Prevention of Dimethylsulfoxide-Related Nausea and Vomiting by Prophylactic Administration of Ondansetron for Patients Receiving Autologous Cryopreserved Peripheral Blood Stem Cells

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Autologous peripheral blood stem cell transplantation (ASCT) is used most commonly for the treatment of lymphoma and multiple myeloma, with more than 30,000 ASCTs performed worldwide in 2009 (Pasquini & Wang, 2011). ASCT requires collection and cryopreservation of autologous peripheral blood stem cells (PBSCs). Before the reinfusion of PBSCs, patients must undergo conditioning with high-dose radiation and/or chemotherapy. PBSCs typically are mobilized from patients using chemotherapy and hematopoietic growth factors such as filgrastim or granulocyte macrophage–colony-stimulating factor, or growth factors alone. Once the PBSCs have been mobilized from the bone marrow into the blood, they are collected by apheresis and then cryopreserved for reinfusion at a later time point. To protect the cells from damage associated with freezing and thawing, a cryoprotectant is required in the cryopreservation process. Common methods of cryopreservation include 10% v/v dimethylsulfoxide (DMSO), or 5% v/v DMSO with or without hydroxyethyl starch (Abrahamsen, Rusten, Bakken, & Bruserud, 2004; Kessinger & Sharp, 2003; Liseth et al., 2009; Rowley, MacLeod, Heimfeld, Holmberg, & Bensinger, 1999). PBSCs can be frozen for an extended period of time, although a maximum duration has not yet been established (Berz, McCormack, Winer, Colvin, & Quesenberry, 2007).

After mobilization chemotherapy and PBSC collection and storage, most patients are given about 30 days to recover before proceeding with the high-dose transplantation conditioning regimen. Different high-dose agents are used depending on the underlying disease and clinical setting. After completion of high-dose therapy, cryopreserved PBSCs usually are thawed rapidly at the bedside and infused without further manipulation beginning on "day 0." Prior to the infusion, patients require IV hydration. To prevent reactions related to histamine release caused by the DMSO,

Purpose/Objectives: To evaluate the effectiveness of ondansetron for the prevention of nausea and vomiting from dimethylsulfoxide (DMSO) during autologous stem cell transplantation (ASCT) infusion.

Design: Nonrandomized cohort using historical control.

Setting: Comprehensive cancer center outpatient infusion department.

Sample: 50 patients receiving ASCT in the outpatient setting.

Methods: Patients were assessed for nausea and vomiting on their infusion day using the Multinational Association of Supportive Care in Cancer Antiemesis Tool (MAT) at arrival, pre-ASCT infusion, pre-ondansetron administration, prior to the first bag, and after each bag of stem cells. A standard script was used to ensure consistency. Ondansetron, 16 mg IV, was administered 30–90 minutes prior to each ASCT infusion. Number and volume of stem cells bags, as well as infusion rate and emesis episodes, were recorded. Nausea scores and vomiting episodes were compared to historical data.

Main Research Variables: Subjectivity of nausea, potential Hawthorne Effect.

Findings: Forty-five percent of patients had an MAT score greater than 2 on arrival, decreasing to 18% after receiving ondansetron before the first bag. Twenty-four percent had MAT increases of more than two points by infusion end compared to 58% in the historic control group. Eighteen percent of patients vomited compared to 28% of historic controls.

Conclusions: The administration of 16 mg of IV ondansetron significantly reduced DMSO-related nausea and episodes of vomiting in patients receiving ASCT.

Implications for Nursing: Prophylactic administration of ondansetron had a positive effect on reducing nausea symptoms and episodes of vomiting during ASCT infusions. These results prompted a change in clinical practice. More research is required to determine whether the inclusion of other antiemetic agents would provide even greater benefit.

Knowledge Translation: To date, no other published studies have explored the benefits of premedicating patients with ondansetron prior to ASCT infusions. This study is the first to establish efficacy of ondansetron for an unlabeled indication. These results may pave the way for future research in decreasing nausea and vomiting in this setting.

patients also are premedicated with oral acetaminophen, IV diphenhydramine, and hydrocortisone. In addition, patients commonly experience nausea and vomiting from the DMSO. Each bag of thawed PBSCs is administered rapidly and sequentially by gravity through a central venous catheter. Patients receive an additional IV hydration following the last bag of PBSC infusion to flush from the system the cellular debris, red blood cell hemolysate, and DMSO that accompany the product. Cryopreserved autologous PBSCs generally are infused without manipulation to remove DMSO because this process may result in a loss of stem cells. Nursing care during an autologous PBSC reinfusion requires diligent, continuous monitoring at the bedside, specifically assessing vital signs and respiratory status. Because PBSCs are infused by gravity, careful attention must be given to the infusion rate, typically beginning at 3–5 ml per minute and increasing to as fast as tolerated (Sauer-Heilborn, Kadidlo, & McCullough, 2004). Depending on the volume of the bag and patient tolerance, each bag can take anywhere from 5–20 minutes to infuse. Relatively fast infusions are desired because of concerns about potential clumping of thawed cells and additional exposure of the cells to the DMSO.

Dimethylsulfoxide

DMSO, a dipolar aprotic solvent, is metabolized by oxidation to dimethyl sulfone or by reduction to dimethyl sulfide (Gaylord, 2007). DMSO was approved by the U.S. Food and Drug Administration in 1978 as an aqueous solution for intravesicular irrigation to treat interstitial cystitis (Jacob & de la Torre, 2009). Off-label uses have included topical treatment for extravasation injury, herpes zoster, and scleroderma, although little or no evidence supports its use for those indications (Micromedex, 2010). IV DMSO infusion is not an approved route of administration. Therefore, very little research exists regarding side effects outside of the realm of transplantation using cryopreserved PBSCs. Within the transplantation context, a number of common adverse effects have been identified, including neurotoxicity, cardiovascular toxicity, respiratory toxicity, renal toxicity, histamine-mediated allergic reactions, nausea, vomiting, abdominal cramps, diarrhea, facial flushing, throat irritation, and coughing (Berz et al., 2007; Calmels et al., 2007; Rowley et al., 1999; Syme et al., 2004).

Odor

DMSO has a strong characteristic odor, sometimes described as being similar to creamed corn, garlic, salmon, or oysters (Jacob & de la Torre, 2009). When given via IV, DMSO is rapidly excreted through the respiratory, dermatologic, and renal systems, with 44% recovered in the urine within 24 hours (Egorin, Rosen, Sridhara, Sensenbrenner, & Cottler-Fox, 1998; Gaylord, 2007). Nurses involved with ASCT reinfusions immediately notice the exhaled odor, often before the patient is aware (Prior, Mitchell, Nebauer, & Smith, 2000).

Nausea and Vomiting

One of the most common side effects of receiving cryopreserved PBSCs is nausea and vomiting. Other toxicities include allergic reactions, hypotension, hypertension, rash, fever, chills, dyspnea, and chest pain. Nausea and vomiting associated with ASCT infusions generally is transient and occurs during the infusion with symptoms diminishing once the stem cell reinfusion has been completed. However, infusions of multiple bags can take up to 60 minutes, depending on the stem cell volume, diameter of the central venous catheter, and patient tolerance. Despite the routine aggressive antihistamine premedications and the relative brevity of infusions, nausea and vomiting remains a frequent and distressing adverse event (Bojanic et al., 2008; Kim et al., 2007; Okamoto et al., 1993; Stroncek et al., 1991; Zambelli et al., 1998).

A number of complex pathways are responsible for the subjective sensation of nausea, and for vomiting, a distinct but related objective response (Hawkins & Grunberg, 2009; Quigley, Hasler, & Parkman, 2001). Little is known about the precise mechanism of nausea and vomiting related to DMSO. Therefore, directly comparing patient risk factors and interventions with those used for chemotherapy-induced nausea and vomiting (CINV) is difficult.

Studies have documented the incidence of nausea and vomiting associated with DMSO, ranging from 23%–65% (Bojanic et al., 2008; Kim et al., 2007; Okamoto et al., 1993; Stroncek et al., 1991; Zambelli et al., 1998). However, these reports are heterogeneous in nature, and no universally agreed-upon definition of nausea was used. Often, nausea and vomiting are grouped together, further obscuring the true incidence of each. Other factors, including the volume of stem cell product and the granulocyte content in the product, also can contribute to side effects, which may be difficult to distinguish from the direct effect of DMSO (Bojanic et al., 2008; Donmez et al., 2007; Milone et al., 2007).

The potential contribution of the odor associated with DMSO on PBSC infusion-related nausea and vomiting should not be underestimated. Prior et al. (2000) reported the noxious effects of DMSO on nurses caring for patients receiving stem cell infusions preserved with DMSO and noted that nursing staff complained of nausea as a result of the smell. Strong, unpleasant odors can be carried by the mouth or nose to the cranial nerve and then to the cortex (Comeau, Epstein, & Migas, 2001). Because DMSO is excreted into saliva, the unpleasant taste sensation also can trigger nausea.

Background

A review of the literature was performed using PubMed and CINHL® databases for published studies on the efficacy of antiemetics for prevention of DMSO-related nausea and vomiting. No studies specifically on the efficacy of antiemetics were identified. In 2009, a phone survey performed by the authors of four transplantation centers in California, Nebraska, Texas, and New York revealed a wide variation in antiemetic practices for ASCT reinfusions. Sauer-Heilborn et al. (2004) discussed the possible benefit of adding an antiemetic to other premedications, but specific drugs or dosages were not delineated. In a study of 33 patients, Ferrucci et al. (2000) used 8 mg of ondansetron as part of their premedication protocol and reported a low rate of gastrointestinal symptoms, but a systematic analysis of nausea and vomiting was not included.

None of the currently available antiemetics are approved for DMSO-induced nausea and vomiting, and no data exist to demonstrate efficacy of a particular agent. The investigators were interested in testing the effectiveness of a single antiemetic added to standard diphenhydramine and hydrocortisone prior to infusion of thawed, DMSO-cryopreserved PBSCs.

Several antiemetics initially were considered as candidate drugs to evaluate in this study. Prochlorperazine is safe for CINV but was ruled out because of concerns about its ability to produce hypotension, also a known side effect of DMSO. Lorazepam is useful for anticipatory nausea and is prescribed as a PRN antiemetic for patients receiving chemotherapy at the authors' center; however, it was not felt to have sufficient potency for this trial. Aprepitant, a novel substance P/neurokinin 1 receptor antagonist, generally has been avoided in ASCT because of its long half-life and CYP3A4 interactions with certain medications such as cyclophosphamide and thiotepa (Egerer et al., 2010).

Ondansetron, a member of the 5-HT_3 antagonist family of antiemetics, has demonstrated effectiveness for CINV and is well tolerated with a shorter half-life. In the authors' center, the drug is standardly used in mobilization and transplantation conditioning regimens. Ondansetron also provides effective prophylaxis for postanesthesia (Jokela et al., 2009). For those reasons, ondansetron was selected for the study.

The Seattle Cancer Care Alliance (SCCA) is a leading cancer treatment center associated with the Fred Hutchinson Cancer Research Center (FHCRC), the University of Washington Medical Center, and Seattle Children's Hospital. When possible, patients undergoing ASCT receive their cryopreserved reinfusions in the SCCA ambulatory clinic infusion room. A previous study of 60 patients in the center examined the feasibility of using an orange to decrease throat symptoms such as tickling and irritation associated with cryopreserved PBSC infusions (Potter, Eisenberg, Cain, & Berry, 2011). A secondary aim was to assess the potential benefit of the orange intervention for reducing nausea and vomiting. Patients randomized to treatment arms were instructed to smell a sliced naval orange or sweet orange extract in an aromatherapy sampler during their PBSC infusion. Nausea was evaluated using a component of the Multinational Association of Supportive Care in Cancer Antiemesis Tool (MAT) (Molassiotis et al., 2007). The MAT is an eight-item tool designed to assess nausea and vomiting for patients receiving chemotherapy, and has been validated against the Rhodes Index for nausea, vomiting, and retching. MAT items include occurrence, duration, and frequency of acute and delayed nausea and vomiting. Because of the relatively transient nature of DMSO-related nausea and vomiting, item number 4 of the MAT, a scale that rates nausea from 0 (none) to 10 (as much as possible), was adopted for this study, as well. Without the use of oranges, 58% of the 60 patients had infusion-related nausea scores greater than one, and the scores were greater than four in 43% of the 60 total patients (n = 26) (data not published). In addition, as observed and counted by the study personnel, 28% (n = 17) of the patients vomited.

The purpose of the current study is to determine whether administration of a 16 mg IV dose of ondansetron prior to cryopreserved PBSC infusion would decrease the incidence of nausea and vomiting, using the benchmark data from the orange study for efficacy comparison. Secondary analyses evaluated the effects of product volume size, number of bags infused, infusion rate, and gender on nausea.

Methods

Setting and Sample

The SCCA ambulatory clinic provides outpatient care for the FHCRC blood and marrow transplantation recipients. About 250 autologous transplantations are performed annually, and many patients receive their stem cells in the clinic's infusion department. The study was designed by two outpatient nurses involved in the multidisciplinary committee that ensures standardization of best practices within the transplantation population. The nurses sought to determine whether a single 16 mg IV dose of ondansetron given prior to the first bag of autologous cryopreserved PBSC infusion decreased the rate of nausea and number of vomiting episodes associated with DMSO as compared to historical controls in the orange study. The investigators also were interested in determining whether the rate of infusion and total stem cell volume had effects on nausea independent of premedication. Two physicians were included in the research team for oversight and prescribing purposes,

Inclusions
- Autologous peripheral blood stem cell (PBSC) transplantation patient
- Aged 21 years or older
- English-speaking
- Planned cryopreserved PBSC infusion at the Seattle Cancer Care Alliance outpatient clinic

Exclusions
- History of prior autologous transplantation
- Younger than 21 years
- Non-English speaking
- Planned cryopreserved PBSC infusion at the University of Washington Medical Center inpatient unit
- Infusion of cryopreserved PBSCs that are thawed and washed to removed dimethylsulfoxide prior to infusion
- Allergy or adverse reaction to ondansetron

Figure 1. Eligibility Criteria

and an FHCRC biostatistician assisted with the analysis. The study was approved by the FHCRC investigational review board. All patients signed an informed consent form prior to participation. An infusion room nurse and a clinical nurse specialist were responsible for all data collection and remained with patients throughout their reinfusions.

The study was designed to provide 91% power to observe a nausea rate that is statistically significantly lower (at the two-sided level of 0.05) than the fixed historical rate of 58% if the assumed-true rate with ondansetron is 35%. Similarly, if the assumed-true rate of vomiting with ondansetron premedication is 10%, 50 patients provide 90% power to observe a statistically significantly lower rate than the fixed historical rate of 28%.

Eligibility

Patient eligibility and exclusion criteria are described in Figure 1. Patients who were scheduled to be admitted to the inpatient service for their infusion were not approached because the study nurses were assigned to the outpatient clinic and would not be able to follow patients in the inpatient setting. Eligibility was determined by study personnel. Informed consent was obtained by the study staff and attending physicians prior to initiating conditioning chemotherapy. A total of 58 patients were approached. Four patients were admitted to the inpatient service between the time of consenting and their day of infusion and were not treated in the study. Four other patients declined to participate in the study. One patient was not eligible for infusion because of a change in the transplantation conditioning regimen.

Instrument

Nausea and vomiting was evaluated using the same item (number 4) of the MAT that had been used with the previous orange study (Molassiotis et al., 2007). A preprinted script was used by study staff to ensure that all patients received identical information about how the tool would be used and at what time points. Nausea was defined as an increase in the MAT score of two or more points from the preinfusion (baseline) score. Episodes of retching or actual vomiting would be documented by the study personnel as they occurred.

Procedures

Patients were first evaluated by study personnel on arrival to the infusion room on day 0 to assess initial nausea and to obtain antiemetic history from the preceding 24 hours. Ascertaining what degree of nausea patients were experiencing prior to their infusions was important because all patients had received high-dose chemotherapy within the prior 36 hours and had been given prescriptions for prochlorperazine, lorazepam, and diphenhydramine. Nutritional intake from midnight the night before the infusion was assessed along with any additional antiemetics taken by patients at home or given to those who visited the infusion room one day prior to the stem cell infusion. Diagnosis, weight, and body surface area (BSA) were recorded along with major comorbidities.

All patients were hydrated for two to three hours prior to their infusion. Ondansetron 16 mg IV then was administered via IV 30–90 minutes prior to the thawing of the cells at the bedside. Patients receiving stem cells spanning multiple days received a dose of ondansetron on each day of infusion and were assessed at the same time points on each day of infusion. Patients who experienced breakthrough nausea and vomiting during their infusion were permitted to receive IV lorazepam if needed.

The time and dosage of standard premedications (i.e., diphenhydramine, hydrocortisone, and acetaminophen) were recorded on the case report form. The volume of each infused stem cell bag along with the start and stop times were used to determine the rate of infusion because cryopreserved PBSCs are infused by gravity. In addition to study personnel obtaining an initial nausea score on arrival, patients were asked to rate their nausea prior to the first PBSC bag, which was designated as the baseline nausea score. Nausea then was reassessed prior to each subsequent bag and after completion of the last bag. Retching and vomiting were recorded as discrete events, along with the time of occurrence. All of the cryopreserved PBSC products contained 10% DMSO solutions. Study personnel remained with all patients during all infusions. As per the FHCRC Standard Practice Committee policy, patients received less than 1.63 x 10^9 total nucleated cells/kg per day (Khera et al., 2012).

Statistical and Data Analysis

The degree of nausea and the incidence of vomiting each were compared to historical data using a one-sample

binomial test. The one-sample t test was used to test the null hypothesis that the change in nausea score was equal to zero. The two-sample t test was used to compare the average of the various parameters (e.g., age, weight, BSA, number of days of reinfusion, number of bags, mean infusion rates) between patients with and without nausea. The chi-square test was used to compare the proportion of women between nauseated and non-nauseated patients.

Results

During a period of seven months, 49 patients were treated and evaluable for the study. The majority were Caucasian (18 women and 29 men), and the remaining 4% were Asian (two women). Diagnoses were as follows: 28 patients had multiple myeloma, nine had non-Hodgkin lymphoma, 10 had Hodgkin lymphoma, and two had germ cell cancer. No adverse events were associated with the ondansetron.

Nausea

Twenty-three patients (45%) had initial (arrival) pre-ondansetron MAT scores greater than two. Of those, six had a baseline MAT of zero after ondansetron (before infusion of bag 1), and eight had a MAT of zero by the end of their last bag of PBSCs. Nine patients (18%) had a baseline MAT greater than two immediately prior to their first bag. Baseline nausea ratings for all patients ranged from 0–8, with a mean of 1.3 (SD = 1.93). Individual post-bag MAT scores were compared to each patient's preinfusion scores. Twelve patients (24%) had a greater than two-point increase from baseline by the end of their infusions. That rate compares favorably to the historic rate of 58% ($p < 0.0001$). The mean change in MAT score from baseline to after the last bag was 0.43 ($p = 0.16$), although in general, scores decreased relative to the baseline ($\bar{X} = -0.78$, $p = 0.05$).

Vomiting

Eighteen percent (n = 9) of the patients vomited compared to the historic rate of 28% ($p = 0.03$). Of the nine patients who vomited, only three also had nausea. Of the 12 patients who had a greater than two-point increase from baseline nausea by the end of their infusions, only three vomited. Five of the nine patients who vomited had retching.

Gender and Weight

Twenty women enrolled in the study. Of the 12 nauseated patients, six (50%) were women compared to 14 of 37 (38%) non-nauseated patients ($p = 0.46$). Mean ages for nauseated and non-nauseated patients were 49 and 51 years, respectively ($p = 0.52$). The mean weight for nauseated patients was 85 kg, and 81 kg for non-nauseated patients ($p = 0.99$). Similarly, the mean BSAs for nauseated and non-nauseated patients were 2.02 and 1.97, respectively ($p = 0.55$).

Infusion Rate and Volume

A wide variation in infusion rates was noted, with a range from 216–760 ml per hour (see Table 1). In addition, infusion times varied from 3–26 minutes. The mean infusion rates among nauseated and non-nauseated patients were 307 ml per hour and 392 ml per hour, respectively, which represented a significant difference ($p = 0.02$). Although an increase in nausea with larger volumes of stem cell product was anticipated because of the increased amount of DMSO, the opposite effect was observed, with a trend for less nausea associated with greater total infused volume ($p = 0.04$).

The mean duration of infusion time for the first bag of stem cells was 8.59 minutes, with a range of 3–17 minutes (SD = 3.23). Most patients received either two or four bags of cells ($\bar{X} = 2.65$, range = 1–6). Mean number of days of infusion in nauseated and non-nauseated patients was 1.25 and 1.16, respectively ($p = 0.55$). Mean

Table 1. First Day Infusion Rate and Bag Volumes (N = 49)

Bags Infused	n	$\bar{X}$ Length (Minutes)	Median Length (Minutes)	Range (Minutes)	SD	Mean Rate[a]	Slowest Rate[a]	Fastest Rate[a]	Median Rate[a]	Median Volume (ml)
1	49	8.59	9	4–9	3.23	417	216	760	394	54
2	42	10.02	9	5–26	4.77	346	120	624	346	50
3	23	9.55	8.5	5–19	3.72	346	164	620	323	49
4	14	10.85	10	5–24	5.23	323	130	576	336	49
5	3	13	12	5–22	6.97	296	130	528	230	46
6	1	5	5	5	0	528	528	528	528	54

[a] Measured in ml per hour

number of bags in nauseated patients was 3, and 2.5 for non-nauseated patients ($p < 0.27$). Forty-two patients were infused in one day, six over two days, and one patient, who received 11 bags, was infused over three days. No patient received more than six bags in a single day.

Discussion

Despite numerous published reports of DMSO-related nausea associated with infusion of cryopreserved PBSCs, this study is the first, to the authors' knowledge, that systematically addressed the potential efficacy of ondansetron to prevent infusion-related nausea and vomiting. The frequency and severity of nausea and vomiting from the recent historical cohort of cryopreserved PBSC recipients (Potter et al., 2011) are similar to rates reported by others (Bojanic et al., 2008; Kessinger, Schmit-Pokorny, Smith, & Armitage, 1990; Kim et al., 2007; Okamoto et al., 1993; Stroncek et al., 1991; Zambelli et al., 1998). The current study demonstrates that prophylactic ondansetron, in combination with standard antihistamine premedications, markedly decreases the incidence of nausea ($p < 0.0001$) and episodes of vomiting ($p = 0.03$) compared with the historical rates.

Thirty-eight participants (77%) reported having eaten food and 49 (100%) had consumed liquids during the time between midnight and their arrival in the infusion room on day 0. Similar to the orange study, the use of other antiemetic therapy was not prohibited prior the administration of the ondansetron on the day of infusion. Eighty-eight percent (n = 43) reported taking at least one of the prescribed oral antiemetics (e.g., prochlorperazine, diphenhydramine, lorazepam) at home within the 24-hour period prior to day 0, and 28% (n = 14) had received one or more of these medications via IV in the clinic on the prior day, but not the day of infusion. Given that the mean half-lives of oral prochlorperazine, diphenhydramine, and lorazepam are 8.6 hours, 13 hours, and 12 hours, respectively (Hessell, Lloyd-Jones, Muir, Parr, & Sugden, 1989; Micromedex, 2012; Simons, Watson, Martin, Chen, & Simons, 1990), these agents were unlikely to have a significant effect on nausea and vomiting scores, particularly considering the percentage of patients who were nauseated on arrival on day 0.

No relationship was observed between infusion rates and increased nausea, refuting a long-held belief by nursing staff that faster infusions induced more severe nausea. Indeed, a faster rate of infusion was associated with significantly less nausea ($p = 0.02$). At least two possible explanations exist for that. First, because prophylactic ondansetron effectively reduced the overall incidence of nausea and/or vomiting, it also may ameliorate a potential emetogenic effect of bolus PBSC infusion. Second, this study was not designed to assess changes in the degree of nausea associated with increasing or decreasing the infusion rate during each bag, and the low overall rates of nausea and/or vomiting may have led to a type II statistical error. A randomized blinded study would be needed to accurately assess the effects of infusion rate on the incidence and severity of nausea and vomiting. Such a study would require that the bag, tubing, and drip chamber be masked to negate any potential bias of nausea reporting based on the patient's visual observation of the volume change. In addition, the patient's nausea would need to be assessed at multiple set time points during the infusion of each bag.

Limitations

This study had several limitations. First, the number of patients enrolled was relatively small and was almost exclusively Caucasian. Second, a double-blinded, placebo-control design would have increased the strength of the conclusions. In addition, other factors might induce nausea and vomiting during PBSC infusions. Milone et al. (2007) reported that in addition to patient age, the inclusion of more than 0.5×10^8/kg nonmononuclear cells with the stem cell and bone marrow products may play a role in noncardiac side effects, including nausea and vomiting. The potential effect of age could not be evaluated because the median age of nauseated and non-nauseated patients in this study was statically nonsignificant. A study by Calmels et al. (2007) concluded that the number of granulocytes present in the PBSC bag was a contributor to nausea and vomiting in autografts in which the DMSO had been removed after thawing. In addition, infusing large quantities of cold IV fluids may induce a vagal response, which in turn can produce nausea and vomiting unrelated to DMSO (Ferrucci et al., 2000). Although the authors' center limits the number of total nucleated cells that can be infused to a patient to 1.63×10^9 total nucleated cells/kg per day (Khera et al., 2012), data are not routinely collected on the number of nonmononuclear cells in each PBSC product. Therefore, what effect, if any, the nonmononuclear cell content may have had on the study results cannot be determined. However, a report by Khera et al. (2012) found no difference in nonserious infusion-related adverse events (which included nausea and vomiting) in the ASCT population who received cryopreserved PBSC infusions that were limited to 1.63×10^9 total nucleated cells/kg per day. Nausea and vomiting scores in the current study also may have been influenced by the Hawthorne Effect, whereby the participants' responses are influenced by having study personnel focused on their nausea and vomiting (Campbell-Yeo, Ranger, Johnston, & Fergusson, 2009).

Implications for Nursing

Symptom management is an important component of oncology nursing care. Oncology nurses understand the rationale for administering antiemetics prior to chemotherapy, as the efficacy of these antiemetics have been proven in numerous studies. To the authors' knowledge, the current study is the first to specifically examine the role of ondansetron for DMSO-related nausea and vomiting. However, because many patients still experienced breakthrough nausea and vomiting, additional investigation using a combination of antiemetics in a large multicenter study should be undertaken. The results of such a trial would provide additional knowledge to further reduce the unpleasant symptoms associated with DMSO.

Conclusion

When compared with highly emetogenic chemotherapy, DMSO has a significantly lower potential to produce nausea and vomiting and has a relatively short duration. In addition, although the emotional effects of DMSO-related nausea and vomiting have not been studied, the emotionally distressing effects of CINV have been well demonstrated (Tompkins Stricker & Eaby, 2010). Preventing nausea and vomiting, regardless of its cause, should be a priority for oncology nurses.

Although not 100% effective, the use of ondansetron in this setting appears to be beneficial in significantly reducing the incidence and severity of nausea, along with episodes of vomiting. As a consequence, 16 mg of IV ondansetron prior to DMSO-preserved PBSC infusions has become the standard of care for adult patients at the study facility.

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