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Implementation of National Pediatric Guidelines to Prevent Chemotherapy Induced Nausea and Vomiting in Children with Cancer

Taryn Sandheinrich
tgfqn5@mail.umsl.edu

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Taryn Sandheinrich
M.S.N., Masters of Science in Nursing, University of Missouri-St. Louis, 2014
B.S.N., Bachelors of Science in Nursing, St. Louis University, 2011

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Advisory Committee

Susan Dean-Baar, PhD, RN, CENP, FAAN.
Chairperson

Lisa Merritt, DNP, APRN, CPNP-PC/AC, PMHS.

Deborah Robinson, DNP, MSNR, APRN, PPCNP-BC, CPHON

Implementation of National Pediatric Guidelines

Abstract

Purpose: The purpose of this study was to assess the use of supplemental, as needed (prn) pharmacologic interventions for uncontrolled acute chemotherapy induced nausea and vomiting (CINV) in children with cancer after implementation of new pediatric CINV prophylaxis guidelines. **Description of Project:** A retrospective chart review was completed on forty-three children admitted to the hospital for chemotherapy during a 3 month period in 2017 to document the use of medications given for acute breakthrough CINV. The pre-implementation group received anti-emetics based on the institutional standard of care. A second retrospective chart review was completed on thirty-three children admitted to the hospital for chemotherapy during a 3 month period in 2018 to evaluate use of medications for acute breakthrough CINV. The post-implementation group received anti-emetics based on the new published pediatric guidelines. Patient characteristics, treatment information, and provider compliance with guidelines were collected. **Results/Conclusions:** Implementation of the guideline by the institution was successful with 91% of patients in the post-intervention group receiving the new anti-emetic regimen to prevent nausea and vomiting. The mean anti-emetic dose in all patients for breakthrough CINV pre-implementation was 4.837±10.4857. Post-implementation, the mean anti-emetic dose for all patients was 3.394±6.432. This was not statistically significant ($p = 0.462$). For patients under 12, the mean anti-emetic dose pre-implementation was 5.8±12.5333 and post-implementation was 3.882±8.1. This was also not statistically significant ($p = 0.55$). Data collected from this project did demonstrate a decrease in the number of breakthrough anti-emetics used in children under 12 years of age likely related to the addition of the drug aprepitant. Although clinical guidelines provide excellence guidance to clinicians, they must always be evaluated for risk versus benefit; adapted to individual patient circumstances as appropriate; and used within the context of expert clinician judgement.

Introduction

Childhood cancer is the second leading cause of death in children 5-14 (Ward, DeSantis, Robbins, Kohler, & Jemal,2014). In the United states 1 in 285 children under the age of 20 are diagnosed with cancer each year (Ward et al., 2014). Chemotherapy induced nausea and vomiting (CINV) is a common side effect that can cause significant physical and emotional distress. Chemotherapy induced nausea and vomiting can be divided into different categories. Acute nausea and vomiting includes all episodes each day the chemotherapy is administered, and for 24 hours after the last dose. Delayed nausea and vomiting starts 24 hours after the last dose and can last up to one week. Anticipatory nausea and vomiting occurs prior to chemotherapy administration. It can be triggered by smells, tastes, and anxiety (Jordan, Kasper, & Schmoll, 2005).There are many risk factors that are associated with a higher incidence of CINV. These include but are not limited to female gender, younger age, and previous exposure to highly emetogenic agents (Haiderali, Menditto, Good, Teitelbaum, &Wegner, 2011).

Chemotherapy agents classified as highly emetogenic have a greater than 90% frequency of emesis in the absence of prophylaxis (Dupuis et al. 2013). The majority of patients at some time point in their cancer treatment protocol will receive chemotherapy classified as highly emetogenic. Uncontrolled nausea or vomiting from chemotherapy causes not only a burden on the patient, it can also impact the overall quality of care provided. Some of the direct costs that are associated with managing nausea or vomiting symptoms include: additional anti-emetic medications; unplanned doctor visits; unexpected hospitalizations, and visits to the emergency room. Indirect costs of CINV include loss of work productivity, and missed work for patient and/or caregiver

(Haiderali et al., 2011). In a study by Haiderali et al. (2011), it was estimated that the combined indirect and direct cost of CINV per patient per round of chemotherapy was on average $778.53 per patient. This number only accounts for the cycle of chemotherapy. The standard of care for children with Ewing's sarcoma is 12 cycles of highly emetogenic chemotherapy. That would mean an increased cost of around $9342.36 per patient with this diagnosis each year.

CINV is one of the most feared side effects prior to chemotherapy treatment, and unfortunately it is relatively common. Anti-emetic medications to control the unwanted effects of chemotherapy are available, but they are not always administered according to international guidelines. Insufficient administration of anti-emetics can lead to suboptimal management of side effects resulting in a significant impact on quality of life (QoL) (Lorusso et al., 2016) Many studies have shown that CINV negatively affects QoL in patients receiving treatment for malignancy. In a study by Ballatori et al. (2007), more than 90% of the patients at 7 different Italian centers with acute and delayed onset CINV reported impact on daily life on the Functional Living Index-Emesis (FLIE) questionnaire. The FLIE questionnaire is the only validated nausea and vomiting specific patient reported outcome tool.

Until recently, there had been no pediatric published guidelines for management and prophylaxis of CINV. In 2013, The Pediatric Oncology Group of Ontario (POGO) published evidence based guidelines for management of CINV in pediatric cancer patients. In 2016, the Children's Oncology Group (COG) the national pediatric clinical trial organization supported by the National Cancer Institute (NCI) adopted these evidence based guidelines for CINV management. These guidelines have since been

amended in 2017. One of the biggest changes in the 2017 guidelines was the use of the drug aprepitant for children greater than 6 months of age. These changes were based on recommendations of Patel et al., (2017). Aprepitant is an anti-emetic medication designed to treat delayed vomiting, however the original FDA approval for this medication was in the adult population and in adolescents greater than 12 years. These evidence based guidelines give health care providers an approach to help reduce the incidence of both acute and delayed nausea and vomiting caused by chemotherapy in the pediatric population (Dupuis et al., 2013).

Purpose

The purpose of this project was to evaluate if there was a decrease in the use of supplemental pharmacologic intervention to treat breakthrough acute CINV after implementation of new adapted St. Louis Children's Hospital (SLCH) guidelines based on a published evidenced-based national guideline. The guideline was expected to have the most impact on children less than 12 years of age, thus this group was analyzed separately. The second purpose was to assess provider compliance with the new guideline. The scope of this project includes only those patients who received highly emetic chemotherapy; and the data collection occurred only during the acute phase of CINV including all days the patient actually received chemotherapy.

The standard definition in the literature for optimal control of acute CINV is stated as: no vomiting, no retching, no nausea, and no use of anti-emetic agents other than those given for CINV prevention. This level of control is to be achieved on each day of chemotherapy administration. For this project, each time a patient received an anti-emetic

in a 24 hour period, was considered a failure of the regimen at that point in time. Each dose of breakthrough anti-emetics was counted for each day of chemotherapy for all patients in the sample.

Setting

This project was completed at a large urban academic pediatric hospital. The hospital has a nationally recognized pediatric oncology program and is an active member of the COG. The hospital had developed an institutional standard of care for prophylaxis of both acute and delayed vomiting caused by chemotherapy including a defined breakthrough regimen. This institutional standard was based on the adult American Society of Clinical Oncology (ASCO) guideline (Basch et al., 2011) and the published literature regarding symptom management of pediatric patients receiving chemotherapy. The institutional standard was implemented with a general pre-built anti-emetic order set with clinical guidance, but it was ultimately left up to the providers to prescribe as they desired for their patient's individual needs and preferences.

Anti-Emetic Medications

There are 3 major categories of anti-emetic agents that will be discussed in this project. 5- HT3 receptor antagonists such as ondansetron are the mainstay of treatment for acute CINV. Corticosteroids such as dexamethasone enhance the activity of ondansetron and are given concurrently. Neurokinin 1 receptor antagonists such as aprepitant augment the anti-emetic regimen and primarily treat delayed vomiting. The standard of care for anti-emetics previous to dissemination of the new COG guidelines was to prescribe ondansetron for prophylaxis of CINV scheduled every 6 hours during

each day of chemotherapy and for 24-48 hours afterward. Aprepitant, to prevent delayed vomiting, was prescribed for patients older than 12 years of age. For patients that were able to receive steroids, dexamethasone was given every 24 hours. Diphenhydramine and metoclopramide were used as second line for breakthrough nausea and vomiting, and lorazepam was used as third line treatment for breakthrough symptoms. The timing and dosing of this standard anti-emetic regimen was based on adult guidelines; published pediatric studies; and institutional provider preference related to adverse events from these medications.

A multi-disciplinary task force at the pediatric hospital (where the data was collected) reviewed the new pediatric anti-emetic guidelines and the associated evidence. The team decided to implement the guidelines with a few minor deviations based on the level of evidence; clinical contributions from team members; and the potential for increased toxicity. The guidelines endorsed by the Children's Oncology Group were adapted and then disseminated to the hematology/oncology division at Saint Louis Children's Hospital (SLCH) in October of 2017 as a new adapted anti-emetic guideline. The differences in the COG guidelines and the new SLCH adapted guideline are outlined in Table 1. In these adapted guidelines the interval of administration of dexamethasone for anti-emetic prophylaxis was changed from the recommended every 6 hour to every 12 hours. The task force intentionally modified this recommendation for dexamethasone as the published evidence review was graded, and every 6 hour dosing was a weak recommendation with a low quality of evidence (for highly emetic chemotherapy agents).

Evidence Identification and Synthesis

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A review of the literature regarding the previous standard of antiemetic regimens to control CINV in pediatric patients was performed. The search terms used were: therapeutics, child, nausea, oncology or cancer. The National Center for Biotechnology Information (NCBI) database and PubMed were searched using these terms with the filters of less than 18 years old and only articles in English. There were 67 results to be screened after duplicates were removed. Of these 67 results, 56 record were excluded for titles and abstracts not applicable. Eleven full articles were assessed for eligibility. Six records were included in the synthesis.

In the study published by Cubeddu, Hoffmann, Fuenmayor, & Finn (1990), the efficacy of ondansetron to treat CINV in a double blind randomized controlled trial was evaluated. This study demonstrated that ondansetron was superior to a placebo in all aspects of antiemetic efficacy. This historical study was included in the synthesis as it set the standard for ondansetron as the mainstay of antiemetic therapy for pediatric patients receiving chemotherapy. There were no more recent studies evaluating the efficacy of ondansetron in CINV; and 5-HT3 antagonists (like ondansetron) remain the backbone of ASCO and POGO recommendations for control of CINV.

Anti-emetic agents given in combination with ondansetron have been inconsistent in pediatric oncology practice even though there is data to suggest that multi-agent treatment for CINV is the most efficacious. The Oncology Nursing Society (ONS) has published practice recommendations that are applicable to the pediatric population that include 5-HT3 (ondansetron or second generation drug) for prophylaxis of CINV (Oncology Nursing Society, 2014). Triple drug therapy with 5-HT3 agonist, dexamethasone, and aprepitant is the adult standard of care in ONS guidelines. A meta-

analysis of antiemetic medications for the prevention and treatment of CINV concluded that 5-HT3 antagonists remain the gold standard and are more effective than older agents, and that the addition of dexamethasone to this regimen improves efficacy (Phillips et al., 2016). Aprepitant is a newer medication that is recommended for adults receiving chemotherapy in addition to 5-HT3 antagonists and dexamethasone. There was limited data regarding aprepitant in pediatric patients and previous to the new COG guidelines, it was not recommended for children under the age of 12 years. A study of aprepitant was completed in 2014 to assess the effect and safety of aprepitant in children receiving highly emetogenic chemotherapy. The results of this study concluded that much like adult data has shown, aprepitant is a safe and effective drug that significantly decreases CINV in pediatric patients when used in conjunction with dexamethasone and ondansetron (Bakhshi et al., 2015).

A second literature review was performed regarding the adoption and use of new evidence based guidelines by healthcare providers. The search terms used were: barriers or obstacles, provider, guidelines or protocols, implementation. These terms were used to search the Medline database. A total of 251 records were identified and screened. Two hundred thirty seven records were excluded for title or by abstract. Fourteen full text articles were assessed for eligibility. Only records in English were evaluated.

According to Okene & Zapka (2000) despite dissemination of clinical practice guidelines, adherence to these guidelines for clinical care is often low. Inconsistent use of clinical practice guidelines remains a continued challenge to improve public health (Chan et al., 2017). There are many barriers to implementation of clinical practice guidelines. Some providers do not believe there is a need for a change in clinical standards that are

well established. Although many studies have shown that evidence based guidelines and/or clinical practice guidelines can have a positive impact on patient outcomes, many clinicians do not readily accept changes to their current practice (Okene & Zapka, 2000). Improved dissemination and education could improve provider compliance to evidence based practice guidelines (Okene & Zapka, 2000). A study by Zeng et al. (2017) showed that even though providers were aware of clinical practice guidelines, only a small percentage of them implemented the findings. Of the providers surveyed, the most frequently reported barriers to guideline implantation were: lack of training, lack of access, and lack of awareness. Although there is scant literature regarding barriers to clinical practice guideline implementation, what does exist reflects that a lack of knowledge and education on the guidelines remain the primary barriers to changing practice.

Method

The overall design of this project was a retrospective chart review to evaluate the adherence to implementation of the new pediatric guideline; and to assess outcomes for patients who were treated according to the new guideline. Documentation of "breakthrough" medications was used as the key outcome measure to assess if the guideline medications worked as intended to control all symptoms of nausea and vomiting after chemotherapy. The adapted guidelines were disseminated to the hematology/oncology division at SLCH in October of 2017. Charts at this single institution were reviewed for patients who received chemotherapy during a planned chemotherapy admission between January 2017 and March 2017. Inclusion criteria for the chart review included all planned admissions with a patient receiving chemotherapy

classified as highly emetogenic per COG anti emetic guidelines. Exclusion criteria for the chart review were the following: outpatient chemotherapy treatments; patients that received therapy categorized as moderately or mildly emetogenic as delineated in the COG antiemetic guidelines; patients that were unable to receive 5-HT3 antagonist for comorbid conditions such as prolonged QT; and patients unable to receive steroids. Conditions for which steroids are contraindicated as prophylaxis for CINV include but are not limited to: patients receiving therapy for leukemia, patients being treated for brain tumors, and comorbid conditions such as avascular necrosis.

The patients who were admitted from January 1, 2017- March 31, 2017 were accessed through a list of pre-certifications for insurance approval on a shared drive within the division. All patients that were directly admitted to the inpatient oncology service, or admitted through the outpatient oncology clinic were on this master list. These patients were screened for any exclusion criteria. Patients that had more than one admission within this time frame were treated as separate encounters for the chart review. The same lists was accessed for January 1, 2018- March 31, 2018. For both chart reviews all patients were screened for: administration of chemotherapy categorized as highly emetogenic; greater than 6 months of age as this is the youngest patient able to receive aprepitant; and no contraindications for use of ondansetron or dexamethasone. These contraindications included, but are not limited to: prolonged QTc and allergy to 5-HT3 agonists.

Each patient chart that met criteria for inclusion had the following data extracted from the chart: age, gender, number of days patient admitted for treatment, and number and type of PRN medications received for breakthrough CINV. In the review of the first

quarter of 2018, it was evaluated if the guidelines were followed when prescribing the chemotherapy for each admission, and if that provider was an APN or MD. Results were tracked using the data collection tool (Appendix A). All patient identifiers were removed. Each patient chart was only accessed once. Data was numbered sequentially starting with number 1. Data collected from patient charts from January1, 2017- March 31, 2017 will be coded with the letter "a" following the number. Data collected from patient charts from January 1, 2018-March 31, 2018 will be coded with the letter "b" after the number.

Results

Seventy-six patient's charts met eligibility criteria and underwent review. Forty-three of those charts were patient admissions between January 1, 2017 and March 31, 2017. The remaining thirty-three charts reviewed were patient admissions between January 1, 2018 and March 31, 2018. In 2017, the sample included 58%, and 58% of the children were less than twelve years old. In 2018, the sample included 64%; and 52% of the children were less than twelve years old. The mean age of patients in 2017 was 9.07±6.19; and in 2018 the mean patient age was 9.47±6.15.

A t-test was used to compare the mean number of combined anti-emetic doses for all patients in the first quarter of 2017, with the sample from the first quarter of 2018. The mean anti-emetic dose for breakthrough CINV in 2017 was 4.837±10.4857, and in 2018 the mean anti-emetic dose was 3.394±6.432. This was not statistically significant ($p = 0.462$) as shown in Table 3. It was then compared by the number of patients in each sample. In the first quarter of 2017, 21 patients (49%) received anti-emetics for breakthrough CINV as compared to 15 patients (46%) in 2018. A chi square was

performed and this was found not to be statistically significant (p =0.77). Both of these results are shown in Table 2.

The patients were then divided into two groups by age for additional analysis. The age of 12 years was chosen as the new guideline had the greatest potential impact on children less than 12 years of age who were now able to get three agents up front to control their nausea and vomiting (ondansetron, dexamethasone and aprepitant). A t-test was performed to compare the mean number of combined anti-emetic doses for patients <12 years old in the first quarter of 2017, and in the first quarter of 2018. The mean anti-emetic dose for 2017 was 5.8±12.5333; and in 2018 the mean was 3.882±8.1. This was found to not be statistically significant (p =0.55) as shown in Table 4.

Conclusion

The data from this project did demonstrate that there was excellent adherence with use of the new SLCH adapted pediatric anti-emetic guideline in this population of patients. Of the 33 patient charts reviewed, 30 patients (91%) received anti-emetics recommended in the adapted guideline. In reviewing the analysis of the need for anti-emetic doses to treat breakthrough CINV, it can be concluded that in the population of children evaluated in this project, there was not a statistically significant difference in control of acute nausea/vomiting after implementation of the new adapted pediatric guideline. This data may suggest that the previous institutional standard regimen at the hospital was successful in managing acute nausea and vomiting prior to the recommended changes in the new pediatric guideline. However, in the age group of children less than 12 years of age, children did receive 2 fewer prn anti-emetic

medications for breakthrough symptoms each admission for chemotherapy treatment after guideline implementation. The small sample size in children less than 12 years likely impacted the ability to achieve any statistical significance. Although the data in the sample did not achieve statistical significance, this decrease in anti-emetics in children less than 12 years of age is clinically significant. Fewer doses of breakthrough medications for symptoms of nausea or vomiting would have significantly impacted the patient's overall CINV control; and their quality of life if this would have been an outcome measure.

Discussion

One of the biggest changes in the new adapted pediatric guideline was a significant increase in the dosing of dexamethasone (twice the dose). These findings illustrate similar control of acute CINV with once daily dosing of dexamethasone as opposed to the new guideline standard of every 12 hours. The acute side effects of dexamethasone used for CINV were studied by Vardy, Chiew, Galica, Pond, & Tannock (2006). The four symptoms reported were: insomnia, gastro-esophageal reflux, agitation and depression. In fact, 27% of patients reported moderate to severe symptoms in two of four categories in the weeks following dexamethasone administration; and 32% reported moderate to severe symptoms in at least three of these categories. These severe side effects from the anti-emetic itself may negatively impact quality of life. While the use of dexamethasone has been well established as an effective agent to prevent both acute and delayed nausea and vomiting, the unwanted side effects of increased doses may be substantial without increased efficacy. CINV has negative effects on QoL, however, there are many factors that affect QoL. Patients with minimal CINV may have decrease

in QoL from the side effects of dexamethasone for CINV prophylaxis (Vardy et al, 2006). Providers should take into consideration that a similar dose of dexamethasone once daily in this population of patients, was just as effective as an every 12 hour dose for the duration of therapy without the risk of increased adverse side effects secondary to high dose steroid administration for CINV.

The second major change in the new pediatric guideline was the use of aprepitant in all children older than 6 months of age. Aprepitant was designed to control delayed vomiting in the time frame from 2-8 days post chemotherapy treatment. Previously, patients younger than 12 years old, did not receive aprepitant for CINV. Although aprepitant has been shown to be a highly effective ameliorator of delayed CINV, these effects may not be seen while the patient is still admitted but would occur after the child is discharged from the hospital. The prevalence of delayed vomiting in children after moderately high or highly emetogenic chemotherapy was reported to be as high as 32% in a study by Robinson & Carr (2007) specifically addressing the prevalence and pattern of these symptoms in children. The data collected for this project was only during the admission for actual treatment and did not include any post treatment follow up. Although data collected in the project did not show a statistical difference in acute vomiting control; the use of aprepitant in children is still highly recommended as the goal is the prevention of delayed vomiting that occurs up to one week after treatment.

In terms of adaptation of the new pediatric guideline, the pediatric oncology team was very successful with a greater than 90% compliance with the new recommendations. Provider compliance with new evidence based guidelines has been well studied. However, there is a paucity of literature on effective ways to increase use of guidelines in

practice. Studies have shown 30-40% of patients do not receive medical care based on scientific evidence, and 25-30% of care is not needed or potentially harmful (Grol & Grimshaw, 2003). Barriers to provider use of guidelines at many different points of care. These barriers exists at the level of the patient, the provider, the healthcare team, the health care organization and the healthcare environment (Grol & Grimshaw, 2003). Lack of knowledge by the provider continues to be the most studied barrier to new guideline implementation (Maue, Segal, Kimberlan, & Lipowski, 2004).

The new adapted guidelines for the prophylaxis of CINV were disseminated via division email and discussed at team meetings. There was no formal education on the use of the new guidelines prior to or after dissemination. However, there were pre-built anti-emetic order sets in the provider order entry system that provided clinical guidance on the drugs and dosing directly from the new pediatric guidelines. Future interventions to improve provider use of institutional guidelines could include focused education with providers who are prescribers of chemotherapy. Increased education of bedside nurses who are administering highly emetogenic chemotherapies may also be beneficial. The bedside nurse could play a crucial role by recognition that a patient receiving highly emetogenic chemotherapy was being undertreated for CINV and alert a provider.

Limitations

The findings of this study are limited by the review of patient charts at a single institution, and by a small sample size. In addition, the incidence of nausea and vomiting in young children may be effected by the child's inability to verbalize nausea. Discomfort in a child may be perceived by the caregiver as pain or general irritability, and therefore

not treated. There are also limited validated tools in pediatrics to clearly assess and rate the distressing symptoms of nausea for children of all ages.

Conclusions

CINV is a distressing symptom of treatment for cancer that negatively impacts the patient's quality of life. This side effect is equally as distressing for children as it is adults. While treatment for CINV has been well studied in adults, there is less definitive evidence for effective prevention in the pediatric population. Recent guidelines have been published to specifically address prophylaxis of nausea and vomiting in children receiving chemotherapy. Providers who prescribe anti-emetics for children receiving highly emetic chemotherapy need to carefully review the current data; new published guidelines; level of evidence; drug interactions; and side effect profile of available anti-emetics, and make informed choices in the clinical care of their patients. As always, individual tolerance and patient preference should be a part of clinical care. Process measures and outcome measures after implementation of any new guideline are crucial to follow the success of the implementation; and to continually improve the supportive care we provide to both adults and children with cancer.

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Table 1. Changes to Anti-emetic prescribing recommendations.

Previous Institutional Standard of Care	New Children's Oncology Group Guidelines	Adapted Guidelines now used at St. Louis Children's Hospital
Ondansetron Every 6 hours while receiving chemotherapy	**Ondansetron or Granisetron** Prior to initiation of chemotherapy and then q 8 hours	**Ondansetron** Every 6 hours while receiving chemotherapy
Dexamethasone 0.2mg/kg every 24 hours if unable to receive aprepitant. 0.1mg/kg every 24 hours if concurrently receiving aprepitant	**Dexamethasone** 6 mg/m2 every 6 hours if unable to receive aprepitant 3 mg/m2 every 6 hours if concurrently receiving aprepitant	**Dexamethasone** 6 mg/m2 every 12 hours if unable to receive aprepitant 3 mg/m2 every 12 hours if concurrently receiving aprepitant
Aprepitant 125mg on day 1 of chemotherapy 80mg on days 2 & 3 of chemotherapy only in patients greater than 12 years old	**Aprepitant** 125mg on day 1 of chemotherapy or 3mg/kg for patients old but greater than 6 months old and less than 12 years old 80mg on days 2&3 of chemotherapy or 2mg/kg for patients greater than 6 months old and less than12 years old and greater than 6 months old	**Aprepitant** 125mg on day 1 of chemotherapy or 3mg/kg for patients old but greater than 6 months old and less than 12 years old 80mg on days 2&3 of chemotherapy or 2mg/kg for patients greater than 6 months old and less than12 years old and greater than 6 months old
Benadryl PRN 1mg/kg every 6 hours concurrently with metoclopramide	***No recommendations for breakthrough nausea and vomiting***	**Benadryl** PRN 1mg/kg every 6 hours concurrently with metoclopramide
Metoclopramide PRN 0.3mg/kg every 6 hours		**Metoclopramide** PRN 0.3mg/kg every 6 hours
Lorazepam PRN 0.02mg/kg every 6 hours		**Lorazepam** PRN 0.02mg/kg every 6 hours

Table 2. T-Test Comparison of Mean Anti-Emetic Doses Between 2017 & 2018									
Year	N		Mean			Std. Deviation		Std. Error Mean	
2017	43		4.837			10.4857		1.599	
2018	33		3.394			6.432		1.1197	
Independent Samples Test									
	Levine's Test for Equality of Variances		T-Test for Equality of Means						
	F	Sig.	t	df	Sig.	Mean Difference	Std Error Difference	95% CI Lower	95%CI Upper
Equal Variance assumed	1.887	0.174	0.696	74	0.489	1.4433	2.0739	-2.6888	5.5753
Equal Variance not Assumed			0.739	0.462	0.462	1.4433	1.9521	-2.4492	5.3357

Table 3. Chi Square Comparison of Anti-Emetic Doses Between 2017 & 2018			
Received Anti-Emetics	2017 n(%)	2018 n(%)	p-value*
Yes	21 (49%)	15(46%)	0.770
No	22 (51%)	18(54%)	

*Pearson Chi Square Test

Table 4. Comparison of Mean Anti-Emetic Doses Between 2017 & 2018 (<12 years old)									
Year	N		Mean			Std. Deviation		Std. Error Mean	
2017	25		5.8			12.533		2.5067	
2018	17		3.882			8.1		1.9645	
Independent Samples Test									
	Levine's Test for Equality of Variance		T-Test for Equality of Means						
	F	Sig.	T	Df	Sig.	Mean Difference	Std. Error Difference	95% CI lower	95% CI upper
Equal Variance Assumed	0.756	0.39	0.556	40	0.581	1.1976	3.4507	-5.0566	8.8919
Equal Variance Not Assumed			0.602	0.55	0.55	1.9176	3.1848	-4.5193	8.3546

Appendix

Data Collection Form

Year _____ Chart # _____ Gender_____ Age_____

Days in hospital _____

Number of doses of:

Benadryl_____

Metoclopramide_____

Lorazepam_____

- ☐ Used anti-emetic prescribing guidelines

- ☐ Did not use anti-emetic prescribing guidelines
  - Greater than 6 months and did not receive aprepitant
  - Did not get correct steroid dose/interval