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Chemotherapy-induced Nausea and Vomiting Prophylaxis: Practice Within the Children's Oncology Group

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Abstract

Background—The Children's Oncology Group (COG) has endorsed a clinical practice guideline (CPG) for acute chemotherapy-induced nausea and vomiting (CINV) prophylaxis in children with cancer. This project aims to describe current acute CINV prophylaxis practice at COG sites and the gap between this practice and CPG recommendations.

Procedure—Two surveys were developed. The first survey, sent to 94 Cancer Control and Supportive Care Responsible Individuals (CCL RIs) at 94 COG institutions, asked if the institution

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had a standardized approach to practice and focused on antiemetic agent choice. The second survey, sent to 54 pharmacists at COG sites where the CCL RI indicated there was a standardized approach to CINV prophylaxis practice, focused on antiemetic dosing. Survey results were described and analyzed for consistency with the CPG recommendations.

Results—Among the 69 respondents to the first survey, 54 (78%) stated that their institutions have a standardized approach to CINV prophylaxis practice. However, antiemetic choice practices varied widely among respondents. Results from the 36 respondents to the second survey also demonstrated significant antiemetic dosing practice variability. Frequent sources of deviation from CPG recommendations were: antiemetic choice when corticosteroids are contraindicated, dexamethasone dosing, aprepitant use in children less than 12 years and aprepitant use in the presence of a known or suspected drug interaction.

Conclusions—There is great diversity in the CINV prophylaxis provided to children with cancer at COG sites. Concerted strategies are required to improve awareness of the current CINV prophylaxis CPG and to facilitate CPG-consistent CINV prophylaxis.

Keywords

nausea; vomiting; supportive care; chemotherapy-induced vomiting; antiemetic; pediatrics

Introduction

Chemotherapy-induced nausea and vomiting (CINV) is an important concern of children with cancer and their parents, having a significant negative impact on a child's quality of life.[1-3] Parents of children with cancer receiving chemotherapy have ranked nausea as one of the most bothersome treatment-related symptom experienced by their children.[1] Providing CINV prophylaxis that is consistent with recommendations of evidence-based clinical practice guidelines (CPG) improves CINV control in adult cancer patients.[4,5] The Children's Oncology Group (COG) is the world's largest clinical trials consortium dedicated exclusively to pediatric cancer research. In 2013, the COG Cancer Control and Supportive Care (CCL) Committee recognized the need to endorse high quality supportive care CPGs to disseminate alongside therapeutic clinical trials.[6] In the COG CPG endorsement effort,[7] care is taken to ensure endorsed CPGs are evidence-based and consistent with the criteria from the Institute of Medicine[8] and the National Guidelines Clearinghouse.[9] In August 2014, the COG endorsed a CPG for the prevention of acute CINV in pediatric cancer patients.[10] The extent to which practice in COG member institutions is consistent with this CPG is unknown. Understanding the gap between the CINV prophylaxis provided at COG member institutions and the CPG recommendations will help inform the need for, and the development of, specific knowledge implementation strategies and quality improvement initiatives. Furthermore, this information will be important to the planning of future antiemetic trials within the COG.

In this quality improvement project, COG members were surveyed to determine current CINV prophylaxis practice at COG member institutions. We aimed to describe practice across COG sites with respect to: commonly used antiemetic agents and doses in children receiving highly emetogenic chemotherapy (HEC; chemotherapy that has greater than 90%

chance of causing nausea and vomiting in the absence of prophylaxis); the restrictions systematically applied to the use of dexamethasone and aprepitant; indications for palonosetron use; and the level of awareness of the current CPG for CINV prophylaxis.

Methods

This project was approved by the Quality Management Department at The Hospital for Sick Children in January 2015. Two surveys were designed using REDCap (Research Electronic Data Capture), a secure, web-based application designed to support data capture for research studies. REDCap provides 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources. Study data were collected and managed using REDCap electronic data capture tools hosted at The Hospital for Sick Children.[11]

Survey Development

A survey was developed by two authors (PP and LLD) to determine practice regarding the selection of antiemetic agents for CINV prophylaxis, antiemetic dosing and awareness of the current CPG. The survey was intended to be sent to Cancer Control and Supportive Care Responsible Individuals (CCL RIs) at COG institutions. The CCL RI program was developed in 2013 by the COG CCL Committee when it was recognized that a local champion was an important determinant of success of COG CCL trials at the institutional level.[12] The CCL RI is charged with the responsibility for the conduct of CCL trials at their institution.

In regard to the survey questions, if a respondent indicated that they practiced at an institution where CINV prophylaxis was standardized, the questions were framed to ascertain what CINV prophylaxis was usually administered at that specific institution, in the opinion of that respondent. Respondents who indicated that they did not practice at an institution with a standardized approach to CINV prophylaxis were asked to describe their own personal practice.

To determine which antiemetic regimens were commonly provided for children receiving HEC, respondents completed three case-based questions. The scenarios were as follows: 1) child under the age of 12 years receiving HEC not known or suspected to interact with aprepitant; 2) child over the age of 12 years receiving HEC not known or suspected to interact with aprepitant; and 3) child over the age of 12 years receiving HEC known or suspected to interact with aprepitant. When respondents indicated that dexamethasone would be used as a part of their antiemetic regimen, a follow-up question asked what antiemetic regimen would be selected if corticosteroids were contraindicated in the same case. The survey also included questions regarding the respondent's professional role and their awareness of the current CPG.

Survey questions were pilot-tested at The Hospital for Sick Children, Toronto by an inter-professional group of clinicians (physicians, nurse practitioners, pharmacists) with experience in CINV prophylaxis selection. For the pilot-testing, each participant completed

the electronic survey. Immediately thereafter, one of the study investigators (PP or LLD) conducted a 10 to 15 minute, face-to-face, semi-structured interview with each participant to elicit opinions regarding the clarity, ease of survey completion, survey length, and appropriateness of questions. Pilot-testing was done in blocks of one to two interviews. Revisions were made after each block until no substantive changes were suggested by two consecutive interviewees. Changes made to the survey included revisions to wording to be more specific and clear, addition of more response options and areas for comments, and reduction in the length of the survey.

After conducting seven interviews, feedback regarding survey clarity and feasibility was also solicited from the COG Cancer Control and Supportive Care Steering Committee members. At their suggestion, the survey was split into two. The first survey focused on antiemetic selection and was aimed at CCL RIs. The second survey focused on antiemetic dosing and was aimed at pharmacists at COG institutions. After these changes were made, each survey was pilot-tested as described previously until no further, substantive changes were suggested. The first survey (Supplemental Appendix A) was pilot-tested by an additional four healthcare professionals, and the second survey (Supplemental Appendix B) by an additional four pharmacists.

Survey Distribution

An electronic link to the first survey was e-mailed to 94 CCL RIs at 94 institutions in February 2015 (6 months after CPG endorsement by COG). CCL RIs were given the option of forwarding the survey to another person at their institution better equipped to address questions related to CINV prophylaxis. CCL RIs who did not respond within 7 days were reminded with an e-mail and/or telephone call. Weekly reminders were sent for a period of 4 weeks.

COG institutions with a standardized approach to CINV prevention were identified from the responses to the first survey. One pharmacist at each of these institutions was e-mailed an electronic link to the second survey. Pharmacists who did not respond received weekly reminders by e-mail and/or telephone for a period of 4 weeks.

Analysis of Survey Responses

Survey responses were collated and summarized. Partially completed surveys were not included in the analysis. REDCap allowed for branching logic to be used such that a follow-up question could be asked depending on the respondent's response to the initial survey question. As a result, the number of respondents to each question varied.

The consistency between answers to the case-based and dosing survey questions and the current CPG was determined. A list of responses that were considered to be CPG-consistent for each of the case-based questions in each of the surveys is presented in Supplemental Appendix C.

Results

Survey of CCL RIs

Sixty-nine fully completed surveys (response rate: 73%; 69/94) were received. One partially completed survey was excluded from analysis. Respondent demographics are presented in Table I. Most respondents (78%; 54/69), stated that their institution had a standardized approach to CINV prophylaxis, with the majority (59%; 32/54) stating that the approach was institution-specific. The Pediatric Oncology Group of Ontario CINV prophylaxis CPG (the CPG for CINV prophylaxis currently endorsed by the COG) was used at 28% (15/54) of institutions. 67% (46/69) of respondents had read the current CPG for CINV prophylaxis endorsed by COG although only 4% (3/69) stated that all of its recommendations had been implemented at their institution. Another 20% (14/69) of respondents knew the CPG existed, but were not familiar with its content.

Choice of Antiemetic Agents—Complete survey results for the case-based questions are presented in the Supplemental Appendix D. A total of 18 different CINV prophylaxis regimens (i.e. combination of antiemetic agents used irrespective of dose) were offered in response to the scenario describing a child less than 12 years of age receiving HEC that is not known or suspected to interact with aprepitant. Less than half of surveyed respondents (41%; 28/69) offered regimens that were consistent with the current CPG (Table II). A common source of CPG-inconsistent antiemetic agent choice was the use of aprepitant in this age group (35%; 24/69) (Table III).

A total of 21 and 24 different CINV prophylaxis regimens were offered for CINV prophylaxis in response to the scenarios of children 12 years of age and older receiving HEC that was or was not known or suspected to interact with aprepitant, respectively. CPG-consistent antiemetic agents were selected by 26% (18/69) and 13% (9/69) of respondents in the scenarios with and without a known or suspected interaction with aprepitant, respectively. A common source of CPG-inconsistent antiemetic selection was the use of aprepitant in a child receiving chemotherapy known or suspected to interact with aprepitant (30%; 21/69) (Table III).

No respondent selected an antiemetic regimen that was consistent with the current CPG in the 3 scenarios in which the use of a corticosteroid for CINV prophylaxis was contraindicated. Lorazepam [33% (19/58) to 38% (17/45)], scopolamine [10% (6/58) to 20% (9/45)] and diphenhydramine [21% (8/39) to 28% (16/58)] were commonly reported in these scenarios. None are consistent with the CPG recommendations. Another CPG-inconsistent antiemetic choice, the combination of aprepitant and granisetron/ondansetron, was also commonly [23% (9/39) to 33% (19/58)] chosen in these cases.

Reasons identified by respondents for avoiding the use of aprepitant were: known or suspected drug interaction with the patient's chemotherapy (68%; 47/69), patient's age less than 12 years (35%; 24/69), and patient's body weight less than 40kg (35%; 24/69). Reasons identified by respondents for avoiding the use of corticosteroids as an antiemetic were: diagnosis of acute lymphoblastic leukemia (80%; 55/69), acute myelogenous leukemia (59%; 41/69), brain tumor (51%; 35/69) or osteosarcoma (1%; 1/69) and receipt of

hematopoietic stem cell transplant conditioning (28%; 19/69). Palonosetron was used in 29% (20/69) of institutions, primarily when other antiemetic regimens had failed (90%; 18/20).

Survey of COG Pharmacists

The second survey was sent in March 2015 (7 months from CPG endorsement by COG) to COG pharmacists at the 54 institutions which, according to the respondents to the first survey, had a standardized approach to CINV prophylaxis. Thirty-six completed surveys were received (response rate: 67%; 36/54). One partially completed survey was not included in the analysis. Among respondents, 44% (16/36) stated that their institution followed institution-specific guidelines and 28% (10/36) of respondents indicated that their institution followed the CPG currently endorsed by the COG (Table I).

Choice of Antiemetic Agents—Aprepitant was recommended by the institutions' respective CINV prophylaxis guideline at 75% (27/36) of respondents' sites. In an additional 8 institutions (22%; 8/36), aprepitant was used despite not being specifically recommended in their guideline. Aprepitant was unlikely to be recommended for children who were under the age of 12 years by 40% (14/35) of respondents.

Dexamethasone was recommended for CINV prophylaxis at 89% (32/36) of institutions. An additional 2 respondents (6%; 2/36) indicated that dexamethasone was used without a specific guideline recommendation. In 2 institutions (6%; 2/36), dexamethasone was never recommended as an antiemetic regardless of the patient situation.

Palonosetron was recommended by the CINV prophylaxis guideline in place at 14% (5/36) of the respondents' sites. It was considered as a potential option for CINV prophylaxis at an additional eight institutions and thus was available for use at 36% (13/36) of institutions overall.

Dosing of Antiemetic Agents—Supplemental Appendix E presents all of the dosing recommendations provided by survey respondents for aprepitant, dexamethasone and palonosetron.

Aprepitant dosing: For children 12 years of age and older, 11 different aprepitant dosing regimens were in use across 35 institutions. Most respondents (60%; 21/35) stated that the adult dose of aprepitant [13] (125 mg on day 1 followed by 80 mg on days 2 and 3) was administered. This dose is consistent with the current CPG.[10]

At the 21 institutions where aprepitant was administered to children under the age of 12 years, 13 different dosing regimens were described. These 13 dosing regimens varied primarily with respect to the weight tiers used for dosing. Some institutions (23%; 8/35) used the adult dose in children weighing greater than 20kg, whereas other institutions would not administer the adult dose unless the child weighed greater than 40kg (20%; 7/35).

Dexamethasone dosing: In total, respondents from 34 institutions offered 29 different dexamethasone dosing recommendations for children receiving HEC. Few respondents (9%;

3/34) indicated that the dexamethasone dose recommended in the current CPG (6mg/m²/dose IV/PO q6h)[10] would be administered at their institution. Dexamethasone doses varied from 6.75 mg/m²/day to 30 mg/m²/day with doses given every 6 to 8 hours. Four institutions (12%; 4/34) indicated that dexamethasone doses were fixed within given body surface area tiers for children less than 12 years; three institutions did the same for children 12 years of age and older. At 2 institutions (6%; 2/34) dexamethasone dosing was fixed regardless of weight or body surface area for children less than 12 years of age and in 3 (9%; 3/34) institutions for children 12 years of age and older. Two respondents (6%; 2/34) stated that there was no standard dexamethasone dosing regimen at their institution.

Palonosetron dosing: Thirteen respondents stated that palonosetron was used at their institution for CINV prophylaxis. Of these, 4 (31%; 4/13) indicated that palonosetron was not used in children under the age of 12 years. The recommended adult dose (0.25 mg IV x 1 dose pre-therapy)[14] was the most commonly administered (46%; 6/13) in children 12 years of age and older. The FDA-approved palonosetron dose for pediatric patients (<17 years: 20 mcg/kg (max: 1.5 mg) IV x 1 dose pre-therapy)[14] was recommended by 23% (3/13) of respondents in children less than 12 years and by 15% (2/13) of respondents in children over the age of 12 years.

Discussion

The COG CCL RIs and COG pharmacists responding to our surveys have reported that a consistent approach to CINV prophylaxis is in place at most institutions. While this is encouraging, this approach is most often institution-specific and practice is highly variable across COG sites. The endorsement of a CINV prophylaxis CPG by the COG has not yet translated into uniform antiemetic choice or dosing across COG sites for CINV prevention. Implementation of CPG-consistent CINV prophylaxis represents a major challenge to improve CINV outcomes in pediatric oncology.

In general, there was excellent awareness of the current CINV CPG among CCL RIs, especially given that only 6 months had passed since the COG had endorsed it. Since we surveyed CCL RIs, who are institutional champions of supportive care, awareness of the current CPG is likely higher among our respondents than in the general pediatric oncology community. However, CPG awareness did not translate into CPG-consistent practice. Although awareness of the current CPG may be further improved now that all COG Supportive Care Endorsed CPGs are publicly and readily available (see: <https://childrensoncologygroup.org/index.php/cog-supportive-care-guidelines>), focused efforts are required to promote CPG implementation. Educational outreach programs,[4,15,16] providing clinicians with feedback on a patient's CINV experience,[17] and informing prescribers when their prescribing is CPG-inconsistent are methods that have facilitated practice change in adult medicine.[18] It is possible that attitudes and behaviours regarding CPG implementation are different within the pediatric oncology community. As a result, there is a need to develop and evaluate CPG implementation strategies tailored to pediatric oncology.

The current CPG for CINV prophylaxis contains both strong and weak recommendations as defined by the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system for CPG development.[10,19,20] Strong recommendations may be implemented as a policy since there is a high level of confidence that the desirable effects outweigh undesirable effects. Conversely, implementation of a weak recommendation should take place only after an evaluation of values and preferences of those involved, as the guideline panel makes the recommendation in the belief that desirable and undesirable effects are finely balanced or that appreciable uncertainty exists about the magnitude of effect.[19,20] Therefore, some of the practice variation described in our survey results understandably stems from the number of weak recommendations within the current CPG. For example, no respondent selected CINV prophylaxis that was consistent with the weak CPG recommendation to administer ondansetron or granisetron plus chlorpromazine or nabilone to children receiving HEC when corticosteroids were contraindicated. In contrast, 41% (28/69) of respondents selected CINV prophylaxis consistent with the strong CPG recommendation to administer ondansetron or granisetron plus dexamethasone to children less than 12 years receiving HEC.[10]

Fundamentally, practice variation with respect to CINV prophylaxis, including criteria for use and optimal dosing of antiemetic agents, is likely a result of the significant evidence gaps that exist in this area and the lack of high quality evidence upon which to base strong recommendations. The use of aprepitant in young children is one such gap. At the time of this survey, there was little direct evidence to support the administration of aprepitant to children less than 12 years old. Nevertheless, it was reported to be the practice at 35% (24/69) of institutions. This may reflect the eagerness of pediatric clinicians to offer children a drug shown to be of benefit in adults and/or familiarity with a then on-going, now published, pediatric aprepitant trial.[21]

A second area of practice variation stemming from an evidence gap is the co-administration of aprepitant with chemotherapy whose dose intensity may increase as a result of an interaction. When directly queried, 68% (47/69) of respondents indicated that aprepitant would be avoided in the presence of a drug interaction. Nevertheless, 30% (21/69) of respondents selected aprepitant for CINV prophylaxis in the case-based question involving such a situation. This may indicate that healthcare professionals are unaware of potential drug interactions with aprepitant or that there is disagreement regarding their clinical significance.

Thirdly, lack of high quality evidence also leads to variation in the dosing of antiemetic agents. For example, respondents to our survey reported a more than three-fold variation in the dexamethasone dose for children receiving HEC. Since the ability of dexamethasone to control CINV is dose-dependent in adults,[22] studies to determine the optimal pediatric dose of dexamethasone for CINV prophylaxis are sorely needed.

Our surveys describe CINV prophylaxis practices in a large number of North American pediatric oncology centers, all of whom are members of the COG. While a potential limitation of our surveys was our reliance on the respondents to understand the questions and to convey an accurate reflection of their institutional practice, we do not feel that this

was a concern given that these issues were not identified during the final rounds of pilot-testing of the surveys. The strength of our findings lies in the wide geographical representation of the respondents and the involvement of an inter-professional group of clinicians with a self-declared interest in supportive care and pharmacists with a professional interest in drug dosing. As a result, our findings are likely to be generalizable across COG member institutions. Future studies will evaluate actual practice at COG sites to determine the degree of CPG-consistent versus CPG-inconsistent care actually delivered and the associated clinical outcomes.

Conclusion

CINV prophylaxis provided to children with cancer at COG institutions is diverse. At the time of the survey, no institution had a guideline in place that was entirely consistent with the current CPG for CINV prophylaxis. Focused efforts to improve uptake of the COG Supportive Care Endorsed Guidelines among COG members and studies to improve the quality of evidence available to support CPG recommendations are critical to ensure that children with cancer receive optimal supportive care.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Dupuis LL, Milne-Wren C, Cassidy M, Barrera M, Portwine C, Johnston D, Silva M, Sibbald C, Leaker M, Routh S, Sung L. Symptom assessment in children receiving cancer therapy: the parents' perspective. *Support Care Cancer*. 2010; 18(3):281–299. [PubMed: 19513763]
2. Rodgers C, Kollar D, Taylor O, Bryant R, Crockett K, Gregurich MA, Hockenberry M. Nausea and vomiting perspectives among children receiving moderate to highly emetogenic chemotherapy treatment. *Cancer Nurs*. 2012; 35(3):203–210. [PubMed: 21915041]
3. Rodgers C, Norville R, Taylor O, Poon C, Hesselgrave J, Gregurich MA, Hockenberry M. Children's coping strategies for chemotherapy-induced nausea and vomiting. *Oncol Nurs Forum*. 2012; 39(2):202–209. [PubMed: 22374494]
4. Aapro M, Molassiotis A, Dicato M, Pelaez I, Rodriguez-Lescure A, Pastorelli D, Ma L, Burke T, Gu A, Gascon P, Roila F. investigators P. The effect of guideline-consistent antiemetic therapy on chemotherapy-induced nausea and vomiting (CINV): the Pan European Emesis Registry (PEER). *Ann Oncol*. 2012; 23(8):1986–1992. [PubMed: 22396444]
5. Gilmore JW, Peacock NW, Gu A, Szabo S, Rammage M, Sharpe J, Haislip ST, Perry T, Boozan TL, Meador K, Cao X, Burke TA. Antiemetic guideline consistency and incidence of chemotherapy-induced nausea and vomiting in US community oncology practice: INSPIRE Study. *J Oncol Pract*. 2014; 10(1):68–74. [PubMed: 24065402]

6. Sung L. Priorities for quality care in pediatric oncology supportive care. *J Oncol Pract.* 2015; 11(3): 187–189. [PubMed: 25758449]
7. Children's Oncology Group Supportive Care Guidelines Committee. [2015 October 26] Endorsement Policy. https://childrensoncologygroup.org/downloads/Endorsement_Policy_COG_Guidelines_Comm_August_25_2015.pdf
8. Institute of Medicine. Clinical practice guidelines we can trust. National Academies Press; <http://www.iom.edu/Reports/2011/Clinical-Practice-Guidelines-We-Can-Trust/Standards.aspx> Published 2011 March 23 [2015 October 26]
9. National Guideline Clearinghouse. Inclusion Criteria. U.S. Department of Health & Human Services; <http://www.guideline.gov/about/inclusion-criteria.aspx>. Published 2014 June 1 [2015 October 26]
10. Dupuis LL, Boodhan S, Holdsworth M, Robinson PD, Hain R, Portwine C, O'Shaughnessy E, Sung L. Pediatric Oncology Group of Ontario. Guideline for the prevention of acute nausea and vomiting due to antineoplastic medication in pediatric cancer patients. *Pediatr Blood Cancer.* 2013; 60(7):1073–1082. [PubMed: 23512831]
11. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform.* 2009; 42(2):377–381. [PubMed: 18929686]
12. Vanhoff D, Hesser T, Kelly KP, Freyer D, Stork S, Sung L. Facilitating accrual to cancer control and supportive care trials: the clinical research associate perspective. *BMC Med Res Methodol.* 2013; 13:154. [PubMed: 24380578]
13. Merck & Co., Inc. [2015 September 15] Emend (aprepitant) Product Monograph. http://www.merck.com/product/usa/pi_circulars/e/emend/emend_pi.pdf. Published 2015 August
14. Eisai Inc. [2015 September 15] Aloxi (palonosetron HCl injection) Product Monograph. <http://www.aloxi.com/docs/pdf/PI.pdf>. Published 2014 September 19
15. Peterson DE, Bensadoun RJ, Lalla RV, McGuire DB. Supportive care treatment guidelines: value, limitations, and opportunities. *Semin Oncol.* 2011; 38(3):367–373. [PubMed: 21600365]
16. Roila F. Transferring scientific evidence to oncological practice: a trial on the impact of three different implementation strategies on antiemetic prescriptions. *Support Care Cancer.* 2004; 12(6): 446–453. [PubMed: 15045572]
17. Mertens WC, Higby DJ, Brown D, Parisi R, Fitzgerald J, Benjamin EM, Lindenauer PK. Improving the care of patients with regard to chemotherapy-induced nausea and emesis: the effect of feedback to clinicians on adherence to antiemetic prescribing guidelines. *J Clin Oncol.* 2003; 21(7):1373–1378. [PubMed: 12663729]
18. Wood M, Hall L, Hockenberry M, Borinstein S. Improving Adherence to Evidence-Based Guidelines for Chemotherapy-Induced Nausea and Vomiting. *J Pediatr Oncol Nurs.* 2015; 32(4): 195–200. [PubMed: 25576315]
19. Guyatt GH, Oxman AD, Kunz R, Falck-Ytter Y, Vist GE, Liberati A, Schunemann HJ, Group GW. Going from evidence to recommendations. *BMJ.* 2008; 336(7652):1049–1051. [PubMed: 18467413]
20. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, Schunemann HJ, Group GW. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ.* 2008; 336(7650):924–926. [PubMed: 18436948]
21. Kang HJ, Loftus S, Taylor A, DiCristina C, Green S, Zwaan CM. Aprepitant for the prevention of chemotherapy-induced nausea and vomiting in children: a randomised, double-blind, phase 3 trial. *Lancet Oncol.* 2015; 16(4):385–394. [PubMed: 25770814]
22. Italian Group for Antiemetic Research. Double-blind, dose-finding study of four intravenous doses of dexamethasone in the prevention of cisplatin-induced acute emesis. *J Clin Oncol.* 1998; 16(9): 2937–2942. [PubMed: 9738561]

Abbreviations

CCL Cancer Control and Supportive Care

CCL RI	Cancer Control and Supportive Care Responsible Individual
CINV	chemotherapy-induced nausea and vomiting
CPG	clinical practice guideline
COG	Children's Oncology Group
HEC	highly emetogenic chemotherapy
REDCap	Research Electronic Data Capture

TABLE I

Characteristics of Respondents to Two Chemotherapy-induced Nausea and Vomiting Prophylaxis Practice Surveys

Characteristic	Survey of CCL RIs N = 69 (%)	Survey of Pharmacists N = 36 (%)
Profession:		
Nurse Practitioner	15 (22)	-
Pharmacist	7 (10)	36 (100)
Physician	46 (67)	-
Nurse	1 (1)	-
Use of Clinical Practice Guidelines:		
No	15 (22)	-
Yes	54 (78)	36 (100)
American Society of Clinical Oncology	3 (6)	3 (8)
2009 Children's Oncology Group	4 (7)	-
2014 Children's Oncology Group	12 (22)	5 (14)
Institution-Specific	32 (59)	16 (44)
Pediatric Oncology Group of Ontario	3 (6)	5 (14)
Other	-	7 (19)
Awareness of 2014 COG Supportive Care Endorsed Guidelines:		
Read and apply all of the recommendations in daily practice	3 (4)	-
Read and apply some of the recommendations in daily practice	43 (62)	-
Know they are available, but have not read them	14 (20)	-
Did not know they are available	9 (13)	-

CCL RI: Cancer Control and Supportive Care Responsible Individual

TABLE II

Proportion of Respondents Selecting Antiemetic Regimens Consistent with the Clinical Practice Guideline Endorsed by the Children's Oncology Group

Scenario	Number of respondents (%)		
	Standardized practice (N=54)	Not standardized practice (N=15)	Total (N=69)
Child <12 years receiving HEC with no known or suspected aprepitant drug interaction	22 (41)	6 (40)	28 (41)
Child 12 years receiving HEC with no known or suspected aprepitant drug interaction	8 (15)	1 (7)	9 (13)
Child 12 years receiving HEC with known or suspected aprepitant drug interaction	17 (31)	1 (7)	18 (26)
Child <12 years receiving HEC with a contraindication to the use of corticosteroids	0 (0)	0 (0)	0 (0)
Child 12 years receiving HEC with a contraindication to the use of corticosteroids	0 (0)	0 (0)	0 (0)

HEC: highly emetogenic chemotherapy

TABLE III

Antiemetic Choices Inconsistent with the Clinical Practice Guideline Endorsed by the Children's Oncology Group

Inconsistent Antiemetic Choice ^a	Number of respondents (%)		
	Standardized practice (N=54)	Not standardized practice (N=15)	Total (N=69)
Aprepitant for a child <12 years	16 (30)	8 (53)	24(35)
Aprepitant in the presence of a suspected drug interaction	16 (30)	5 (33)	21 (30)
CPG-inconsistent antiemetic regimens in the case where corticosteroids are contraindicated	54 (100)	15 (100)	69 (100)
Scheduled use of diphenhydramine	Case 1: 4 (7)	Case 1: 0 (0)	Case 1: 4 (6)
	Case 2: 6 (11)	Case 2: 1 (7)	Case 2: 7 (10)
	Case 3: 7 (13)	Case 3: 1 (7)	Case 3: 8 (12)
Scheduled use of lorazepam	Case 1: 6 (11)	Case 1: 1 (7)	Case 1: 7 (10)
	Case 2: 7 (13)	Case 2: 1 (7)	Case 2: 8 (12)
	Case 3: 9 (17)	Case 3: 1 (7)	Case 3: 10 (14)
Scheduled use of scopolamine	Case 1: 3 (6)	Case 1: 0 (0)	Case 1: 3 (4)
	Case 2: 7 (13)	Case 2: 1 (7)	Case 2: 8 (12)
	Case 3: 7 (13)	Case 3: 1 (7)	Case 3: 8 (12)

^a All sources refer to cases where corticosteroids are not contraindicated, unless otherwise noted; CPG: clinical practice guideline