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## Original Article

# Study of chemotherapy induced nausea and vomiting in children with malignancy

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## Abstract

**Introduction:** Chemotherapy induced nausea and vomiting (CINV) can be a major problem for children undergoing cancer treatment. The experience of vomiting creates physical distress for child and family. the purpose of studying the incidence of chemotherapy induced nausea and vomiting (CINV) and analysing the use and effectiveness of anti-emetics, and to suggest if any changes are required to optimize the management of CINV in this setting.

**Method:** This was a prospective observational study, which assessed the current usage, Chemotherapy cycles in subjects, which met the eligibility criteria were studied for chemotherapy induced nausea and vomiting (CINV), using National Cancer Institute (NCI) Common Toxicity Criteria. A total of 50 patients who met the study criteria were enrolled in to the study. All the data pertaining to reason for the antiemetic agents used were based on the emetogenic potential of the chemotherapy protocols.

**Result and Discussion:** It was observed in our study that use of ondansetrone was according to standard guidelines. Hence although fairly good control of emesis was recorded for moderate emetogenic regimens, strategies for further improvement in antiemetic schedule for high emetogenic schedules should be considered. vincristine-actinomycin-cyclophosphamide had the highest rate of emesis while high dose methotrexate had the best control.

**Conclusion:** Among the various chemotherapy schedules used, it was observed that rate of acute emesis control was poorest with vincristine-actinomycin-cyclophosphamide and best control was observed with high dose methotrexate. This observation may be kept in mind when planning the anti-emetic protocol for these regimes.

## 1.Introduction

Chemotherapy-induced nausea and vomiting (CINV) can be major problem for children with cancer. Children are especially vulnerable to electrolytes imbalance, dehydration and weight loss, and poor nutrition may affect their tolerance of additional chemotherapy. The experience of vomiting creates physical and emotional distress for child and family or carers: as early as 1983 it was shown that, for patients, treatment-related nausea and vomiting were among the most dreaded adverse effects[1]. The distress can affect the person's normal activities and quality of life significantly[2].

Children receiving chemotherapy are not at equal risk for developing CINV. Individual characteristics and chemotherapeutic agents are among the factors affecting risk, and the later are probably the most significant (Anti-emetic Subcommittee of the Multinational Association of Supportive Care in Cancer (ASMASCC)[3][4]. Variation in the management of CINV in children exists nationally and internationally. The aim of the present study is to present finding from an audit undertaken at the national Irish pediatric Cancer centre of the use and effective of anti-emetic and the resulting change in the management of CINV. Nausea vomiting and retching must be clearly defined for accurate assessment as separate concepts[5][6].

The objective of the study was to check out chemotherapy induced nausea and vomiting (CINV) and efficacy of antiemetics in children (<18 years of age) for pediatric cancers with chemotherapy regimens having moderate or high emetogenic potential.

### 1.1 Objective

To study chemotherapy induced nausea and vomiting (CINV) and efficacy of antiemetics in children (<18 years of age) treated for pediatric cancers with cancers chemotherapy regimens having moderate or high emetogenic potential.

## 2. Material and Method

The present study was a prospective observational, single centre study conducted in the Department of Pediatric Hematology Oncology at Rajiv Gandhi Cancer Hospital and Research Centre from November 2012 to May 2013. Chemotherapy cycles in subjects which met the eligibility criteria were studied for chemotherapy induced nausea and vomiting (CINV), using National Cancer Institute (NCI) Common Toxicity Criteria. The anti-emetic agents used were based on the emetogenic potential of the chemotherapy protocol. The main objective was to document the prescribing and administration of antiemetics and collect data on the incidence of CINV with the purpose of studying the effectiveness of antiemetic medication used.

### 2.1 Inclusion Criteria

1. Patients age < 18 years of age
2. Patients has a prognosis >3 months
3. Patients with confirmed diagnosis of pediatric solid tumors
4. Chemotherapy protocols with moderate or high emetogenic potential

**2.2 Exclusion Criteria**

1. Solid tumor patients would be excluded
2. Critically ill patients in ICU or critical setting
3. Patients shifted to ICU from ward

## 3. Result and Discussion

### 3.1 Demographic details

Among 50 patients of childhood cancer, 235 cycles of chemotherapy were studied. The gender incidence revealed that males constituted 66% and females 34%. The age distribution revealed that median age was 12 years; 18% of patients were <5 years of age, 24% percent of patients were 6-10 years of age, 38% of patients were 11-15 years of age and 20% of patients were >15 years of age. The different types of childhood tumors studied were Ewing's sarcoma (38%), osteosarcoma (26%) rhabdomyosarcoma (8%) germ cell tumor (8%) medulloblastoma (6%) Wilms tumor (4%) retinoblastoma (2%) and neuroblastoma (2%) in reducing order of frequency. The details of the different chemotherapy regimens revealed that High dose Methotrexate (23%), Ifosfamide-Etoposide (22%), Vincristine-Adriamycin-Cyclophosphamide (14%), Vincritine-Cyclophosphamide (13%), Cisplatin-Adriamycin (11%), Bleomycin-Etoposide-Cisplatin (7%), were the most frequently administered chemotherapy regimen in reducing order of frequency.

**Table 1: Demographic and disease related features involved in chemotherapy induced nausea and vomiting**

| Total no | No (%) |
|---|---|
| | 50 (100) |
| **Age**( in years) | |
| <5yr | 9(18) |
| 6-10yr | 12(24) |
| 11-15 | 19(38) |
| >15yr | 10(20) |
| **Gender** | |
| Male | 33(66) |
| Female | 17(34) |
| **Diagnosis** | |
| Ewing's sarcoma | 19(38) |
| Osteosarcoma | 13(26) |
| Germ cell tumor | 4(8) |
| Rhabdomyosarcopma | 4(8) |
| Synovial sarcoma | 3(6) |
| Wilm's tumor | 2(4) |
| Retinoblastoma | 1(2) |
| Medulloblastoma | 3(6) |
| Neuroblastoma | 1(2) |
| **Chemotherapy** | |
| Cisplatin 100mg/m²/Adriamycin 75mg/m² | 28(11.91) |
| Vincristin 1.5mg/m²/Adriamycin 75mg/ m²/Cyclophosphamide 1.2mg/m² | 34(14.46) |
| Vincristine 1.5mg/m²/ Actinomycin 2.5mg/m² /Cyclophosphamide 1.2-2.2mg/m² | 21(8.93) |
| Vincristine 1.5mg/m²/Cisplatin 100mg/m²/Etoposide 100mg/m² | 8(3.40) |
| Ifosfamide 1.8mg/m²/Adriamycin 25mg/m² | 4(1.70) |
| Vincristine 1.5mg/m²/Cyclophosphamide 1.2mg/m² | 13(5.53) |
| Ifosfamide 1.8mg/m²/Etoposide 100mg/m² | 53(22.55) |
| High Dose Methotrexate 12gm/m² | 54(22.97) |
| Vincristine 1.5mg/m²/Carboplatin 560mg/m²/Etoposide 100mg/m² | 6(2.55) |
| Bleomycin 18mg/m²/Etoposide 100mg/m²/Cisplatin 20mg/m² | 7(2.97) |
| Cyclophosphamide1.2gm/m² /Topotecan 1mg/m² | 6(2.55) |
| Vincristine 1.5mg/m² | 1(0.42) |

### 3.2 The details of the antiemetic drug schedules that were used with the different types of chemotherapy protocols

Ondansetrone was used in all cases; dexamethasone and aprepitant were additional antiemetic agents that were used in patients with high emetogenic potential. Among the highly emetogenic chemotherapy protocols, ondansetrone alone was administered in 10% of cycles, and both ondansetrone and aprepitent in 77%. For the moderate emetogenic chemotherapy protocols, ondansetrone alone was administered in 9% of cycles, and both ondansetrone and aprepitent in 44%. For the Low emetogenic chemotherapy aprepitant was not used and Ondansetrone alone was used in all (100%) cycles.

**Table 2: Antiemetic schedule of ondansetron and its combination with Aprepitant and Dexamethasone by chemotherapy protocol**

| Chemotherapy Type | Cycles N % | Ondansetrone (%) | Ondansetrone+ Aprepitant (%) | Ondansetrone+ Dexamethasone (%) | Ondansetrone + Aprepitant + Dexamethasone (%) |
|---|---|---|---|---|---|
| **High Emetogenic Chemotherapy** | **100 (43)** | **10(10)** | **25(25)** | **13(13)** | **52(52)** |
| Cisplatin/Adriamycin | 28 | 0(0) | 3(10) | 6(21) | 19(67) |
| Vincristine/Adriamycin/Cyclophosphamide | 34 | 3(8) | 18(52) | 3(8) | 10(29) |
| Vincristine/Actinomycin/Cyclophosphamide (dose-2.2gm/m²) | 17 | 0(0) | 3(17) | 1(5) | 13(58) |
| Vincristine/Cyclophosphamide | 13 | 7(53) | 1(7) | 1(7) | 4(30) |
| Vincristine/Cisplatin/ Etoposide | 4 | 0(0) | 0(0) | 2(50) | 2(50) |
| Ifosfamide/Adriamycin | 4 | 0(0) | 0(0) | 0(0) | 4(100) |
| **Moderate Emetogenic Chemotherapy** | **128 (54)** | **12(9)** | **35(27)** | **59(46)** | **22(17)** |
| Ifosfamide/Etoposide | 53 | 1(1) | 31(58) | 3(5) | 18(33) |
| High Dose Methotrexate | 54 | 1(1) | 1(1) | 52(96) | 0(0) |
| Vincristine/Actinomycin/Cyclophosphamide (dose-1.2gm/m²) | 4 | 0(0) | 2(50) | 0(0) | 2(50) |
| Vincristine/Cisplatin/ Etoposide | 4 | 4(100) | 0(0) | 0(0) | 0(0) |
| Vincristine/Carboplatin/ Etoposide | 6 | 6(100) | 0(0) | 0(0) | 0(0) |
| Bleomycin/Etoposide /Cisplatin | **7** | 0(0) | 1(14) | 4(57) | 2(28) |
| **Low Emetogenic Chemotherapy** | **7 (3)** | **7(100)** | **0(0)** | **0(0)** | **0(0)** |
| Cyclophosphamide/ Topotecan | 6 | 6(100) | 0(0) | 0(0) | 0(0) |
| Vincristine | 1 | 1(100) | 0(0) | 0(0) | 0(0) |

### 3.3 Frequency of vomiting with different chemotherapy protocols

Emesis free cycles were observed in 40% of high emetogenic chemotherapy schedule, 46% of moderate emetogenic chemotherapy, and 57% of low emetogenic chemotherapy. Anticipatory emesis was observed in 47% of high emetogenic chemotherapy cycles, and 75% of moderate emetogenic chemotherapy cycles, and 71% of low emetogenic chemotherapy. Acute emesis was observed in 46% of high emetogenic chemotherapy cycles and 75% of moderate emetogenic chemotherapy, and 71% of low emetogenic chemotherapy. Delayed emesis was observed in 55% of high emetogenic chemotherapy cycles 53% of moderate emetogenic chemotherapy, and 14% of low emetogenic chemotherapy. Rescue drug therapy was not required in 81% cycles of high emetogenic chemotherapy, 92% cycles of moderate emetogenic chemotherapy and none of the low emetogenic chemotherapy protocols.

**Figure 1: Graph showing high emetogenic potential data of chemotherapy induced emesis**

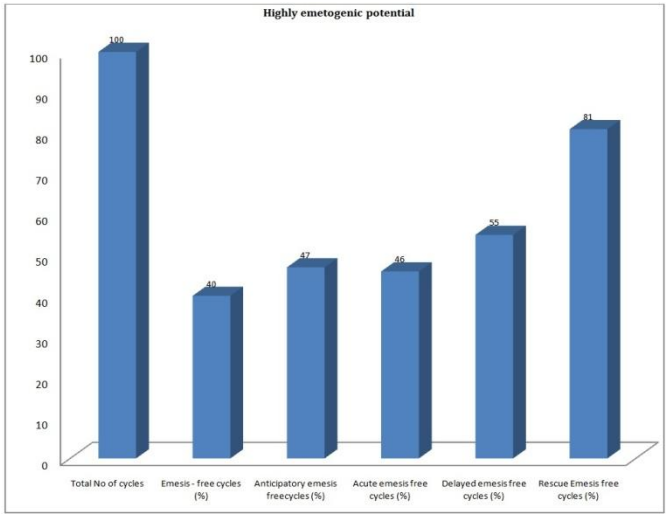



**Figure 2: Graph showing Moderate emetogenic potential data of chemotherapy induced emesis**

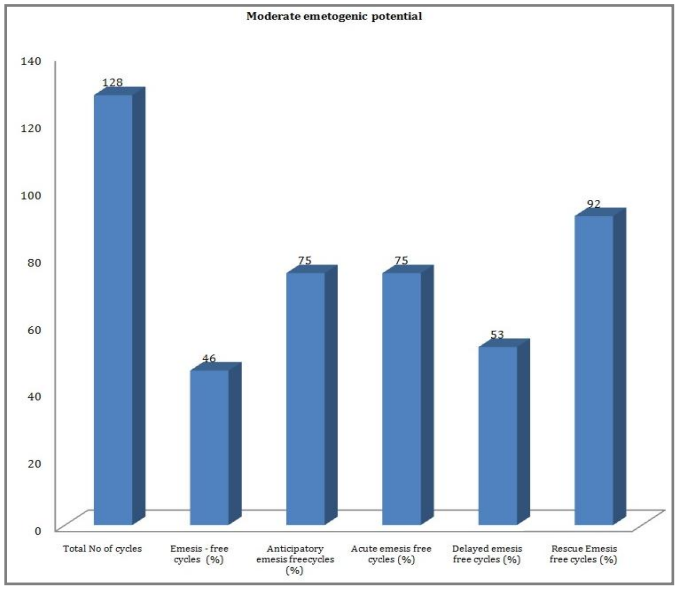
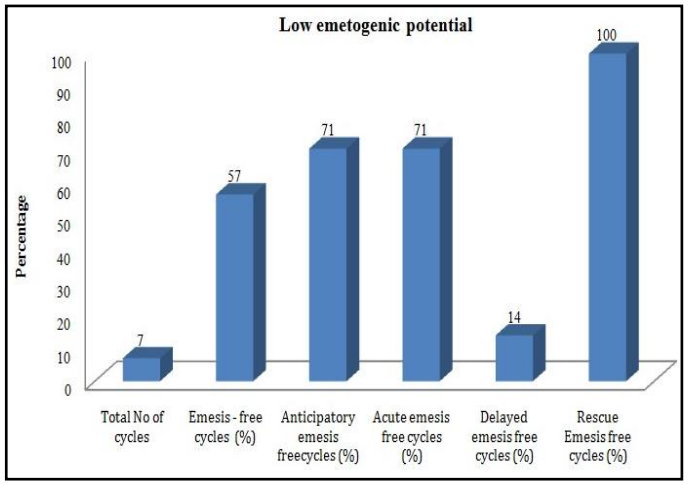



**Figure 3: Graph showing Low emetogenic potential data in chemotherapy induced emesis**




### 3.4 Frequency of nausea with different chemotherapy protocols

Nausea free cycles were observed in 45% of high, 30% of moderate and 58% of low emetogenic chemotherapy schedule. Anticipatory nausea free cycles were observed in 43% of high emetogenic chemotherapy cycles, 43% of moderate emetogenic chemotherapy 66% of low emetogenic chemotherapy. Acute nausea free cycles were observed in 32% of high emetogenic chemotherapy cycles, 33% of moderate emetogenic chemotherapy and 66% of low emetogenic chemotherapy. Delayed nausea free cycles were observed in 38% of high emetogenic chemotherapy cycles, 28% of moderate emetogenic chemotherapy, 66% of low emetogenic chemotherapy. Rescue drug therapy was not required in 94% cycles of high emetogenic chemotherapy, 88% cycles of moderate emetogenic chemotherapy and none of the low emetogenic chemotherapy protocols.

**Figure 4: Graph showing high emetogenic potential data in chemotherapy induced nausea**

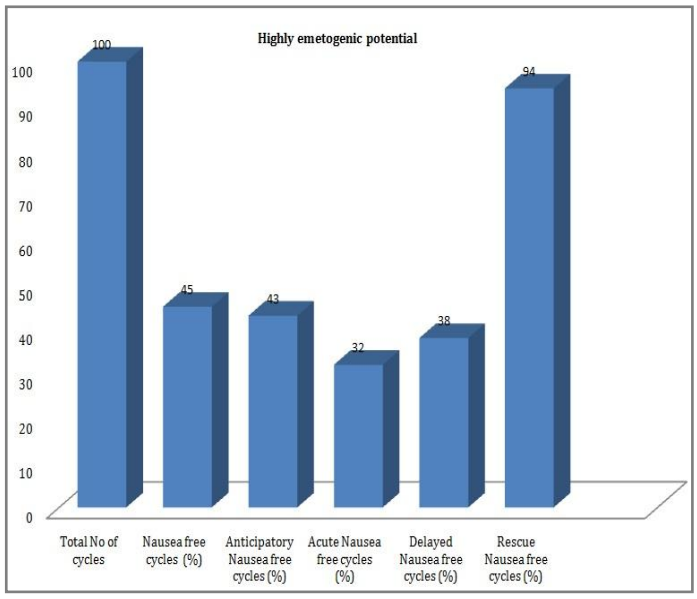


**Figure 5: Graph showing moderate emetogenic potential data in chemotherapy induced nausea**

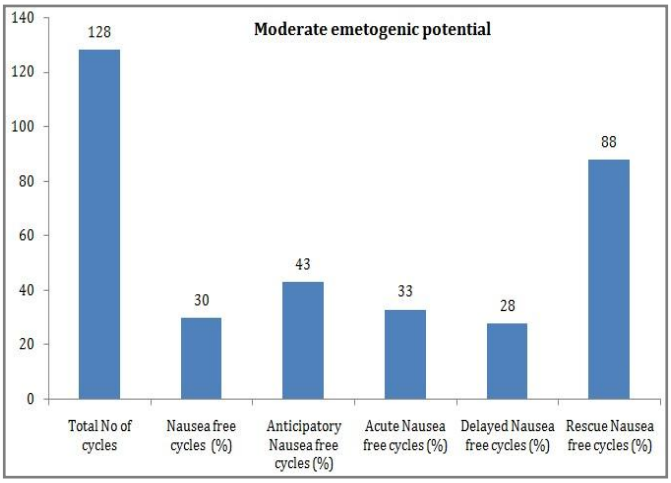
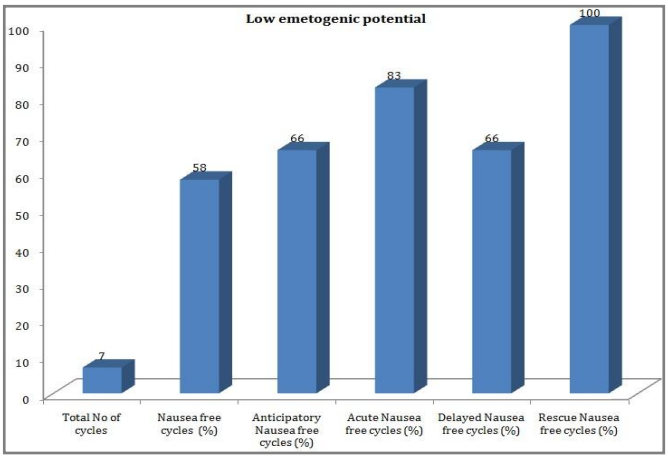



**Figure 6: Graph showing low emetogenic potential data in chemotherapy induced nausea.**




## 4. Conclusion

This was an observational study of CINV, among 50 patients, diagnosed with different types of pediatric solid malignancy, receiving 235 cycles of chemotherapy. Of these, the high emetogenic chemotherapy constituted 42% of cycles and moderate emetogenic chemotherapy 54%.

The antiemetic schedule involved ondansetrone in 100% of cycles and in combination with other agents in more than 90% of all chemotherapy cycles. The 5-$HT_3$ anatgonist, aprepitant, was used in significantly larger number of high emetogenic chemotherapy as compared to moderate ones (77% vs 44%, $p < 0.01$). These observations were in sync with the National Comprehensive Cancer Network guidelines. It was observed that acute emesis was more frequently observed with high emetogenic chemotherapy in comparison with moderate emetogenic chemotherapy (54% vs 25%, $p < 0.001$), this difference was statistically significant. Furthermore, the grade of vomiting was worse in high as compared to moderate emetogenic chemotherapy, as a CTC grade of ≥2 occurred in 33% vs 19% of cycles respectively with a significant p value of 0.02. Hence although fairly good control of emesis was recorded for moderate emetogenic regimens, strategies for further improvement in antiemetic schedule for high emetogenic schedules should be considered. The incidence of delayed emesis was similar for the high (45%) and moderate (48%) emetogenic chemotherapy ($p=0.6$, NS). This reveals need for better delayed emesis control. It is also emphasizes the importance of counseling parents to administer proper antiemetic after discharge. Dexamethasone is very effective for delayed emesis and we can ensure that these patients do receive it prophylactically. Among the various chemotherapy schedules used, it was observed that rate of acute emesis control was poorest with vincristine-actinomycin-cyclophosphamide and best control was observed with high dose methotrexate (p value was significant). This observation may be kept in mind when planning the anti-emetic protocol for these regimes.

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