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ORIGINAL REPORT

Delayed Nausea and Vomiting Continue to Reduce Patients' Quality of Life After Highly and Moderately Emetogenic Chemotherapy Despite Antiemetic Treatment

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ABSTRACT

Purpose
Chemotherapy-induced nausea and vomiting (CINV) are major adverse effects of cancer chemotherapy. We compared the impact of acute (during the first 24 hours postchemotherapy) and delayed (days 2 through 5 postchemotherapy) CINV on patients' quality of life (QoL) after highly or moderately emetogenic chemotherapy (HEC and MEC, respectively).

Patients and Methods
This prospective, multicenter, multinational study was conducted in 14 medical practices on cancer patients undergoing either HEC or MEC treatment. Patients recorded episodes of nausea and vomiting in a diary. Patients completed the Functional Living Index-Emesis (FLIE) questionnaire at baseline and on day 6.

Results
A total of 298 patients were assessable (67 HEC patients, 231 MEC patients). Emesis was reported by 36.4% of patients (13.2% acute, 32.5% delayed) and nausea by 59.7% (36.2% acute, 54.3% delayed). HEC patients reported significantly lower mean FLIE total score than MEC patients (95.5 *v* 107.8 respectively; $P = .0049$). Among all patients, the nausea score was significantly lower than the vomiting score (50.0 and 55.3, respectively; $P = .0097$). Of the 173 patients who experienced neither vomiting nor nausea during the first 24 hours postchemotherapy, 22.9% reported an impact of CINV on daily life caused by delayed CINV.

Conclusion
CINV continues to adversely affect patients' QoL despite antiemetic therapy even after treatment with only moderately emetogenic chemotherapy regimens, and even in the subgroup of patients who do not experience nausea and vomiting during the first 24 hours. On the basis of the FLIE results in this study, nausea had a stronger negative impact on patients' daily lives than vomiting.

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INTRODUCTION

Chemotherapy-induced nausea and vomiting (CINV) remain major adverse effects of cancer chemotherapy.[1] Antiemetic treatments, including serotonin (5-HT_3) receptor antagonists and corticosteroids, have been instrumental in improving the control of vomiting among patients receiving chemotherapy.[2,3] However, recent studies have demonstrated the need for improved therapeutic intervention in a number of areas.[4] For example, Roscoe et al[5] report that after the introduction of 5-HT_3 receptor antagonists, the incidence of nausea may actually have risen despite the reduction in the incidence of vomiting. Furthermore, antiemetic treatments have been less effective in improving delayed nausea and vomiting than acute nausea and vomiting.[6] Two meta-analyses of clinical trials have shown that 5-HT_3 receptor antagonists with or without corticosteroids are not effective against delayed emesis and nausea.[7,8]

The lack of adequate CINV control may be partly attributed to the fact that antiemetic treatment regimens are guided by risk factors, including level of emetogenicity of chemotherapeutic agents.[9] Emetic risk categories are based on experience rather than specific data, and the categories refer to acute emesis only.[6,10] Moreover, the neuropharmacologic mechanism of delayed CINV (> 24 hours postchemotherapy) is not well understood, and prevention of delayed CINV has largely been based on empiric results.

CINV adversely impact patients' quality of life[11-14] From a list of chemotherapy-related adverse effects, patients rated nausea as their first and vomiting as their third most feared symptom.[15] In a

recent study, ovarian cancer patients included complete to almost complete control from CINV among the most favorable health states, just below perfect health and clinical remission.[16]

Against this background, the Anti Nausea Chemotherapy Registry (ANCHOR) study was designed to address two issues; (i) to prospectively compare, under current practice patterns, the incidence of acute and delayed nausea and emesis after highly and moderately emetogenic chemotherapy (HEC and MEC, respectively), and (ii) to assess the impact of acute and delayed nausea and vomiting after HEC and MEC on patients' quality of life (QoL). The Functional Living Index-Emesis (FLIE), a validated nausea- and vomiting-specific patient-reported outcome measure was used to evaluate the impact of CINV on patients' daily lives.[17,18] Results on the incidence of CINV after HEC or MEC are reported elsewhere.[19] In the following, we address the impact of CINV on patients' daily life.

PATIENTS AND METHODS

Study Design and Setting

This prospective, multicenter, observational study was conducted in 14 medical practices in Denmark, France, Italy, Germany, the United Kingdom, and the United States during 2001 to 2002. All centers were experienced in the administration of cancer chemotherapy. Centers were selected to allow for enrollment of a broad spectrum of patients requiring chemotherapy.

Patient Selection Criteria

Patients were eligible for inclusion if they were adults (> 18 years of age), never had chemotherapy before study entry (chemotherapy naïve), and were scheduled for treatment with either HEC (ie, at least one chemotherapeutic agent of Hesketh Level 5 emetic potential; eg, > 50 mg/m^2 of cisplatin or > 1,500 mg/m^2 of cyclophosphamide) or (ie, at least one chemotherapeutic agent of Hesketh Levels 3 or 4 emetic potential; eg, > 20 mg/m^2 of doxorubicin or < 1,500 mg/m^2 of cyclophosphamide).[10]

Patients were not eligible for participation in the study if they were scheduled to receive multiple-day chemotherapy, or if they had vomited during the 24-hour period preceding chemotherapy administration.

The protocol was approved by the ethics committees/institutional review boards according to the requirements in each participating country. Written and signed informed consent was obtained from all patients before study entry.

Data Collection

Patients who agreed to participate received a diary covering the 24 hours before chemotherapy, the day of chemotherapy administration (day 1) and the following 4 days (day 2 through 5). Patients were instructed to use the diary every day to record each emetic episode and to provide daily nausea assessments using a 100-mm visual analog scale (VAS) to rate the severity of nausea experienced during the preceding 24 hours. Patients also recorded all rescue antiemetic medications, which were taken in addition to what was prescribed at baseline to prevent nausea and vomiting. No nausea was defined as a VAS less than 5 mm on the 100-mm scale. A patient was considered to have had acute nausea or acute emesis if nausea (VAS ≥ 5mm) or at least one episode of vomiting was reported during the first 24 hours after start of chemotherapy. Any episodes of nausea and/or vomiting thereafter up to 5 days after chemotherapy was considered delayed.[6]

In addition, patients were asked to complete the FLIE, a self-administered questionnaire used to evaluate the impact of CINV on patients' daily lives. The development of the FLIE has been described previously.[17,18] The FLIE instrument was modeled after the Functional Living Index-Cancer, a patient-completed multidimensional quality of life instrument. The FLIE is a validated nausea- and vomiting-specific patient-reported outcome instrument composed of two domains (vomiting and nausea) with nine identical items in each domain. The FLIE-item score was assessed at baseline (prechemotherapy) and on the morning of day 6 postchemotherapy. The first item in each domain asked the patient to rate how much nausea and vomiting he or she had experienced during the previous 5 days. The remaining eight items covered different sections influencing the patient's quality of daily life (ie, "recreation or leisure activities," "make meal/do tasks," "ability to enjoy meal," "enjoy drinking fluids," "see family/ friends," "daily functioning," "personal hardship," "hardship on others"). The FLIE-score was determined by summing the responses to the 18 questions on a seven-point analog scale. Therefore, the range of total scores possible is between 18 (all one responses on each scale) and 126 (all seven responses on each scale). A higher score corresponds to a higher QoL or less impact of CINV on daily life.[20]

No or minimal impact on daily life (NIDL) was defined as an average FLIE item score of more than 6 on the seven-point continuous visual analog scale or a total FLIE-Score of more than 108.

Data Analysis

Descriptive statistics were used to summarize patient demographics and survey responses. The *t* test for paired and unpaired observations was used as appropriate for comparison of group means. Differences in the proportion of patients that reported NIDL between MEC and HEC treated patients were analyzed using χ^2 tests (Fisher's exact test).

RESULTS

Description of Patient Sample

A total of 322 patients from 14 centers were enrolled in the study (patient disposition is shown in Fig 1). One patient was lost to follow-up, one patient died during the observation period; no questionnaires could be obtained from six patients. Questionnaires from 16 further patients had to be excluded from the analysis because of incomplete data or protocol violations. Hence, 298 patients were assessable: 85 were male, 213 were female, and the mean age was 55.5 years (standard deviation, 12.1 years). The most frequent diagnoses were breast (49.3%) and lung (17.8%) cancers. Sixty-seven (22.5%) patients received HEC; of these, 61 (91%) received cisplatin, and six (9%) dacarbazine. Two hundred thirty-one patients(77.5%) received MEC; of these 163 (70%) received regimens containing cyclophosphamide, doxorubicin, and/or epirubicin; 59 (25%) received carboplatin-containing regimens; and nine (5%) received other regimens.[19]

Antiemetic therapy consistent with the guidelines[6,21,22] in force at the time and place of the study was used in most of the patients, and has been described in detail previously.[19] Briefly, 282 patients (96.6%) received 5-HT$_3$ receptor antagonists, and 227 (77.7%)

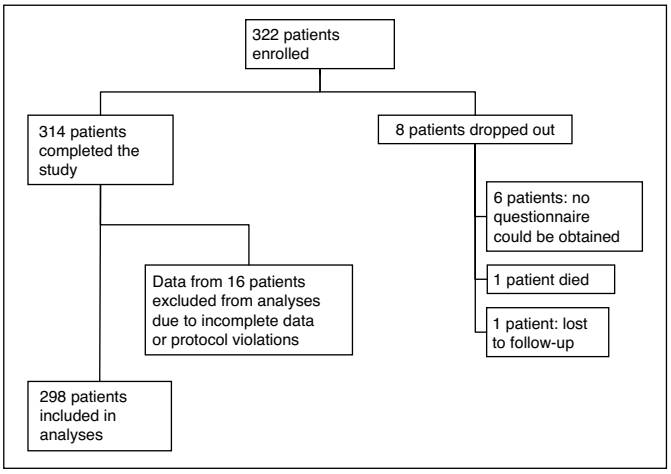

Fig 1. Patient disposition chart.

received corticosteroids. Two hundred fifty patients (85.6%) received prophylaxis for delayed CINV (> 24 hours postchemotherapy). The most common duration of 5-HT_3 receptor antagonist therapy and corticosteroid therapy was 3 days, with 71% of patients receiving 5-HT_3 receptor antagonists and 55% of patients receiving a corticosteroid for at least that long.

Frequency of Emetic Episodes and Nausea During the 5-Day Period After Chemotherapy

Results on the incidence of acute and delayed CINV across chemotherapy treatment groups are reported elsewhere.[19] In summary, 13.2% of the patients reported emetic episodes, and 36.2% nausea, during the 24-hour period after administration of chemotherapy, whereas delayed emesis was reported by 32.5% of the patients and delayed nausea by 54.3%.

The daily incidence of emesis and its prevalence are reported in Table 1 and Figure 2. The prevalence of acute emesis was similar between HEC- and MEC-treated patients (11.9% and 13.2%, respectively), but HEC treated patients were significantly more likely to report delayed emesis than MEC treated patients ($P < .05$). On average, HEC treated patients reported more emetic episodes per day per patient than MEC treated patients for both the acute (3.1 *v* 2.5, respectively) and the delayed phase (1.4 *v* 1.2, respectively).

The daily incidence and severity of nausea are summarized in Table 2 and Figure 2. The rate of nausea plateaued between days 2 and 3. There were no significant differences in the rate of acute and delayed nausea between HEC- and MEC-treated patients, but HEC-treated patients reported greater nausea severity especially in days 2 through 5, as indicated by the mean VAS score during each period (Table 2).

Impact of Nausea and Vomiting on Patients' Daily Life

At baseline, 95.3% of the patients reported NIDL with an average total FLIE score of 122.9. There was no difference between patients scheduled for HEC (93.9% NIDL, total FLIE score 123.1) and MEC (95.6% NIDL, total FLIE score 122.9) at baseline.

Results from all items of the FLIE obtained on day 6 are summarized in Table 3. On day 6 postchemotherapy, the mean total FLIE score was 105.4; however, 61.0% of all patients reported that CINV had no or minimal impact on their daily life (ie, total FLIE score > 108). The average FLIE score indicates that patients receiving HEC experienced a greater impact of CINV on their daily life than patients receiving MEC (95.5 *v* 107.8, respectively $P = .0049$). Significantly fewer HEC than MEC patients (47.2% and 64.5%, respectively) reported NIDL ($P = .0272$).

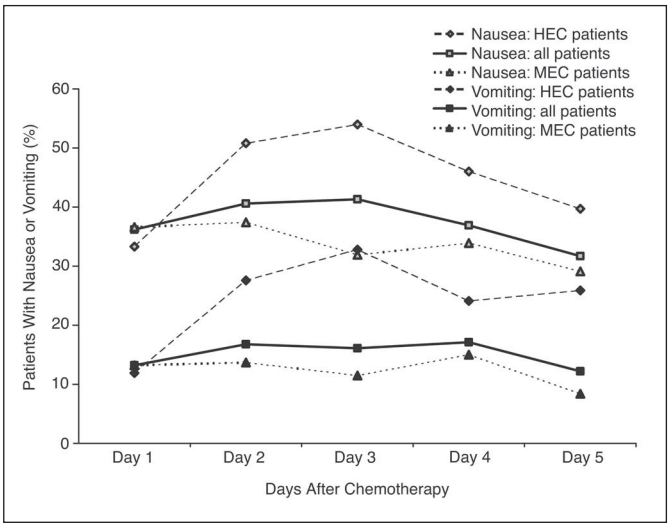

Fig 2. Frequency of nausea and vomiting during the 5-day period after chemotherapy. HEC, highly emetogenic chemotherapy; MEC, moderately emetogenic chemotherapy.

Among all patients, the mean FLIE nausea domain score on day 6 was 50.0 (44.7 for HEC and 51.4 for MEC; $P = .0024$), whereas the mean FLIE vomiting domain score was 55.3 (50.3 for HEC and 56.5 for MEC; $P = .0097$), indicating that nausea had a stronger impact on daily life than vomiting (Table 3). This is also reflected by the NIDL data because only 53.1% of patients reported NIDL for nausea, compared with 73.4% with NIDL for vomiting (Fig 3). The greater impact of nausea on daily life is also emphasized by results from individual FLIE items shown in Figure 4: The change from baseline to day 6 was more pronounced for all individual nausea domain items than for the corresponding vomiting domain items.

Impact of Acute and Delayed CINV on Patients' Daily Life

Table 4 reports the proportion of patients reporting NIDL for those with acute or delayed vomiting or nausea. On the basis of the total FLIE score, the observed trend is that patients with neither acute

Table 1. Frequency of Emetic Episodes During the 5-Day Period After Chemotherapy

	All Patients				HEC Patients				MEC Patients			
	Patients				Patients				Patients			
Days After Chemotherapy	Missing Values	Total No.	%	Episodes (No.)	Missing Values	Total No.	%	Episodes (No.)	Missing Values	Total No.	%	Episodes (No.)
1 (acute emesis)	38	287	13.2	99	7	59	11.9	22	30	226	13.2	74
2	48	286	16.8	122	16	58	27.6	45	31	226	13.7	75
3	46	286	16.1	109	19	58	32.8	48	26	226	11.5	60
4	49	286	17.1	89	14	58	24.1	28	34	226	15.0	57
5	35	286	12.2	58	15	58	25.9	24	19	226	8.4	31
2-5 (delayed emesis)	93	286	32.5	378	29	58	50.0	167	63	226	27.9	297

NOTE. A total of 298 patients were enrolled. This includes three patients for whom there was no sufficient information to classify them as HEC or MEC. The smaller number of patients reporting emesis reflects missing values.
Abbreviations: HEC, highly emetogenic chemotherapy; MEC, moderately emetogenic chemotherapy.

Table 2. Nausea Assessment–Incidence and Severity

Day After Chemotherapy	All Patients: Patients Missing Values	All Patients: Patients Total No.	All Patients: Patients %	All Patients: Nausea VAS (mean ± SD)	HEC Patients: Patients Missing Values	HEC Patients: Patients Total No.	HEC Patients: Patients %	HEC Patients: Nausea VAS (mean ± SD)	MEC Patients: Patients Missing Values	MEC Patients: Patients Total No.	MEC Patients: Patients %	MEC Patients: Nausea VAS (mean ± SD)
Prechemotherapy period	15	293	5.1	1.1 ± 4.5	6	63	9.5	1.8 ± 5.8	8	227	3.5	0.8 ± 3.8
1 (acute nausea)	106	293	36.2	12.8 ± 23.2	21	63	33.3	13.1 ± 24.1	83	227	36.6	12.4 ± 22.6
2	119	293	40.6	14.6 ± 24.2	32	63	50.8	25.8 ± 34.1	85	227	37.4	11.3 ± 19.7
3	121	293	41.3	15.0 ± 25.0	34	63	54.0	25.7 ± 31.9	85	227	31.9	11.9 ± 21.8
4	108	293	36.9	11.1 ± 19.7	29	63	46.0	18.0 ± 25.8	77	227	33.9	9.0 ± 16.9
5	93	293	31.7	8.7 ± 17.8	25	63	39.7	15.9 ± 25.7	66	227	29.1	6.4 ± 13.9
2-5 (delayed nausea)	159	293	54.3		38	63	60.3		119	227	52.4	

NOTE. The measurements are based on a 100-mm VAS for nausea. No nausea was defined as nausea VAS score < 5 mm. A total of 298 patients were enrolled. These data includes three patients for whom there was no sufficient information to classify them as HEC or MEC. The smaller number of patients reporting emesis reflects missing values.

Abbreviations: HEC, highly emetogenic chemotherapy; MEC, moderately emetogenic chemotherapy; VAS, Visual Analog Scale; SD, standard deviation.

nor delayed nausea or vomiting are more likely to report NIDL than patients who reported both acute and delayed nausea or vomiting (78.3% *v* 20.8% for vomiting, 94.4 for *v* 26.5 for nausea). On average, patients with neither acute nor delayed nausea or vomiting report higher FLIE total scores than patients with both acute and delayed nausea or vomiting (115.9 *v* 72.1 for vomiting, 121.9 for *v* 86.2 for nausea).

Data in Table 4 show that only 155 (66.8%) of 232 patients without acute vomiting reported NIDL on day 6. Similarly, among the 168 patients who experienced no acute nausea, 129 (76.7%) reported NIDL on day 6.

DISCUSSION

It may seem self-evident that nausea and vomiting after chemotherapy have a negative impact on patients' health-related QoL, but there are

Table 3. QoL Assessment and Test of Differences in QoL by Treatment Type Based on Responses to the FLIE Questionnaire on Day 6 Postchemotherapy

FLIE Item	All Patients: No. With NIDL Missing Values	All Patients: No. With NIDL Total No.	All Patients: No. With NIDL %	All Patients: FLIE Score	HEC Patients: No. With NIDL Missing Values	HEC Patients: No. With NIDL Total No.	HEC Patients: No. With NIDL %	HEC Patients: FLIE Score	MEC Patients: No. With NIDL Missing Values	MEC Patients: No. With NIDL Total No.	MEC Patients: No. With NIDL %	MEC Patients: FLIE Score	FLIE Score *P**	NIDL *P*†
FLIE total score	163	267	61.0	105.39	25	53	47.2	95.50	138	214	64.5	107.83	.0049	.0272
Nausea domain total score	144	271	53.1	50.03	20	55	36.4	44.74	124	216	57.4	51.37	.0024	.0063
"Had nausea"	149	271	55.0	5.57	21	55	38.2	4.96	128	216	59.3	5.72	.0029	.0062
"Recreation or leisure activities"	166	271	62.3	5.58	28	55	50.9	5.17	138	216	63.9	5.69	.0740	.0889
"Make meal/do tasks"	159	270	58.9	5.42	28	55	50.9	5.14	131	215	60.9	5.50	.2308	.2192
"Ability to enjoy meal"	148	271	54.6	5.31	21	55	38.2	4.40	127	216	58.8	5.54	.0014	.0095
"Enjoy drinking fluids"	171	271	63.1	5.69	29	55	52.7	5.02	142	216	65.7	5.86	.0098	.0857
"See family/friends"	170	269	63.2	5.63	25	54	46.3	4.96	145	215	67.4	5.80	.0036	.0069
"Daily functioning"	155	269	57.6	5.49	26	54	48.1	5.09	129	215	60.0	5.59	.0842	.1255
"Personal hardship"	150	269	55.8	5.48	23	54	42.6	4.86	127	215	59.1	5.64	.0071	.0326
"Hardship on others"	178	269	66.2	5.89	28	54	51.9	5.25	150	215	69.8	6.05	.0094	.0159
Vomiting domain total score	196	267	73.4	55.26	32	53	60.4	50.31	164	214	76.6	56.49	.0097	.0233
"Had nausea"	210	268	78.4	6.29	34	54	63.0	5.67	176	214	82.2	6.45	.0071	.0049
"Recreation or leisure activities"	204	267	76.4	5.97	36	54	66.7	5.60	168	213	78.9	6.06	.1168	.0725
"Make meal/do tasks"	210	267	78.7	6.18	35	53	66.0	5.55	175	214	81.8	6.34	.0153	.0155
"Ability to enjoy meal"	210	267	78.7	6.18	33	53	62.3	5.51	177	214	82.7	6.35	.0089	.0023
"Enjoy drinking fluids"	214	267	80.1	6.28	33	53	62.3	5.57	181	214	84.6	6.45	.0056	.0008
"See family/friends"	207	265	78.1	6.07	37	53	69.8	5.71	170	212	80.2	6.16	.1091	.1360
"Daily functioning"	213	265	80.4	6.28	35	53	66.0	5.83	178	212	84.0	6.39	.0430	.0061
"Personal hardship"	203	265	76.6	6.16	31	53	58.5	5.44	172	212	81.1	6.35	.0041	.0009
"Hardship on others"	190	265	71.7	5.81	31	53	58.5	5.47	159	212	75.0	5.90	.1795	.0258

NOTE. A total of 298 patients were enrolled. Smaller numbers are due to individual missing values from some patients.

Abbreviations: QoL, quality of life; HEC, highly emetogenic chemotherapy; MEC, moderately emetogenic chemotherapy; FLIE, Functional Living Index-Emesis questionnaire; NIDL, average FLIE item score of > 6 on the seven-point scale.

*Based on *t* tests of the hypothesis that the mean scores of the FLIE items between MEC and HEC patients are not different.

†Based on χ^2 tests of the hypothesis of no association between treatment type (MEC versus HEC) and effect on daily living measured by NIDL.

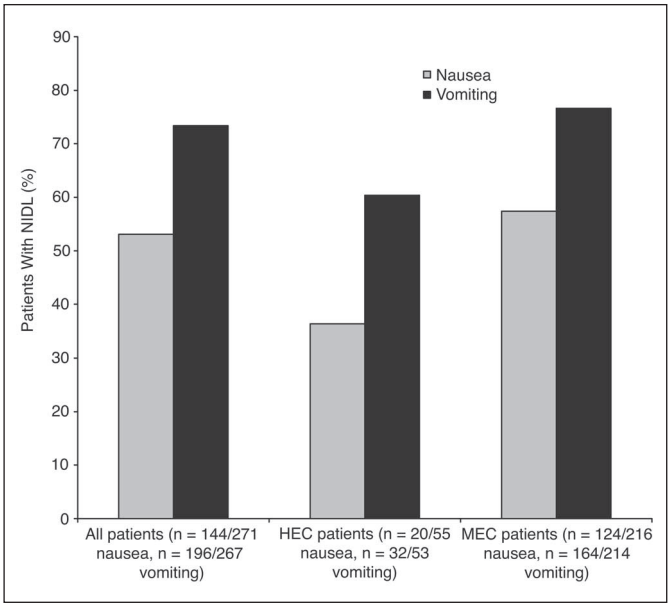

Fig 3. Proportions of patients reporting "no impact on daily life" (NIDL) for nausea and vomiting domains on day 6 postchemotherapy, by treatment type. Results indicate that vomiting had an impact on fewer patients' quality of life than nausea. HEC, highly emetogenic chemotherapy; MEC, moderately emetogenic chemotherapy.

Table 4. Percentage of Patients Reporting NIDL and Mean and Median FLIE Total Score by Acute and/or Delayed CINV Based on Responses to the FLIE Questionnaire on Day 6 Postchemotherapy

Occurrence of CINV (acute, delayed)	No. of Patients	Patients Reporting NIDL		Total FLIE Score	
		%	No.	Mean	Median
Vomiting					
(+, +)	24	20.83	5	72.10	67.23
(+, –)	10	30.00	3	94.61	102.51
(–, +)	57	31.58	18	89.65	84.84
(–, –)	175	78.29	137	115.94	121.44
Nausea					
(+, +)	83	26.51	22	86.22	87.96
(+, –)	15	80.00	12	114.79	117.36
(–, +)	61	45.90	28	100.80	104.28
(–, –)	107	94.39	101	121.94	125.94

NOTE. Ordered pairs of + and – indicate the presence and absence respectively of the relevant condition. The first element of an ordered pair refers to the acute phase and the second to the delayed phase. NIDL is based on FLIE total score.

Abbreviations: NIDL, no or minimal impact on daily life; CINV, chemotherapy-induced nausea and vomiting; FLIE, Functional Living Index-Emesis questionnaire.

little data from prospective clinical trials to demonstrate and quantitatively assess this adverse effect of treatment.[20] Moreover, most studies of the QoL effects of nausea and vomiting are characterized by narrow patient selection criteria and are limited to well-defined chemotherapy regimens. Hence, it is not known to what extent the nausea- and vomiting-induced deterioration of QoL differs after chemotherapy regimens of different levels of emetogenicity. However, data on QoL deterioration would be useful to inform the choice of preventive antiemetic regimens. We set out to directly compare the incidence and QoL impact of nausea and vomiting after HEC and MEC in a representative sample of oncology patients under patterns of daily clinical practice.

Incidence rates of CINV in our patients are in agreement with results from previous, similar studies.[23,24] The central findings from this study were that both HEC and MEC patients reported delayed nausea and vomiting more often than acute nausea and vomiting. Although delayed emesis occurred in almost twice as many HEC as MEC patients, the rate of delayed nausea was unexpectedly similar after HEC and MEC treatment (60.3% *v* 52.4%, respectively). This indicates that level of emetogenicity may not be as strong a predictor of delayed nausea as might be assumed. The potential clinical relevance of this observation is emphasized by the finding that nausea had a stronger negative impact on QoL than vomiting. This was consistent across all items of the FLIE score (Fig 3), and more patients experienced an impact on daily life from nausea than from vomiting (Table 3; Fig 2). This is in concordance with the finding that 5-HT_3 receptor antagonists, such as ondansetron and granisetron, have been successful in preventing vomiting, but less effective in the prevention of nausea.[25]

Both absolute FLIE scores and the proportions of patients reporting NIDL were significantly different between HEC- and MEC-treated groups, demonstrating that HEC patients suffered more of an impact

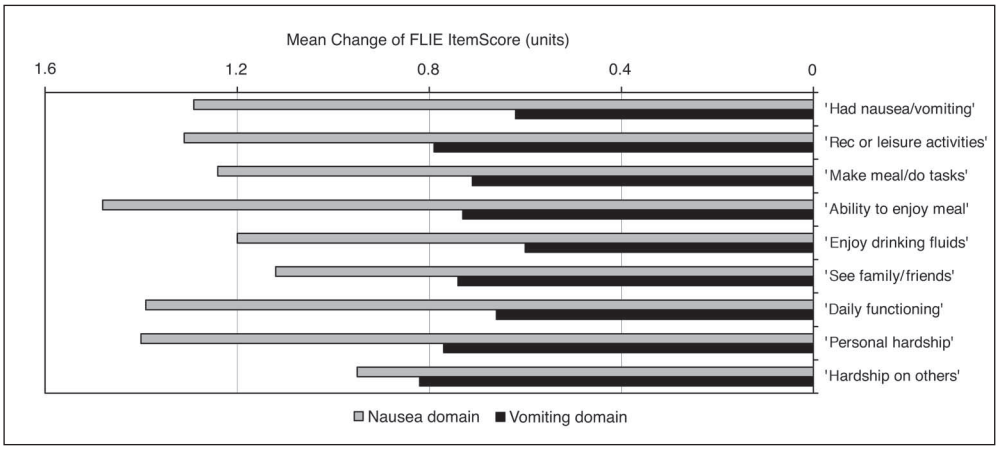

Fig 4. Impact of nausea and vomiting on patients' quality of life: mean change in Functional Living Index-Emesis (FLIE) items score from baseline. A greater negative change means a greater impact of the symptom on that aspect of quality of life. Results indicate that nausea had a stronger negative impact on all FLIE items than vomiting.

on QoL. This finding, although not unexpected, has not, to our knowledge, been described previously. Nonetheless, our data (Table 3) indicate that the percentage of MEC patients who experienced an impact on daily living was as high as 35.5 for the FLIE total score and 42.6 for the nausea domain score (corresponding to 64.5% and 57.4% NIDL, respectively). This indicates that nearly one in two patients suffered an impact on daily life, primarily from nausea, even though they received only moderately emetogenic regimens. Our findings highlight the need for adequate prevention of CINV, even after MEC. Considering that most of our MEC patients received antiemetic treatment consistent with guidelines relevant at the time of this study, this also supports the notion that management of MEC patients may not have been adequately addressed, even in treatment guidelines for prevention of CINV.[24]

Results from this study may also be applied to assess the usefulness of acute CINV as a predictor of impact on QoL: It could be argued that the subgroup of patients who do not experience acute CINV are unlikely to suffer a negative impact on QoL and, hence, might be accorded lower priority for prevention of delayed CINV. This is not supported by our findings, as shown in Table 4. A considerable number of patients who had reported no episodes of nausea or vomiting during the first 24 hours after treatment suffered an impact on QoL during the postchemotherapy period. Results shown in Table 4 also indicate that patients who experienced delayed but not acute nausea were more likely to report an impact on daily living than patients who experienced only acute nausea. The corresponding FLIE scores indicate that delayed CINV has a more severe impact on daily living than acute CINV. This may be attributed to the greater length of time over which delayed CINV could be experienced.

Several methodologic aspects of our study deserve discussion. Our prospective investigation was based on the FLIE score, a validated instrument with questions specifically addressing the impact of CINV on the physical abilities, social and emotional function, and ability to enjoy meals.[20] Patient management and data acquisition were performed by experienced centers and personnel. The study was not restricted to a particular cancer type, and we have deliberately enrolled a heterogeneous group of cancer patients receiving a broad range of chemotherapies. This is expected to make our results relevant for extrapolation to most cancer patient populations on highly or moderately emetogenic treatments.

The importance of the time of administration after chemotherapy of the QoL assessment has been addressed previously. Because CINV is most intense during the first 3 days after chemotherapy, it is critical that these days be included in the observation period. Moreover, the observation period must not be overly long to minimize recall bias that may result in loss of assay sensitivity.[20,26] In this study, we administered the FLIE questionnaire in the morning of day 6, a period that was judged to be adequate on the basis of results from a previous study on the timing of QoL assessment of CINV[26] and further validated in a clinical trial sample.[18] Furthermore, the 5-day period is expected to include most CINV-related events without a relevant level of recall bias.

Only treatment-naïve patients were enrolled in this study. This may limit extrapolation of our findings to the first cycle of chemotherapy because previous experience has shown that the antiemetic effect decreases during subsequent cycles.[27] Hence, results of our study may underestimate the overall impact of CINV on patient's daily life during subsequent cycles of their chemotherapy.

Guidelines on antiemetic prophylaxis for patients undergoing HEC have been amended since the time when this study was conducted.[28] For these patients, a three-drug combination, including a neurokinin-1 receptor antagonist, may now offer better protection, but for MEC patients current guidelines are still in line with the practice pattern in our study.[29]

In conclusion, our findings support the notion that CINV continues to adversely affect patients' QoL, even after treatment with moderately emetogenic regimens, and even in the subgroup of patients who do not experience nausea and vomiting during the first 24 hours. Nausea has a stronger negative impact on QoL than vomiting. Patients in this study were included at the first cycle of chemotherapy. It is well known that the antiemetic effect of a serotonin receptor antagonist and a corticosteroid declines through subsequent cycles of HEC[30] or MEC.[31] This emphasizes the need for new and potent antiemetics.

Recently, the American Society of Clinical Oncology has updated its guidelines for antiemetic use in oncology. The updated guidelines state that before patients are receiving chemotherapy of high emetic risk (eg, an anthracycline and cyclophosphamide), a three-drug regimen of a 5-HT_3 serotonin receptor antagonist, dexamethasone, and aprepitant is recommended.[32] The two-drug combination of dexamethasone and aprepitant is recommended for the prevention of delayed emesis in patients receiving cisplatin or other agents of high emetogenicity. Future studies will show whether this updated regimen will translate into an improved QoL for patients undergoing chemotherapy.

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