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Comparison of Drugs and Intravenous Crystalloid in Reduction of Postoperative Nausea and Vomiting after Laparoscopic Surgery

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Abstract

Background: Nausea and vomiting are frequent after general anesthesia ,the most important causes of morbidity after anesthesia and surgery are postoperative nausea and vomiting.

Methods: A comparative analysis of published articles was done to determine the relative efficacy and safety of ondansetron, droperidol, metoclopramide, dexamethasone, and intravenous crystalloid fluid for the prevention of postoperative nausea and vomiting. I performed a literature search of English references using both the MEDLINE database and a manual search. Double-blinded, randomized, controlled trials comparing the effect of these agents in reduction or prevention of postoperative nausea and vomiting.

Results: A total of 60 studies were identified, of which 6 were excluded for methodological concerns. For each comparison of drugs, ondansetron ($P < 0.001$), droperidol ($P < 0.001$) were more effective than metoclopramide in preventing vomiting. We conclude that ondansetron and droperidol are more effective than metoclopramide in reducing postoperative nausea and vomiting. The incidence of vomiting was reduced in the intravenous administration of crystalloid 30 mg/kg in healthy adults ($P = 0.001$) and for dexamethasone is ($P < 0.03$).

Conclusion: In summary, both ondansetron and droperidol were more effective than metoclopramide, intravenous crystalloid fluid and dexamethasone in preventing postoperative vomiting.

Keywords: Laparoscopy postoperative nausea and vomiting, droperidol, metoclopramide, ondansetron, IV crystalloid.

INTRODUCTION

Postoperative nausea and vomiting (PONV) remains one of the most common postoperative complications and is experienced by up to 70% of patients (Hofer and colleagues).[1] It is a limiting factor in the early discharge of ambulatory surgery patients and is a leading cause of unanticipated hospital admission.[2,3] There is still controversy concerning the best approach to managing postoperative nausea and vomiting (PONV).[4] PONV can lead to increased recovery room time, expanded nursing care, and potential hospital admission—all factors that may increase total health care costs. Patients report that avoidance of PONV is of greater concern than avoidance of postoperative pain.[5] The optimal approach to PONV management remains unclear to many clinicians. Guidelines for prevention and treatment of PONV based on data from systematic reviews of randomized trials have been published.[6,7] Patients incur a fluid deficit by mandatory preoperative fasting. Guided intravenous fluid therapy improves outcomes in major surgery.[8,9] It has been suggested that relative hypovolemia may be a factor in such adverse outcomes after surgery and that preoperative administration of intravenous fluids reduces their incidence.[10] Gan and colleagues showed an earlier return to bowel function, decreased length of hospital stay and a reduction in PONV by using esophageal Doppler with goal-directed therapy aimed at maintaining stroke volume.[11] While they studied a major surgery group with expected blood loss in excess of 500 ml, their work supports our hypothesis that reduced bowel mucosal perfusion may be a factor in PONV. I, therefore performed a meta-analysis of published, randomized, controlled trials of prophylactic antiemetic therapy to determine the relative efficacy and safety of ondansetron, metoclopramide, droperidol, intravenous crystalloid fluid and dexamethasone for preventing PONV.

METHODS

An initial list of published studies was obtained by searching the MEDLINE database from (1996 to 2007) using the terms (MeSH as well as text search) "prevention," "postoperative complications," "nausea and vomiting" separately for "ondansetron," "droperidol," "metoclopramide, dexamethasone, and intravenous crystalloid fluid." The list was expanded by a manual search of table of contents in English anesthesiology journals and reference lists from all articles, review articles, correspondence, and abstracts related to PONV. Only English-language references were included.

Articles that met the following criteria were included in the meta-analysis:

1. The study was a double-blinded, randomized, controlled trial;
2. Patients underwent general anesthesia for laparoscopy;
3. Vomiting, nausea, or the use of rescue antiemetic therapy were identified as outcomes;
4. Antiemetic therapy was administered prophylactically, not just in the treatment of PONV;
5. At least two drugs (metoclopramide 10 mg, droperidol 20 microgram, ondansetron 2 mg, dexamethasone 2 mg IV crystalloid fluid 10 ml/kg and 30 ml/kg) were compared.

The meta-analyses were designed to determine the relative efficacy of ondansetron, droperidol, metoclopramide, dexamethasone and IV crystalloid fluid compared with each other in reducing the odds of PONV. Separate meta-analyses were performed for the different drug combinations. All patients from the included studies were categorized as having postoperative vomiting or nausea or using rescue antiemetic medication under each two-drug comparison. In some studies, counts were calculated from percentages identified in tables or figures. Studies with different drug doses within the therapeutic range. In the study where the patients received crystalloid fluid (JJ magner)[12] divided the patient into two group the CSL-10 group ($n = 70$) received compound sodium lactate (CSL) 10 ml kg–1; the CSL-30 group ($n = 70$) received CSL 30 ml kg–1. CSL contains sodium 131 mmol litre–1, potassium 5 mmol litre–1, calcium 2 mmol litre–1, chloride 111 mmol litre–1 and lactate 29 mmol litre–1. To maintain patient and investigator blinding, intravenous fluid administration was initiated in the preoperative area.

RESULT

The details of the articles involving a total of 676 patients included in the meta-analyses. The meta-analysis comparing the efficacy of ondansetron versus metoclopramide included 175 patients (Tables 1 and 2).[12] Droperidol versus metoclopramide analysis included (Table 2).[13] The ondansetron

TABLE 1: Demographic and clinical characteristic of patient population (N = 175)

Group (n)	*Age (yr)*	*Body weight (kg)*	*History of motion sickness*	*History of PONV*
Ondansetron (58)	34 ± 10	58 ± 11	18	NPAE = 16 PAEP = 24 NPAE = 18
Metoclopramide (57)	36 ± 10	56 ± 8	19	NPAE = 13 PAEP = 26 PAENP = 18
Placebo (60)	35 ± 12	56 ± 10	21	NPAE = 26 PAENP = 17

Age and body weight data are presented as mean = No. History of motion sickness and PONV data as presented as the number of patient. PONV = postoperative nausea and vomiting. NPAE = no previous anesthetic experience, PAEP = previous anesthetic experience with PONV, PANP = previous anesthetic experience without PONV.

TABLE 2: Odds ratio (95% confidence interval of one hour efficacy of antiemetic regimen in 175 patients)

Variables	*Odds ratio*		
	Nonadjusted	*Adjusted*	*P value**
Age (SD 10.8 yr)	0/85 (0.62-1.15)	1.02 (0.66-1.57)	0.927
Body weight (SD 9.6 kg)	0.78 (0.57-1.06)	0.67 (0.43-1.06)	0.080)
Motion sickness (present versus absent)	1.19 (0.61-2.32)	1.85 (0.75-4.56)	0.175
Past history			
PAEP versus NPAE	0.51 (0.24-1.11)	0.51 (0.18-1.49)	
PAENP versus NPAE	1.35 (0.55-3.27)	1.31 (0.38-4.55)	0.151
Duration (SD 32.5 min)	0.76 (0.56-1.03)	1.07 (0.60-1.93)	0.812
Fentanyl (SD 159 µg)	0.56 (0.41-0.78)	0.33 (0.17-0.62)	< 0.001
Treatment			
Ondansetron versus metoclopramide	6.73 (2.13-2.14)	17.8 (3.97-79.7)	
Placebo versus metoclopramide	0.27 (0.1300.58)	0.18 (0.07-0.45)	< 0.001

Odds ratio were derived from a logistic regression model. Odds ratios for continuous variables were computed on the basis of an increase in the values of 1 SD. NPAE = no previous anesthetic experience, PAEP = previous anesthetic experience with postoperative nausea and vomiting, PAENP = previous anesthetic experience without postoperative nausea and vomiting. *P = values were computed controlling for all other variables.

TABLE 3: Postoperative nausea and vomiting

	Comparison of drug 1st versus drug 2nd		
	Ondansetron versus metoclopramide	*Ondansetron versus droperiodol*	*Droperiodol versus* metoclopramide
Nausea	10	13	15
No of studies	907/1697 (53)	1587/2743 (58)	473/1021 (46)
Nausea/no of patients (%)			
Incidence nausea (5)			
Drug 1	48	57	41
Drug 2	59	58	52
Pooled OR (95% CI)	0.70 (0.45, 1.10)	0.99 (0.66, 1.47)	0.66 (0.48, 0.90)
P	0.125	> 0.9	0.008
Vomiting			
No of studies	17	22	20
Vomiting/no. of patients (%)	955/2272 (42)	1435/3750 (38)	412/1374 (30)
Incidence vomiting (%)			
Drug 1	35	34	26
Drug 2	50	42	34
Pooled OR (95% CI)	0.43 (0.31, 0.61)	0.70 (0.52, 0.94)	0.68 (0.54, 0.85)
P	< 0.001	0.018	< 0.001

OR = odds ratio, *Drugs 1—the first drug in each comparison, Drug 2—the second drug in each comparison.

versus droperidol (Table 3)[14] and the difference between them in 1st day (Fig. 1).

This prospective, randomized, double-blind clinical investigation has shown a beneficial effect of rapid infusion of 30 ml kg–1 compared with 10 ml kg–1 of crystalloid solution in reducing the incidence of PONV after gynecologic laparoscopy in ASA 1 female patients. However, there were no significant differences in the subjective symptoms of dizziness, thirst or opioid consumption at any time. Sore throat was transiently increased in the CSL-30 group on emergence from anesthesia (Table 4).

TABLE 4: Subject characteristics

	Ondansetron (n = 80)	*Droperidol (n = 78)*
Age (yr)	33 (18-49)	32 (19-50)
Weight (kg)	70 (43-128)	68 (46-110)
Operative time (min)	25 (7-75)	28 (5-106)
Anesthesia time (min)	52 (28-105)	53 (28-152)
Type of surgery		
Tubal ligation	52	56
Diagnostic lap	17	12
Pelviscopy	11	10
Time in PACU (min)	128 (75-268)	118 (42-220)
Fentanyl dose (µg)	206 (0-550)	178 (0-575)

Values are mean (range). There were no significant differences between groups.
Lap = Laparoscopy, PACU = postanesthesia care unit.

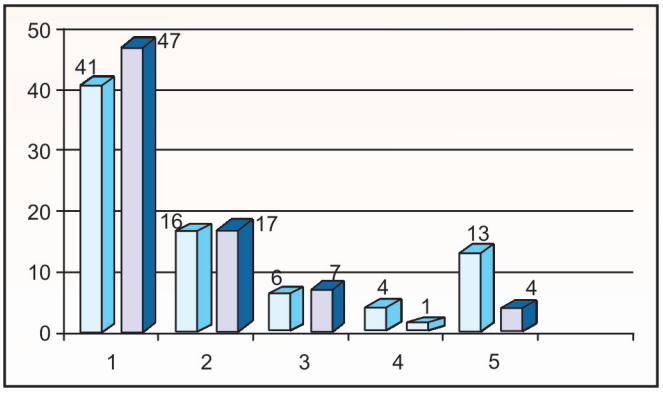

Fig. 1: Distribution for nausea and vomiting postoperatively in 1st 24 h light bars = ondesteron, dark bars = droperidol, p = 0.115 for the comparisons in the study for the patient receiving crystalloid fluid. In the first 48 h after anesthesia, the incidence of vomiting was lower in the CSL-30 group than in the CSL-10 group (8.6% vs 25.7%, P = 0.01). Antiemetic use was less in the CSL-30 group at 0.5 h (2.9% vs 14.3%, P = 0.04). The incidence of severe nausea was significantly reduced in the treatment group at awakening (2.9% vs 15.7%, P = 0.02), 2 h (0.0% vs 8.6%, P = 0.04) and cumulatively (5.7% vs 27.1%, P = 0.001)[12]

The result for dexamethasone in comparison with metaclopramide as in Tables 5 to 7.[15] Patients in group I reported a lower incidence of PONV and requested less rescue antiemetics than those in group III during the first four postoperative hours ($P < 0.01$). Patients in group I reported a lower incidence of PONV than those in groups II ($P < 0.05$) and III ($P < 0.01$) during the 24 hr postoperative period. Groups II and III did not differ

TABLE 5: Postoperative nausea and vomiting cumulative refers to number of patient affected or treated, not number of episodes CSL = compound sodium lactate

	CSL 10 ml kg⁻1	*CSL 30 ml kg⁻1*	*P-value*
Vomiting			
Preoperative	0 (0.0)	0 (0.0)	0.886
0.5 h	9 (12.9)	2 (2.9)	0.06
2 h	7 (10.0)	1 (1.4)	0.07
24 h	6 (8.6)	3 (4.4)	0.52
48 h	1(1.5)	1 (1.5)	0.49
Cumulative	18 (25.7)	6 (8.6)	0.01
Nausea: severe only			
Preoperative	0 (0.0)	0 (0.0)	0.886
0.5 h	11 (15.7)	2 (2.9)	0.02
2 h	6 (8.6)	0 (0.0)	0.04
24 h	5 (7.1)	2 (2.9)	0.46
48 h	0 (0.0)	1 (1.5)	0.99
Cumulative	19 (27.1)	4 (5.7)	0.001
Nausea: severe with antiemetic given			
Preoperative	0 (0.0)	0 (0.0)	0.886
0.5 h	10 (14.3)	2 (2.9)	0.04
2 h	6 (8.6)	0 (0.0)	0.04
24 h	3 (4.5)	1 (1.4)	0.58
48 h	0 (0.0)	1 (1.5)	0.99
Cumulative	16 (22.3)	4 (5.7)	0.008
Nausea: total			
Preoperative	0 (0.0)	0 (0.0)	0.886
0.5 h	17 (24.3)	19 (27.1)	0.85
2 h	11 (15.7)	8 (11.4)	0.62
24 h	8 (11.4)	3 (4.4)	0.23
48 h	3 (4.3)	2 (3.0)	0.97
Cumulative	26 (37.1)	26 (37.1)	0.86
Antiemetic use			
Preoperative	0 (0.0)	0 (0.0)	0.886
0.5 h	10 (14.3)	2 (2.9)	0.035
2 h	7 (10.0)	2 (2.9)	0.168
24 h	3 (4.29)	1 (1.47)	0.63
48 h	0 (0)	1 (1.5)	0.98
Cumulative	16 (22.9)	8 (11.9)	0.146

from each other in the incidence of PONV and the proportion of patients who requested rescue antiemetics.

From the result we can see that the Prophylactic intravenous dexamethasone 5 mg significantly reduces the incidence of PONV in women undergoing ambulatory laparoscopic tubal ligation. At this dose, dexamethasone is more effective than metoclopramide 10 mg or placebo.[16]

DISCUSSION

The clinical benefits of routine antiemetic prophylaxis for high-risk surgical patients have been well documented in the anesthesia literature.[4,20-25] These benefits were not limited to cost savings for treatment of emetic episodes but also included improved patient satisfaction compared with simply treating presenting symptoms.[22,23] Although multimodal antiemetic regimens involving up to three antiemetic drugs are justified in patients at high risk of developing PONV,[20] the possibility of adverse drug interactions increases as a function of the number of drugs administered. In this meta-analysis, I demonstrated that the prophylactic administration of ondansetron and droperidol was more effective than that of metoclopramide, dexamethasone and intravenous crystalloid in preventing postoperative nausea and vomiting. The droperidol is less cost than ondasetron and the intravenous crystalloid have same effect in decreasing the postoperative nausea and vomiting, so we can use droperidol and crystalloid for prophylactic antiemetic effect. The results were sometimes variable, and most studies individually lacked the power to detect differences in efficacy among the different drugs. In such settings, the use of a meta-analysis has been advocated to provide greater power to detect differences among the drugs and to obtain a more precise estimate of effect size.[17,18] The results of the meta-analyses in the present study are strengthened by the remarkable consistency of the large number of individual studies for most drug comparisons. A meta-analysis merits more confidence when the individual ORs for each study are predominately on the same side of the no difference line, an OR of 1.0.[19] This consistency of results occurred with both the ondansetron versus metoclopramide and the droperidol versus ondansetron analyses. This meta-analysis suggests that the usual clinical doses of either ondansetron or droperidol, rather than metoclopramide, dexamethasone, and intravenous crystalloid fluid should be administered for the greatest antiemetic efficacy. Droperidol and ondansetron were similarly effective in preventing PONV in adults.

CONCLUSION

All methods were associated with low incidence of postoperative nausea and vomiting. I conclude that

TABLE 6: Patients characteristics

	Dexamethasone (Group I)	Metoclopramide (Group II)	Saline (Group III)
No.	39	38	38
Age (yr)	32 (27–35)	34 (31–36)	35 (30–37)
Weight (kg)	54 (42–72)	56 (46–75)	56 (45–76)
Height (cm)	158 (145–172)	157 (138–170)	156 (139–173)
		Interval since last menstrual period (days)	
0–8	12	11	11
9–16	7	9	10
16–28	11	12	9
>28	9	6	8
Duration of anesthesia (min)			
65 (45–78)	68 (49–78)	64 (51–76)	
Duration of surgery (min)	41 (32–63)	45 (38–65)	42 (38–64)

Values given as numbers or median (range).

TABLE 7: Incidence of nausea and vomiting after laparoscopic tubal ligation

	Dexamethasone (Group I)	Metoclopramide (Group II)	Saline (Group III)
No.	39	38	38
		In the PACU (0-4 hr postoperatively)	
- Nausea	6 (15)	8 (21)	12 (32)
- Vomiting	3 (8)	6 (16)	10 (26)
- Total	9 (23)	14 (37)	22 (58)
- Rescue antiemetic	4 (10)	10 (26)	16 (42)
		After discharge (4-24 hr postoperatively)	
- Nausea	4 (10)	6 (15)	8 (21)
- Vomiting	1 (3)	4 (11)	3 (8)
- Total	5 (13)	10 (26)	11 (29)
		From 0-24 hr postoperatively	
- Nausea	8 (21)	12 (32)	13 (34)
- Vomiting	3 (8)	8 (21)	11 (29)
- Total	11 (28)*	20 (53)	24 (63)
Successful protection	28 (72)*	18 (47)	14 (37)

Values are numbers of patients (%). PACU = postanesthetic care unit. Successful protection was defined as no nausea, no vomiting and no antiemetic medication.*$P < 0.05$ when compared with group II; $P < 0.01$ when compared with group III using 3×22 test followed by 2×22 test.

ondansetron, droperidol were more effective than the anther in laparoscopy. Equivalents effectiveness for ondansetron, droperidol, and significant cost saving may be obtained by using droperidol prophylactically for laparoscopic surgery.

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