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Intraoperative prochlorperazine for prevention of postoperative nausea and vomiting

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.

Postanaesthetic nausea and vomiting can result in significant morbidity for some patients. The incidence of postanaesthetic nausea and vomiting ranges from 25–35 per cent, with the age group 0–19 years old affected most.^{1, 2} There is an increased incidence in the adult female population, one to three times greater than in men.¹ Factors such as narcotic premedication can increase the incidence of nausea and vomiting while atropine has an antiemetic effect.³ Many of the inhalational agents used in anaesthesia have the tendency to produce emetic symptoms with a dose-response and time relationship.⁴ Therefore, the duration of anaesthesia is also significant. Among the factors increasing the emetic response are the site of the operation (especially intra-abdominal or the head and neck region), pre-existing medical illnesses (e.g., uraemia), motion sickness, obesity, history of postanaesthetic vomiting, and administration of anticholinesterase drugs to reverse muscle relaxants.⁵

Prochlorperazine is an acknowledged antiemetic agent

for chemotherapy and radiotherapy.^{6–9} The present study was designed to determine the effectiveness of prochlorperazine in preventing postoperative nausea and vomiting, as compared to placebo when given intraoperatively.

Methods

The study was approved by the McMaster University Ethics Review Committee. One hundred adult patients, ASA physical status I or II, scheduled for elective surgery (intra-abdominal or head and neck procedures) were included. Patients were excluded if they had a known allergy to the drug, were currently taking phenothiazines, were pregnant or nursing, or had any condition associated with nausea and vomiting. Any history of previous postoperative nausea and vomiting, motion sickness, or migraine headaches was elicited.

The study design was prospective, randomized, and double-blinded. Informed consent was signed by each patient. The effect of prochlorperazine on blood pressure and heart rate during anaesthesia was assessed. The relationship of treatment outcome to motion sickness, migraine headaches, and a previous history of postanaesthetic nausea and vomiting was also studied.

Syringes of sterile water and prochlorperazine were prepared by the pharmacy in coded syringes which were identical in appearance. Patients were randomized within blocks of four and two using a random numbers table, to two treatment groups: Group I received 10 mg prochlorperazine and Group II received sterile saline (placebo). The anaesthetists, patients, and nursing staff involved were blinded to the nature of the treatment received. Each group consisted of 50 patients.

The contents of the syringe containing either control or drug was administered into the patient's indwelling IV line approximately 10 min after the induction of anaesthesia was accomplished, provided that all vital signs were stable. Heart rate and blood pressure were recorded prior to injection, one minute postinjection, and five minutes postinjection and an ECG and Dynamap were used during anaesthesia. A standardized anaesthetic was administered

Key words

COMPLICATIONS: nausea, vomiting; VOMITING: antiemetics, prochlorperazine.

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TABLE I Patients' demographic data and duration of anaesthesia

	Placebo		Prochlorperazine	
	Mean $\pm$ SEM	n	Mean $\pm$ SEM	n
Age (Years)	37.3 $\pm$ 1.7	49	40.7 $\pm$ 1.8	50
Sex (M)	—	7	—	8
(F)	—	42	—	42
Height (cm)	154 $\pm$ 2.1	48	160 $\pm$ 2.1	45
Weight (kg)	64.8 $\pm$ 2.2	49	66.8 $\pm$ 1.9	50

to each study patient and included thiopentone 1–5 mg·kg⁻¹, succinylcholine 1–2 mg·kg⁻¹, fentanyl less than 2 µg·kg⁻¹·hr⁻¹, nitrous oxide, isoflurane, and a muscle relaxant of choice. The only premedication allowed was oral diazepam.

The occurrence of patient nausea and vomiting was elicited in the recovery room. The minimum recovery room stay was one hour. Nausea and vomiting were assessed on two occasions: prior to receiving narcotics in the recovery room and again after narcotics were given for pain relief, if required. Recovery from anaesthesia was judged by the achievement of a full Glasgow Coma Score. Following this, nausea was assessed as being present or absent: vomiting was scored using a four point scale; 0 – no vomiting, 1 – retching only, 2 – vomiting only once, and 3 – vomiting more than once.

The results were analyzed statistically using a Chi square for categorical data and an unpaired Student's *t* test to compare continuous data. For the purpose of this study a *P* value < 0.05 was regarded as being statistically significant.

Results

Of the 100 patients entered into the study 99 outcomes (prochlorperazine = 50, control = 49) were available for evaluation. One patient was excluded because the needle dislodged from the syringe at the time of injection and the study medication was wasted. Patient demographic data are presented in Table I. In only one patient was the

trachea not intubated and the lungs mechanically ventilated, although there were no study restrictions regarding airway management and ventilation. The duration of anaesthesia for both groups was similar. There were no statistically significant changes in the heart rate or blood pressure between the two groups. The incidence of nausea and vomiting in each group is presented in Table II. There is a difference in sample size in Table II as many patients did not require narcotics while in the recovery room. The difference between the two groups, both before and after receiving narcotics, did not reach statistical significance. A history of motion sickness, migraine and previous postoperative nausea and vomiting were analyzed for correlation with postoperative nausea and vomiting and are shown in Table III. Only a history of postanaesthetic nausea and vomiting was statistically significant.

Discussion

No statistically significant difference existed in the frequency of postoperative nausea and vomiting between the treatment (prochlorperazine) and control groups. Prochlorperazine was given in a parenteral dose (10 mg) recommended by the manufacturer, and was given before emergence from anaesthesia so that adequate blood levels would be present in the postoperative period. A single dose acts within 30 minutes and maintains its antinauseant effect for four hours.⁶ We chose prochlorperazine for our trial as it has good success as an antinauseant following chemotherapy and radiotherapy, both potent emetic treatments. It has been used as the "gold standard" for comparison of other antiemetic agents.^{10–14}

Since prochlorperazine has a good record as an anti-nauseant, our findings were unexpected. Whenever a negative result is obtained one must consider the study design and power. The study design was prospective, randomized and double-blinded to minimize any bias. In addition, we standardized many variables in the anaesthetic technique. We also selected a high-risk population to ensure that our study patients would have the highest incidence of nausea and vomiting.

TABLE II The incidence of nausea and vomiting before and after narcotic administration in the recovery room

	Before narcotics						After narcotics					
	Nausea		Vomiting				Nausea		Vomiting			
	none	present	0	1	2	3	none	present	0	1	2	3
Placebo	35	14	39	7	2	1	31	10	31	7	2	1
Prochlorperazine	37	13	36	11	2	1	30	9	29	9	1	0
χ ² for difference	0.08	(NS)		0.51	(NS)	*	0.02	(NS)		0.02	(NS)	*

*Categories of vomiting (1 + 2 + 3) grouped for analysis.

TABLE III The relation of postoperative nausea to previous postoperative nausea, motion sickness and migraine

	Prior history		Motion sickness		Migraine	
	Yes	No	Yes	No	Yes	No
No nausea	26	46	18	54	14	58
Nausea	17	10	8	19	8	19
χ^2 for difference	4.72		0.22		1.18	
	(P < 0.05)		(NS)		(NS)	

Despite a standardized anaesthetic technique, there may have been minor variations in each case, for example isoflurane concentration. Alternatively, the stimulus for nausea and vomiting may have been too potent for the antinauseant ability of prochlorperazine. Lastly, the dose of 10 mg was based on efficacy in a different patient population (chemotherapy, radiotherapy) and may be inappropriately low for anaesthetic and surgically induced nausea and vomiting.

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References

- 1 Smessaert A, Schehr EA, Artusio JF. Nausea and vomiting in the immediate postanesthetic period. *JAMA* 1959; 170: 2072-6.
- 2 Burtles R, Peckett BW. Postoperative vomiting. Some factors affecting its incidence. *Br J Anaesth* 1957; 29: 114-23.
- 3 Riding JE. Postoperative vomiting. *Proc Roy Soc Med* 1960; 53: 671-7.
- 4 Belleville JW, Bross IDJ, Howland WS. Postoperative nausea and vomiting. IV: Factors related to postoperative nausea and vomiting. *Anesthesiology* 1960; 21: 186-93.
- 5 Purkis IE. Postoperative vomiting. *Can Anaesth Soc J* 1964; 11: 335-53.
- 6 Conner PK, Moyer J. Preliminary clinical observations on a potential antiemetic agent, prochlorperazine (compazine). *AM&CT* 1957; 4: 508-14.
- 7 Frytak S, Moestel CG. Management of nausea and vomiting in the cancer patient. *JAMA* 1981; 245: 393-7.
- 8 Dundee JW, Moore J. Studies of drugs given before anaesthesia. VI: The phenothiazines. *Br J Anaesth* 1965; 37: 332-53.
- 9 Gray WD. An appraisal of a new antiemetic drug: prochlorperazine. *Int Rec Med* 1957; 170: 469-72.
- 10 Bardfeld PA. A controlled double blind study of trimethobenzamide, prochlorperazine, and placebo. *JAMA* 1966; 196: 796-8.
- 11 Carr B, Bertrand M. A comparison of the antiemetic efficacy of prochlorperazine and metoclopramide for the treatment of cisplatin induced emesis: a prospective randomized double blind study. *J Clin Oncol* 1985; 3: 1127-32.
- 12 Herman TS, Einhorn LH. Superiority of nabilone over prochlorperazine as an antiemetic in patients receiving cancer chemotherapy. *N Engl J Med* 1979; 300: 1295-8.
- 13 Moertel CG, Rutemeier E. A controlled clinical evaluation of antiemetic drugs. *JAMA* 1963; 186: 116-9.
- 14 Sallan SE, Cronin C. Antiemetics in patients receiving chemotherapy for cancer. *N Engl J Med* 1980; 302: 135-9.

Résumé

La prochlorperazine est un anti-émétique populaire en chimiothérapie. Nous en avons comparée une dose péri-opératoire intraveineuse de 10 mg à un placebo, dans le cadre d'une étude portant sur la prévention des nausées et des vomissements post-opératoires. L'étude conduite à double insu chez 100 patients randomisés a révélé que l'incidence de nausées et de vomissements, évaluée en salle de réveil avant et après l'injection d'analgésiques opiacés était semblable d'un groupe à l'autre.