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Antiemetic Effectiveness of Intramuscularly Administered Domperidone

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Domperidone, a new antiemetic, does not cause the cardiovascular and central nervous system side effects associated with other antiemetics. In previous studies, a 10-mg dose of domperidone administered iv proved more effective than placebo in treating postoperative nausea and vomiting.[1–3] Since the intramuscular route should produce a longer duration of action and the intravenous route is not always available, we compared the effectiveness of domperidone with that of a placebo when they were given intramuscularly to treat postoperative nausea and vomiting.

MATERIALS AND METHODS

Five-hundred and twelve women, ASA physical status 1 or 2, who were not taking drugs with antiemetic properties were scheduled for gynecological surgical procedures signed consent forms after being fully informed of the nature of the study.‡ Of these, 46 vomited postoperatively and were assigned by a table of random numbers to receive domperidone 10 mg (5 mg/ml), im, or a placebo. The vehicle for domperidone served as the placebo. A coded, single-dose ampule was provided for each patient and the medication was administered within 5 min of the occurrence of symptoms.

Nausea, vomiting and side effects were recorded by one of us (N.C.) at half-hourly intervals for four hours after treatment. Complaints of nausea were spontaneous or in response to a neutral question, *i.e.*, "How do you feel?" When symptoms persisted for half an hour, a second dose of the initial medication was administered im. When symptoms persisted for another half hour (one hour after the initial symptoms) or returned after the first hour and the patient requested treatment, a standard antiemetic (benzquinamide or prochlorperazine) was administered, and the outcome with domperidone or placebo considered a treatment failure.

Table 1. Premedicants, Anesthetic Agents and Surgical Procedures

	Domperidone	Placebo
Premedicants*		
Narcotic	11	9
Diazepam	5	7
Barbiturate	0	1
Atropine	8	11
None	9	7
Anesthetic agents†		
N_2O + fentanyl	13	7
N_2O + fentanyl + enflurane	1	3
N_2O + enflurane	9	11
N_2O	0	2
Surgical procedures		
Minor gynecologic		
Abortion‡	7	8
Other	4	3
Laparoscopy	8	8
Abdominal tubal ligation	1	2
Major gynecologic	3	2

* Some patients had more than one drug.
† All patients received thiopental induction.
‡ Patients received oxytocic drugs.

The numbers of patients who received second injections, were classified as treatment failures, had no further symptom, and experienced recurrences of nausea and/or vomiting in the first two hours were determined for each group.

Patients' ages and weights were compared by the Student *t* test. Other data were analyzed using the chi-square test; $P < 0.05$ was considered significant.

RESULTS

The mean ages and weights of patients in the two groups were similar (domperidone, 34.6 years, range 19–59; placebo, 34.3 years, range 20–51; domperidone, 66 kg, range 45–90, and placebo, 61 kg, range 48–95). The surgical procedures performed and the anesthetic agents and premedicant drugs used were similar in the two groups. (table 1). Side effects were not seen in any patient. The data in table 2 show no significant difference between the results in patients who received domperidone and those who received a placebo.

DISCUSSION

Domperidone, 10 or 20 mg, im, was ineffective for control of nausea and vomiting postoperatively. Since

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TABLE 2. Responses to Treatment with Domperidone Compared with Responses to Placebo

	No Further Symptom*	Recurrent Nausea	Recurrent Vomiting	Second Dose Given	Treatment Failure
Domperidone (n = 23)	7	16	15	8	10
Placebo (n = 23)	4	19	16	9	8

* No further nausea or vomiting after treatment.

There was no significant difference between responses to domperidone and placebo.

we previously reported a protective effect against further nausea and vomiting when domperidone, 10 mg, was administered iv to a similar patient population, we felt it important to report and try to explain these findings.

Possible explanations include: 1) the necessity of an initial high blood level for effectiveness; 2) poor absorption from intramuscular sites; 3) insufficient dose; 4) a reduced potency of domperidone in the particular drug lot that we were using.

Either an initial high blood level, obtained with intravenous administration, is necessary for a therapeutic effect, or a larger intramuscular dose is necessary to maintain blood levels in the therapeutic range. Blood levels obtained when domperidone, 20 mg, iv, was given to treat apomorphine-induced vomiting in man were much higher, exceeding for an hour even the peak levels obtained after dosing with 10 mg, im (50 times higher at 15 min, ten times higher at 30 min, 2.4 times higher at 60 min, and two times higher at 120 min).§ These are the only clinical data available for comparison of blood levels achieved by intramuscular and intravenous routes.

Pharmacokinetic studies in human volunteers have shown peak plasma levels are reached 15–30 min after intramuscular administration.¶

Janssen R & D, Inc., analyzed the drug from the lot used and found normal activity.

Since side effects are absent at an intravenously administered dose of 20 mg, a higher intramuscular dose should be studied. However, domperidone's insolubility would require too large a solvent volume to be practical for larger doses.

We conclude that patients are not protected from postoperative nausea or vomiting when domperidone, 10 mg, is administered intramuscularly in single or repeated injections.

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§ Unpublished data, personal communication of December 8, 1978, Jack D. Proctor, M.D., Associate Professor of Medicine, Medical College of Virginia, Richmond, Virginia 23298.

¶ Unpublished research reports supplied by Janssen R & D, Inc., New Brunswick, New Jersey.

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Transient Left-bundle-branch Block during Anesthesia

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Cardiac conduction blocks during anesthesia are uncommon. We present the case of a patient in whom transient left-bundle-branch block developed in association with an episode of hypertension during anesthesia for cholecystectomy.

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REPORT OF A CASE

A 79-year-old woman admitted with the diagnosis of cholecystitis was scheduled for elective cholecystectomy. The patient had had a diaphragmatic hernia repair 15 years previously. She was not diabetic, was not taking digitalis or psychotropic drugs, and had no history of hypertension.

The patient weighed 50 kg. Blood pressure was 120/80 torr and

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