Randomized, Double-Blind Comparison of a Prochlorperazine-Based versus a Metoclopramide-Based Antiemetic Regimen in Patients Undergoing Autologous Bone Marrow Transplantation

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Background. **Highly emetogenic combination alkylator therapy is routinely used in autologous bone marrow transplantation for treatment of eligible patients with solid tumors. Antiemetic therapy remains less than optimal in this setting.**

Methods. **One hundred twenty-six patients with cancer receiving high dose cisplatin, cyclophosphamide, and carmustine with autologous bone marrow support were randomized to receive one of four double-blinded antiemetic regimens: 4-day continuous infusion prochlorperazine (6 mg/m² intravenous [i.v.] loading dose followed by 1.5 mg/m²/hour) or metoclopramide (80 mg/m² iv loading dose followed by 20 mg/m²/hr) each with either dronabinol 5 mg/m² or placebo capsules for two doses before carmustine on the last day of chemotherapy. All subjects received scheduled lorazepam and diphenhydramine throughout the 4-day study period. Efficacy was measured by the Emetic Process Rating Scale and the Rhodes Index of Nausea and Vomiting (INV) Form 2.**

Results. **One hundred six patients completed the study and were fully evaluable. The median number of emetic episodes on the metoclopramide study arm were: 1 (0–7, day −6), 1 (0–6, day −5), 2 (0–9, day −4), and 2 (0–10, with dronabinol day −3) or 2 (0–7, no dronabinol day −3) and on the prochlorperazine study arm were: 4 (0–12, day −6), 0 (0–8, day −5), 0 (0–12, day −4) and 2.5 (0–9, with dronabinol day −3) or 2 (0–12, no dronabinol day −3). Metoclopramide was significantly better on the first day of therapy (day −6, $P < .002$) and prochlorperazine was significantly better on the third day of therapy (day −4, $P < 0.002$). There was no significant difference among any of the four arms on the last day of chemotherapy (day −3), or when the median number of emetic episodes over the total study period were compared. The patients' assessment of nausea, vomiting, and retching on the INV Form 2 was consistent with the observer ratings. Toxicities requiring dose reduction or discontinuation of antiemetic drugs included diarrhea, cardiac arrhythmias, sedation, anxiety, and akathisia.**

Conclusions. **Both metoclopramide and prochlorperazine in combination with lorazepam and diphenhydramine offer good control of nausea and vomiting although the sedation and low risk for cardiac toxicity limit the regimen to an inpatient setting with close monitoring. No regimen was clearly superior during the entire treatment period but prochlorperazine offered more consistent control after the first day. *Cancer* 1995;76:2330–7.**

Key words: antiemetic therapy, metoclopramide, prochlorperazine, dronabinol, high dose chemotherapy, autologous bone marrow transplantation.

Nausea, retching, and vomiting are well recognized side effects of chemotherapy and are particularly associated with administration of high dose alkylating agents. Although this is rarely a life-threatening side effect, it is

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one of the most dreaded toxicities that patients with cancer experience.[1] Cisplatin is often used as model for evaluating control of emesis due to its predictable, dose-related pattern of producing emesis. Other highly emetogenic agents such as cyclophosphamide, carmustine, and busulfan are commonly used in preparative regimens for autologous bone marrow transplantation (ABMT) programs. The emetic patterns (severity, onset, and duration) associated with high dose combination chemotherapy are poorly described in the literature and probably differ from that occurring with standard dose platinum-containing regimens. Typically, high dose combination alkylating agents require multiple anti-emetic agents for adequate emetic control. Controlled clinical trials of anti-emetic combination therapy approaches have rarely been conducted in the ABMT setting.

The spectrum of standard anti-emetic agents that have been combined in clinical practice includes metoclopramide, lorazepam, dexamethasone, diphenhydramine, prochlorperazine, thiethylperazine, and haloperidol.[2-4] The phenothiazines have been widely used for many years and offer good to moderate emetogenic control in many settings at a reasonable cost. Metoclopramide, which works similarly to the phenothiazines by binding dopamine receptors in the chemoreceptor trigger zone, as well as by peripheral stimulation of gastrointestinal motility, is thought by many investigators to be superior to the phenothiazines.[5,6] Recently, the Serotonin-3 antagonists, ondansetron and granisetron, have become available. This class of drugs is highly effective in controlling emesis on day 1 of cisplatin or cyclophosphamide-containing chemotherapy.[7] These agents have not been proven to be effective in the control of emesis associated with high dose alkylating agents administered over 4 days. Metoclopramide binds at a lower affinity to the serotonin-3 receptor and this observation has been evoked to explain its superior anti-emetic efficacy in many trials.[8] Dronabinol (THC) has been shown to possess anti-emetic activity in single-agent trials, although the mechanism of this effect is not well understood.[9,10] There have been two studies that combined dronabinol with prochlorperazine and found the combination to be superior to prochlorperazine or dronabinol alone, or placebo.[11,12] The purpose of this trial was to compare the efficacy and toxicity of four combination anti-emetic regimens in autologous bone marrow transplant patients receiving cisplatin, cyclophosphamide, and carmustine, (Fig. 1). The study drugs were selected on the basis of their differing mechanisms of action and preliminary experience with these anti-emetics in this patient population. The serotonin-3 antagonists were not available at the time this study was designed.

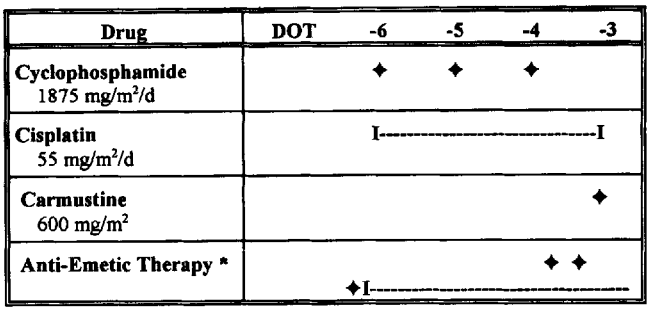

Figure 1. Chemotherapy and antiemetic treatment schema. *Patients were randomized to either (1) metoclopramide 80 mg/m² loading dose (LD) followed by 20 mg/m²/hour plus dronabinol 5 mg/m² orally every 6 hours × 2 on day −3 of therapy; (2) metoclopramide 80 mg/m² LD followed by 20 mg/m²hour plus placebo capsules orally every 6 hours × 2 on day −3 of therapy; (3) prochlorperazine 6 mg/m² LD followed by 1.5 mg/m²/hour plus dronabinol 5 mg/m² orally every 6 hours × 2 on day −3 of therapy; or (4) prochlorperazine 6 mg/² LD followed by 1.5 mg/m²/hour plus placebo capsules orally every 6 hours × 2 on day −3 of therapy. All patients received lorazepam 1 mg/m² every 4 hours and diphenhydramine 25 mg every 6 hours.

Methods

Patient Selection

One hundred twenty-six patients admitted to the adult bone marrow transplant unit between September, 1989, and July, 1991, for high dose cisplatin, cyclophosphamide, and carmustine chemotherapy and autologous bone marrow rescue were entered into the study. All patients met the Duke standard transplant eligibility criteria.[13] Exclusion criteria were: age less than 18 years; pregnancy; concurrent use of corticosteroids, other anti-emetics, hypnotics, or anxiolytics during the study period; prior history of drug or alcohol abuse; known allergies, or history of significant side effects to any of the study drugs; history of pheochromocytoma.

Upon admission to the unit, all patients had a complete history and physical with baseline electrocardiogram, blood counts, serum chemistries, and liver function tests. Eligible patients received a detailed explanation of the study and written informed consent was obtained. Complete demographic information was obtained for all study patients. The study was approved by all research review committees before its initiation at our institution.

While on study, patients were monitored according to transplant protocol, including daily electrocardiograms, daily complete blood counts, twice-daily chemistries, and twice-weekly liver function tests. After completion of the study, follow-up included bloodwork as above.

Chemotherapy Treatment

All patients on study received high dose cyclophosphamide, cisplatin, and carmustine (Fig. 1), which has been described previously.[12] Patients were hydrated with D_5NS containing meq/l of potassium chloride at 200 ml/m^2/hour beginning 12 hours before the start of chemotherapy and continuing until 12 hours after completion of chemotherapy. Patients were placed on cardiac monitors throughout chemotherapy administration and daily electrocardiograms were obtained.

Study Design and Antiemetic Treatment

This study was a double-blind two-by-two factorial design that evaluated the efficacy and toxicity of four combination antiemetic regimens (Fig. 1). Patients were randomized to one of the four treatment arms before the start of chemotherapy. All patients received diphenhydramine 25 mg every 6 hours and lorazepam 1 mg/m^2 intravenously every 4 hours. A randomization list was computer generated and patients were randomized by the pharmacy upon notification of eligibility and patient consent. Patients received study antiemetics starting 30 minutes prechemotherapy and remained on their designated regimen until 12 hours postchemotherapy. The study was discontinued in patients who experienced significant side effects possibly related to the antiemetic agents under study. Patients were declared treatment failures and removed from study if they reported continuous moderate to severe nausea or experienced more than five episodes of vomiting and/or retching in a 12 hour period. For patients experiencing grade 1 diarrhea during the study period, diphenoxylate hydrochloride 2.5 mg orally as needed was prescribed for patients testing negative for C. difficile toxin. If grade 3 diarrhea occurred, the study drug continuous infusion rate was reduced by 25%. If severe diarrhea persisted for the next 8 hours, the patient was removed from study. The lorazepam dose was cut 50% for patients excessively sedated.

Instruments and Patient Evaluation Procedures

The Emetic Process Rating Scale (EPRS) and the Rhodes Index of Nausea and Vomiting Form 2 (INV Form 2) were used to collect data on antiemetic efficacy. The EPRS is an observer-rated scale designed to measure episodic variations in the intensities of nausea, vomiting, and retching.[14] Intensities are measured using 50 mm visual analogue scales on the EPRS rating sheet. Five-point operational definitions are provided for guidance in judging intensities. Although initial reports from the use of the EPRS suggest that it has acceptable reliability and content validity, further research is needed in this area.[15] Before beginning this study, interrater reliability was assessed using paired RN assessments of eight randomly selected emetic episodes. As testing revealed low scores (Spearman's rho = 0.60 for total score; nausea = 0.84, retching = 0.44, vomiting = 0.49), extensive training of staff RNs in the use of this tool was performed during the study period to enhance reliability. The bone marrow transplantation clinical nurse specialist worked individually with all new RNs on the unit to assure their proficiency in the use of the tool.

One-to-one nurse-patient ratios were provide during high dose chemotherapy administration. Nurses provided close observation of all study patients by sitting outside their respective rooms and monitoring patients for occurrences of emetic episodes. All rooms had glass windows and doors, which facilitated easy visualization of the patient. Emetic Process Rating Scale ratings were performed after emetic episodes during chemotherapy administration and for 12 hours after completion of the chemotherapy. As only numbers of emetic episodes and intensities of vomiting were used from this instrument in the data analysis, total numbers of episodes and intensity scores were obtained for each patient on each day under study. Reliability of numbers of emetic episodes was double-checked by the investigators by comparing EPRS with nursing flowsheet documentation.

The Rhodes INV Form 2 was used to evaluate patients' perceptions of their response to the study drugs during the study period. The Rhodes INV Form 2 is an eight-item, five-point Likert-type self-report form that measures the patient's perceived duration of nausea, distress from nausea, number of nausea episodes, frequency of vomiting, distress from vomiting, amount of vomiting, frequency of dry heaves, and distress from dry heaves.[16] The items on each subscale give the patient a 12-hour time reference. An INV total score can be derived that reflects the patient's total symptom experience. Subscale scores can also be obtained to analyze particular components of the emetic response separately. Internal reliability of the INV was determined using a split half procedure and Cronbach's Alpha and yields estimates of 0.90 and 0.98 respectively.[17,18] Concurrent validity was established using Spearman's correlation coefficient ($r = 0.87$, $n = 18$, $P = 0.001$).[17] In addition, construct validity was determined by using the Wilcoxon–Mann Whitney U Test and factor supports distinctness of each of the three subscales.[17] In summary, the Rhodes INV has acceptable reliability, is brief, and could be completed by the high dose chemotherapy subjects under study.

All study patients were given their first Rhodes INV

form to complete just before initiation of high dose in the morning of day −6. The nursing staff delivered INV forms to patients for completion every 12 hours throughout the study period until 12 hours post-chemotherapy. If patients had difficulty reading the form, nurses assisted them by reading the questions aloud and marking the patient's chosen response. Despite varying degrees of sedation, most patients were able to complete the questionnaire. At the end of the study period, numerical scores were calculated for each dimension measured by the INV on each form (patients had a total of eight forms per study period) according to the directions provided by the author of this instrument. Scores ranged from 0 (least) to 4 (most) for each of the eight parameters measured; subscale scores for nausea, retching, vomiting and total INV scores were calculated as well.

Patients were permitted to take fluids orally or food as desired. None of the patients in this sample utilized behavioral methods for nausea and vomiting control such as relaxation techniques or tapes.

Toxicity data was collected by the investigators and staff nurses during the study period using a separate toxicity checkoff sheet completed every 12 hours. This sheet indicated the presence or absence of typical side effects known to occur with the drugs under study. Reasons for early study withdrawal were recorded on the toxicity sheets at the time of study drug discontinuation.

Other data was collected by the co-investigators, in addition to the instruments mentioned above. All patients were interviewed by one of the investigators to ascertain presence of anticipatory nausea and vomiting, previous cannabinoid use, and previous use of sedatives, narcotics, or anxiolytics. Age was recorded for each patient. As part of monitoring for toxicity, laboratory parameters, hemodynamic parameters (maximum/minimum blood pressures and heart rates), oral intake, and diarrheal outputs were recorded on a separate sheet for each patient on each day during the study period.

Statistics

Patients were analyzed according to the randomization and were included in analyses as long as they could contribute some data. For example, the analyses comparing the antiemetic regimens over the three days of combined cyclophosphamide and cisplatin included patients with data for at least one of the days. Patients leaving the study early because of toxicity were scored for the toxicity on their last day in the study. Nonparametric methods, such as the Kruskal–Wallis test or the Wilcoxon Rank-sum test were used to compare treatment groups.[19] All quoted P values are two-sided. Treatment comparisons attaining statistical significance less than 0.05 were deemed significant. Fisher's exact test was used to analyze cross-classification tables, for example when comparing the four treatment regimens with respect to toxicities or side effects.

Results

One hundred twenty-six patients were randomized to one of four treatment arms, 122 were evaluable for toxicity, and 103 patients were fully evaluable. The characteristics of all randomized patients are shown in Table 1. One patient was inevaluable due to the presence of brain metastases that had been previously undetected

Table 1. Patient Characteristics

	Metoclopramide + placebo	Metoclopramide + dronabinol	Prochlorperazine + placebo	Prochlorperazine + dronabinol	*P* value
No. of patients					
Randomized	31	31	32	32	
Evaluable	24	27	28	27	NS
Age (yrs)					
Median	39	42	42	42	
Range	24–53	25–52	32–57	26–57	NS
Sex					
Female	30	30	32	31	
Male	1	1	0	2	NS
Type of cancer					
Breast carcinoma	30	30	31	31	
Melanoma	1	1	1	2	NS
Prior dronabinol use	3	2	2	5	NS
Anticipatory N/V	5	5	3	3	NS

N/V: nausea and vomiting; NS: not significant.

Table 2. Incidence of Toxicity Associated With Discontinuation or Dose Reduction of Study Drugs

Toxicity	Metoclopramide (n = 56) (%)	Prochlorperazine (n = 57) (%)
Diarrhea*	2 (3.6)	0
Cardiac†	1 (1.8)	3 (5.3)
Sedation	1 (1.8)	0
Anxiety‡	3 (5.4)	2 (3.5)
Akasthesia	1 (1.8)	4 (7.0)

* Greater than Grade 2 uncontrolled by diphenoxylate.

† One case of second degree heart block on both arms, one case each of bradycardia, and ventricular ectopy with multifocal PVCs on prochlorperazine arm.

‡ Anxiety was associated with lack of sedation and poor emetic control; five patients were removed from study for these reasons.

and another patient was rendered inevaluable by her continued narcotic requirements. Two patients were inevaluable due to missing data. Eight patients (4 receiving metoclopramide and 4 receiving prochlorperazine) were declared failures and removed from study. Failures were defined as either more than five emetic episodes within a 12-hour period, or patient request to come off study. Study failures were associated with increased anxiety, lack of sedation, and poor emetic control. The remaining 11 inevaluable patients were removed from study for toxicities associated with antiemetic therapy (Table 2). Akasthisia was more commonly associated with prochlorperazine whereas diarrhea was more common from metoclopramide-containing regimens. Table 3 shows the median number of emetic episodes per day of transplant for patients receiving metoclopramide or prochlorperazine combinations with or without dronabinol. The patterns of response are different for the two antiemetic agents with metoclopramide demonstrating significant better control on the first day of chemotherapy and prochlorperazine offering superior control of emesis on subsequent days. The addition of dronabinol to either three-drug regimen before carmustine administration had no effect on the number of episodes of vomiting on day −3 and all four arms of the study were similar on this day.

The intensity of emetic episodes, as rated by the nurse observers on the EPRS, is shown in table 4. The only significant differences were seen on day −6 and, between metoclopramide with or without dronabinol, on day −3. Overall there was no difference between any of the study arms.

Patient self-assessment data from the Rhodes INV was analyzed and revealed no significant difference between the four treatment arms over the entire four day treatment period or between metoclopramide and prochlorperazine on days −6 though −4. There was a trend toward less distress from nausea, vomiting, and retching in patients receiving dronabinol versus placebo but this was not statistically significant (Table 5). The patients' assessment of frequency, quantity, and distress from nausea, vomiting, and retching followed the same patterns of response as observed with the EPRS data shown when each treatment day was analyzed separately.

Discussion

This study was designed to address the specific problems associated with control of nausea and vomiting during high dose cisplatin, cyclophosphamide, and carmustine. We used an intensive 4-day treatment protocol that results in moderate emesis on the first three days and acute, severe emesis and retching on the fourth day after carmustine administration. Given the complexity of the therapy, patients generally prefer to be sedated throughout their treatment. Because the predominant opinion, at the time the study was designed, was that metoclopramide would be significantly more efficacious than prochlorperazine (our standard agent), a double-blind, randomized strategy was employed. The severity of carmustine-associated emesis observed in these patients led to the evaluation of dronabinol as a fourth antiemetic agent on day −3. This drug was not used for the entire treatment period due to concerns that excessive central nervous system toxicities would occur. Administration of just two doses of dronabinol before de-

Table 3. Median Number of Emetic Episodes per Day of Transplant

	Day of transplant				
	*−6**	*−5*	*−4**	*−3*	Total
Metoclopramide (n = 56)	1 (0–7)	1 (0–6)	2 (0–9)		
Prochlorperazine (n = 57)	4 (0–12)	0 (0–8)	0 (0–12)		
Metoclopramide + dronabinol (n = 31)				2 (0–10)	7 (1–21)
Metoclopramide + placebo (n = 25)				2 (0–7)	6 (1–19)
Prochlorperazine + dronabinol (n = 28)				2.5 (0–9)	8 (1–23)
Prochlorperazine + placebo (n = 29)				2 (0–12)	10 (1–20)

* $P < 0.002$.

Table 4. Intensity of Emetic Episodes per Day of Transplant

	Day of transplant				
	−6	*−5*	*−4*	*−3*	Total
Metoclopramide (n = 56)	12.3 (0.7–33.9)	15.3 (0–35)	17 (1.8–41)		
Prochlorperazine (n = 57)	19.2 (6.9–37.2)	20 (0–40)	20 (4.5–35.5)		
Metoclopramide + dronabinol (n = 31)				22* (4.7–49.5)	20.4 (2.6–34)
Metoclopramide + placebo (n = 25)				30 (14.3–48)	20.8 (11.3–40.1)
Prochlorperazine + dronabinol (n = 28)				22.8 (0–37.3)	18.9 (8–33.8)
Prochlorperazine + placebo (n = 29)				25.1 (3.5–49.5)	20.8 (11.6–33.9)

Possible scores are from 0 to 50 mm, with 50 mm representing the maximum emetic intensity.
* $P < 0.02$ for DOT −6 metoclopramide vs. prochlorperazine and DOT −3 metoclopramide + placebo vs. metoclopramide + dronabinol.

livery of carmustine was well tolerated and no increase in sedation or other CNS side effects was observed. Dronabinol did not affect the average number of emetic episodes when combined with prochlorperazine or metoclopramide. There was a trend toward better patient acceptance and less nausea with the regimens that contained dronabinol instead of placebo, but no variable on the INV Form 2 was statistically significant.

When the four arms of the study are compared over the entire treatment period, no statistically significant differences are found. Interestingly, different patterns of efficacy can be observed when metoclopramide- and prochlorperazine-containing regimens are compared on each day of treatment separately. Metoclopramide is initially more effective but antiemetic efficacy declines on the third and fourth day of treatment. Prochlorperazine was least effective on day −6 and offered improved emetic control during the next 3 days. Although the median number of emetic episodes was not different after carmustine therapy (day −3 of therapy), 25% of patients receiving prochlorperazine were completely protected from emesis on this day as compared with only 12% of patients receiving metoclopramide. A similar observation has been made by Olver et al.,[20] in a randomized, double-blind study of high dose intravenous prochlorperazine versus metoclopramide in patients receiving various chemotherapy treatments. The duration of vomiting in patients vomiting after cisplatin was less with prochlorperazine (5 vs. 15 hours, $P = 0.03$) than with metoclopramide. The peripheral serotonin receptor antagonist effect of metoclopramide is likely to account for the superior emetic control observed with this agent on the first day of chemotherapy. On subsequent days, mechanisms of delayed emesis and nausea, which are much less clearly understood and not thought to be related to the serotonin-3 receptor, may account for the decrease in emetic control by metoclopramide. The anti-emetic studies in the literature typically report day 1 results and do not describe patterns of response. We have observed a similar decline in anti-emetic efficacy over time with various 4- and 5-day emetogenic chemotherapy regimens employing ondansetron at our institution.

The inclusion of lorazepam and diphenhydramine to the study regimens resulted in minimal problems with extrapyramidal side effects. Akasthisia was the only extrapyramidal side effect noted and it was easily managed by discontinuing the study infusion and administering extra diphenhydramine or beztropine mesylate. The sedation associated with these agents varied considerably and often correlated with prior benzodiazepine use by patients. In this setting, sedation was not considered an adverse event unless the patient was not appropriately arousable. Only six of 122 patients required lorazepam dosage reduction for excessive sedation. Five patients were removed from study for lack of sedation and uncontrolled emesis.

It is unclear whether the cardiac toxicities observed were related to the antiemetic agents or to the administration of high dose cyclophosphamide. Second-degree heart block also has been observed in similar ABMT patients receiving continuous infusion perphenazine.[21] Cyclophosphamide is dose-limited in the ABMT setting by cardiomyopathy, which usually occurs acutely, during or immediately after therapy. In its milder form, it may be manifested by various dysrhythmias, including bradycardia and multifocal premature ventricular contractions.[22] There were no serious consequences of the cardiac side effects observed in the patients on this study. However, 24-hour cardiac monitoring and one-to-one nursing was employed throughout the study period. This regimen is not appropriate for outpatient administration or settings in which close patient monitoring is not feasible.

Both prochlorperazine and metoclopramide in combination with lorazepam and diphenhydramine were well tolerated and offered good control of nausea and vomiting associate with high dose alkylating agents administered over 4 days. Although no regimen was clearly superior, the prochlorperazine arms offered

Table 5. Median INV Scores for Vomiting, Nausea, and Retching per Day of Transplant

	Day of transplant				
	−6	*−5*	*−4*	*−3*	Total
Metoclopramide*					
Vomiting	2.5 (0–7)	2 (0–8)	3.5 (0–4)		
Nausea	2 (0–15)	2 (0–8)	3.5 (0–5)		
Retching	0.5 (0–9)	0.5 (0–10)	1.5 (0–3)		
Prochlorperazine†					
Vomiting	3.5 (0–4.5)	2 (0–3)	2 (0–4)		
Nausea	3 (0–5)	1.5 (0–4.5)	2 (0–5)		
Retching	1 (0–1.5)	0.5 (0–1)	0.5 (0–1.5)		
Metoclopramide + dronabinol					
Vomiting				5 (0–12)	3 (0–7)
Nausea				5.5 (0–12)	3.5 (0–7)
Retching				2 (0–7)	1 (0–4)
Metoclopramide + placebo					
Vomiting				6 (0–12)	3 (0–7)
Nausea				8 (0–11)	3 (0–11)
Retching				3 (0–7)	1 (0–6.5)
Prochlorperazine + dronabinol					
Vomiting				4 (0–11)	2.5 (0–5)
Nausea				4 (0–11)	2.5 (0–7)
Retching				1 (0–7)	0.5 (0–3)
Prochlorperazine + placebo					
Vomiting				5 (0–10)	3 (0–6)
Nausea				3.5 (0–9)	3 (0–7.5)
Retching				1 (0–7)	1 (0–4)

INV: index of nausea and vomiting.

Maximum scores for vomiting and nausea are 12 and for retching are 8. These represent the sum of the subscale scores in each category, with 0 representing no episodes or distress and 12 or 8 representing the highest distress from the three symptoms.

* Metochlopramide regimen superior on day of transplant −6 for vomiting ($P < 0.01$) and nausea ($P < 0.02$).

† Prochlorperazine regimen superior on day of transplant −4 for vomitingg, nausea, and retching ($P < 0.005$). Prochlorperazine regimen superior on day of transplant −3 for nausea ($P < 0.01$).

more complete emetic control on three of four study days. The cost of the prochlorperazine regimen is also significantly less than the metoclopramide regimen. Prochlorperazine when given as a continuous infusion with scheduled lorazepam and diphenhydramine offers a reasonable, efficacious and cost-effective alternative to more expensive antiemetic combinations that may not prove superior in highly emetogenic, multiple-day chemotherapy treatment programs. This regimen is currently serving as the control arm for studies to investigate the role for serotonin antagonists in patients receiving the identical high dose chemotherapy.

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