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Abstract

This paper presents findings of an audit on the management of chemotherapy induced nausea and vomiting (CINV) in children/adolescents being treated in the national Irish paediatric cancer unit. Over a three month time period, the prescribed antiemetic medication and the incidence of CINV in 50 consecutive patient episodes was recorded. Twenty five children with a variety of malignancies were included. Results of the audit revealed that antiemetics were not prescribed relative to the emetogenic potential of the chemotherapy received. Dexamethasone as an antiemetic was only used by one patient. 40% of patients did not take any antiemetics when discharged from hospital. It was concluded that the potential negative effects of Dexamethasone may be anecdotally influencing prescribing. As a result of this audit, evidence-based guidelines incorporating antiemetics proportional to chemotherapy emetogenic potential were established.

Key words: adolescent, anti-emetics, audit, chemotherapy, nausea, oncology, paediatric, vomiting.

Introduction

Chemotherapy induced nausea and vomiting (CINV) can be a major problem for children with cancer. Children are especially vulnerable to electrolyte imbalance, dehydration and weight loss. In addition poor nutrition may impact on their intolerance to additional chemotherapy. The actual experience of vomiting creates physical and emotional distress for both the child and the parents. As early as 1983 it was shown that the possibility of experiencing treatment-related nausea and vomiting was considered to be one of the most important and dreaded side effects for patients (Coates et al., 1983, de Boer-Dennert et al., 1997). This distress can effect the patient's normal activities and quality of life significantly (McRonald and Fleisher 2005, Robinson and Carr 2007). All patients who receive chemotherapy are not at equal risk for developing CINV. Patient characteristics and chemotherapy agents are among the contributing factors; the latter probably the most significant risk factor (Bloechl-Daum et al., 2006, MASCC, 2006). Variation in the management of CINV in children exists nationally and internationally. The aim of this paper is to present findings from an audit undertaken at the national Irish paediatric cancer centre of the use, and effectiveness, of antiemetics and to demonstrate the resulting change in practice in the management of CINV.

Background

Nausea, vomiting and retching are discrete symptoms; therefore, they must be clearly defined and understood in order to accurately assess and measure these separate concepts (Molassiotis and Borjeson 2006, Robinson and Carr 2007). Nausea is a subjective, unobservable phenomenon of an unpleasant sensation often associated with a feeling that

vomiting is imminent. It is often associated with unpleasant sensations experienced in the back of the throat and can be accompanied by autonomic nervous system activity such as pupil dilation, sweating and salivation (Morrow et al., 2002, Robinson and Carr 2007).

Retching is an attempt to vomit without bringing anything up and can be measured both subjectively and objectively. It may be described as 'dry heaves', 'gagging' or attempting to vomit without results. Patients can readily differentiate the frequency of occurrence and the actual distress experienced from the sensation of retching. The process of retching or vomiting is definitive, obvious to the observer and patient and not dependent on the patient's impressions (Rhodes and McDaniel 2001). Vomiting is the forceful expulsion of the contents of the stomach through the oral or nasal cavity and in contrast to nausea, can be objectively measured (Morrow et al., 2002).

Chemotherapy induced nausea and vomiting is classified into three categories: acute onset, occurring within 24 hours of the initial administration of chemotherapy, delayed onset, occurring 48 hours to five days after initial treatment and anticipatory nausea and vomiting which is observed in patients whose emetic episodes are triggered by taste, odours, sights, thoughts or anxiety secondary to a history of poor response to anti-emetic agents (Fromer 2005, Robinson and Carr 2007, Hesketh 2008).

The mechanism by which chemotherapy induces nausea and vomiting is complex. Mechanisms for acute CINV are different than the mechanisms for delayed or anticipatory nausea and vomiting. Furthermore, the mechanism associated with one

chemotherapy agent may be different to another agent and the schedule or dose of one drug may be affected by another. The impact of combining chemotherapy with radiotherapy or biotherapy may also influence the profile of the patient's nausea and vomiting (MASCC 2006).

Management of CINV in children is challenged by a paucity of evidence in that studies on the prevention of CINV are few and far between. However, the 5-HT_3 receptor antagonists are more effective than metoclopramide or phenothiazines and the 5-HT_3 receptor antagonists alone are inferior to the combination of dexamethasone and 5-HT_3 receptor antagonists. Patients receiving moderate to highly emetogenic chemotherapy seem to benefit from this combination. The use of dexamethasone remains controversial not because of its efficacy but rather due to the possibility of decreasing the cytotoxic potential of chemotherapy. In-vitro data exists demonstrating dexamethasone to inhibit the action of chemotherapy in certain solid tumour cell lines (Zhang et al., 2006). A recent Cochrane review of antiemetic medication for prevention and treatment of CINV in children concluded that it remains uncertain how the known antiemetic benefit of dexamethasone is to be balanced with this reduction of chemotherapy sensitivity (Phillips et al., 2011). Collaborative guidelines for antiemetic treatment in CINV, incorporating the above general recommendations, have been published both by the Multinational Association of Supportive Care in Cancer (MASCC) (in conjunction with the European Society of Medical Oncology since 2004) and the American Society of Clinical Oncology (ASCO) from 1997, with these guidelines subsequently being revised and updated at least twice (Jordan et al., 2011).

With this background a need was identified in the national paediatric cancer unit in Ireland to audit the management of CINV. This need was reinforced by the lack of use of dexamethasone as an antiemetic together with the lack of local institutional guidelines to manage CINV in children. The national paediatric unit is a centralised, single centre providing care in conjunction with 16 shared-care centres across the country, to all patients diagnosed with cancer under the age of 16 yrs in Ireland (approximately 160 patients per year).

Aim and Objectives

The aim of this audit was to document the current management of CINV in children/adolescents in an attempt to revise and align practice to recently published contemporary guidelines. The main objective of the audit was to document the current prescribing and administration practice of antiemetic therapy with a secondary objective being to collect data on the effectiveness, where possible, of current antiemetic medication used.

Method

a) Setting

The audit took place in the In-patient Haematology/Oncology ward, Our Lady's Children's Hospital Crumlin, Dublin. It was limited to in-patients, as compared to out-patients, for the ease of time accessibility to patients and their parents and in order for patients/parents to become familiar with the assessment instruments (see instrument section below).

b) Sample

Fifty consecutive patient episodes were recorded, with an episode being a single-case/patient admission for chemotherapy administration. For inclusion into the audit, the patient had to be ≥ 4years, to be suitable to utilise the instrument to assess nausea (see below – instruments).

c) Time

The audit was conducted over a 3 month period, August to October 2008

d) Procedure

A prospective design was used, with each patient episode involving a daily (from day 1 of admission to discharge) interview of the patient, conducted by the first author to assess degree of nausea and vomiting experienced, utilising two instruments (see below – instruments). Antiemetic medication and chemotherapy received, including dosage, was documented on each day. MASCC diaries were given to the patient/parent on their first day of admission for chemotherapy. On the day following discharge the patient/parent was contacted by telephone by the first author to (1) assess nausea intensity and vomiting frequency following discharge from hospital and (2) to record what antiemetic medication was given to the patient to take home on discharge. Although the interviewer/first author may have been involved peripherally in the clinical care of the patient, she had no role or influence in the prescribing of antiemetic medication, a task performed exclusively by the medical staff of the ward. Medical and nursing staff were aware of the audit process.

e) Emetogenic grading of chemotherapy

The emetogenic potential of each chemotherapy agent was classified, retrospectively, as low, moderate, high and very high (Dupuis et al., 2008) (Table 1). Patients were stratified according to these criteria (Dupuis et al., 2008). For instance, the most emetogenic chemotherapy agent received, for e.g. Vindesine- low (10-30% chance of emesis if no antiemetic administered), Cyclophosphamide < 750mg/m^2 - moderate (30%-60%), Doxorubicin > 60mg/m^2 - high (60%-90%) and Cisplatin> 50mg/m^2- very high (>90%). Children and adolescents receive a combination of chemotherapy over a number of days and therefore the chemotherapy agent with the highest emetogenicity directed the appropriate antiemetics that were required.

f) Instruments

Two instruments were utilised to assess the degree of nausea and vomiting experienced: the Pediatric Nausea Assessment Tool (PeNAT) (Dupuis et al., 2006), and the Multinational association of supportive care in oncology tool (MASCC Antiemesis Tool (MAT) (Molassiotis, 2007).

The PeNAT was used to assess patients' level of nausea. This tool was devised to assess nausea intensity in children age 4 years or older and utilises four facial expression scales (Figure 1). This instrument has moderate construct and convergent validity scores (Baxter et al., 2011). It was the only instrument of its kind especially developed for children available at the time of the audit. Another pictorial children's nausea scale has since been developed (Baxter et al., 2011). Two standard scripts were developed for administering the instrument; one for children older than 8 years and the other for children between 4 –

8 years. For children older than 8 years, all four faces of the PeNAT tool were presented simultaneously. For the younger children, PeNAT faces were presented in successive adjacent pairs to block their tendency to choose the extremes of the scale.

The PeNAT has an accompanying information sheet which explains the correct way to present the PeNAT instrument, and this was used in the audit. Before the first author presented the instrument, a discussion regarding each individual family's familiar terms for nausea and vomiting were discussed and when using the PeNAT instrument this term was used. If the child aged 4-8yrs states that they have 'no nausea', faces 1 and 2 are shown. If the child says 'some nausea', faces 3 and 4 are shown and the child was asked 'which face is more like you now'? Regarding the child older than 8 years, the PeNAT states that children who receive chemotherapy feel nauseous (use family term) and some do not. These faces show children who feel no nausea at all, who feel a little bit nauseous, who feel even more nauseous, and who feels nauseous a whole lot. The first author pointed to each face at the appropriate time and then asked 'which face is more like you now'?

On discharge, the first author provided the parents a copy of the PeNAT instrument and demonstrated to the parents on how to present the instrument to their children at home.

The MASCC Antiemesis Tool (MAT) (Molassiotis, 2007) is a validated eight item scale which assesses both acute and delayed nausea and acute and delayed vomiting (Wood et al., 2011). This instrument records occurrence (four subscales), duration (two subscales)

and frequency (two subscales) of nausea and helps identify patients who are not being appropriately treated with anti-emetic therapy (Molassiotis et al., 2008, Yamaguchi et al., 2009). In a review of patient self-report tools for chemotherapy nausea and vomiting (Brearley et al., 2008), the MAT's strengths are highlighted as its conciseness and its ability to be administered at the end of a 2 or 3-week cycle. The patient/carer was requested to record using the instrument as directed: i.e. 24 hours following the administration of chemotherapy for acute emesis and for delayed emesis up to 2 days following completion of chemotherapy.

g) Classification and grading of vomiting

Vomiting was classified as: anticipatory (within 24 hour period preceding chemotherapy administration), acute (defined as ≥ 1 vomit in a 24 hour period) during chemotherapy administration, delayed (defined as ≥ 1 vomit in the 48 hour period following completion of chemotherapy). Intensity of vomiting was defined according to the Common Toxicity Criteria (CTC) (NCCN 2008) – see table (2).

h) Administrative

Informed consent was obtained from the parents/guardians of all patients and where appropriate, assent from the patients was obtained. As the audit was prospective, involving direct patient/parent contact, approval from the Ethics Committee of Our Lady's Children's Hospital to conduct this audit was obtained.

Audit results

Fifty inpatient episodes were recorded, involving 25 patients (10 female and 15 male) with a variety of malignancies – see Table (3). Days in hospital ranged from 1 to 10 days.

The majority of patients in this audit (98%) received a combination of a 5-HT_3 antagonist and metoclopramide. Only 1 out of the 25 patients received dexamethasone. There was no correlation between antiemetic prescribed and emetogenic potential of received chemotherapy - see Table (4).

Thirty five patients (70%) experienced some degree of nausea on days 1-5.

In total, the majority (90%) of patients experienced no or only 'a little nausea' (PeNAT 1 or 2) as compared to 10% of patients who experienced more nausea or a lot of nausea (PeNAT 3 or 4) (Table 5).

Anticipatory vomiting occurred in 2 (4%) patient episodes, a 10yr old girl and a 7yr old boy. Acute vomiting was experienced in approximately 35% of patient episodes, averaged over 5 days of chemotherapy administration. Delayed vomiting occurred in 24 (48%) patient episodes. Twenty patients (40%) did not take any antiemetics when discharged from hospital. Eleven of these 20 patients were not prescribed antiemetics on discharge.

No vomiting (CTC grade 0) was experienced in 72%, 59%, 62%, 67% and 67% patient episodes on days 1-5 of chemotherapy administration respectively. In contrast only 14%, 28%, 23%, 11% and 17% of patient episodes were characterised by CTC grade 2 to 4 (> 2-5 vomiting episodes in 24 hours)- see Table 2

Discussion

This is the first audit to be undertaken in this institution to assess patients' level of nausea and degree of vomiting following their scheduled chemotherapy. Inconsistencies and variation in prescribing in the management of CINV was evident in the audit, with the two major findings being that the emetogenic potential of the chemotherapy administered was not taken into consideration when prescribing antiemetics and secondly, the very low use of dexamethasone as an antiemetic.

Dexamethasone was prescribed for only one patient despite current international literature recommending its use in the management of acute or delayed CINV. National Comprehensive Cancer Network (NCCN), Multinational Association of Supportive Care in Oncology (MASCC) and ASCO all discuss that dexamethasone plays a major role in the prevention of acute and delayed CINV and is an integral component of almost all anti-emetic regimens (Kris et al., 2006). Factors that favour the use of dexamethasone are its proven benefit in clinical trials, widespread availability in oral form, low cost and incremental effectiveness in patients receiving chemotherapies of high emetic risk. Dexamethasone is the standard of care for the management of acute emesis in very high emetogenic chemotherapy. However, the reported side effects with Dexamethasone, such as avascular necrosis and suppression of the immune system may be anecdotally influencing prescribing. In addition, there is preclinical data to suggest dexamethasone has a protective effect on tumour growth, therefore further raising concerns on its use (Antonarakis et al., 2004, Zhang et al., 2006). The use of dexamethasone as an antiemetic historically has been avoided in this institution due to the concerns of long term sequelae

and /or possible effects on the underlying disease and prognosis. Acknowledging the controversies of using dexamethasone for the management of CINV, it remains an international effective agent and therefore its use should be considered for use in the development of guidelines.

Arguably the most likely reason for the above two major findings of this audit could be attributed to the absence of formal comprehensive guidelines for the management of CINV within the unit allowing for more anecdotal experience to influence antiemetic prescribing.

Regarding the efficacy of the antiemetic treatment prescribed, 10% had troublesome nausea (PeNAT grade 3 or 4) while 70% of patients experienced some degree of nausea. This compares with Sullivan et al., (1992) who examined the effectiveness of ondansetron for nausea and found that 40% (6) of children reported severe nausea as per World Health Organisation (WHO) guidelines. Nausea and vomiting was abolished in subsequent courses in 67% (4) of these children by increasing the ondansetron dose frequency to six hourly (Sullivan et al., 1992).

The PeNAT scale was relatively easy to utilise. However, young children (i.e. younger than 8 years of age) could only describe how they felt at the point of asking rather than give a retrospective decision on their nausea over the previous 24hrs. Importantly, the PeNAT scale has not been validated for retrospective nausea assessment. The level of nausea documented may not therefore be reflective of their true state of nausea over the

preceding 24 hours. The MAT instrument was also easy to understand and use, with sufficient space for the parent to write in their child's number of vomits as instructed.

Anticipatory vomiting documented among 4% of patient episodes is comparable with other studies. Anticipatory vomiting occurs prior to the administration of chemotherapy and like delayed CINV appears linked to poor emetic control during previous chemotherapy treatments. In children, pre-school and school age, the incidence of anticipatory vomiting has been reported to range from 15% to 54% depending on research methods and antiemetic prophylaxis history (Foot and Hayes, 1994, Tyc et al., 1997). Anticipatory nausea and vomiting is thought to be caused by behavioural process of classical conditioning, behavioural interventions are appropriate for use in treatment (King, 1997). Both ASCO and the NCCN guidelines suggest the use of nonpharmologic methods such as relaxation, systematic desensitization, hypnosis, guided imagery, music therapy, acupuncture or acupressure for controlling anticipatory nausea and vomiting (Kris et al., 2006, NCCN, 2008).

Acute CINV was experienced in 35% of patient episodes. This is tending towards the goal set out by Jordan et al., (2007) who reported that CINV can be prevented in 70-80% of adults. In a study reported by Holdsworth et al., (2006), 224 children completed surveys, assessing the complete response of antiemetic retrospectively. Complete control of nausea and vomiting was more likely in children ages birth to 3 years than in older children. For moderately emetogenic regimens, nausea and vomiting in the acute and delayed phases was controlled well. In the children aged between 4-11years the rate of

complete response was 73% and in the adolescent group 12-20years, complete response rate was 63.9% during the acute phase. With moderate antiemetic prophylaxis it is reported that 76%-86% of children receiving a variety of emetogenic chemotherapy agents are emesis free (Foot and Hayes, 1994, Kusnierczyk et al., 2002).

Age and gender had no significant effect on delayed vomiting. However, the relative high incidence at 48% of delayed vomiting is of concern specifically when considering that 40% of patients did not take antiemetics following discharge. This compliance may be related to the perceived underestimation of the risk after being discharged or the deficiency of the medical/nursing team to inform and stress the importance of such to patients and their parents, or a combination of the above. Also of importance is that eleven patients did not have a prescription for antiemetics on discharge. This may also have increased the number of patients who experienced delayed vomiting in this study. Mertens et al., (2003) conclude that the prevention of delayed emesis is not as well controlled as it is not as dramatic as the presentation of acute emesis. In addition, current treatments do not reduce symptoms to the same degree that $5HT_3$ antagonist and corticosteroids achieve in acute emesis. The high incidence of delayed vomiting revealed in this audit needs to be addressed with education to all members of the multidisciplinary team and parents about the need for antiemetics post discharge to help with the impact of vomiting in the delayed phase.

In this audit, of the 48% who experienced delayed vomiting, only 13% (3) received Cisplatin, 8% (2) received Carboplatin, 8% (2) received cyclophosphamide and 21% (5)

received Ifosfamide. Delayed CINV is more commonly associated with the use of cisplatin, carboplatin and/or cyclophosphamide as well as vomiting during the acute phase (Dupuis and Nathan, 2003).

Limitations

Clinical audit can improve the quality of health care but this approach to evaluation has many limitations (Johnson et al., 2000). There is an absence of a 'commonly defined method of audit' (Bowie et al, 2007, p. 353) and many clinical audits are often of poor quality and therefore have no positive impact on patient care (Naveen et al., 2011). Specific issues with this audit included the instruments used. The nausea tool that was utilised may have limited how children younger than 8 years of age could use it since they could only describe how they felt at the point of being asked. They could not provide a retrospective decision on their nausea in the previous 24hours. Only nausea at that point in time therefore was documented and may not have reflected these children's true state of nausea over the preceding 24 hours. Nausea was also very difficult to assess when the child had been discharged from hospital. However, parents were given a copy of the PeNAT scale upon discharge and then the first author asked the patient and their guardian which face described their feeling of nausea and vomiting at that point of contact.

Data related to dietary intake and degree of nausea was not obtained in this paediatric population in contrast to the study reported by Dupuis et al., (2006). The difficulty of

assessing nausea on discharge needs to be addressed in future studies to capture the 'real state' of nausea and not just a point in time of each day.

MASCC diaries were given to the patient's carer/parent on their first day of admission for chemotherapy. However, the compliance rate for completing the diary was less than 4%. Parents used their own personal diary to document their child's episodes of vomits.

Finally, the sample size was small and therefore it is acknowledged that the interpretation of the efficacy of antiemetic treatment is done so with caution.

Implications for practice

This audit highlighted the disparity in the management of CINV relative to available international published guidelines, thereby helping to facilitate a change of practice. As a direct result of this audit, new institutional antiemetic guidelines have been developed and introduced based on best available evidence on the management of CINV in this clinical setting. The introduction of these guidelines to the unit has provided consistency and standardised the antiemetic prescribing in guiding the medical team in the management of CINV. With the introduction of these guidelines, antiemetics are prescribed and administered early in the patient's treatment based on the highest emetogenic chemotherapy being administered, which may help to reduce the incidence of CINV. These guidelines also address the patient's previous anti-emetic treatment and if the patient experienced anticipatory, breakthrough or delayed vomiting on previous chemotherapy cycles. These guidelines may also lead to further education of patients and

parents/carers regarding the effectiveness of the new anti-emetic regimens. It is also important to take note of the patients and parents/carers' perspective of the new anti-emetic treatment to help improve the patient's overall care and experience of their cancer treatment. Plans are currently underway to re-audit the management of CINV now that the new guidelines are established.

This audit has highlighted the importance of auditing current clinical practice to improve the supportive care of children with cancer by offering a consistent, evidence based approach to improvement in ongoing patient care.

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References

Antonarakis, E S., Evans, J L., Heard, G F., Noonan, L M., Pizer, B L., Hain, R D W., 2004. Prophylaxis of acute chemotherapy-induced nausea and vomiting in children with cancer: what is the evidence. Pediatric Blood Cancer 43, 651-658.

Baxter, AL., Watcha, MF., Baxter, WV., Leong, T. & Wyatt, MM., 2011. Development and validation of a pictorial nausea rating scale for children. *Pediatrics* 127, e1542-e1549.

Bloechl-Daum, B., Deuson, R R., Mavros, P., Hansen, M., Herrstedt, J., 2006.

Delayed nausea and vomiting continue to reduce patients' quality of life after highly and moderately emetogenic chemotherapy despite antiemetic treatment. Journal of Clinical Oncology 24 (27), 4472-4478.

Bowie, P., Cooke, S., Lo, P., McKay, J. & Lough, M., 2007. The assessment of criterion audit cycles by external peer review - When is an audit not an audit? *Journal of Evaluation in Clinical Practice* 13(3), 352-357.

Brearley, S.G., Clements, C.V. & Molassiotis, A., 2008. A review of patient self-report tools for chemotherapy-induced nausea and vomiting. *Supportive Care in Cancer* 16, 213-1229.

Coates, A., Abraham, S., Kaye, S B., 1983. On the receiving end-patient perception of the side effects of cancer chemotherapy. European Journal Cancer Clinical Oncology 19 (2), 203-208.

de Boer-Dennert, M., de Wit, R., Schmitz, P I., Djontono, J., Beurden, V., Stoter, G., Verweij, J., 1997. Patient perceptions of the side effects of chemotherapy: the influence of 5HT3 antagonists. British Journal of Cancer 76 (8), 1055-1061.

Dupuis, L L., Nathan, P C., 2003. Options for the prevention and management of acute chemotherapy-induced nausea and vomiting in children. Pediatric Drugs 5 (9), 597-613.

Dupuis, L L., Taddio, A., Kerr, E N., Kelly, A., MacKeigan, L., 2006. Development of the Pediatric Nausea Assessment Tool for use in children receiving antineoplastic agents. Pharmacotherapy 26(9), 1221-1231.

Dupuis, L L., Maloney, A M., Nathan, P., Naqvi, A., Tabori, U., 2008. Antiemetic selection for children receiving antineoplastics and/or radiotherapy. (Unpublished work) Department of Pharmacy, The Hospital for Sick Children, Toronto

Foot, A B M., Hayes, C., 1994. Audit of guidelines for effective control of chemotherapy and radiotherapy induced emesis. Archives of Disease in Childhood 71, 475-480.

Fromer, M J., 2005. Chemotherapy-induced nausea and vomiting: Research update on improving control. Oncology Times 1**,** 21-23.

Hesketh, P J., 2008. Chemotherapy-induced nausea and vomiting. The New England Journal of Medicine 358 (23), 2482-2494.

Holdsworth, M T., Raisch, D W., Frost, J., 2006. Acute and delayed nausea and emesis control in pediatric oncology patients. Cancer 106 (4), 931-940.

Johnston, G., Crombie, I.K., Davies, H.T.O., Alder, E.M. & Millard, A., 2000. Reviewing audit: Barriers and facilitating factors for effective clinical audit. *Quality in Health Care* 9(1), 23-36.

Jordan, K., Sippel, C., Joachim Schmoll, H., 2007. Guidelines for antiemetic treatment of chemotherapy-induced nausea and vomiting: past, present, and future recommendations. The Oncologist 12, 1143-1150.

Jordan, K., Roila, F., Molassiotis, A., Maranzano, E., Clark-Snow, R A., Feyer, P., 2011. Antiemetics in children receiving chemotherapy. MASCC/ESMO guideline update 2009. Support Care Cancer 19 (1), S37-S42.

King, C R., 1997. Nonpharmacologic management of chemotherapy-induced nausea and vomiting. Oncology Nursing Forum 24 (7), 41-48.

Kris, M G., Hesketh, P J., Somerfield, M R., Feyer, P., Clark-Snow, R., Koeller, J M., Morrow, G R., Chinnery, L W., Chesney, M J., Gralla, R J., Grunberg, S M., 2006. American Society of Clinical Oncology guideline for antiemetics in oncology: update 2006. Journal of Clinical Oncology 24 (18), 2932-2947.

Kusnierczyk, N M A., Saunders, E F., Dupuis, L L., 2002. Post- transplant complications Outcomes of antiemetic prophylaxis in children undergoing bone marrow transplantation. Bone Marrow Transplantation 20, 119-124.

McRonald, F E., Fleisher, D R., 2005. Anticipatory nausea in cyclical vomiting. BMC Pediatrics 5 (3), 1-4.

MASCC The Antiemetic Subcommittee of the Multinational Association of Supportive Care in Cancer (MASCC) (MAT) (2006) Prevention of chemotherapy- and radiotherapy – induced emesis: results of the 2004 Perugia International Antiemetic consensus conference. Annals of Oncology 17, 20-28.

Mertens, W C., Higby, D J., Brown, D., Parisi, R., Fitzgerald, J., Benjamin, E M., Lindenauer, P K., 2003. 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. Journal of Clinical Oncology 21(7), 1373-1378.

Molassiotis, A., Borjeson, S., 2006. Nausea and Vomiting. In: Kearney, N., Richardson, A., (Eds), Nursing Patients with Cancer Principles and Practice. Churchill Livingstone, London.

Molassiotis, A., 2007. A prospective observational study of chemotherapy-related nausea and vomiting in routine practice in a UK cancer centre. Support Care Cancer Internet: Accessed 13th November 2007, http://lib.bioinfo.pl/auth:Molassiotis,A

Molassiotis, A., Saunders, MP., Valle, J., Wilson, G., Lorigan, P., Wardley, A., Levine, E., Cowan, R., Loncaster, J., Rittenberg, C., 2008. A prospective observational study of chemotherapy-related nausea and vomiting in routine practice in a UK cancer centre. *Supportive Care in Cancer* 16, 201-208.

Morrow, G R., Roscoe, J A., Hickok, J T., Andrews, P L R., Matteson, S., 2002. Nausea and emesis: evidence for a biobehavioural perspective. Support Care Cancer 10**,** 96-105.

National Comprehensive Cancer Network (NCCN) 2008 Types of Nausea. Retrieved May 2nd,2008 from: http://www.nccn.org/patients/patient_gls/english/_nausea_and_vomiting/3_types.asp

Naveen, A., Vemanna, S., Shankar, N. & Praveena, V., 2011. Basics in research methodology - The clinical audit. *Journal of Clinical and Diagnostic Research* 5(3), 679-682.

Phillips, R S., Gopaul, S., Gibson, F., Houghton, E., Craig, J V., Light, K., Pizer, B., 2011. Antiemetic medication for the treatment of chemotherapy induced nausea and vomiting in childhood (Review). *The Cochrane Library.* Issue 2.

Rhodes, V A., McDaniel, R W., 2001. Nausea, Vomiting and Retching: Complex problems in palliative care. CA Cancer Journal Clinicians 51, 232-248.

Robinson, D L., Carr, B A., 2007. Delayed vomiting in children with cancer after receiving moderately high or highly emetogenic chemotherapy. Journal of Pediatric Oncology Nursing 24**,** 70-80.

Sullivan, M J., Abbott, G D., Robinson, B A., (1992) Ondansetron antiemetic therapy for chemotherapy and radiotherapy induced vomiting in children. New Zealand Medical Journal. 105(942), 369-371.

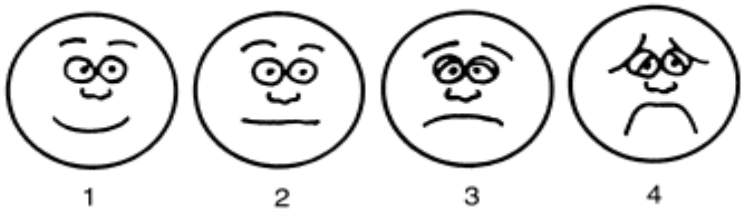
Tyc, V L., Mulhern, R K., Barclay, D R., Smith, B F., Bieberich, A A., 1997. Variables associated with anticipatory nausea and vomiting in pediatic cancer patients receiving ondansetron antiemetic therapy. Journal of Pediatric Psychology 22(1), 45-58.

Wood, J.M., Chapman, K. Eilers, J., 2011. Tools for assessing nausea, vomiting, and retching: A literature review. *Cancer Nursing* 34, E14-E24.

Yamaguchi, M., Ogawa, T., Watanabe, M., Anami, S., Kamigaki, S., Nishikawa, N., Ono, T. Furukawa, H., 2009. Assessment of chemotherapy-induced nausea and vomiting (CINV) using MASCC antiemesis tool. *Japanese Journal of Cancer and Chemotherapy* 36, 1691-1696.

Zhang, C., Beckermann, B., Kallifatidis, G., Liu, Z., Rittgen, W., Edler, L., Buchler, P., Klaus, M D., Buchler, M W., Friess, H., Herr, I., 2006. Corticosteroids induce chemotherapy resistance in the majority of tumour cells from bone, brain, breast, cervix, melanoma and neuroblastoma. International Journal of Oncology 29, 1295-1301.

Figure 1: Pediatric Nausea Assessment Tool (PeNAT)



Face 1: no nausea, to face 4, worst nausea.

Table 1: Emetogenic classification of chemotherapy agents (from Dupuis et al., 2008)

Very High (>90%)	**High (60%-90%)**	**Moderate (30%-60%)**	**Low (10-30%)**
Carmustine > 250mg/m^2	Carboplatin*	Amsacrine	Docetaxel
Cisplatin > 50mg/m^2*	Carmustine < 250mg/m^2	Busulfan IV	Etoposide < 60mg/m^2
Cyclophosphamide >1500mg/m^2	Cisplatin < 50mg/m^2*	Cyclophosphamide < 750mg/m^2	Fludarabine Oral
Dacarbazine	Cyclophosphamide > 750 - 1500mg/m^2 *	Cyclophosphamide: oral	Fluorouracil
	Cytarabine> 1000mg/m^2	Cytarabine > 100 to 1000mg/m^2	Gemcitabane
	Dactinomycin	Daunomycin < 60mg/m^2	Melphalan
	Daunomycin > 60mg/m^2	Doxorubicin < 60mg/m^2	Methotrexate 51-249mg/m^2
	Doxorubicin > 60mg/m^2	Epirubicin < 90mg/m^2	Paclitaxel
	Methotrexate> 1000mg/m^2	Etoposide > 60mg/m^2	Thiotepa
	Procarbazine	Etoposide: oral	Vindesine
	Topotecan	Intrathecal therapy	
		Idarubicin	
		Ifosfamide	
		Imatinib	
		Irinotecan	
		Methotrexate 250-1000mg/m^2	
		Mitoxantrone < 15mg/m^2	
		Temozolomide	
		Vinorelbine: oral	

Table 2

Common Toxicity Criteria (CTC) (NCCN 2008)

	Vomiting
0	None
1	1 episode in 24hrs: IV fluids indicated < 24hrs
2	2-5 episodes in 24hours
3	> 6 episodes in 24hrs: IV fluids, or TPN indicated > 24hrs
4	Life Threatening consequences-Requiring TPN or ICU

	CTC grade				
	0	1	2	3	4
Day 1	72%	14%	14%	0%	0%
2	59.4%	12.5%	25%	3.1%	0%.
3	61.5%	15.4%	15.4%	7.7%	0%
4	66.7%	22.2%	11.1%	0%	0%
5	66.6%	16.7%	16.7%	0%	0%

Table 3 Patient characteristics

Number of patients	N=25	
Females	N=10	
Males	N=15	
Age Range	4-8 years	8
	8.1-12years	7
	12.1-16years	8
	> 16years	2
Cancer diagnosis	CNS tumour	4
	Osteogenic sarcoma	3
	PNET/Ewing's sarcoma	3
	Leukaemia	3
	Rhabdomysosarcoma	2
	Non Hodgkin's lymphoma	2
	Neuroblastoma	2
	Wilms'	1
	Pleuropulmonary Blastoma	1
	Optic Glioma	1
	Relapsed ALL	1
	Acute Myeloid leukaemia	1
	Hodgkin's lymphoma	1
Inpatient chemotherapy days per episode		
1 day	16	
2 days	17	
3 days	5	
4 days	3	
5 days	5	
>5 days	4	

Table 4

Antiemetics prescribed in each chemotherapy group as an inpatient and on discharge are shown in Table 2

Antiemetics prescribed	**Very High**	**High**	**Moderate**	**Low**
Inpatient	Ondansetron Metoclopramide	Ondansetron Metoclopramide Promethazine Cyclizine Lorazepam Dexamethasone	Ondansetron Metoclopramide Promethazine	Ondansetron Metoclopramide Domperidone
On discharge	Ondansetron Metoclopramide	Ondansetron Metoclopramide Promethazine Cyclizine	Ondansetron Metoclopramide Promethazine	Ondansetron

Table 5: PeNAT Scores days 1-5

Face 1: No Nausea, Face 2: A little bit nauseous
Face 3: feel even more nauseous Face 4: A lot of nausea

	PeNAT			
	1	2	3	4
Day 1	36	8	5	1
2	26	15	8	1
3	33	11	3	3
4	32	15	3	0
5	39	10	1	0