 17 trials were analyzed: 598 received dexamethasone; 582 received ondansetron, granisetron, droperidol, metoclopramide, or perphenazine; 423 received a placebo; and 343 received a combination of dexamethasone with ondansetron or granisetron. With placebo, the incidence of early and late PONV was 35% and 50%, respectively. Sixteen different regimens of dexamethasone were tested, most frequently, 8 or 10 mg IV in adults, and 1 or 1.5 mg/kg IV in children. With these doses, the number needed to treat to prevent early and late vomiting compared with placebo in adults and children was 7.1 (95% CI 4.5 to 18), and 3.8 (2.9 to 5), respectively. In adults, the number needed to treat to prevent late nausea was 4.3 (2.3 to 26). The combination of dexamethasone with ondansetron or granisetron further decreased the risk of PONV; the number needed to treat to prevent late nausea and vomiting with the combined regimen compared with the 5-HT₃ receptor antagonists alone was 7.7 (4.8 to 19) and 7.8 (4.1 to 66), respectively. There was a lack of data from comparisons with other antiemetics for sensible conclusions. There were no reports on dexamethasone-related adverse effects. **IMPLICATIONS:** When there is a high risk of postoperative nausea and vomiting, a single prophylactic dose of dexamethasone is antiemetic compared with placebo, without evidence of any clinically relevant toxicity in otherwise healthy patients. Late efficacy seems to be most pronounced. It is very likely that the best prophylaxis of postoperative nausea and vomiting currently available is achieved by combining dexamethasone with a 5-HT₃ receptor antagonist. Optimal doses of this combination need to be identified.

Can J Anaesth. 2000 Oct;47(10):1008-18.

5-HT₃ receptor antagonists vs traditional agents for the prophylaxis of postoperative nausea and vomiting.

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PURPOSE: Numerous antiemetics have been studied for the prevention of postoperative nausea and vomiting (PONV) including traditional agents (metoclopramide, perphenazine, prochlorperazine, cyclizine and droperidol) and the 5-HT₃ receptor antagonists (ondansetron, dolasetron, granisetron and tropisetron). The results have been divergent and inconsistent. The purpose of this quantitative systematic review was to evaluate the effectiveness of 5HT₃ receptor antagonists compared to traditional antiemetics for the prevention of PONV **METHODS:** A systematic search of the English language literature using computerized MEDLINE, EMBASE, and Pre-MEDLINE databases from 1966 to October 1999 and a manual search of references from retrieved articles were performed. Individual efficacy and adverse effect data was extracted from each of the studies according to a predefined protocol. The summary odds ratios were calculated using the Dersimonian and Laird method under a random effects model. **RESULTS:** A total of 41 trials met our pre-defined inclusion criteria and were included in our analysis. Results in the 32 studies examining PONV indicated a 46% reduction in the odds of PONV in the 5-HT₃-treated group (0.54 [95% CI 0.42-0.71], P < 0.001). Evaluation of PONV by traditional antiemetic agent demonstrated a 39% reduction compared with droperidol (0.61 [95% CI 0.42-0.89], P < 0.001) and a 56% reduction compared with metoclopramide (0.44 [95% CI 0.31-0.62], P < 0.001). Results in the 34 studies examining vomiting indicated a 38% reduction in the odds of vomiting in the 5-HT₃-treated group (0.62 [95% CI 0.48-0.81], P < 0.001). **CONCLUSIONS:** The 5-HT₃ receptor antagonists are superior to traditional antiemetic agents for the prevention of PONV and vomiting. The reduction in the odds of PONV and vomiting is significant in the overall analysis and the subgroup analyses comparing 5-HT₃ receptor antagonists with droperidol and metoclopramide.

Acta Anaesthesiol Scand. 2000 Nov;44(10):1252-7.

Droperidol and 5-HT₃-receptor antagonists, alone or in combination, for prophylaxis of postoperative nausea and vomiting. A meta-analysis of randomised controlled trials.

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BACKGROUND: Droperidol and 5-HT₃-receptor antagonists are among the most potent antiemetics to prevent postoperative nausea and vomiting (PONV). Combinations of these drugs have been used to increase the efficacy of

antiemetic treatment. However, so far the quantitative effect of this combination has not been evaluated systematically. METHODS: Results from randomised controlled trials investigating the efficacy of 5-HT₃-receptor antagonists or droperidol alone versus the combination of both drugs to prevent PONV were included in a meta-analysis. Studies were systematically searched using Medline, EMBASE, the Cochrane-Library, and by manually screening the reference lists of matching review articles and current issues of locally available peer-reviewed anaesthesia journals. Seven papers with data on granisetron published by Fujii and co-workers were not considered. The main end point in each study was defined as occurrence of nausea, retching, or vomiting within 6 h ("early PONV") and within 48 h ("late PONV") after surgery. The relative risks (RR) and the numbers needed to treat (NNT) of the pooled data with their corresponding 95% confidence intervals (given in parentheses) were calculated using a random effects model. RESULTS: Eight studies with 881 patients (adults: n=801; children (mean age: 8 yr): n=80) were included in the analysis. Droperidol was applied to 340 patients, 5-HT₃-receptor antagonists to 198, and 343 were treated with a combination of both drugs. Seven out of these eight studies reported increased antiemetic efficacy of the combination group compared with the single drugs (droperidol and 5-HT₃-receptor antagonists respectively). However, in none of the trials did this difference reach statistical significance. When a meta-analytic analysis based on these results was performed the combination of droperidol with a 5-HT₃-receptor antagonist was not associated with a significantly increased antiemetic efficacy. In 12 to 13 patients a 5-HT₃-receptor antagonist has to be added to droperidol prophylaxis to prevent one additional patient from PONV who would have had suffered from PONV when treated with droperidol alone (RR "early PONV": 1.52 (0.95-2.44); RR "late PONV": 1.24 (0.89-1.74)). Similar results were obtained when the antiemetic effect of adding droperidol to a prophylaxis with 5-HT₃-receptor antagonists was analysed. In this case 10 to 12 patients have to be treated with the 5-HT₃-droperidol combination instead of with a 5-HT₃-receptor antagonist alone to prevent one additional patient from PONV (RR "early PONV": 1.55 (0.68-3.52); RR "late PONV": 1.29 (0.77-2.17)). There were no reports of an increased incidence of adverse effects. CONCLUSION: The data on the combination of droperidol with 5-HT₃-receptor antagonists suggest that there is a trend towards increased efficacy of the combination therapy compared to the single drugs. However, so far there are insufficient data to recommend this combination treatment for prophylaxis.

Anaesthesist. 2000 Aug;49(8):713-20.

[Dexamethasone for prophylaxis of postoperative nausea and vomiting. A meta-analysis of randomized controlled studies]

[Article in German]

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OBJECTIVE: Randomised controlled trials investigating the efficacy of dexamethasone alone or in combination with other antiemetics to prevent postoperative nausea and vomiting (PONV) were included in a meta-analysis to estimate the relative efficacy of these treatments. METHODS: Studies were systematically searched using Medline, EMBASE, the Cochrane-Library, and by manual screening the reference lists and current issues of locally available anaesthesia journals. Studies identified were divided into four different groups. For each subgroup an independent analysis was performed: 1. Dexamethasone vs. placebo, 2. Dexamethasone + other antiemetic vs. other antiemetic alone, 3. Dexamethasone + other antiemetic vs. dexamethasone alone, 4. Dexamethasone vs. other antiemetics. The main end point in each study was defined as complete absence of nausea, retching, and vomiting after prophylactic antiemetic treatment. The pooled odds-ratios, the relative risk (RR) and the numbers-needed-to-treat (NNT) with their corresponding 95%-confidence intervals (given in parentheses) were calculated using a random effects model. RESULTS: A total of 26 studies with 2561 patients were analysed. 1. As a sole antiemetic agent dexamethasone is superior to placebo to prevent PONV (RR: 0.49 (0.15-0.42); NNT: 3.4 (2.5-5.3)). 2. When dexamethasone and an other antiemetic (e.g. a 5-HT₃-antagonist) are combined this drug combination is significantly more effective than the single antiemetic without dexamethasone (RR: 0.60 (0.46-0.78); NNT: 7.3 (5.7-10.2)). 3. A similar result was obtained when the dexamethasone combination was compared with dexamethasone alone. The combination is statistically superior (RR: 0.16 (0.08-0.32); NNT: 3.2 (2.2-6.3)). 4. Dexamethasone was usually compared with 5-HT₃-antagonist and to a less extent also with dopamine antagonists. Summarising these studies, there was no significant difference concerning effectiveness (RR: 1.35 (0.99-1.85); NNT: 10.6 (5.6-92.6)). CONCLUSION: Dexamethasone has antiemetic effects that are superior to placebo treatment and are comparable with conventional antiemetic agents (e.g. 5-HT₃-antagonist, dopamine antagonists). The drug is especially useful in combination with other antiemetics and increases the efficacy of the antiemetic partner drug.

Br J Anaesth. 1999 Nov;83(5):761-71.

Metoclopramide in the prevention of postoperative nausea and vomiting: a quantitative systematic review of randomized, placebo-controlled studies.

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Metoclopramide has been used for almost 40 yr to prevent postoperative nausea and vomiting (PONV). We have reviewed the efficacy and safety of metoclopramide for the prevention of PONV. A systematic search (MEDLINE, EMBASE, manufacturers' databases, hand searching, bibliographies, all languages, up to June 1998) was performed for full reports of randomized comparisons of metoclopramide with placebo in surgical patients. Relevant end-points were prevention of early PONV (within 6 h after operation), late PONV (48 h) and adverse effects. Combined data were analysed using relative

benefit/risk and number-needed-to-treat/harm. In 66 studies, 3260 patients received 18 different regimens of metoclopramide, and 3006 controls received placebo or no treatment. There was no evidence of dose-responsiveness with oral, i.m., intranasal or i.v. metoclopramide in children and adults. In adults, the best documented regimen was 10 mg i.v. There was no significant anti-nausea effect. The numbers-needed-to-treat to prevent early and late vomiting were 9.1 (95% confidence intervals 5.5-27) and 10 (6-41), respectively. In children, the best documented regimen was 0.25 mg kg⁻¹ i.v. The number-needed-to-treat to prevent early vomiting was 5.8 (3.9-11). There was no significant late anti-vomiting effect. Minor drug-related adverse effects (sedation, dizziness, drowsiness) were not significantly associated with metoclopramide. There was one adult who experienced extrapyramidal symptoms with metoclopramide.

Anesthesiol Intensivmed Notfallmed Schmerzther. 1999 Sep;34(9):528-36.

[Meta-analysis of controlled randomized studies on droperidol for prevention of postoperative phase vomiting and nausea]

[Article in German]

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OBJECTIVE: Randomised, controlled trials using prophylactic droperidol to prevent postoperative nausea and vomiting (PONV) were included in a meta-analysis to estimate efficiency and dose-response of treatment. **MATERIALS AND METHODS:** Studies were systematically extracted from Medline, the manufacturer's database, and a supplemental search of references lists and current issues of locally available anaesthesia journals. Complete prevention of PONV defined as absence of nausea, retching, and vomiting within 6 hours (early PONV) and within 48 hours (late PONV) was chosen as the main end point. Additional information such as dose of droperidol, time and way of administration, and biometric data of the patients were extracted from each study. The pooled relative risk and the number-needed-to treat (NNT) were calculated. **RESULTS:** A total of 72 studies with 107 comparative subgroups were accepted for analysis according to the prospectively defined criteria. Of these sixty-nine trials reported a lower incidence of PONV with droperidol. The incidence of early and late PONV among the 5370 patients receiving droperidol was 23.4% and 38.2%, respectively. The corresponding incidence among the 3954 control patients was 40.7% and 53.9%. The relative risk for patients receiving prophylactic droperidol of suffering from early PONV was 0.58 and 0.71 for late PONV. The NNT for preventing one patient from PONV was 5.8 and 6.4 for early and late PONV, respectively. Treatment with droperidol was more effective when the baseline risk for PONV was higher than 25% for early PONV and 35% for late PONV. Under these circumstances the NNT was between 2.6 and 5.6. There was no dose response relationship for droperidol when the drug was applied in doses ranging from 0.5 to 300 micrograms.kg⁻¹ body weight. It was not possible to derive reliable information about the incidence of side-effects of the droperidol administration. **CONCLUSION:** Droperidol is an effective antiemetic drug. The drug can be administered to patients with an increased risk of suffering from PONV without antiemetic prophylaxis. Since a positive dose response is lacking, droperidol should only be administered in doses of 1 mg or less.

Eur J Anaesthesiol. 1999 Aug;16(8):556-64.

Prophylactic ondansetron for post-operative emesis: meta-analysis of its effectiveness in patients with and without a previous history of motion sickness.

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The post-operative anti-emetic efficacy of 4 and 8 mg of ondansetron in adult patients with and without a previous history of motion sickness (PHMS) was assessed by meta-analysis. MEDLINE and EMBASE databases were searched for randomized placebo-controlled trials evaluating the anti-emetic effectiveness of ondansetron in a 24-h period. In the 49 studies found, a further selection was with respect to those studies that noted the patient's previous history of motion sickness. Twelve trials involving 2122 patients; 446 previous history of motion sickness(+) patients and 1676 previous history of motion sickness(-) patients met the selection criteria. The dose of 4 mg ondansetron was 71.5% more effective in previous history of motion sickness(+) than in previous history of motion sickness(-) patients. For the 8 mg dose, the odds ratios (95% CI) were: previous history of motion sickness(+) = 3.11 (1.40-6.93) and previous history of motion sickness(-) = 2.08 (1.35-3.21). The calculated number needed to treat was also more favourable in previous history of motion sickness(+) patients for both doses of ondansetron, demonstrating a higher effectiveness in this subgroup of patients.

Acta Anaesthesiol Scand. 1999 Jul;43(6):637-44.

Prophylactic ondansetron for postoperative emesis. Meta-analysis of its effectiveness in patients with previous history of postoperative nausea and vomiting.

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BACKGROUND: The objective of this study was to compare, by means of meta-analysis, the postoperative antiemetic efficacy of ondansetron in patients with and without antecedents of postoperative nausea and vomiting. **METHODS:** MEDLINE and EMBASE databases were searched for randomised placebo-controlled trials which evaluated the antiemetic effectiveness of 4 mg and 8 mg intravenous doses of prophylactic ondansetron in adult patients. A further selection was with respect to those studies which noted the patient's previous history of postoperative nausea and vomiting (PH-PONV) and, for the meta-analysis, the patients were divided into two sub-groups: those with (PH-PONV +) and those without a previous

history of postoperative nausea and vomiting (PH-PONV -). Absence of vomiting was used as the index of effectiveness. RESULTS: Twenty-one trials involving 3984 patients (2446 in ondansetron groups and 1538 in placebo groups; 1163 PH-PONV(+) patients and 2821 PH-PONV(-) patients) met the selection criteria. The effectiveness of the 4 mg dose of ondansetron was: OR (95% CI)=2.40 (1.77-3.26) vs. 2.71 (2.23-3.30) for the patients of PH-PONV(+) and PH-PONV(-) subgroups, respectively. For the 8 mg dose, the effectiveness of ondansetron was: PH-PONV(+)=4.21 (2.66-6.66) and PH-PONV(-)=2.61 (1.81-3.59). For neither of the doses evaluated was there any significant statistical difference between the subgroups. CONCLUSIONS: The effectiveness of ondansetron in the prevention of postoperative vomiting is not affected by the patients' PH-PONV.

Anesth Analg. 1999 Jun;88(6):1370-9.

Comment in: [Anesth Analg. 1999 Dec;89\(6\):1589.](#) [Anesth Analg. 1999 Jun;88\(6\):1200-2.](#)

Comparative efficacy and safety of ondansetron, droperidol, and metoclopramide for preventing postoperative nausea and vomiting: a meta-analysis.

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Postoperative nausea and vomiting are important causes of morbidity after anesthesia and surgery. We performed a meta-analysis of published, randomized, controlled trials to determine the relative efficacy and safety of ondansetron, droperidol, and metoclopramide for the prevention of postoperative nausea and vomiting. We performed a literature search of English references using both the MEDLINE database and a manual search. Double-blinded, randomized, controlled trials comparing the efficiency of the prophylactic administration of ondansetron, droperidol, and/or metoclopramide therapy during general anesthesia were included. A total of 58 studies were identified, of which 4 were excluded for methodological concerns. For each comparison of drugs, a pooled odds ratio (OR) with a 95% CI was calculated using a random effects model. Ondansetron (pooled OR 0.43, 95% CI 0.31, 0.61; $P < 0.001$) and droperidol (pooled OR 0.68, 95% CI 0.54, 0.85; $P < 0.001$) were more effective than metoclopramide in preventing vomiting. Ondansetron was more effective than droperidol in preventing vomiting in children (pooled OR 0.49; $P = 0.004$), but they were equally effective in adults (pooled OR 0.87; $P = 0.45$). The overall risk of adverse effects was not different among drug combinations. We conclude that ondansetron and droperidol are more effective than metoclopramide in reducing postoperative vomiting. IMPLICATIONS: We performed a systematic review of published, randomized, controlled trials to determine the relative efficacy and safety of ondansetron, droperidol, and metoclopramide for preventing postoperative nausea and vomiting. Ondansetron and droperidol were more effective than metoclopramide in reducing postoperative vomiting. The overall risk of adverse effects did not differ.

Anesth Analg. 1999 Jun;88(6):1362-9.

Comment in: [Anesth Analg. 1999 Jun;88\(6\):1200-2.](#)

The use of nonpharmacologic techniques to prevent postoperative nausea and vomiting: a meta-analysis.

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We assessed the efficacy of nonpharmacologic techniques to prevent postoperative nausea and vomiting (PONV) by systematic review. These studies included acupuncture, electroacupuncture, transcutaneous electrical nerve stimulation, acupoint stimulation, and acupressure. Of the 24 randomized trials retrieved by a search of articles indexed on the MEDLINE and EMBASE databases (1980-1997), 19 were eligible for meta-analysis. The primary outcomes were the incidence of nausea, vomiting, or both 0-6 h (early efficacy) or 0-48 h (late efficacy) after surgery. The pooled relative risk (RR) and numbers needed to treat (NNT) were calculated. In children, no benefit was found. Some results in adults were significant. Nonpharmacologic techniques were similar to antiemetics in preventing early vomiting (RR = 0.89 [95% confidence interval 0.47-1.67]; NNT = 63 [10-infinity]) and late vomiting (RR = 0.80 [0.35-1.81]; NNT = 25 [5-infinity]) in adults. Nonpharmacologic techniques were better than placebo at preventing early nausea (RR = 0.34 [0.20-0.58]; NNT = 4 [3-6]) and early vomiting in adults (RR = 0.47 [0.34-0.64]; NNT = 5 [4-8]). Nonpharmacologic techniques were similar to placebo in preventing late vomiting in adults (RR = 0.81 [0.46-1.42]; NNT = 14 [6-infinity]). Using nonpharmacologic techniques, 20%-25% of adults will not have early PONV compared with placebo. It may be an alternative to receiving no treatment or first-line antiemetics. IMPLICATIONS: This systematic review showed that nonpharmacologic techniques were equivalent to commonly used antiemetic drugs in preventing vomiting after surgery. Nonpharmacologic techniques were more effective than placebo in preventing nausea and vomiting within 6 h of surgery in adults, but there was no benefit in children.

Anesth Analg. 1999 Jun;88(6):1354-61.

Comment in: [Anesth Analg. 1999 Jun;88\(6\):1200-2.](#) [Anesth Analg. 2000 Sep;91\(3\):763.](#)

Efficacy and adverse effects of prophylactic antiemetics during patient-controlled analgesia therapy: a quantitative systematic review.

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Nausea and vomiting are frequent adverse effects of patient-controlled analgesia (PCA) with opioids. To identify the optimal prophylactic antiemetic intervention in this setting, we performed a systematic search for randomized trials (MEDLINE, EMBASE, Cochrane library, reference lists, hand-searching, no language restriction) published up to May 1998 that compared prophylactic antiemetic interventions with placebo or no treatment in the postoperative PCA-setting with opioids.

Fourteen placebo-controlled trials (1117 patients) with different regimens of droperidol, ondansetron, hyoscine TTS, tropisetron, metoclopramide, propofol, and promethazine were analyzed. One PCA was with tramadol, all others were with morphine. At 24 h, the cumulative incidence of nausea and vomiting without antiemetics was approximately 50%. Droperidol 0.017-0.17 mg/mg of morphine (0.5-11 mg/d droperidol) was statistically significantly more effective than placebo without evidence of dose-responsiveness; the number needed to treat to prevent nausea compared with placebo was 2.7 (95% confidence interval 1.8-5.2), and that to prevent vomiting was 3.1 (2.3-4.8). Compared with placebo, the incidence of minor adverse effects with droperidol was increased with doses >4 mg/d. IMPLICATIONS: Of 100 patients treated with droperidol added in a patient-controlled analgesia pump with morphine, 30 who would have vomited or been nauseated had they not received droperidol will not suffer these effects. There is no evidence of dose-responsiveness for efficacy with droperidol, but the risk of adverse effects is dose-dependent. There is a lack of evidence for other antiemetics.

Br J Anaesth. 1997 Mar;78(3):247-55.

Propofol anaesthesia and postoperative nausea and vomiting: quantitative systematic review of randomized controlled studies.

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We have analysed randomized controlled studies which reported the incidence of postoperative nausea and vomiting (PONV) after propofol anaesthesia compared with other anaesthetics (control). Cumulative data of early (0-6 h) and late (0-48 h) PONV were recorded as occurrence or non-occurrence of nausea or vomiting. Combined odds ratio and number-needed-to-treat were calculated for propofol as an induction or maintenance regimen, early or late outcomes, and different emetic events. This was performed for all control event rates and within a range of 20-60% control event rates. We analysed 84 studies involving 6069 patients. The effect of propofol on PONV was dependent mainly on the method of administration, time of measurement and range of control event rates. When all studies were included the number-needed-to-treat to prevent PONV with propofol was more than 9 when used for induction of anaesthesia and at best 6 when used for maintenance. Within the 20-60% control event rate range, best results were achieved with propofol maintenance to prevent early PONV: the number-needed-to-treat to prevent early nausea was 4.7 (95% confidence interval 3.8-6.3), vomiting 4.9 (4-6.1) and any emetic event 4.9 (3.7-7.1). Within the 20-60% control event rate, of five patients treated with propofol for maintenance of anaesthesia, one will not vomit or be nauseated in the immediate postoperative period who would otherwise have vomited or been nauseated. This may be clinically relevant. In all other situations the difference between propofol and control may have reached statistical significance but was of doubtful clinical relevance. Treatment efficacy should be established within a defined range of control event rates for meaningful estimates of efficacy and for comparisons.

Br J Anaesth. 1996 Feb;76(2):186-93.

Omitting nitrous oxide in general anaesthesia: meta-analysis of intraoperative awareness and postoperative emesis in randomized controlled trials.

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We have reviewed randomized controlled trials to assess the effectiveness and safety of anaesthetics which omitted nitrous oxide (N₂O) to prevent postoperative nausea and vomiting (PONV). Early and late PONV (6 and 48 h after operation, respectively), and adverse effects were evaluated using the numbers-needed-to-treat (NNT) method. In 24 reports with information on 2478 patients, the mean incidence of early and late vomiting with N₂O (control) was 17% and 30%, respectively. Omitting N₂O significantly reduced vomiting compared with a N₂O regimen; the combined NNT to prevent both early and late vomiting with a N₂O-free regimen was about 13 (95% confidence intervals (CI) 9, 30). The magnitude of the effect depended on the incidence of vomiting in controls. In studies with a baseline risk higher than the mean of all reports, the NNT to prevent both early and late vomiting with a N₂O-free anaesthetic was 5 (95% CI 4, 10). When the baseline risk was lower than the mean, omitting N₂O did not improve outcome. Omitting N₂O had no effect on complete control of emesis or nausea. The NNT for intraoperative awareness with a N₂O-free anaesthetic was 46 compared with anaesthetics where N₂O was used. This clinically important risk of major harm reduces the usefulness of omitting N₂O to prevent postoperative emesis.

Droperidol

N Engl J Med. 2004 Jun 10;350(24):2441-51.

Comment in: [J Urol. 2005 Mar;173\(3\):887.](#)

- [N Engl J Med. 2004 Jun 10;350\(24\):2511-2.](#)
- [N Engl J Med. 2004 Sep 30;351\(14\):1458-9; author reply 1458-9.](#)
- [N Engl J Med. 2004 Sep 30;351\(14\):1458-9; author reply 1458-9.](#)

A factorial trial of six interventions for the prevention of postoperative nausea and vomiting.

[Apfel CC](#), [Korttila K](#), [Abdalla M](#), [Kerger H](#), [Turan A](#), [Vedder J](#), [Zernak C](#), [Danner K](#), [Jokela R](#), [Pocock SJ](#), [Trenkler S](#), [Kredel M](#), [Biedler A](#), [Sessler DI](#), [Roewer N](#); [IMPACT Investigators](#).

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BACKGROUND: Untreated, one third of patients who undergo surgery will have postoperative nausea and vomiting. Although many trials have been conducted, the relative benefits of prophylactic antiemetic interventions given alone or in combination remain unknown. **METHODS:** We enrolled 5199 patients at high risk for postoperative nausea and vomiting in a randomized, controlled trial of factorial design that was powered to evaluate interactions among as many as three antiemetic interventions. Of these patients, 4123 were randomly assigned to 1 of 64 possible combinations of six prophylactic interventions: 4 mg of ondansetron or no ondansetron; 4 mg of dexamethasone or no dexamethasone; 1.25 mg of droperidol or no droperidol; propofol or a volatile anesthetic; nitrogen or nitrous oxide; and remifentanyl or fentanyl. The remaining patients were randomly assigned with respect to the first four interventions. The primary outcome was nausea and vomiting within 24 hours after surgery, which was evaluated blindly. **RESULTS:** Ondansetron, dexamethasone, and droperidol each reduced the risk of postoperative nausea and vomiting by about 26 percent. Propofol reduced the risk by 19 percent, and nitrogen by 12 percent; the risk reduction with both of these agents (i.e., total intravenous anesthesia) was thus similar to that observed with each of the antiemetics. All the interventions acted independently of one another and independently of the patients' baseline risk. Consequently, the relative risks associated with the combined interventions could be estimated by multiplying the relative risks associated with each intervention. Absolute risk reduction, though, was a critical function of patients' baseline risk. **CONCLUSIONS:** Because antiemetic interventions are similarly effective and act independently, the safest or least expensive should be used first. Prophylaxis is rarely warranted in low-risk patients, moderate-risk patients may benefit from a single intervention, and multiple interventions should be reserved for high-risk patients. Copyright 2004 Massachusetts Medical Society

Table 3. Estimated Incidence of Postoperative Nausea and Vomiting as a Function of Baseline Risk, on the Basis of the Assumption That Each Intervention Reduces the Relative Risk by 26 Percent.

Baseline Risk (No Intervention)*	Estimated Incidence of Postoperative Nausea and Vomiting			
	One Intervention	Two Interventions	Three Interventions	Four Interventions
	<i>percent</i>			
10%	7	5	4	3
20%	15	11	8	6
40%	29	22	16	12
60%	44	33	24	18
80%	59	44	32	24

* The baseline risk levels of 10 percent, 20 percent, 40 percent, 60 percent, and 80 percent reflect the presence of 0, 1, 2, 3, and 4 risk factors, respectively, according to a simplified risk score.¹⁷

Baseline Risk of PONV	Number of Interventions Used To Prevent PONV			
	1	2	3	4
10%	38.5	22.1	16.8	14.3
20%	19.2	11.1	8.4	7.1
40%	9.6	5.5	4.2	3.6
60%	6.4	3.7	2.8	2.4
80%	4.8	2.8	2.1	1.8
	Number Needed to Treat (To Prevent One Case of PONV)			

Anesth Analg. 2003 Sep;97(3):816-21.

Erratum in: Anesth Analg. 2004 Jan;98(1):88.

The antiemetic efficacy of droperidol added to morphine patient-controlled analgesia: a randomized, controlled, multicenter dose-finding study.

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The antiemetic dose response of droperidol when it is added to patient-controlled analgesia with morphine is not well known. We randomly allocated adults who received postoperative morphine patient-controlled analgesia (1-mg bolus, 5-min lockout) to one of four regimens: no droperidol (control) or 5, 15, or 50 micro g of droperidol per milligram of morphine. Efficacy and adverse effects were recorded during 24 h and were analyzed with number needed to treat (NNT) and number needed to harm with 95% confidence intervals. Data from 82 controls, 82 patients receiving droperidol 5 micro g, 82 receiving droperidol 15 micro g, and 83 receiving droperidol 50 micro g were analyzed. Average consumption of droperidol per 24 h was 0.2 mg with the 5- micro g regimen, 0.61 mg with the 15- micro g regimen, and 2.04 mg with the 50- micro g regimen. In controls, the incidence of nausea was 48.8%; with droperidol 5 micro g, it was 42.7% (NNT compared with control, 16 [95% confidence interval, 4.7 to -11]); with 15 micro g, it was 32.9% (NNT, 6.3 [3.3-100]); and with 50 micro g, it was 21.7% (NNT, 3.7 [2.4 to 7.6]). In controls, the incidence of vomiting was 24.4%; with droperidol 5 micro g, it was 23.2% (NNT compared with control, 82 [7 to -8.5]); with 15 micro g, it was 22.0% (NNT, 41 [6.5 to -9.6]); and with 50 micro g, it was 12% (NNT, 8.1 [4.2-142]). In controls, the incidence of pruritus was 12.2%; with droperidol 5 micro g, it was 6.1% (NNT compared with control, 16 [6.7 to -37]); and with 15 and 50 micro g, it was 2.4% (NNT, 10 [5.7-52]). In controls, the incidence of sedation was 2.4%; with droperidol 5 micro g, it was 8.5% (number needed to harm (NNH) compared with control, 16 [7.7 to -123]); with 15 micro g, it was 6.1% (NNH, 27 [10 to -40]); and with 50 micro g, it was 18.1% (NNH, 6.4 [4.1-15]). There were no extrapyramidal symptoms and no cardiac adverse events. There was no difference in patient satisfaction. The optimal antiemetic dose of droperidol is 15-50 micro g/mg of morphine. Larger doses may have more antiemetic efficacy but are likely to be unacceptably sedating.

J Clin Anesth. 2002 Mar;14(2):121-5.

Continuous epidural, not intravenous, droperidol inhibits pruritus, nausea, and vomiting during epidural morphine analgesia.

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PURPOSE: To investigate whether continuous epidural droperidol and intravenous (IV) intraoperative droperidol inhibit pruritus and postoperative nausea and vomiting (PONV) during epidural morphine analgesia. **DESIGN:** Randomized, double-blinded, controlled study. **SETTING:** Metropolitan cancer center. **PATIENTS:** 120 ASA physical status I and II patients undergoing thoracic or abdominal surgery with general anesthesia combined with epidural anesthesia. **INTERVENTIONS:** Patients received an intraoperative epidural injection of 2 mg morphine hydrochloride, followed postoperatively by a continuous epidural infusion of morphine hydrochloride 4 mg/day for 4 days. Patients were randomly allocated to four groups: Group A = control group, Group B = intraoperative single IV injection of droperidol (2.5 mg), Group C = postoperative continuous epidural droperidol infusion (2.5 mg/day), and Group D = intraoperative IV injection of droperidol (2.5 mg) and postoperative continuous epidural droperidol infusion (2.5 mg/day). **MEASUREMENTS AND MAIN RESULTS:** The frequency and severity of pruritus and PONV in each group were evaluated during the postoperative period. Continuous epidural infusion of droperidol significantly reduced the frequency and severity of pruritus and PONV induced by epidural morphine without causing significant side effects. Intraoperative single IV injection of droperidol was effective for PONV ($p < 0.05$) but not for pruritus. **CONCLUSION:** Postoperative epidural droperidol infusion significantly decreased both the frequency and severity of pruritus and PONV during postoperative continuous epidural morphine analgesia. IV intraoperative droperidol significantly reduced the frequency and the severity of PONV but not pruritus.

Br J Anaesth. 1998 Sep;81(3):384-6.

High-dose ondansetron regimen vs droperidol for morphine patient-controlled analgesia.

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We have performed a randomized, double-blind study comparing droperidol and high-dose ondansetron mixed with morphine for patient-controlled analgesia (PCA). To detect a reduction in the incidence of postoperative nausea and vomiting from 55% to 20% with a power of 80% at the $P < 0.05$ level, 29 patients per group were required. We studied 60 healthy women undergoing abdominal hysterectomy, anaesthetized using a standard technique. Group D received a bolus dose of droperidol 1.25 mg at induction followed by droperidol 0.1 mg per 1 mg of morphine from the PCA system. Group O received a bolus dose of ondansetron 4 mg at induction followed by ondansetron 0.32 mg per 1 mg of morphine. This dose of ondansetron is more than double that studied previously. Mean nausea and vomiting scores at 4, 8, 12 and 24 h, mean time to first vomit, sedation scores, incidence of side effects, and doses of prochlorperazine did not differ between the groups. In group D, 24 patients did not vomit compared with 23 in group O. The only significant difference between the groups was increased morphine consumption in the ondansetron group up until 12 h after operation ($P < 0.05$), but by 24 h this difference was not significant. The ondansetron regimen was more expensive (at local prices) by a factor of 27, and our results suggested no clinical advantage over droperidol.

Acta Anaesthesiol Scand. 1996 May;40(5):600-5.

Patient-controlled analgesia with morphine and droperidol following caesarean section under spinal anaesthesia.

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BACKGROUND: The addition of droperidol to morphine for patient-controlled analgesia reduces the incidence of nausea and vomiting, but may result in unwanted side effects. **METHOD:** We studied 40 women randomised to receive morphine sulphate with or without added droperidol (10mg droperidol/60 mg morphine) by patient-controlled analgesia following elective caesarean section under spinal anaesthesia. **RESULTS:** Median morphine demand in the 20 h after surgery was 74 mg with morphine alone, and 53 mg with added droperidol, the median consumption of which was 8.8 mg. The incidence of nausea was reduced from 80% to 38.8% ($P < 0.01$), and that of emesis from 55% to 16.7% ($P < 0.05$) by the addition of droperidol. Psychomotor function was significantly impaired to a similar degree in both groups and there was no significant difference in sedation scores or pain scores. Subjective drowsiness which resulted in withdrawal from the study occurred in two patients, both of whom were receiving droperidol, and though all patients who completed the study were satisfied with their analgesia overall, significantly more of those receiving unsupplemented morphine (11/19 compared with 4/18, $P < 0.05$) described it as excellent. **CONCLUSION:** The addition of droperidol 10 mg to morphine 60 mg for PCA following caesarean section under spinal anaesthesia reduces the incidence of nausea and emesis, but may result in drowsiness, limiting the usefulness of the technique.

Anaesthesia. 1995 Dec;50(12):1086-8.

Comment in: [Anaesthesia. 1996 Aug;51\(8\):795.](#)

Comparison of ondansetron and droperidol in reducing postoperative nausea and vomiting associated with patient-controlled analgesia.

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In a randomised, placebo-controlled trial we have compared the efficacy of ondansetron and droperidol in reducing postoperative nausea and vomiting associated with patient-controlled analgesia after orthopaedic surgery. One hundred and forty five patients, ASA 1 and 2, undergoing major orthopaedic surgery were anaesthetised using a standardised technique. They were randomly allocated to receive patient-controlled analgesia as morphine 1 mg.ml⁻¹ alone; morphine as before plus a single dose of 1.25 mg droperidol together with 0.083 mg.ml⁻¹ in the infusion syringe; or morphine as before plus 4 mg ondansetron and 0.13 mg.ml⁻¹ in the syringe. The patient-controlled analgesia bolus dose was set at 1 ml with a 5 min lockout and a 4 h maximum dose of 30 mg morphine. There was no background infusion. The occurrence of nausea, vomiting and sedation was assessed every 4 h. The incidence of vomiting decreased from 59% in the morphine-only group to 35% and 14% in the droperidol ($p < 0.05$) and ondansetron groups ($p < 0.001$) respectively. The number of patients suffering from nausea alone was not significantly different between the three groups, although those in the ondansetron group experienced less severe nausea ($p < 0.05$) when using a two point scale. The droperidol group had significantly higher sedation scores than the other two groups ($p < 0.005$). We conclude that ondansetron is superior to droperidol when used with patient-controlled analgesia and causes less sedation.

Anaesthesia. 1993 Oct;48(10):881-4.

Comment in: [Anaesthesia. 1994 Apr;49\(4\):349-50.](#)

Addition of droperidol to patient-controlled analgesia: effect on nausea and vomiting.

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A double-blind trial of the effect of droperidol on the incidence of nausea and vomiting in patients using patient-controlled analgesia was carried out in 60 healthy women undergoing abdominal hysterectomy. After a standard anaesthetic including

droperidol 2.5 mg as a prophylactic antiemetic, patients were randomly allocated to receive postoperative patient-controlled analgesia with either morphine alone (2 mg.ml⁻¹) or morphine (2 mg.ml⁻¹) with droperidol (0.2 mg.ml⁻¹) added to the syringe. Verbal scores and visual analogue scores for nausea, vomiting, pain and sedation were made at 4, 12 and 24 h postoperatively, and any requirement for intramuscular prochlorperazine noted. There was no difference between the groups at any time in the amount of morphine consumed or in pain scores. At 12 h, patients receiving droperidol experienced significantly less nausea, and over the first 24 h, 31% required prochlorperazine compared with 59.3% of patients not receiving droperidol. The number of patients with sedation at 24 h was significantly greater in the droperidol group. We conclude that the addition of droperidol to morphine both reduces nausea and the need for further antiemetic treatment.

Dexamethasone

Anesth Analg. 2004 Apr;98(4):1066-71, table of contents.

A dose ranging study of dexamethasone for preventing patient-controlled analgesia-related nausea and vomiting: a comparison of droperidol with saline.

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Department of Anesthesiology, Buddhist Tzu-Chi Medical Center, Tzu-Chi University School of Medicine, Hualien, Taiwan. We designed this study to determine the minimum dose of dexamethasone for preventing nausea and vomiting associated with the use of morphine by patient-controlled analgesia (PCA). Two hundred forty female patients were randomly assigned to receive dexamethasone 2, 4, 8, or 12 mg IV immediately before induction of anesthesia. Droperidol (0.1 mg/mL with morphine 1 mg/mL in PCA pump) and saline were used as controls. The complete response (no postoperative nausea and vomiting and no need for rescue antiemetic for a 24-h postoperative period) rates for dexamethasone 8 mg (72.2%) and 12 mg (78.9%) were significantly more than for saline (42.9%) ($P < 0.05$). Patients who received dexamethasone 12 or 8 mg also reported higher patient satisfaction than those who received saline ($P < 0.05$). These results were as effective as adding droperidol 0.1 mg/mL to the morphine PCA without causing drowsiness, restlessness, or arrhythmias. Smaller doses of dexamethasone (4 or 2 mg) were not effective for this propose. The results suggest that dexamethasone 8 mg IV is the minimum effective dose for the reduction of PCA morphine-related nausea and vomiting. IMPLICATIONS: Morphine administration by patient-controlled analgesia (PCA) is often associated nausea and vomiting. In this double-blind study, the minimum effective dose of dexamethasone for reducing this complication was 8 mg. This was as effective as adding droperidol 0.1 mg/mL to the morphine PCA without causing drowsiness, restlessness or arrhythmias.

Br J Anaesth. 2003 May;90(5):665-70.

Prevention of postoperative nausea and vomiting after spinal morphine for Caesarean section: comparison of cyclizine, dexamethasone and placebo.

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BACKGROUND: Low-dose intrathecal (spinal) morphine (0.1-0.2 mg) for Caesarean section delivers excellent postoperative analgesia but is associated with significant nausea and vomiting. We compared the antiemetic efficacy of cyclizine, dexamethasone, and placebo in this clinical setting. METHODS: Ninety-nine women undergoing elective Caesarean section under spinal anaesthesia were allocated randomly, in a double-blind study design, to receive either cyclizine 50 mg, dexamethasone 8 mg, or placebo as a single-dose infusion in saline 0.9%, 100 ml on completion of surgery. Spinal anaesthesia consisted of: hyperbaric bupivacaine 0.5%, 2.0 ml; fentanyl 10 micro g; and spinal morphine 0.2 mg. The primary outcome measure was the incidence of nausea. RESULTS: The incidence of nausea was significantly less in patients receiving cyclizine compared with dexamethasone and placebo (33 vs 60 and 67%, respectively, $P < 0.05$). Severity of nausea and number of vomiting episodes were also less at 3-6 h in cyclizine patients. Overall satisfaction with postoperative care at 24 h, expressed on a 100 mm visual analogue scale, was greater in cyclizine [78 (28)] than either dexamethasone [58 (31), $P = 0.03$] or placebo [51 (28), $P = 0.008$]. CONCLUSION: We conclude that following spinal morphine 0.2 mg and fentanyl 10 micro g analgesia for Caesarean section, cyclizine 50 mg i.v. reduces the incidence of nausea compared with dexamethasone 8 mg i.v. or placebo. It also lessens the severity of nausea and vomiting, and increases maternal satisfaction in the early postoperative period.

Anaesthesia. 2002 Jul;57(7):705-9.

The effect of dexamethasone upon patient-controlled analgesia-related nausea and vomiting.

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Ninety female patients were enrolled in this randomised, double-blind, placebo-controlled study to compare the anti-emetic effect of intravenous dexamethasone 8 mg with saline control in preventing patient-controlled analgesia-related nausea and vomiting following major orthopaedic surgery. The prophylactic administration of dexamethasone 8 mg significantly reduced the overall incidence of patient-controlled analgesia-related nausea and vomiting ($p < 0.001$) and the need for rescue anti-emetics ($p < 0.01$). Furthermore, patients who received dexamethasone showed a higher incidence of complete responses (no vomiting or need for rescue anti-emetic for a 24-h postoperative period) than those who received saline ($p < 0.05$). We conclude that dexamethasone 8 mg may be valuable for preventing patient-controlled analgesia-related nausea and vomiting in women undergoing major orthopaedic surgery.

Br J Anaesth. 2000 Dec;85(6):865-8.

Dexamethasone for prophylaxis of nausea and vomiting after epidural morphine for post-Caesarean section analgesia: comparison of droperidol and saline.

Tzeng JI, Wang JJ, Ho ST, Tang CS, Liu YC, Lee SC.

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We have evaluated the prophylactic effect of i.v. dexamethasone 8 mg in preventing nausea and vomiting during epidural morphine for post-Caesarean section analgesia. Droperidol 1.25 mg and saline served as the control. We studied 120

parturients (n=40 in each group) receiving epidural morphine for post-Caesarean section analgesia, in a randomized, double-blind, placebo-controlled study. All parturients received epidural morphine 3 mg. Both dexamethasone and droperidol significantly decreased the total incidence of nausea and vomiting compared with saline, with incidences of 18, 21 and 51% for the three treatments respectively ($P<0.01$ and $P<0.05$ respectively). Parturients who received droperidol reported a more frequent incidence of restlessness (16%) than those who received dexamethasone ($P<0.05$).

5HT3 antagonists

Paediatr Anaesth. 2004 Sep;14(9):759-67.

The effect of premedication with OTFC, with or without ondansetron, on postoperative agitation, and nausea and vomiting in pediatric ambulatory patients.

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BACKGROUND: The purpose of this study was to evaluate, in the pediatric ambulatory surgical population, the efficacy of: (i) oral transmucosal fentanyl citrate (OTFC), when given preoperatively, to reduce postoperative excitement associated with sevoflurane, and (ii) intravenous ondansetron to reduce postoperative nausea and vomiting (PONV) associated with OTFC. **METHODS:** This randomized, double-blinded, placebo controlled study evaluated the efficacy of OTFC [normal dose (ND) = 10-15 microg x kg(-1) or low dose = 100 microg] compared with placebo in the prevention of postoperative agitation; and the efficacy of ondansetron (0.1 mg x kg(-1) to 4 mg) compared with placebo to reduce PONV associated with OTFC. **RESULTS:** There were 125 patients evaluated (2-10 years old, ASA class I or II and weight 10-40 kg). Preoperatively OTFC was associated with an increased likelihood of cooperation at baseline (P = 0.018). Postoperatively there was a higher incidence of vomiting in children that received OTFC. The anxiety/agitation of patients entering the PACU was significantly less in children who received OTFC ND (P < 0.001). This effect decreased over time. Patients with respiratory adverse events related to the study drug were significantly higher in groups who received OTFC, however, they were not of clinical significance. OTFC was associated with delays in time for eligibility to PACU discharge (P = 0.003). **CONCLUSIONS:** Even though OTFC reduced early postoperative agitation the increase in side effects, namely PONV and prolonged recovery times, limits its clinical usefulness. The study demonstrates the tradeoffs between anxiety and agitation vs vomiting, respiratory events and prolonged recovery times. Ambulatory pediatric patients undergoing procedures in which opioids would be routinely used might benefit the most from OTFC combined with ondansetron as part of the anesthetic technique.

Anesth Analg. 2004 Jan;98(1):264; author reply 264.

Comment on: [Anesth Analg. 2003 Jun;96\(6\):1789-93, table of contents.](#)

Ondansetron for prevention of intrathecal opioids-induced pruritus, nausea and vomiting after cesarean delivery.

Yazigi A, Chalhoub V, Madi-Jebari S, Haddad F.

Plast Reconstr Surg. 2002 Jun;109(7):2487-94.

Comment in: [Plast Reconstr Surg. 2003 Mar;111\(3\):1365-6.](#)

The prevention of emesis in plastic surgery: a randomized, prospective study.

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Perhaps the most unpleasant experience following outpatient plastic surgery procedures is postoperative nausea and vomiting. Postoperative nausea and vomiting often results in delayed recovery time and unintended admission, and it can be a contributing factor to the formation of hematoma following rhytidectomy. Ondansetron (Zofran) has proven benefit in preventing postoperative nausea and vomiting if given before general anesthesia in a variety of surgical procedures. Its utility in cases performed under conscious sedation has not been determined. The purpose of this study was (1) to test the ability of prophylactic ondansetron to prevent postoperative nausea and vomiting in plastic surgery cases performed under conscious sedation, and (2) to determine relative risk factors for postoperative nausea and vomiting and a selection policy for the administration of antiemetic prophylaxis. This was a prospective, randomized, double-blind study. One hundred twenty patients were enrolled after giving informed consent. Patients received a single dose of either placebo or ondansetron (4 mg intravenously) before administration of sedation. Sedation administration followed a standardized institutional protocol, using midazolam and fentanyl. Data were recorded from a series of three questionnaires: preoperatively, immediately postoperatively, and at the time of the first office return. Data were confirmed by means of telephone interview, chart analysis, and nursing documentation. Multivariate analysis was conducted. Nausea and emesis occurred with an overall frequency of 33 percent and 22 percent, respectively. Postoperative nausea and vomiting was associated with statistically longer recovery periods. The incidence of emesis was statistically higher among women, among those undergoing facial rejuvenation, and among those with a history of opioid-induced emesis or postoperative nausea and vomiting following a previous operation (p < 0.05). The incidence of postoperative nausea and vomiting paralleled increases in case duration; the incidence of emesis was zero in cases less than 90 minutes in duration. Ondansetron significantly reduced the incidence of emesis overall (placebo, 30 percent; ondansetron, 13 percent; p < 0.05). Postoperative perception of nausea was significantly lower among those who had received ondansetron (p < 0.05). These results confirm the efficacy of ondansetron for the prevention of postoperative nausea and vomiting in plastic surgery cases under conscious sedation. In those who are at increased risk, prophylaxis should be considered. Such risks include female gender, facial rejuvenation procedures, and a patient history of opioid-induced emesis or postoperative nausea and vomiting following a prior operation. The zero incidence of emesis in cases less than 90 minutes does not support the routine use of prophylaxis in such cases. Patient satisfaction in plastic surgery is derived from the overall subjective experience of the event as much as by the final result. By remaining attentive to patient concerns and optimizing perioperative care, we can improve the subjective experience for our

patients.

Br J Anaesth. 2001 Sep;87(3):502-4.

Prophylactic ondansetron does not improve patient satisfaction in women using PCA after Caesarean section. Cherian VT, Smith I.

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Eighty-one consenting women undergoing elective Caesarean section under spinal anaesthesia were randomly divided into two groups. In Group O patients, ondansetron 4 mg was given intravenously at the end of the surgery and 8 mg added to the morphine solution in the PCA syringe. Patients in Group P received only morphine via PCA syringe. Analgesia and nausea were measured until PCA was discontinued 24 h after the operation. Women in the two groups were similar with respect to age, duration of use of the PCA, amount of morphine used, previous history of PONV, and incidence of motion sickness and morning sickness during the current pregnancy. The number of women who complained of nausea and those needing rescue antiemetic medication was significantly less in Group O. However, there was no statistically significant difference between the two groups in the patient's perception of the control of nausea and their overall satisfaction. It was noted that PONV was more frequent among women who had significant morning sickness during early pregnancy and ondansetron was beneficial in reducing PONV in these women. Although the ondansetron reduced the incidence of PONV and the need for further antiemetic medication, this did not affect patient's satisfaction regarding their postoperative care.

Anaesthesia. 2001 Apr;56(4):365-9.

Patient-controlled analgesia and postoperative nausea and vomiting: efficacy of a continuous infusion of ondansetron. White LA, Vanarase M, Brockbank K, Barrett RF.

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A continuous infusion of ondansetron was compared with a placebo infusion in 80 patients undergoing major breast reconstructive surgery. All patients received a standard anaesthetic and a bolus dose of ondansetron after induction. They were then randomly allocated to receive an intravenous infusion of ondansetron or a placebo infusion for 24 h in a double-blind fashion. Postoperative analgesia was provided by patient-controlled subcutaneous diamorphine. In the ondansetron group, the severity of nausea, measured by a 10-point verbal rating scale, was reduced ($p = 0.01$) and fewer patients stated at postoperative interview that nausea and vomiting was a problem ($p = 0.01$).

Acta Anaesthesiol Sin. 2000 Dec;38(4):201-5.

Failure of prevention against postoperative vomiting by ondansetron or prochlorperazine in patients undergoing gynecological laparoscopy.

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BACKGROUND: Ondansetron has been approved for the treatment and prevention of postoperative emesis. Since it is presumably considered to possess potent antiemetic effect with fewer side effects, the administration of ondansetron to inhibit emesis in patients following gynecological laparoscopic surgery might be recommendable. Hence, we examined the effects of intravenous ondansetron at dosage of 4 and 8 mg in comparison with intravenous prochlorperazine at 5 mg and placebo. **METHODS:** A total of 120 patients were allocated randomly into 3 groups. Group 1 patients who served as control were given NaCl 0.9% 4 mL (placebo) intravenously (i.v.); patients in group 2 and group 3 were given ondansetron 4 mg ondansetron 8 mg i.v. respectively; patients in group 4 were given prochlorperazine 5 mg i.v. Premedication was omitted. **RESULTS:** Logistic regression analysis adjusted for prognostic factors revealed no significant difference between 5 mg prochlorperazine group and 4 mg or 8 mg ondansetron group as compared over the 24 h study period. **CONCLUSIONS:** The results of this study suggest that i.v. 4 or 8 mg ondansetron and 5 mg prochlorperazine were not effective in prevention of postoperative emesis in patients undergoing gynecological laparoscopy. Since the cost of ondansetron is high, its routine use for prevention against postoperative nausea and vomiting is not be recommended clinically because of its uncertain benefit.

Clin Ther. 1999 Jul;21(7):1216-27.

Intravenous ondansetron for the control of opioid-induced nausea and vomiting. International S3AA3013 Study Group.

Sussman G, Shurman J, Creed MR, Larsen LS, Ferrer-Brechner T, Noll D, Allegra J, Montgomery R, Schreck D, Grafstein E, Ramalanjaona G, Patel V, Ducharme J, Ortenwall P, Foster E, Ames M.

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This randomized, double-masked, placebo-controlled, multicenter trial was conducted in 9 countries to assess the safety and efficacy of 2 doses of intravenous ondansetron (8 and 16 mg) for the control of opioid-induced nausea and vomiting. A total of 2574 nonsurgical patients who presented with pain requiring treatment with an opioid analgesic agent participated in this trial. The most common presenting painful condition was back or neck pain, reported by approximately one third of patients. A total of 520 patients (317 females, 203 males) developed nausea or vomiting after opioid administration and were randomly assigned to receive a single dose of 1 of 3 study treatments: placebo ($n = 94$), ondansetron 8 mg ($n = 215$), or ondansetron 16 mg ($n = 211$). Ondansetron 8 and 16 mg led to complete control of emesis in 134 of 215 patients (62.3%) and

145 of 211 patients (68.7%), respectively. Results with both doses were significantly better than those seen with placebo (43 of 94 patients [45.7%]). Complete control of nausea was achieved in 6.8% of placebo patients, 14.8% of ondansetron 8-mg-treated patients, and 19.4% of ondansetron 16-mg treated patients; only ondansetron 16 mg was significantly better than placebo ($P = 0.007$). Significantly more patients who received ondansetron 8 mg than patients who received placebo were satisfied/very satisfied with their antiemetic treatment, as assessed by 4 patient-satisfaction questions. Significantly more patients who received ondansetron 16 mg compared with placebo were satisfied/very satisfied on 2 of 4 satisfaction questions. In conclusion, based on the observed incidence of opioid-induced nausea and vomiting in this study, it may be more appropriate to treat symptoms on occurrence rather than administering antiemetic agents prophylactically. The results of this study demonstrate that intravenous ondansetron in doses of 8 or 16 mg is an effective antiemetic agent for the control of opioid-induced nausea and vomiting in nonsurgical patients requiring opioid analgesia for pain.

Br J Anaesth. 1998 Sep;81(3):384-6.

High-dose ondansetron regimen vs droperidol for morphine patient-controlled analgesia.

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We have performed a randomized, double-blind study comparing droperidol and high-dose ondansetron mixed with morphine for patient-controlled analgesia (PCA). To detect a reduction in the incidence of postoperative nausea and vomiting from 55% to 20% with a power of 80% at the $P < 0.05$ level, 29 patients per group were required. We studied 60 healthy women undergoing abdominal hysterectomy, anaesthetized using a standard technique. Group D received a bolus dose of droperidol 1.25 mg at induction followed by droperidol 0.1 mg per 1 mg of morphine from the PCA system. Group O received a bolus dose of ondansetron 4 mg at induction followed by ondansetron 0.32 mg per 1 mg of morphine. This dose of ondansetron is more than double that studied previously. Mean nausea and vomiting scores at 4, 8, 12 and 24 h, mean time to first vomit, sedation scores, incidence of side effects, and doses of prochlorperazine did not differ between the groups. In group D, 24 patients did not vomit compared with 23 in group O. The only significant difference between the groups was increased morphine consumption in the ondansetron group up until 12 h after operation ($P < 0.05$), but by 24 h this difference was not significant. The ondansetron regimen was more expensive (at local prices) by a factor of 27, and our results suggested no clinical advantage over droperidol.

Anaesthesia. 1999 Mar;54(3):266-71.

Prophylactic anti-emetic efficacy of ondansetron in laparoscopic cholecystectomy under total intravenous anaesthesia. A randomised, double-blind comparison with droperidol, metoclopramide and placebo.

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The prophylactic anti-emetic efficacy and safety of pre-operative intravenous ondansetron was evaluated in a randomised, double-blind, comparison with droperidol, metoclopramide and placebo in 160 ASA grade 1 and 2 patients undergoing laparoscopic cholecystectomy under total intravenous anaesthesia. The patients were randomly allocated to receive ondansetron (4 mg), droperidol (1.25 mg), metoclopramide (10 mg) or placebo given as a single intravenous dose immediately before induction of a standardised general anaesthetic. There were no significant differences between the four study groups with regard to the demographic and anaesthetic data, postoperative analgesia, postoperative sedation scores, duration of postoperative hospital stay and incidence of adverse events. The incidence of nausea and vomiting was significantly lower ($p < 0.05$) between 1 h and 4 h after surgery in the ondansetron group compared with the droperidol, metoclopramide and placebo groups. The incidence of nausea was similar in the four groups in the other study periods: 0-1 h and 4-24 h. The incidence of vomiting was lower in the ondansetron, droperidol and metoclopramide groups than in the placebo group between 1 and 4 h but was the same between 4 and 24 h. As a result of the lower incidence of nausea and vomiting between 1 h and 4 h in the ondansetron group, the overall incidence of nausea and vomiting was lower during the first 24 h after surgery in this group than in the other three groups.

Arch Intern Med. 1998 Oct 26;158(19):2124-8.

Erratum in: Arch Intern Med 1999 Mar 22;159(6):615.

Efficacy of ondansetron and prochlorperazine for the prevention of postoperative nausea and vomiting after total hip replacement or total knee replacement procedures: a randomized, double-blind, comparative trial.

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BACKGROUND: Limited data are available on the efficacy of ondansetron hydrochloride compared with prochlorperazine maleate for the treatment of postoperative nausea and vomiting (PONV). **OBJECTIVE:** To evaluate the comparative efficacy of ondansetron and prochlorperazine for the prophylaxis of PONV in patients undergoing total hip replacement or total knee replacement procedures. **METHODS:** A randomized, double-blind, comparative trial was conducted at a tertiary care, university hospital. Seventy-eight patients undergoing elective total hip or total knee replacement procedures received a single dose of ondansetron hydrochloride ($n = 37$), 4 mg intravenously, or prochlorperazine maleate ($n = 41$), 10 mg

intramuscularly, at the end of the surgical procedure. Rescue therapy was administered every 4 hours as needed during the initial 48 hours. Primary outcome measures were the incidences and severity of PONV. Secondary outcome measures included the number of rescue antiemetic doses required, number of physical therapy cancellations because of PONV, length of hospital stay, and cost of antiemetic agents administered. RESULTS: The incidence of nausea was significantly greater in the ondansetron group compared with the prochlorperazine group (81% vs 56%; odds ratio, 3.4; 95% confidence interval, 1.2-9.4) as was the severity of nausea ($P = .04$). Multivariate analysis identified administration of ondansetron, history of PONV, obesity, and female sex as risk factors for a nausea event. The incidence of vomiting tended to be greater in the ondansetron group (49% vs 32%; odds ratio, 2.0; 95% confidence interval, 0.8-5.0). The need for rescue antiemetic therapy was also greater in the ondansetron group (46% vs 27%; odds ratio, 2.3; 95% confidence interval, 0.9-6.0). The mean antiemetic drug cost per patient was significantly greater for the ondansetron group (\$47.56 vs \$2.47; $P < .001$). However, the proportion of patients who were unable to participate in physical therapy because of PONV and the median length of hospital stay were similar in both groups. CONCLUSION: Prochlorperazine is associated with superior efficacy and significant cost savings compared with ondansetron for the prevention of PONV in patients undergoing total hip and total knee replacement procedures.

Anesth Analg. 1997 Apr;84(4):832-8.

Intravenous ondansetron for postsurgical opioid-induced nausea and vomiting. S3A-255 Study Group.

Rung GW, Claybon L, Hord A, Patel C, Kallgren M, Koppel J, Benedetti C, Creed M, Asgharian A, Bryson J, Milton S. Hershey Medical Center, Pennsylvania State University, 17033, USA.

The use of opioids for postoperative analgesia may be limited by side effects such as nausea and vomiting. Because ondansetron, a selective serotonin type 3 (5-hydroxytryptamine [5-HT₃]) antagonist, is effective for chemotherapy and general anesthesia-induced nausea and vomiting, we hypothesized that it may also be effective for opioid-induced nausea and vomiting. ASA physical status I-III patients undergoing regional anesthesia were eligible for the study. Those who requested an antiemetic after postsurgical opioid administration were randomized to receive a single dose of ondansetron (0.1 mg, 4 mg, or 16 mg intravenously [I.V.]) or placebo in a double-blind fashion. Emetic episodes, nausea and pain ratings, and adverse events were recorded for 24 h after study drug administration. Patient satisfaction scores were obtained 24 h after study drug infusion. A significantly ($P < 0.05$) larger proportion of patients treated with ondansetron 4 mg and 16 mg experienced no emetic episodes, received no rescue antiemetic, and completed the study compared with placebo. Nausea scores and patient satisfaction scores in the ondansetron 16-mg group were significantly ($P < 0.05$) more favorable than in the placebo group. Postsurgical pain scores did not differ among groups. The incidence of adverse events was similarly low across groups. The results of this study support our hypothesis that I.V. ondansetron is effective for postsurgical opioid-induced nausea and vomiting.

Anaesthesia. 1996 Sep;51(9):880-2.

Comment in: [Anaesthesia. 1997 Jan;52\(1\):90-1.](#)

Antiemetic efficacy of ondansetron with patient-controlled analgesia.

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A double-blind, randomised, placebo-controlled study was performed to assess the antiemetic efficacy of ondansetron in women receiving morphine from a patient-controlled analgesia system after total abdominal hysterectomy. Sixty-six ASA grade 1 or 2 patients scheduled for total abdominal hysterectomy were randomly allocated into one of two groups. All patients received a standardised anaesthetic and postoperative patient-controlled analgesia regimen. Group 1 received ondansetron 4 mg at induction of anaesthesia, repeated 8 h later. Group 2 received saline as a placebo at the same times. Pain scores, nausea scores, episodes of vomiting, use of rescue antiemetics and recollection of nausea and vomiting were not different between the groups. Only 15% of patients who received ondansetron and 30% of patients who received the placebo recorded no nausea or vomiting in the first 24 h. We conclude that ondansetron, in the dose studied, does not reduce nausea and vomiting in women receiving morphine from a patient-controlled analgesia system after total abdominal hysterectomy.

Anaesth Intensive Care. 1996 Oct;24(5):538-45.

The prophylactic antiemetic efficacy of prochlorperazine and ondansetron in nasal septal surgery: a randomized double-blind comparison.

[van den Berg AA.](#)

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A prospective, randomized placebo-controlled study was undertaken to compare the effects on heart rate and blood pressure during surgery and on the incidence of nausea, vomiting and headache after surgery of i.m. prochlorperazine 0.2 mg.kg⁻¹, i.v. prochlorperazine 0.1 mg.kg⁻¹ and i.v. ondansetron 0.06 mg.kg⁻¹ given at induction of general anaesthesia to patients undergoing septorhinoplasty. The effects of the test drugs after administration on heart rate and blood pressure were similar, as were the incidences of retching and vomiting in the recovery ward after each test drug. Postoperatively, compared with placebo (7%), nausea per se was most frequent in those given i.v. prochlorperazine (25%, $P < 0.01$), and less frequent in those given i.m. prochlorperazine (2%) and i.v. ondansetron (15%). Vomiting per se was reduced from 24% to 7% ($P < 0.025$) by i.v. prochlorperazine and to 4% ($P < 0.0005$) by i.v. ondansetron. The incidence of nausea with vomiting was reduced from 35% to 15% ($P < 0.025$), 16% ($P < 0.05$) and 11% ($P < 0.005$) by i.m. prochlorperazine, i.v. prochlorperazine

and i.v. ondansetron respectively. I.m. prochlorperazine and i.v. ondansetron increased the frequency (from 35% to 64%, $P < 0.0005$ and to 71%, $P < 0.0005$, respectively) of those experiencing no PONV and delayed the onset of PONV, but only i.m. prochlorperazine reduced the severity of postoperative vomiting. Headache was frequent in the control (69%), i.v. prochlorperazine (62%) and i.v. ondansetron (69%) groups, and least frequent after i.m. prochlorperazine (53%; $P < 0.05$ versus i.v. ondansetron). It is concluded that these drugs have no adverse cardiovascular effects within 10 minutes of administration, i.m. prochlorperazine and i.v. ondansetron reduce PONV more effectively than i.v. prochlorperazine and postoperative headache after septorhinoplasty occurs less frequently in those given i.m. prochlorperazine than in those given i.v. ondansetron.

Can J Anaesth. 1996 Sep;43(9):939-45.

A comparison of ondansetron and prochlorperazine for the prevention of nausea and vomiting after tympanoplasty.
[van den Berg AA.](#)

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PURPOSE: To evaluate the effects on PONV and headache after tympanoplasty of prochlorperazine 0.2 mg.kg⁻¹ i.m., ondansetron 0.06 mg.kg⁻¹ i.v. or placebo (isotonic saline) 0.02 ml.kg⁻¹ i.v. given immediately after induction of anaesthesia prior to tracheal intubation. **METHODS:** The study was randomised, double blind and prospective. One hundred and forty-eight patients, aged 9-61 yr, received a standardised balanced inhalational anaesthetic with controlled ventilation and induced hypotension. Postoperatively, the frequencies of retching and vomiting in the PACU and of nausea, retching, vomiting, headache, analgesic and antiemetic requirements in the surgical ward for 24 hr were recorded. **RESULTS:** The four test groups ($n = 37$ each) were comparable. The incidences of vomiting in the PACU were similar. During the first 24 hr after surgery the antiemetics produced no reductions in the incidence of nausea alone or of vomiting alone. However, the combination of nausea and vomiting was reduced from 53% (placebo) to 16% ($P < 0.0005$), 19% ($P < 0.0005$) and 30% ($P < 0.05$) by i.m. prochlorperazine, i.v. ondansetron and i.v. prochlorperazine, respectively. The frequency of those experiencing no PONV was increased from 27% (placebo) by prochlorperazine i.m. to 57% ($P < 0.01$), by ondansetron i.v. to 62% ($P < 0.005$) and by prochlorperazine i.v. to 43% ($P = NS$). The onset of PONV was delayed in those given prochlorperazine im, and vomiting was less severe in those given ondansetron i.v. Headache occurred with similar frequency in each group. **CONCLUSION:** Prophylactic prochlorperazine 0.2 mg.kg⁻¹ i.m. and ondansetron 0.06 mg.kg⁻¹ i.v. are similarly efficacious in reducing nausea with vomiting after tympanoplasty, while prochlorperazine 0.1 mg.kg⁻¹ i.v. is less efficacious. Neither drug given as described appeared to reduce the frequency of postoperative nausea alone or vomiting alone.

Br J Anaesth. 1996 Mar;76(3):449-51.

Comparison of ondansetron and prochlorperazine for the prevention of nausea and vomiting after adenotonsillectomy.
[van den Berg AA.](#)

Department of Anaesthesia, Riyadh Military Hospital, Kingdom of Saudi Arabia.

This study has compared the incidences of nausea, vomiting and headache after ondansetron 0.06 mg kg⁻¹ i.v., prochlorperazine 0.2 mg kg⁻¹ i.m. and prochlorperazine 0.1 mg kg⁻¹ i.v. given during induction of general anaesthesia to 282 patients undergoing adenotonsillectomy. The cardiovascular effects of the drugs were similar. After operation, nausea per se and vomiting per se occurred with similar frequency, in between 6% and 11% and 11% and 19%, respectively, in each test group. Nausea and vomiting in the same patient was reduced from 29% to 2% by i.v. ondansetron ($P < 0.0005$) and to 3% by i.m. prochlorperazine ($P < 0.0005$), and appeared to be less severe in these groups. Headache was most frequent after i.v. ondansetron (35%; $P < 0.05$), but occurred with similar frequency after i.m. prochlorperazine (32%) and i.v. prochlorperazine (29%).

Other agents

Ann Pharmacother. 2005 Feb;39(2):255-61. Epub 2005 Jan 11.

Promethazine adverse events after implementation of a medication shortage interchange.

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BACKGROUND: Prochlorperazine and droperidol were commonly used antiemetics at the University of Pittsburgh Medical Center-Presbyterian Hospital until a shortage of prochlorperazine occurred and a black box warning was added to droperidol prescribing information. Subsequently, promethazine was selected as the approved intravenous antiemetic for therapeutic interchange in December 2001. Promethazine use and adverse drug events (ADEs) were investigated following review of a serious ADE that identified promethazine use as a probable contributing factor. **OBJECTIVE:** To illustrate ADEs associated with promethazine and characterize high-risk patients. **METHODS:** An ADE database analysis identified promethazine ADEs reported from 2000 to 2003. Promethazine utilization and ADEs were compared with those of other antiemetics during the pre- and post-interchange periods. **RESULTS:** Promethazine utilization increased significantly during the post-interchange period compared with all other antiemetics ($p < 0.001$). Promethazine ADEs increased from one event during the pre-interchange period to 13 events during the post-interchange period. Causality assessment using the Naranjo algorithm ranged from possible to probable. The promethazine ADE rate per 10 000 doses was significantly higher than the combined ADE rate for all other antiemetics ($p < 0.001$; incident rate ratio [IRR] 4.32). Elderly patients (aged $>$ or $=65$ y) experienced more promethazine ADEs than younger patients ($p = 0.005$; IRR 4.68). Concurrent use of opioids and/or sedating drugs contributed to promethazine ADEs in 11 of 14 (78.6%) patients. **CONCLUSIONS:** Geriatric status is a significant risk factor for promethazine ADEs. Concomitant use of sedating drugs may further increase the risk for ADEs. Therapeutic interchange programs should be monitored for both ADEs and utilization.

J Perinatol. 2003 Oct;23(7):531-5.

Comparison of three outpatient regimens in the management of nausea and vomiting in pregnancy.

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OBJECTIVE: This study compares pyridoxine-metoclopramide combination therapy to prochlorperazine and promethazine monotherapies in the outpatient treatment of nausea and vomiting in pregnancy. **STUDY DESIGN:** In total, 174 first trimester, singleton pregnancies were evaluated for nausea and vomiting. Patients were prospectively randomized into three treatment groups: pyridoxine-metoclopramide, prochlorperazine, or promethazine. Prior to, and on the third day, patients recorded their subjective responses to the given treatment and their number of emesis episodes. The three treatment groups were compared for therapy response. **RESULTS:** There were no differences in the number of emesis episodes prior to treatment. Both subjective and objective responses to treatment differed among the three groups when comparing the combination therapy to the monotherapies ($p < 0.05$). **CONCLUSION:** Combination therapy with pyridoxine and metoclopramide appears to be superior to either monotherapy in the treatment of nausea and vomiting in pregnancy.

Ann Emerg Med. 2001 Nov;38(5):491-6.

Comment in: [Ann Emerg Med. 2002 May;39\(5\):576](#).

Intravenous administration of prochlorperazine by 15-minute infusion versus 2-minute bolus does not affect the incidence of akathisia: a prospective, randomized, controlled trial.

[Collins RW](#), [Jones JB](#), [Walthall JD](#), [Chisholm CD](#), [Giles BK](#), [Brizendine EJ](#), [Cordell WH](#).

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STUDY OBJECTIVE: We sought to compare the rate of akathisia after administration of intravenous prochlorperazine as a 2-minute bolus or 15-minute infusion. **METHODS:** We conducted a prospective, randomized, double-blind study in the emergency department of a central-city teaching hospital. Patients aged 18 years or older treated with prochlorperazine for headache, nausea, or vomiting were eligible for inclusion. Study participants were randomized to receive 10 mg of prochlorperazine administered intravenously by means of 2-minute push (bolus group) or 10 mg diluted in 50 mL of normal saline solution administered by means of intravenous infusion during a 15-minute period (infusion group). The main outcome was the number of study participants experiencing akathisia within 60 minutes of administration. Akathisia was defined as either a spontaneous report of restlessness or agitation or a change of 2 or more in the patient-reported akathisia rating scale and a change of at least 1 in the investigator-observed akathisia rating scale. The intensity of headache and nausea was measured with a 100-mm visual analog scale. **RESULTS:** One hundred patients were enrolled. One study participant was excluded after protocol violation. Seventy-three percent (73/99) of the study participants were treated for headache and 70% (70/99) for nausea. In the bolus group, 26.0% (13/50) had akathisia compared with 32.7% (16/49) in the infusion group (Delta=-6.7%; 95% confidence interval [CI] -24.6% to 11.2%). The difference between the bolus and infusion groups in the percentage of participants who saw a 50% reduction in their headache intensity within 30 minutes was 11.8% (95% CI -9.6% to 33.3%). The difference in the percentage of patients with a 50% reduction in their nausea was 12.6% (95% CI -4.6% to 29.8%). **CONCLUSION:** A 50% reduction in the incidence of akathisia when prochlorperazine was administered by means of 15-minute intravenous infusion versus a 2-minute intravenous push was not detected. The efficacy of prochlorperazine in the treatment of headache and nausea likewise did not appear to be affected by the rate of administration, although no formal

statistical comparisons were made.

Emerg Med. 2001 Feb;20(2):113-9.

Slow infusion for the prevention of akathisia induced by prochlorperazine: a randomized controlled trial.

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The utility of intravenous prochlorperazine (PCZ) in the treatment of nausea, vomiting, and headache may be limited by the akathisia that occurs frequently with the recommended 2-min infusion rate. We tested the hypothesis that decreasing the rate of PCZ infusion to 15 min reduces the incidence of akathisia at 1 hour. This double-blinded, randomized, controlled trial was conducted in the Emergency Department of an academic tertiary-care medical center with an annual census of 95,000 emergency patient visits. We enrolled a convenience sample of adult patients who received 10 mg i.v. PCZ for the treatment of nausea, vomiting, or headache. Subjects were randomized to receive either a 2-min infusion of PCZ (10 mg) followed by a 15-min infusion of saline, or a 2-min infusion of saline followed by a 15-min infusion of prochlorperazine. The incidence of akathisia at 1 hour was measured by using explicit diagnostic criteria. One hundred sixty patients were randomly enrolled into two groups, which were comparable with respect to age, gender, weight, and complaint. Akathisia developed in 31 of 84 patients (36.9%) who received the 2-min infusion of PCZ and in 18 of 76 patients (23.7%) who received the 15-min infusion of PCZ ($p = 0.07$), a 36% (95% CI, -5% to 61%) relative reduction. The delta from pre-infusion to postinfusion scores between the two groups was not significant ($p = 0.19$). We conclude that slowing the rate of PCZ infusion does not decrease akathisia.

Ann Emerg Med. 2000 Aug;36(2):89-94.

Comment in: ACP J Club. 2001 Mar-Apr;134(2):47.

Prochlorperazine versus promethazine for uncomplicated nausea and vomiting in the emergency department: a randomized, double-blind clinical trial.

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STUDY OBJECTIVE: Nausea and vomiting related to gastritis or gastroenteritis are common complaints in the emergency department. The most effective antiemetic agent is yet undetermined. This study was conducted to compare the efficacy of prochlorperazine versus promethazine for uncomplicated nausea and vomiting in the ED. **METHODS:** The study was a randomized, double-blind comparison of prochlorperazine (Compazine) and promethazine (Phenergan) for acute ED treatment of gastritis or gastroenteritis. We studied patients 18 years or older with presumed uncomplicated gastritis or gastroenteritis who presented to 2 academic EDs. Patients were randomly assigned to receive either prochlorperazine, 10 mg intravenously, or promethazine, 25 mg intravenously. Visual analog scale readings of patient comfort were obtained at baseline and at 30- and 60-minute intervals. The primary endpoint was degree of relief at 30 and 60 minutes. Secondary endpoints were time to complete relief, need for further antiemetic medication (treatment failures), and side effects. Statistical analysis was performed using the Mann-Whitney U test for nonparametric analysis and repeated-measures analysis of variance (ANOVA). **RESULTS:** Eighty-four patients were enrolled in the study; 42 received prochlorperazine and 42 received promethazine. There were no differences in demographics in the 2 groups. At baseline (time 0), there was no difference in symptoms ($P = .23$). At 30 and 60 minutes after receiving medication, prochlorperazine worked significantly better than promethazine ($P = .004$ and $P < .001$ using nonparametric analysis). Using repeated-measures ANOVA, there was a significant difference in symptoms over time for both groups ($P < .001$) and a significant difference in prochlorperazine versus promethazine ($P = .002$). Time to complete relief was significantly shorter with prochlorperazine ($P = .021$). There were significantly fewer treatment failures with prochlorperazine ($P = .03$, 9.5% versus 31%; difference 21%, 95% confidence interval 5 to 38). There was no difference in incidence of extrapyramidal effects. Prochlorperazine caused significantly fewer complaints of sleepiness ($P = .002$, 38% versus 71%; difference 33%, 95% confidence interval 13 to 53; $P = .002$). **CONCLUSION:** Prochlorperazine works significantly better than promethazine for relieving symptoms of nausea and vomiting more quickly and completely in ED patients with uncomplicated nausea and vomiting.

Eur J Anaesthesiol. 1999 Sep;16(9):638-45.

An assessment of prochlorperazine buccal for the prevention of nausea and vomiting during intravenous patient-controlled analgesia with morphine following abdominal hysterectomy.

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The effectiveness of prochlorperazine buccal as an anti-emetic for the prevention of post-operative nausea and vomiting in patients using intravenous patient-controlled analgesia with morphine following abdominal hysterectomy has been assessed in a randomized, double-blind, placebo-controlled study. Forty-nine female patients participated with 26 allocated to the prochlorperazine buccal group and the remainder to the placebo group. Each received either placebo or prochlorperazine

buccal 6 mg, in each case by the buccal route, 1 h prior to anaesthesia with further doses at 6, 18, 30 and 42 h, respectively. Symptom scores in respect of nausea, pain and sedation, the number without nausea, the number without vomiting and the requirement for rescue anti-emetic therapy were noted for each 4-h period during the 48-h study. Morphine utilization and taste associated with the study material were recorded. Data for 21 patients in the placebo group and 25 patients in the prochlorperazine buccal group were available for analysis. Patients in the prochlorperazine buccal group showed significantly lower mean nausea scores at 4-8 h (placebo group: mean nausea score 0.95; prochlorperazine buccal group: mean nausea score 0.36; $P < 0.05$) and at 16-20 h (placebo group: mean nausea score 1.24; prochlorperazine buccal group: mean nausea score 0.48; $P < 0.05$). Furthermore, the prochlorperazine buccal group showed significantly more patients without nausea at 4-8 h (placebo group: 11 patients out of 21; prochlorperazine buccal group: 20 patients out of 25; $P < 0.05$) and at 16-20 h (placebo group: nine patients out of 21; prochlorperazine buccal group: 18 patients out of 25; $P < 0.05$). The prochlorperazine buccal group showed a significantly higher number of patients rating the taste as unsatisfactory (placebo group: two patients out of 21; prochlorperazine buccal group: nine patients out of 25; $P < 0.05$). Intravenous droperidol is the current gold standard prophylactic anti-emetic in post-operative nausea and vomiting associated with intravenous patient controlled analgesia with morphine usage. This study has demonstrated a peri-operative prochlorperazine buccal regimen to be effective in post-operative nausea and vomiting prophylaxis in the use of intravenous patient controlled analgesia with morphine. Prochlorperazine buccal should be considered as an effective, inexpensive option for the prevention of post-operative nausea and vomiting in post-operative intravenous patient controlled analgesia with morphine administration.

Acta Anaesthesiol Scand. 1995 Oct;39(7):983-6.

Premedication with promethazine and transdermal scopolamine reduces the incidence of nausea and vomiting after intrathecal morphine.

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Intrathecal morphine provides effective postoperative pain relief in major orthopaedic surgery. In use, however, is associated with unpleasant side effects like nausea and vomiting. The effect of different premedications on postoperative emetic sequelae induced by intrathecal morphine was studied in a prospective, double blind study. Sixty patients scheduled for arthroplasty surgery of the lower extremity were anaesthetized with spinal anaesthesia with a combination of isobaric bupivacaine 20 mg and morphine 0.3 mg. For premedication the patients were randomised to three groups of equal size. They received either oral diazepam (5-15 mg), oral promethazine (10 mg) or a combination of promethazine and transdermal scopolamine (1.5 mg). Sixty percent of the patients with both promethazine and transdermal scopolamine were totally free from postoperative nausea and vomiting (PONV) symptoms compared to those premedicated with diazepam (40%) or promethazine alone (30%). Promethazine together with transdermal scopolamine reduced significantly the number of patients with vomiting (to 25%) and also vomiting episodes. This combination was also more efficient in reducing the incidence of nausea (to 25%) and nausea episodes than promethazine alone ($P < 0.05$). Combination also reduced the requests for additional pain relief ($P < 0.05$). PONV occurred in a majority of patients during the first 12 hours of the 24 hour study period and the need for additional analgesics thereafter. The incidence of itching (50-65%) and urinary catheterisation (55-70%) was similar in all groups. In conclusion, the combination of oral promethazine and transdermal scopolamine was most effective in reducing PONV symptoms and also reduced the need for postoperative pain treatment.

Ir Med J. 1993 Nov-Dec;86(6):186-8.

Buccal prochlorperazine as an antiemetic for day care surgery.

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This study compares the antiemetic effect of prochlorperazine in a buccal preparation with a control group as a preoperatively administered antiemetic. Fifty-two female day care patients undergoing gynaecological surgery or breast biopsy were studied. Patients were randomly allocated to two groups. Patients in group one received no antiemetic, while those in group two received 6mg buccal prochlorperazine one hour before surgery. Nausea was assessed with a visual nausea scoring system and interview similar to those used in previous series. Assessment times were before surgery and at one, four and 24 hours after surgery. Patient demographics and type of surgery were similar for the groups. The incidence of postoperative nausea and vomiting for the groups one and two was 57.7% and 15.4% respectively, $p < 0.05$. Most of the patients who experienced nausea in group one and two (86.7% and 50%) gave it a score less than five, indicating mild nausea. The majority of patients did not require treatment for postoperative nausea. The postoperative antiemetic and narcotic requirements were similar in the two groups. This study demonstrates that prochlorperazine at the dose used is effective in preventing postoperative nausea in the patient population studied.

Obstet Gynecol. 1991 Oct;78(4):673-7.

Nausea prophylaxis using transdermal scopolamine in the setting of patient-controlled analgesia.

Harris SN, Sevarino FB, Sinatra RS, Preble L, O'Connor TZ, Silverman DG.

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We evaluated the effectiveness of transdermal scopolamine in patients receiving morphine via patient-controlled intravenous analgesia following intra-abdominal gynecologic surgery. Soon after arrival in the post-anesthesia recovery unit (time 0), patients were randomized either to receive or not receive a postauricular transdermal scopolamine patch. Nausea and vomiting were scored on a 0-3 scale at this time and at 2, 4, 6, and 24 hours. Patients were treated with droperidol as deemed necessary by the primary care nurse. Within 2-4 hours, transdermal scopolamine patients evidenced less nausea and vomiting and required less droperidol than their counterparts who did not receive transdermal scopolamine. A significant decline in the severity of nausea was noted in the transdermal scopolamine group between 2-24 hours; significant inter-group differences were noted for changes in nausea severity during the 0-6-hour and 0-24-hour intervals. Transdermal scopolamine patients evidenced a significant (P less than .05) decrease in the severity of vomiting during the first 2 hours, significantly different from the increase in the non-transdermal scopolamine patients. After the 4-hour assessment, no transdermal scopolamine patients required droperidol; nine doses were administered to the patients who were not given transdermal scopolamine (P less than .05). Thus, transdermal scopolamine therapy appears to be an effective means of treating the nausea and vomiting that are encountered after gynecologic surgery.

Am Rev Respir Dis. 1986 Apr;133(4):558-61.

The effects of combined morphine and prochlorperazine on ventilatory control in humans.

[Olson LG](#), [Hensley MJ](#), [Saunders NA](#).

Recent studies have shown that the antiemetic neuroleptic drug, prochlorperazine, is a potent stimulant of the ventilatory response to hypoxia. To investigate whether or not this effect persisted in the presence of central depression of ventilatory drive, the effects on ventilatory control of morphine with and without prochlorperazine were studied in 12 normal humans. Measurement of resting ventilation and the ventilatory responses to progressive hypercapnia and to transient asphyxia were made before and 15 min after morphine (0.15 mg/kg) given intravenously. Prochlorperazine (12.5 mg) was then administered intravenously to 6 study subjects and saline to 6 control subjects. After a further 10 min, resting ventilation and chemoreceptor function were remeasured. After the administration of morphine, resting ventilation, the ventilatory response to hypercapnia, and the ventilatory response to asphyxia were all significantly decreased (p less than 0.01 in each case; mean effect in control and study group were, respectively, -16 and -17%, -50 and -32%, -46 and -55%). Administration of saline produced no significant additional changes in the 6 control subjects. By contrast, administration of prochlorperazine to the 6 study subjects markedly increased the ventilatory response to asphyxia to levels significantly greater than postmorphine values (p less than 0.005; 2.38 ± 0.22 L . min⁻¹ . % Sao₂ versus 0.80 ± 0.14 L . min⁻¹; mean \pm SEM). Resting ventilation and ventilatory response to hypercapnia were not significantly affected by prochlorperazine. These results were not explained by differences in end-tidal PCO₂ at which hypercapnic hypoxic tests were performed. It is concluded that prochlorperazine reverses the depression of the ventilatory response to asphyxia caused by morphine.

Br Med J (Clin Res Ed). 1985 Apr 20;290(6476):1173-5.

Comparison of the antiemetics metoclopramide and promethazine in labour.

[Vella L](#), [Francis D](#), [Houlton P](#), [Reynolds F](#).

A double blind trial was conducted in 477 mothers in labour to compare the antiemetics metoclopramide 10 mg and promethazine 25 mg and placebo when added to the first dose of pethidine. Metoclopramide and promethazine were equally effective, and both better than placebo, in reducing the incidence of nausea and vomiting after the administration of pethidine. Seventy seven per cent of mothers were drowsy, and 8% slept in the hour after the pethidine injection, with no difference between the groups. The sedative effect was more persistent in the promethazine group, 66% of whom were still drowsy after delivery. One third of the mothers in each group needed further analgesia, with 77% of these ultimately requesting an epidural. The reduction in pain half an hour and one hour after pethidine, assessed by a visual analogue scale, were, respectively, 22% and 22% for placebo; 26% and 23% for metoclopramide; 13% and 9% for promethazine. Analgesia after metoclopramide was significantly better than that after promethazine in terms of pain score, duration of first injection, and need for Entonox. Metoclopramide is therefore to be preferred to promethazine as an antiemetic in labour.

Anesthesiology. 1974 Jun;40(6):581-7.

Comparison of the ventilatory effects of two antiemetics, benzquinamide and prochlorperazine.

[Mull TD](#), [Smith TC](#).

Anesthesiology. 1972 May;36(5):519-20.

The effects of benzquinamide and prochlorperazine, separately and combined, on the human respiratory center.

[Steen SN](#), [Yates M](#).

Curr Med Res Opin. 1998;14(4):203-12.

Comparison of buccal and oral prochlorperazine in the treatment of dizziness associated with nausea and/or vomiting.
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The dizziness inherent in vertiginous disorders is often accompanied by nausea and/or vomiting. While prochlorperazine is effective in relieving nausea and vomiting, its low bioavailability following first pass metabolism in the liver and metabolism in the intestinal wall, compounded by the likelihood of regurgitation in the nauseous patient, may limit the therapeutic value of the oral preparation. A buccal preparation achieves higher plasma concentrations by direct absorption into the systemic circulation. In this randomised, double-blind, double-dummy trial in patients with vestibular disorders, in keeping with previous pharmacokinetic studies, buccal prochlorperazine achieved a significantly faster onset of effect compared with oral prochlorperazine ($p = 0.04$), and was significantly better in reducing the frequency of nausea ($p = 0.02$) and severity of vomiting ($p = 0.05$) at 24-36 hours. The frequency of vomiting was also reduced by buccal prochlorperazine compared with oral prochlorperazine, but this difference was only of borderline significance ($p = 0.07$). Buccal prochlorperazine was well tolerated and well rated by both patients and investigators, having no more adverse effects on the buccal mucosa than placebo and causing less drowsiness and sedation compared with the oral preparation. No advantages were reported for the oral preparation over buccal prochlorperazine. Buccal prochlorperazine is therefore safe and effective, and suitable for the treatment of dizziness associated with nausea and/or vomiting in patients suffering from vertiginous disorders.

Can J Anaesth. 1989 Sep;36(5):565-7.

Intraoperative prochlorperazine for prevention of post-operative nausea and vomiting.

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Department of Anaesthesia, McMaster University, Hamilton, Ontario.

The effectiveness of 10 mg IV prochlorperazine in preventing postoperative nausea and vomiting was compared with placebo when given perioperatively to 100 patients in a prospective double-blind randomized trial. The occurrence of nausea and vomiting was assessed in the recovery room prior to and after narcotic administration for pain relief. No statistically significant difference in the frequency of postoperative nausea and vomiting was found between the treatment and control groups.

Review articles

Drugs. 2000 Feb;59(2):213-43.

Prevention and treatment of postoperative nausea and vomiting.

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Pain, nausea and vomiting are frequently listed by patients as their most important perioperative concerns. With the change in emphasis from an inpatient to outpatient hospital and office-based medical/surgical environment, there has been increased interest in the 'big little problem' of postoperative nausea and vomiting (PONV). Currently, the overall incidence of PONV is estimated to be 25 to 30%, with severe, intractable PONV estimated to occur in approximately 0.18% of all patients undergoing surgery. PONV can lead to delayed postanesthesia care unit (PACU) recovery room discharge and unanticipated hospital admission, thereby increasing medical costs. The aetiology and consequences of PONV are complex and multifactorial, with patient-, medical- and surgery-related factors. A thorough understanding of these factors, as well as the neuropharmacology of multiple emetic receptors [dopaminergic, muscarinic, cholinergic, opioid, histamine, serotonin (5-hydroxy-tryptamine; 5-HT)] and physiology [cranial nerves VIII (acoustic-vestibular), IX (glossopharyngeal) and X (vagus), gastrointestinal reflex] relating to PONV are necessary to most effectively manage PONV. Commonly used older, traditional antiemetics for PONV include the anticholinergics (scopolamine), phenothiazines (promethazine), antihistamines (diphenhydramine), butyrophenones (droperidol) and benzamides (metoclopramide). These antiemetics have adverse effects such as dry mouth, sedation, hypotension, extrapyramidal symptoms, dystonic effects and restlessness. The newest class of antiemetics used for the prevention and treatment of PONV are the serotonin receptor antagonists (ondansetron, granisetron, tropisetron, dolasetron). These antiemetics do not have the adverse effects of the older, traditional antiemetics. Headache and dizziness are the main adverse effects of the serotonin receptor antagonists in the dosages used for PONV. The serotonin receptor antagonists have improved antiemetic effectiveness but are not as completely efficacious for PONV as they are for chemotherapy-induced nausea and vomiting. Older, traditional antiemetics (such as droperidol) compare favourably with the serotonin receptor antagonists regarding efficacy for PONV prevention. Combination antiemetic therapy improves efficacy for PONV prevention and treatment. In the difficult-to-treat PONV patient (as in the chemotherapy patient), suppression of numerous emetogenic peripheral stimuli and central neuroemetic receptors may be necessary. This multimodal PONV management approach includes use of: (i) multiple different antiemetic medications (double or triple combination antiemetic therapy acting at different neuroreceptor sites); (ii) less emetogenic anaesthesia techniques; (iii) adequate intravenous hydration; and (iv) adequate pain control.

Eur J Anaesthesiol. 1998 Sep;15(5):595-9.

The impact of audit in a district general hospital on post-operative nausea and vomiting after major gynaecological surgery.

[Hadji E](#), [Eastwood D](#), [Fear S](#), [Corfield HJ](#).

Arrowe Park Hospital, Upton, Wirral, UK.

An audit of post-operative nausea and vomiting (PONV) was undertaken in 935 female patients who used morphine patient-controlled analgesia (PCA) for pain relief after major gynaecological operations in a district general hospital. We investigated retrospectively five different antiemetic policies and a reference group without policy from January 1993 to July 1995. The department's computerized audit system was used to analyse the observations. At the beginning of the audit, the incidence of nausea and vomiting was as high as 71.5%. But as a consequence of this audit, a departmental policy was adopted 3 years later, which had an incidence of PONV of only 51.7%. During this time the compliance with antiemetic protocols increased from 41% to 76%. There was significantly less PONV if an antiemetic protocol was followed ($P = 0.002$). This emphasizes the importance of corporate involvement in the development, formulation and evaluation of departmental protocols if compliance is to be high. We conclude that audit as a corporate effort improves the acceptance of departmental protocols. This reduces PONV significantly irrespective of the type of antiemetic drug used.

Eur J Cancer. 1994;30A(9):1223-7.

Comment in: [Eur J Cancer. 1994;30A\(9\):1217.](#)

The roles of patient and observer assessments in anti-emetic trials.

[Olver IN](#), [Matthews JP](#), [Bishop JF](#), [Smith RA](#).

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The endpoints assessed by both patients and nurses were compared in three anti-emetic studies. In a parallel subjects study, there was no significant difference between the patients' and nurses' assessment of the number of vomiting episodes, but the duration of vomiting, the severity and duration of nausea, and the side-effects of the anti-emetic were given higher scores by the nurses. In two cross-over studies, the patients recorded more vomiting episodes than the nurses, while the nurses recorded more anxiety and sedation than the patients. This resulted in the patients detecting a difference between the side-effects of the anti-emetics being compared that was not apparent from the nurses' forms. Many of the differences reflect differences in the timing and frequency of data collection. Nurses collected data regularly during the assessment period whereas patients reported their experiences only at the completion of 24 h. Both assessments provide useful perspectives on the study outcomes.

- JAMA. 1966 May 30;196(9):796-8.
A controlled double-blind study of trimethobenzamide, prochlorperazine, and placebo.
[Bardfeld PA.](#)