Supportive Care in Cancer (2023) 31:505
https://doi.org/10.1007/s00520-023-07978-y

REVIEW

Prevalence and predictors of long-delayed (> 120 h) chemotherapy-induced nausea and vomiting (CINV)—a systematic review and individual patient data meta-analysis

Ronald Chow[1] · Leyi Bellinda Yin[1] · Wafa Baqri[1] · Ryan Huang[1] · Gabriel Boldt[2] · Jawaid Younus[2] · Michael Lock[2] · Elizabeth Prsic[3] · Camilla Zimmermann[1] · Jørn Herrstedt[4]

Received: 27 March 2023 / Accepted: 28 July 2023 / Published online: 3 August 2023

Abstract

Introduction Although there have been reports of chemotherapy-induced nausea and vomiting (CINV) beyond 120 h, its overall prevalence has not been systematically examined. The aim of this review and meta-analysis was to report on the prevalence of this long-delayed CINV.

Methods This review was registered on PROSPERO (CRD42022346963). PubMed (Medline), Embase, and Cochrane Central were searched from inception until August 2022. Articles were included if they reported on CINV > 120 h after initiation of the chemotherapy regimen and patients received a single-agent highly emetogenic (HEC) or moderately emetogenic (MEC) antineoplastic agent for 1 day alone or in combination with low/minimal emetogenic chemotherapy. For all eligible articles, individual study authors were contacted and requested to provide individual patient-level data of demographics, emetogenicity of chemotherapy regimens, and daily incidence of nausea and vomiting. Forward stepwise logistic regression identified predictors for the incident day's CINV based on prior day's CINV episodes, controlling for patient demographics, and stratified by regimen emetogenicity.

Results A total of 2048 patients from 2 studies were included in this individual patient data meta-analysis: 1333 patients (65%) received HEC and 715 (35%) received MEC. Among those receiving HEC, 325 (24%) experienced acute, 652 (49%) delayed, and 393 (31%) long-delayed nausea; 107 (8%) experienced acute, 179 (14%) delayed, and 79 (6%) long-delayed vomiting. Among those receiving MEC, 48 (7%) experienced acute, 272 (38%) delayed, and 167 (24%) long-delayed nausea; 12 (2%) experienced acute, 97 (14%) delayed, and 42 (6%) long-delayed vomiting. Nausea in the long-delayed phase was as severe as in the delayed phase. Patients experiencing nausea and vomiting on days 4 and 5 were at significant risk of experiencing long-delayed CINV.

Conclusion While not as prevalent as delayed nausea and vomiting, long-delayed CINV affects a significant proportion of patients and severity is similar. Patients with delayed CINV, specifically on days 4–5, are at risk of experiencing long-delayed CINV.

Keywords Chemotherapy-induced nausea and vomiting · Delayed phase · Long-delayed phase

Introduction

Chemotherapy-induced nausea and vomiting (CINV) is a highly prevalent and significant adverse event for patients undergoing emetogenic chemotherapy [1]. CINV can lead to poor quality of life and treatment nonadherence [2]. The incidence of CINV is commonly documented as occurring in the acute (0–24 h post-chemotherapy) and delayed (24–120 h post-chemotherapy) phases [3]. Over the past several decades, there has been extensive research and development of antiemetics for patients experiencing

✉ Ronald Chow
ronald.chow@uhn.ca

1 Temerty Faculty of Medicine, University of Toronto, Toronto, ON, Canada

2 Schulich School of Medicine & Dentistry, University of Western Ontario, London, ON, Canada

3 Yale School of Medicine, Yale University, New Haven, CT, USA

4 University of Copenhagen, Copenhagen, Denmark

acute and delayed phase CINV [4–6]. As a result, patients treated with highly emetogenic chemotherapy (HEC) or carboplatin-based chemotherapy are currently recommended to be treated with prophylactic regimens, of a combination of 5-HT_3 receptor antagonist, an NK_1 receptor antagonist, dexamethasone, and/or olanzapine [7, 8].

Recent reports have explored long-delayed CINV or symptoms persisting more than 120 h after receipt of HEC. [9, 10] No study has focused explicitly on long-delayed CINV, isolated separately from delayed CINV. Therefore, the overall prevalence of long-delayed CINV (CINV beyond 120 h) is still unknown. Furthermore, the underlying mechanism, and therefore the method of treatment, may differ between delayed CINV and long-delayed CINV. Given the wide use of HEC, this is an important topic to explore. The aim of this systematic review and meta-analysis is therefore to report on the prevalence of long-delayed CINV.

Methods

This review was registered a priori on PROSPERO (CRD42022346963) and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline.

Search strategy

PubMed (Medline), Embase, and Cochrane Central were searched from database inception up until August 2022, using Medical Subject Headings (MeSH) and keywords to identify papers reporting on delayed CINV. Limits were applied to restrict to human studies only. No language restrictions were applied. The complete search strategy is reported in the Appendix.

Screening and eligibility

After duplication removal and a calibration exercise, at least two review authors (RC, BY, WB, RH) independently screened each article according to a pre-specified eligibility criterion. Articles were included or excluded by consensus. If consensus could not be achieved, a third review author (CZ) assisted in discussion and helped achieve consensus.

Articles were included after level 1 title and abstract screening if they reported on delayed CINV. These articles were further screened and eligible after level 2 if they reported on the incidence of delayed CINV beyond 120 h after the initiation of the chemotherapy regimen, and reported on patients receiving a single highly emetogenic or moderately emetogenic antineoplastic agent for 1 day alone or in combination with low/minimal emetogenic chemotherapy as defined by the 2016 MASCC/ESMO antiemetic guidelines [8].

Data extraction

For all eligible articles, individual study authors were contacted and requested to provide individual patient-level data of patient demographics, emetogenicity of chemotherapy regimens (highly emetogenic or moderately emetogenic), and incidence of nausea and vomiting for each day of follow-up during the study period. If no response was received, a follow-up email was sent at 2 to 4 weeks, after which the study was excluded due to no response from authors. Articles were included in the meta-analysis only if data was supplied by authors. Because the objective of this review was to report on prevalence using individual study data, all studies were treated as observational studies, regardless of their study design. Thus, quality of the included studies was assessed using the Risk of Bias in Observational Studies of Exposures (ROBINS-E) tool [11].

Data analysis

Patient demographics of age, sex, and cancer diagnosis were summarized across the merged datasets. Incidence of nausea and vomiting for each day and pre-defined periods of acute (0–24 h), delayed (24–120 h), and long-delayed (> 120 h) CINV were reported using descriptive statistics, stratified by whether patients received highly emetogenic chemotherapy (HEC) or moderately emetogenic chemotherapy (MEC). Forward stepwise logistic regression was used to identify predictors for the incident day's CINV based on prior day's CINV episodes, controlling for patient demographics, and stratified by emetogenicity of chemotherapy regimen. Type I error was set at 0.05. All analyses were conducted using Stata/BE 17.0.

Results

A total of 3677 articles were identified from database search. After duplicate removal, 3651 articles were screened at level and 589 were screened at level 2. Authors for 73 articles [12–84] were contacted to request data. No data was provided for 71 articles. Authors for 46 articles [12, 17–19, 21, 24, 26, 31, 33, 34, 36–40, 42–45, 47–54, 63, 65–67, 69–76, 78, 80–84] could not be contacted. Sixteen authorship teams [13, 14, 20, 22, 27, 28, 32, 41, 55–60, 62, 64] informed that they no longer had access to the dataset, six [23, 29, 30, 35, 61, 69] informed that they were checking for the data but did not supply the data after multiple follow-ups, and three [16, 46, 79] advised

that they did not have the requested data. Ultimately, two studies [68, 77] with an amalgamated sample size of > 2000 patients were included in this individual patient data meta-analysis (Fig. 1).

Both included studies were performed in Japan. Sagae et al. [68] reported on a single-institution randomized cross-over study of 69 women receiving MEC for uterine or ovarian cancer; this study was considered as a 138-person observational study in this review. Tamura et al. [77] reported on a national multi-institution observational study of 108 institutions across Japan, with a total sample size of 1910 patients receiving MEC or HEC. The two studies were of good study quality as observational studies, with no concerns in any domain as evaluated by ROBINS-E. Of note, Sagae et al. was not a high-quality randomized trial, with no emphasis on randomization or drop-outs. However, based on methodological assessment when re-classified as an observational study for our review, there are no significant concerns about Sagae et al.'s data as it pertains to prevalence rates of long-delayed CINV. As well, the Tamura et al. study accrued and reported on substantially more patients, accounting for the majority of patients in this meta-analysis.

A total of 2048 patients were included in this individual patient data meta-analysis. The average age was 59.7 years ± 11.9 years. Fifty-seven percent were female. The most common cancer diagnosis was breast (21%), followed by non-small cell lung (16%), esophageal (9%), colorectal (9%), and ovarian (8%). Just under two-thirds of patients (65%) were treated with HEC. The most common prophylactic antiemetic regimen was a 5-HT_3 receptor antagonist with dexamethasone (Table 1). Both studies reported on days 6 and 7 CINV endpoints.

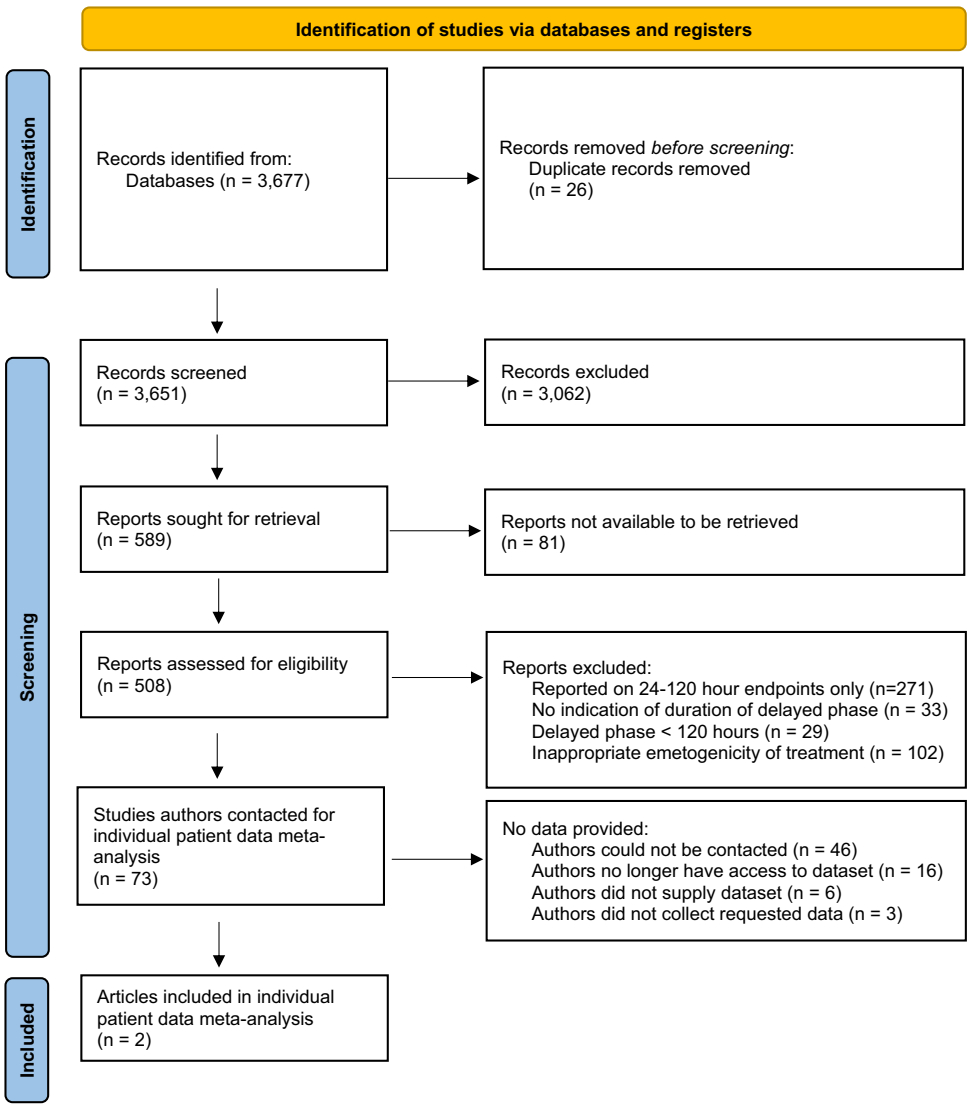

Fig. 1 PRISMA flow diagram

Table 1 Patient demographics

Age (years)	59.7 ± 11.9
Sex	
Female	1175 (57%)
Male	873 (43%)
Cancer diagnosis	
Breast	429 (21%)
Cervical	54 (3%)
Cholangiocarcinoma	70 (3%)
Colorectal	190 (9%)
Endometrial	134 (7%)
Esophageal	192 (9%)
Hodgkin lymphoma	8 (< 1%)
Non-Hodgkin lymphoma	140 (7%)
Leukemia	38 (2%)
Liver	20 (1%)
Multiple myeloma	11 (1%)
Non-small cell lung	326 (16%)
Ovarian	154 (8%)
Pancreatic	10 (< 1%)
Small cell lung	88 (4%)
Stomach	152 (7%)
Other	32 (2%)
Chemotherapy emetogenicity	
Highly emetogenic	1333 (65%)
Moderately emetogenic	715 (35%)
Antiemetic regimen	
5HT3RA alone	42 (2%)
5HT3RA + dexamethasone	715 (35%)
5HT3RA + methylprednisolone	27 (1%)
5HT3RA + dexamethasone + aprepitant	1195 (58%)
5HT3RA + methylprednisolone + droperidol	69 (3%)

Patients treated with highly emetogenic chemotherapy (HEC)

Patients treated with HEC ($n = 1333$) had an average age of 58.7 years ± 12.0 years. Fifty-eight percent were female, and the most common cancer diagnoses were breast (27%), esophageal (14%), and stomach (11%). Almost 90% of patients had a prophylactic regimen of a 5-HT_3 receptor antagonist, dexamethasone, and aprepitant (Table 2).

A total of 325 (24%) of patients experienced any acute nausea, 625 (49%) experienced any delayed nausea, and 393 (31%) experienced any long-delayed nausea. One hundred seven (8%) experienced acute vomiting, 179 (14%) experienced delayed vomiting, and 79 (6%) experienced long-delayed vomiting (Table 3). Severity of nausea across time periods was similar; the severity of long-delayed nausea was similar to delayed nausea (Table 4).

Episodes of nausea and vomiting in prior days were predictors of incident nausea and vomiting. Specifically, day 5 nausea was a significant predictor for long-delayed nausea (OR 14.31; 95% CI: 10.41–19.67) and day 5 vomiting was a significant predictor for long-delayed vomiting (OR 17.46; 95% CI: 10.17–29.99) (Table 5).

Patients treated with moderately emetogenic chemotherapy

Among patients treated with MEC ($n = 715$), the average age was 61.6 years ± 11.4 years. Fifty-six percent were female. The most common cancer diagnoses were non-small cell lung (27%) and colorectal (27%). All patients were treated with a 5-HT_3 receptor antagonist and dexamethasone, possibility with the addition of aprepitant for patients receiving regimens containing carboplatin, irinotecan, ifosfamide, or methotrexate [77] (Table 2).

Forty-eight (7%) and 12 (2%) of patients experienced acute nausea and acute vomiting, respectively. Two hundred seventy-two (38%) patients reported delayed nausea and 97 (14%) reported delayed vomiting. One hundred sixty-seven (24%) patients reported episodes of long-delayed nausea and 42 (6%) reported episodes of long-delayed vomiting (Table 3). Severity of long-delayed nausea was similar to delayed nausea (Table 4).

Episodes of nausea and vomiting in the prior days were predictors of incident nausea and vomiting. Specifically, for long-delayed nausea, day 4 nausea (OR 2.43; 95% CI: 1.41–4.21) and day 5 nausea (OR 21.14; 95% CI: 12.24–36.52) were significant predictors. For long-delayed vomiting, day 5 vomiting (OR 20.63; 95% CI: 12.24–36.52) was a significant predictor (Table 6).

Discussion

To our knowledge, this is the first study to specifically describe the phenomenon of long-delayed CINV (> 120 h). While not as prevalent as delayed nausea and vomiting, it is still relatively prevalent and affects a substantial proportion of patients. As well, the severity of nausea in the long-delayed phase is as severe as that experienced in the delayed phase. Furthermore, patients experiencing nausea and vomiting on days 4 and 5 were at significant risk of experiencing long-delayed CINV.

No previous studies have separately reported on CINV after > 120 h. Published studies have reported on non-standard definitions of delayed CINV, defined as an episode of nausea or vomiting in the time window of 24 h to > 120 h (often 144 to 168 h after the initiation of

Table 2 Patient demographics by emetogenicity of chemotherap

	HEC ($n=1333$)	MEC ($n=715$)
Age (years)	58.7 ± 12.0	61.6 ± 11.4
Sex		
Female	778 (58%)	397 (56%)
Male	555 (42%)	318 (44%)
Cancer diagnosis		
Breast	354 (27%)	75 (10%)
Cervical	27 (2%)	27 (4%)
Cholangiocarcinoma	69 (5%)	1 (< 1%)
Colorectal	0 (0%)	190 (27%)
Endometrial	81 (6%)	53 (7%)
Esophageal	181 (14%)	11 (2%)
Hodgkin lymphoma	8 (1%)	0 (0%)
Non-Hodgkin lymphoma	134 (10%)	6 (1%)
Leukemia	34 (3%)	4 (1%)
Liver	12 (1%)	8 (1%)
Multiple myeloma	4 (< 1%)	7 (1%)
Non-small cell lung	133 (10%)	193 (27%)
Ovarian	79 (6%)	75 (10%)
Pancreatic	8 (1%)	2 (< 1%)
Small cell lung	43 (3%)	45 (6%)
Stomach	150 (11%)	2 (< 1%)
Other	16 (1%)	16 (2%)
Antiemetic regimen		
5HT3RA alone	42 (3%)	0 (0%)
5HT3RA + dexamethasone	0 (0%)	715 (100%)
5HT3RA + methylprednisolone	27 (2%)	0 (0%)
5HT3RA + dexamethasone + aprepitant	1195 (90%)	0 (0%)
5HT3RA + methylprednisolone + droperidol	69 (5%)	0 (0%)

chemotherapy), which may include episodes experienced in the long-delayed period. However, this endpoint is difficult to interpret, as nausea and vomiting experienced on day 6 or 7 is likely markedly different than day 2 or 3, both physiologically and in terms of management strategy. In fact, guidelines are unclear on how to manage CINV many days beyond the initiation of chemotherapy, as it may not necessarily be considered as breakthrough CINV. The identification of patient population with long-delayed CINV presents an opportunity to clarify management and supportive care for these patients.

There seems to be a significant proportion of patients who still experience CINV between 120–168 h after initiation of chemotherapy—31% of patients receiving HEC experienced long-delayed nausea and 6% experienced long-delayed vomiting; and 24% of patients receiving MEC reported long-delayed nausea and 6% reported episodes of long-delayed vomiting. Of note, based on the reporting from Sagae et al. [68] and Tamura et al. [77] many patients receiving HEC were administered cisplatin as part of their antineoplastic treatment. Furthermore, the severity of nausea in this phase is similar to the severity of nausea in the preceding time intervals. However, as the proportion of patients experiencing acute and delayed CINV may differ between the results of this meta-analysis and individual study centers based on antineoplastic treatment agents and antiemetic regimen, it is important to interpret overall percentages and trends. When interpreted broadly, patients were more likely to experience delayed nausea, followed by long-delayed nausea, and then finally acute nausea. A similar trend was observed for vomiting, with the exception that patients receiving HEC more often reported acute vomiting over long-delayed vomiting. Long-delayed CINV is a distinct adverse event related to chemotherapy that should be further investigated, as in how acute and delayed phase CINV have been extensively studied in terms of both incidence and management.

Currently, no other studies exist on long-delayed CINV. As a result, despite only having two studies in this

Table 3 Incidence of acute, delayed and long-delayed chemotherapy-induced nausea, and vomiting

	HEC	MEC
Acute (0–24 h)		
Any acute nausea	325/1333 (24%)	48/715 (7%)
Any acute vomiting	107/1333 (8%)	12/715 (2%)
Delayed (24–120 h)		
Any delayed nausea	652/1330 (49%)	272/711 (38%)
Any delayed vomiting	179/1325 (14%)	97/713 (14%)
Day 2 nausea	400/1333 (30%)	89/714 (12%)
Day 2 vomiting	117/1332 (9%)	18/714 (3%)
Day 3 nausea	456/1331 (34%)	157/713 (22%)
Day 3 vomiting	86/1331 (6%)	41/714 (6%)
Day 4 nausea	437/1330 (33%)	189/713 (27%)
Day 4 vomiting	72/1329 (5%)	53/713 (7%)
Day 5 nausea	387/1324 (29%)	184/712 (26%)
Day 5 vomiting	50/1325 (4%)	42/713 (6%)
Long-delayed (> 120 h)		
Any long-delayed nausea	393/1282 (31%)	167/703 (24%)
Any long-delayed vomiting	79/1275 (6%)	42/702 (6%)
Day 6 nausea	342/1314 (26%)	149/711 (21%)
Day 6 vomiting	59/1314 (4%)	31/711 (4%)
Day 7 nausea	291/1274 (23%)	121/703 (17%)
Day 7 vomiting	58/1274 (5%)	24/702 (3%)

Table 4 Severity of acute, delayed, and long-delayed nausea (visual analog scale of 100 points)

	HEC	MEC
Acute (0–24 h)		
Day 1	44.5 ± 29.0	26.8 ± 27.6
Delayed (24–120 h)		
Day 2	36.8 ± 25.2	34.3 ± 26.8
Day 3	35.1 ± 24.7	39.7 ± 26.6
Day 4	37.5 ± 25.2	41.0 ± 28.0
Day 5	37.1 ± 26.6	39.7 ± 26.7
Long-delayed (> 120 h)		
Day 6	39.7 ± 29.4	35.6 ± 25.5
Day 7	40.3 ± 29.2	35.1 ± 27.2

meta-analysis (albeit having a very large sample size of over 2000 patients across 100 + institutions in Japan), this is the only available evidence documenting the incidence of this important adverse event. Similarly, no studies exist exploring the management of patients experiencing long-delayed CINV. Currently, it is unclear whether routine prophylactic regimens should be extended to provide coverage for a prolonged time period, or whether additional antiemetic agents, prophylactic, and/or rescue, should be used in this setting. Future studies could confirm whether long-delayed CINV is a significant concern in their patient population, examine patterns of recurrence, and explore potential management strategies.

We found that patients experiencing nausea and vomiting on days 4 and 5 were at greatest risk of experiencing long-delayed CINV. This was also observed for delayed CINV, where nausea and vomiting in the acute phase and/or the preceding days of the delayed phase were significant predictors of long-delayed CINV. Patients who experience CINV late in the delayed phase should therefore be managed with greater vigilance and may be prescribed rescue antiemetics for any long-delayed CINV. Future studies could focus on this patient population and explore optimal management strategies, both prophylactic and rescue options.

This study had limitations. The strength of the conclusions of a meta-analysis is only as strong as the weakest included study. Both studies have low risk for bias, and together, report on over 2000 patients across 100 + institutions in Japan. The majority of patients were from one study (Tamura et al. [77]). Study quality is therefore of minimal concern. There could be concern regarding generalizability: disappointingly, the majority of authorship teams could not be contacted. Finally, patients included in this dataset had their CINV managed in accordance with guidelines available at the time of their study, which have changed over time. However, due to the evolving landscape and revision of guidelines over the past decade, those antiemetic regimens are discordant with today's guidelines and best practices. Accordingly, interpretation of the prevalence of long-delayed CINV should be interpreted relative to acute and delayed CINV, rather than as an epidemiologic metric. As a corollary, it is uncertain whether current recommendations will better prevent long-delayed CINV. It is unclear whether NK_1 receptor antagonists or olanzapine may be effective in reducing the incidence of long-delayed CINV, or alternatively whether the incidence of long-delayed CINV could be worse, with recommendations of single-day rather than multi-day corticosteroid regimens. The findings of this review should serve as encouragement for further investigation, to validate whether long-delayed CINV is a significant concern.

In conclusion, this is the first study to report on the phenomenon of long-delayed CINV. We found that a significant proportion of patients experienced long-delayed CINV. Future studies could validate this phenomenon and explore options for prophylactic and rescue management.

Table 5 Significant predictors of chemotherapy-induced nausea and vomiting among patients receiving highly emetogenic chemotherapy

Delayed (24–120 h)	
Any delayed nausea	Any acute nausea: OR 10.40; 95% CI: 7.41–14.60
Any delayed vomiting	Any acute Nausea: OR 1.72; 95% CI: 1.19–2.48 Any acute vomiting: OR 6.88; 95% CI: 4.22–11.21
Day 2 nausea	Any acute nausea: OR 16.86; 95% CI: 12.62–22.54
Day 2 vomiting	Any acute nausea: OR 3.57; 95% CI: 2.11–6.01 Any acute vomiting: OR 15.93; 95% CI: 8.86–28.65
Day 3 nausea	Any acute nausea: OR 1.70; 95% CI: 1.15–2.51 Any acute vomiting: OR 0.52; 95% CI: 0.27–0.97 Day 2 nausea: OR 15.98; 95% CI: 11.67–21.87 Day 2 vomiting: OR 10.88; 95% CI: 5.50–21.51
Day 3 vomiting	Any acute vomiting: OR 1.86; 95% CI: 1.02–3.38 Day 2 nausea: OR 2.90; 95% CI: 1.81–4.65 Day 2 vomiting: 14.92; 95% CI: 8.98–24.78
Day 4 nausea	Any acute nausea: OR 1.53; 95% CI: 1.05–2.23 Day 2 nausea: OR 1.55; 95% CI: 1.08–2.24 Day 3 nausea: OR 21.60; 95% CI: 15.95–29.25
Day 4 vomiting	Day 2 vomiting: OR 1.79; 95% CI: 1.01–3.15 Day 3 nausea: OR 3.00; 95% CI: 1.81–4.97 Day 3 vomiting: OR 8.71; 95% CI: 5.08–14.92
Day 5 nausea	Day 2 nausea: OR 1.45; 95% CI: 1.03–2.06 Day 3 nausea: OR 1.50; 95% CI: 1.04–2.18 Day 4 nausea: OR 20.55; 95% CI: 14.74–28.65 Day 4 vomiting: OR 1.64; 95% CI: 1.01–2.68
Day 5 vomiting	Day 3 vomiting: OR 5.63; 95% CI: 3.41–9.29 Day 4 nausea: OR 6.79; 95% CI: 3.85–11.97
Long-delayed (> 120 h)	
Any long-delayed nausea	Day 2 nausea: OR 2.00; 95% CI: 1.45–2.78 Day 4 nausea: OR 1.85; 95% CI: 1.31–2.63 Day 4 vomiting: OR 1.75; 95% CI: 1.05–2.93 Day 5 nausea: OR 14.31; 95% CI: 10.41–19.67
Any long-delayed vomiting	No acute nausea: OR 2.47; 95% CI: 1.36–4.48 Any delayed nausea: OR 2.21; 95% CI: 1.21–4.03 Day 2 nausea: OR 2.04; 95% CI: 1.17–3.58 Day 3 vomiting: OR 3.01; 95% CI: 1.70–5.31 Day 5 vomiting: OR 17.46; 95% CI: 10.17–29.99
Day 6 nausea	Day 2 nausea: OR 1.53; 95% CI: 1.11–2.12 Day 3 vomiting: OR 1.95; 95% CI: 1.17–3.24 Day 4 nausea: OR 2.13; 95% CI: 1.50–3.03 Day 5 nausea: OR 16.37; 95% CI: 11.77–22.76
Day 6 vomiting	Any delayed nausea: OR 2.69; 95% CI: 1.34–5.40 Day 3 vomiting: OR 3.54; 95% CI: 1.92–6.52 Day 5 vomiting: OR 24.31; 95% CI: 13.75–43.00
Day 7 nausea	Day 5 nausea: OR 3.17; 95% CI: 2.22–4.55 Day 6 nausea: OR 23.06; 95% CI: 15.91–33.42 Day 6 vomiting: OR 2.56; 95% CI: 1.39–4.70
Day 7 vomiting	Day 5 vomiting: OR 2.38; 95% CI: 1.16–4.90 Day 6 nausea: OR 4.62; 95% CI: 2.41–8.89 Day 6 vomiting: OR 23.49; 95% CI: 11.90–6.35

Table 6 Significant predictors of chemotherapy-induced nausea and vomiting, among patients receiving moderately emetogenic chemotherapy

Delayed (24–120 h)	
Any delayed nausea	Any acute nausea: OR 16.01; 95% CI: 6.21–41.32
Any delayed vomiting	Any acute nausea: OR 2.30; 95% CI: 1.05–5.03 Any acute vomiting: OR 7.08; 95% CI: 1.68–29.92
Day 2 nausea	Any acute nausea: OR 21.47; 95% CI: 10.92–42.22
Day 2 vomiting	Any acute nausea: OR 4.25; 95% CI: 1.01–17.84 Any acute vomiting: OR 17.53; 95% CI: 3.23–94.11
Day 3 nausea	Any acute nausea: OR 3.04; 95% CI: 1.30–7.11 Day 2 nausea: OR 21.46; 95% CI: 11.55–39.88
Day 3 vomiting	Day 2 nausea: OR 4.72; 95% CI: 2.22–10.03 Day 2 vomiting: OR 7.52; 95% CI: 2.48–22.81
Day 4 nausea	Day 2 nausea: OR 3.64; 95% CI: 1.78–7.44 Day 3 nausea: OR 22.31; 95% CI: 13.27–37.51
Day 4 vomiting	Any acute nausea: OR 3.19; 95% CI: 1.29–7.87 Day 3 nausea: OR 2.87; 95% CI: 1.35–6.09 Day 3 vomiting: OR 14.22; 95% CI: 6.06–33.37
Day 5 nausea	Day 2 nausea: OR 2.41; 95% CI: 1.29–4.48 Day 4 nausea: OR 20.83; 95% CI: 13.13–33.06
Day 5 vomiting	Day 3 vomiting: OR 4.98; 95% CI: 2.21–11.22 Day 4 nausea: OR 5.05; 95% CI: 2.45–10.39
Long-delayed (> 120 h)	
Any long-delayed nausea	Day 4 nausea: OR 2.43; 95% CI: 1.41–4.21 Day 5 nausea: OR 21.14; 95% CI: 12.24–36.52
Any long-delayed vomiting	Day 4 nausea: OR 3.04; 95% CI: 1.45–6.38 Day 5 vomiting: OR 20.63; 95% CI: 9.42–45.17
Day 6 nausea	Day 4 nausea: OR 2.33; 95% CI: 1.32–4.12 Day 5 nausea: OR 25.34; 95% CI: 14.06–45.65
Day 6 vomiting	Day 3 vomiting: OR 3.17; 95% CI: 1.05–9.59 Day 5 vomiting: OR 41.50; 95% CI: 17.08–100.84
Day 7 nausea	Day 5 nausea: OR 3.81; 95% CI: 1.91–7.60 Day 6 nausea: OR 32.31; 95% CI: 16.02–65.20
Day 7 vomiting	Any delayed nausea: OR 4.75; 95% CI: 1.50–15.05 Day 6 vomiting: OR 27.39; 95% CI: 10.49–72.16

Appendix. Search strategy

PubMed/ Medline (2286 Results)

(neoplasms [mh] OR cancer*[tw])

AND

(anti-eme*[tw] OR antieme*[tw] OR induced nausea*[tw] OR associated nausea*[tw] OR cinv[tw] OR vomit*[tw] OR vomiting[mh] OR nausea*[tw] OR Nausea[mh] OR emesis[tw] OR Emetics[mh] OR emetic*[tw] OR retch*[tw])

AND

(chemotherapy [tw] OR drug therapy [mh] OR Antineoplastic Combined Chemotherapy Protocols[mh])

AND

(time to treatment [mh] OR time factors [mh] OR patient care [tw] OR delay*[tw])

Filters: Humans

EMBASE (1352) & Cochrane (39)

(exp neoplasm/ or cancer*.mp.)

and

(anti-eme*.mp. or chemotherapy induced emesis/ or exp antiemetic agent/ or antieme*.mp. or vomiting/ or nausea/ or induced nausea*.mp. or associated nausea*.mp. or exp "chemotherapy induced nausea and vomiting"/ or cinv.mp. or vomit*.mp. or nause*.mp. or emesis.mp. or Emetics.mp. or exp emetic agent/ or exp retching/ or retch*.mp.)

and

(exp cancer chemotherapy/ or chemotherapy.mp. or exp chemotherapy/ or exp cancer combination chemotherapy/ or exp drug therapy/)

and

(exp time to treatment/ or exp time factor/ or exp patient care/ or exp therapy delay/ or delay*.mp.)

Limit to human and exclude Medline journals

Limit to human and Cochrane Library

Author contribution Conceptualization: RC.
Data curation: RC and GB.
Formal analysis: RC.
Investigation: RC, BY, WB, RH, GB, and JH.
Methodology: RC and JH.
Project administration: RC and CZ.
Resources: RC, GB, and CZ.
Supervision: CZ and JH.
Writing—original draft preparation: RC.
Writing—review and editing: all authors.

Data availability Not applicable.

Declarations

Ethical approval Not applicable.

Competing interests The authors declare no competing interests.

References

1. Cohen L, de Moor C, Eisenberg P, Ming EE, Hu H (2007) Chemotherapy-induced nausea and vomiting: incidence and impact on patient quality of life at community oncology settings. Support Care Cancer 15:497–503
2. Osoba D, Zee B, Warr D, Latreille J, Kaizer L, Pater J (1997) Effect of postchemotherapy nausea and vomiting on health-related quality of life. The Quality of Life and Symptom Control Committees of the National Cancer Institute of Canada Clinical Trials Group. Support Care Cancer 5(4):307–13
3. Chow R, Navari RM, Terry B, DeAngelis C, Prsic EH (2022) Olanzapine 5 mg vs 10 mg for the prophylaxis of chemotherapy-induced nausea and vomiting: a network meta-analysis. Support Care Cancer 30(2):1015–1018
4. Chow R, Herrstedt J, Aapro M et al (2021) Olanzapine for the prophylaxis and rescue of chemotherapy-induced nausea and vomiting: a systematic review, meta-analysis, cumulative meta-analysis and fragility assessment of the literature. Support Care Cancer 29(7):3439–3459
5. Chow R, Valdez C, Chow N et al (2020) Oral cannabinoid for the prophylaxis of chemotherapy-induced nausea and vomiting—a systematic review and meta-analysis. Support Care Cancer 28(5):2095–2103
6. Chow R, Warr DG, Navari RM et al (2018) Should palonosetron be a preferred 5-HT3 receptor antagonist for chemotherapy-induced nausea and vomiting? An updated systematic review and meta-analysis. Support Care Cancer 26(8):2519–2549
7. Hesketh PJ, Kris MG, Basch E et al (2017) Antiemetics: American Society of Clinical Oncology Clinical Practice Guideline update. J Clin Oncol 35(28):3240–3261
8. Roila F, Molassiotis A, Herrstedt J et al (2016) 2016 MASCC and ESMO guideline update for the prevention of chemotherapy- and radiotherapy-induced nausea and vomiting and of nausea and vomiting in advanced cancer patients. Ann Oncol 27:v119–v133
9. Zelek L, Debourdeau P, Bourgeois H et al (2021) A pragmatic study evaluating NEPA versus aprepitant for prevention of chemotherapy-induced nausea and vomiting in patients receiving moderately emetogenic chemotherapy. Oncologist 26(10):e1870–e1879
10. Hata A, Okamoto I, Inui N et al (2021) Randomized, double-blind, phase III study of fosnetupitant versus fosaprepitant for prevention of highly emetogenic chemotherapy-induced nausea and vomiting: CONSOLE. J Clin Oncol 40(2):180–188
11. Higgins J, Morgan R, Rooney A et al (2022) Risk of Bias In Non-randomized Studies - of Exposure (ROBINS-E). https://www.riskofbias.info/welcome/robins-e-tool
12. Aapro MS, Thuerlimann B, Sessa C, De Pree C, Bernhard J, Maibach R (2003) A randomized double-blind trial to compare the clinical efficacy of granisetron with metoclopramide, both combined with dexamethasone in the prophylaxis of chemotherapy-induced delayed emesis. Ann Oncol 14(2):291–297
13. Hilarius DL, Kloeg PH, Van Der Wall E, Van Den Heuvel JJG, Gundy CM, Aaronson NK (2012) Chemotherapy-induced nausea and vomiting in daily clinical practice: a community hospital-based study. Pharm Weekbl 147(42):168–176
14 Börjeson S, Hursti TJ, Tishelman C, Peterson C, Steineck G (2002) Treatment of nausea and emesis during cancer chemotherapy. Discrepancies between antiemetic effect and well-being. J Pain Symptom Manag 24(3):345–58
15. Baba Y, Baba H, Yamamoto S et al (2017) Chemotherapy-induced nausea and vomiting is less controlled at delayed phase in patients with esophageal cancer: a prospective registration study by the CINV Study Group of Japan. Dis Esophagus 30(2):1–7
16 Naik RD, V S, Singh V, Pillai AS, Dhawan D, Bakhshi S (2020) Olanzapine for prevention of vomiting in children and adolescents receiving highly emetogenic chemotherapy: investigator-initiated, randomized, open-label trial. J Clin Oncol 38(32):3785–93
17. Barton DL, Thanarajasingam G, Sloan JA et al (2014) Phase III double-blind, placebo-controlled study of gabapentin for the prevention of delayed chemotherapy-induced nausea and vomiting in patients receiving highly emetogenic chemotherapy, NCCTG N08C3 (Alliance). Cancer 120(22):3575–3583
18. Bossi P, Cortinovis D, Fatigoni S et al (2017) A randomized, double-blind, placebo-controlled, multicenter study of a ginger extract in the management of chemotherapy-induced nausea and vomiting (CINV) in patients receiving high-dose cisplatin. Ann Oncol 28(10):2547–2551
19. Chow KS, Iceton S (1999) Evaluation of a diary card for tailoring antiemetic therapy for children with cancer. Can J Hosp Pharm 52(6):371–377
20. Chua DT, Sham JS, Au GK et al (1996) The antiemetic efficacy of tropisetron plus dexamethasone as compared with conventional metoclopramide-dexamethasone combination in Orientals receiving cisplatin chemotherapy: a randomized crossover trial. Br J Clin Pharmacol 41(5):403–408
21. Cabanillas Stanchi KM, Vek J, Schlegel P et al (2020) Antiemetic prophylaxis with fosaprepitant and granisetron in pediatric patients undergoing allogeneic hematopoietic stem cell transplantation. J Cancer Res Clin Oncol 146(4):1089–1100
22. de Wit R, van den Berg H, Burghouts J et al (1998) Initial high anti-emetic efficacy of granisetron with dexamethasone is not maintained over repeated cycles. Br J Cancer 77(9):1487–1491
23. Di Renzo N, Musso M, Scimè R et al (2020) Efficacy and safety of multiple doses of NEPA without dexamethasone in preventing nausea and vomiting induced by multiple-day and high-dose chemotherapy in patients with non-Hodgkin's lymphoma undergoing autologous hematopoietic stem cell transplantation. Bone Marrow Transplant 55(11):2114–2120
24. Dibble SL, Casey K, Nussey B, Israel J, Luce J (2004) Chemotherapy-induced vomiting in women treated for breast cancer. Oncol Nurs Forum 31(1):E1-8
25. Dibble SL, Isreal J, Nussey B, Casey K, Luce J (2003) Delayed chemotherapy-induced nausea in women treated for breast cancer. Oncol Nurs Forum 30(2):E40–E47
26. Lee J, Dibble SL, Pickett M, Luce J (2005) Chemotherapy-induced nausea/vomiting and functional status in women treated for breast cancer. Cancer Nurs 28(4):249–255
27 Franchi M, Donadello N, Zanaboni F, Tusei A, Scorbati E (1995) Oral ondansetron and intravenous dexamethasone in the

prevention of cisplatin-induced emesis. A phase II trial in women. Oncology 52(6):509–12
28. du Bois A, Vach W, Thomssen C et al (1994) Comparison of the emetogenic potential between cisplatin and carboplatin in combination with alkylating agents. Acta Oncol 33(5):531–535
29. Dupuis LL, Kelly KM, Krischer JP et al (2018) Acupressure bands do not improve chemotherapy-induced nausea control in pediatric patients receiving highly emetogenic chemotherapy: a single-blinded, randomized controlled trial. Cancer 124(6):1188–1196
30. Dupuis LL, Tamura RN, Kelly KM et al (2019) Risk factors for chemotherapy-induced nausea in pediatric patients receiving highly emetogenic chemotherapy. Pediatr Blood Cancer 66(4):e27584
31. Fujii M, Ohno Y, Tokumaru Y et al (2001) Manifest Anxiety Scale for evaluation of effects of granisetron in chemotherapy with CDDP and 5FU for head and neck cancer. Support Care Cancer 9(5):366–371
32. Garcia-del-Muro X, Vadell C, Pérez Manga G et al (1998) Randomised double-blind study comparing tropisetron alone and in combination with dexamethasone in the prevention of acute and delayed cisplatin-induced emesis. Eur J Cancer 34(1):193–195
33. Gershanovich M, Kolygin B, Pirgach N (1993) Tropisetron in the control of nausea and vomiting induced by combined cancer chemotherapy in children. Ann Oncol 4(Suppl 3):35–37
34. Van Belle S, Lichinitser MR, Navari RM et al (2002) Prevention of cisplatin-induced acute and delayed emesis by the selective neurokinin-1 antagonists, L-758,298 and MK-869. Cancer 94(11):3032–3041
35. Hata A, Shiraishi Y, Inui N et al (2022) Exploratory analysis comparing fosnetupitant versus fosaprepitant for prevention of highly emetogenic chemotherapy-induced nausea and vomiting (CINV): a randomized, double-blind, phase 3 study (CONSOLE). Oncol Ther 10(1):253–262
36. Ando Y, Hayashi T, Ito K et al (2016) Comparison between 5-day aprepitant and single-dose fosaprepitant meglumine for preventing nausea and vomiting induced by cisplatin-based chemotherapy. Support Care Cancer 24(2):871–878
37. Hayashi T, Shimokawa M, Matsuo K et al (2021) Chemotherapy-induced nausea and vomiting (CINV) with carboplatin plus pemetrexed or carboplatin plus paclitaxel in patients with lung cancer: a propensity score-matched analysis. BMC Cancer 21(1):74
38. Hayashi T, Shimokawa M, Matsuo K et al (2021) 5HT(3) RA plus dexamethasone plus aprepitant for controlling delayed chemotherapy-induced nausea and vomiting in colorectal cancer. Cancer Sci 112(2):744–750
39. Hayashi T, Shimokawa M, Mizuki F et al (2021) Efficacy of one-day versus multiple-day dexamethasone for chemotherapy-induced nausea and vomiting in lung cancer patients receiving carboplatin-based chemotherapy: a propensity score-matched analysis. Support Care Cancer 29(9):5029–5035
40. Shimokawa M, Hayashi T, Kogawa T et al (2019) Evaluation of combination antiemetic therapy on CINV in patients with gynecologic cancer receiving TC chemotherapy. Anticancer Res 39(1):225–230
41. Hursti TJ, Avall-Lundqvist E, Börjeson S et al (1996) Impact of tumour burden on chemotherapy-induced nausea and vomiting. Br J Cancer 74(7):1114–1119
42. Iihara H, Fujii H, Yoshimi C et al (2016) Control of chemotherapy-induced nausea in patients receiving outpatient cancer chemotherapy. Int J Clin Oncol 21(2):409–418
43. Iihara H, Ishihara M, Fujii H et al (2016) Comparison of the control of nausea and vomiting among several moderately emetic-risk chemotherapy regimens. J Cancer 7(5):569–575
44. Ikari Y, Ogata K, Nakashima Y et al (2014) Safety and pharmacokinetic evaluation of repeated intravenous administration of palonosetron 0.75 mg in patients receiving highly or moderately emetogenic chemotherapy. Support Care Cancer 22(7):1959–64
45. Ikeda M, Yasui M, Fukunaga H et al (2005) Clinical usefulness of oral granisetron hydrochloride for alleviation of delayed nausea and vomiting induced by CPT-11. Eur J Cancer Care (Engl) 14(5):435–439
46. Kunitomi Y, Nakashima M, Seki T, Ide K, Kawakami K (2021) Intergenerational comparison of 5-HT(3)RA in the prevention of chemotherapy-induced nausea and vomiting in gastric cancer patients receiving cisplatin-based chemotherapy: an observational study using a Japanese administrative claims database. Support Care Cancer 29(7):3951–3959
47. Liaw CC, Wang CH, Chang HK, Kao CY, Huang JS (2000) Control of cisplatin-induced emesis with intravenous ondansetron plus intravenous dexamethasone: a crossover study of triple 8-mg dose of ondansetron. Am J Clin Oncol 23(3):253–257
48. Wu CE, Liaw CC (2012) Using aprepitant as secondary antiemetic prophylaxis for cancer patients with cisplatin-induced emesis. Support Care Cancer 20(10):2357–2361
49. Dong X, Huang J, Cao R, Liu L (2011) Palonosetron for prevention of acute and delayed nausea and vomiting in non-small-cell lung carcinoma patients. Med Oncol 28(4):1425–1429
50. Ye P, Pei R, Wang T et al (2022) Multiple-day administration of fosaprepitant combined with tropisetron and olanzapine improves the prevention of nausea and vomiting in patients receiving chemotherapy prior to autologous hematopoietic stem cell transplant: a retrospective study. Ann Hematol 101(8):1835–1841
51. Eisenberg P, MacKintosh FR, Ritch P, Cornett PA, Macciocchi A (2004) Efficacy, safety and pharmacokinetics of palonosetron in patients receiving highly emetogenic cisplatin-based chemotherapy: a dose-ranging clinical study. Ann Oncol 15(2):330–337
52. Maisano R, Spadaro P, Toscano G, Caristi N, Pergolizzi S, Salimbeni V (2001) Cisapride and dexamethasone in the prevention of delayed emesis after cisplatin administration. Support Care Cancer 9(1):61–64
53. Marx W, McCarthy AL, Ried K et al (2017) The effect of a standardized ginger extract on chemotherapy-induced nausea-related quality of life in patients undergoing moderately or highly emetogenic chemotherapy: a double blind, randomized, placebo controlled trial. Nutrients 9(8):867. https://doi.org/10.3390/nu9080867
54. Miyata Y, Yakushijin K, Inui Y et al (2016) A prospective study of the antiemetic effect of palonosetron in malignant lymphoma patients treated with the CHOP regimen. Int J Hematol 104(6):682–691
55. Molassiotis A (2000) A pilot study of the use of progressive muscle relaxation training in the management of post-chemotherapy nausea and vomiting. Eur J Cancer Care (Engl) 9(4):230–234
56. Molassiotis A, Aapro M, Dicato M et al (2014) Evaluation of risk factors predicting chemotherapy-related nausea and vomiting: results from a European prospective observational study. J Pain Symptom Manag 47(5):839–48.e4
57. Molassiotis A, Mok TS, Yam BM, Yung H (2002) An analysis of the antiemetic protection of metoclopramide plus dexamethasone in Chinese patients receiving moderately high emetogenic chemotherapy. Eur J Cancer Care (Engl) 11(2):108–113
58. Molassiotis A, Russell W, Hughes J et al (2014) The effectiveness of acupressure for the control and management of chemotherapy-related acute and delayed nausea: a randomized controlled trial. J Pain Symptom Manag 47(1):12–25
59. Molassiotis A, Yam BM, Yung H, Chan FY, Mok TS (2002) Pretreatment factors predicting the development of postchemotherapy nausea and vomiting in Chinese breast cancer patients. Support Care Cancer 10(2):139–145
60. Münstedt K, Wunderlich I, Blauth-Eckmeyer E, Zygmunt M, Vahrson H (1998) Does dexamethasone enhance the efficacy of

alizapride in cis-platinum-induced delayed vomiting and nausea? Oncology 55(4):293–299
61. Naito Y, Kai Y, Ishikawa T et al (2020) Chemotherapy-induced nausea and vomiting in patients with breast cancer: a prospective cohort study. Breast Cancer 27(1):122–128
62. Olver I, Paska W, Depierre A et al (1996) A multicentre, double-blind study comparing placebo, ondansetron and ondansetron plus dexamethasone for the control of cisplatin-induced delayed emesis. Ondansetron Delayed Emesis Study Group. Ann Oncol 7(9):945–52
63. Olver IN, Grimison P, Chatfield M et al (2013) Results of a 7-day aprepitant schedule for the prevention of nausea and vomiting in 5-day cisplatin-based germ cell tumor chemotherapy. Support Care Cancer 21(6):1561–1568
64. Pater JL, Lofters WS, Zee B et al (1997) The role of the 5-HT3 antagonists ondansetron and dolasetron in the control of delayed onset nausea and vomiting in patients receiving moderately emetogenic chemotherapy. Ann Oncol 8(2):181–185
65. Peterson C, Hursti TJ, Börjeson S et al (1996) Single high-dose dexamethasone improves the effect of ondansetron on acute chemotherapy-induced nausea and vomiting but impairs the control of delayed symptoms. Support Care Cancer 4(6):440–446
66. Poon RT, Chow LW (1998) Comparison of antiemetic efficacy of granisetron and ondansetron in Oriental patients: a randomized crossover study. Br J Cancer 77(10):1683–1685
67. Rodgers C, Kollar D, Taylor O et al (2012) Nausea and vomiting perspectives among children receiving moderate to highly emetogenic chemotherapy treatment. Cancer Nurs 35(3):203–210
68. Sagae S, Ishioka S, Fukunaka N et al (2003) Combination therapy with granisetron, methylprednisolone and droperidol as an antiemetic prophylaxis in CDDP-induced delayed emesis for gynecologic cancer. Oncology 64(1):46–53
69. Babu G, Saldanha SC, Kuntegowdanahalli Chinnagiriyappa L et al (2016) The efficacy, safety, and cost benefit of olanzapine versus aprepitant in highly emetogenic chemotherapy: a pilot study from South India. Chemother Res Pract 2016:3439707. https://doi.org/10.1155/2016/3439707
70. Sorbe B (1993) Tropisetron in the prevention of chemotherapy-induced nausea and vomiting: the Nordic experience. Ann Oncol 4(Suppl 3):39–42
71. Sorbe B, Andersson H, Schmidt M et al (1994) Tropisetron (Navoban) in the prevention of chemotherapy-induced nausea and vomiting–the Nordic experience. Support Care Cancer 2(6):393–399
72. Sorbe B, Högberg T, Himmelmann A et al (1994) Efficacy and tolerability of tropisetron in comparison with a combination of tropisetron and dexamethasone in the control of nausea and vomiting induced by cisplatin-containing chemotherapy. Eur J Cancer 30A(5):629–634
73. Sorbe BG (1994) Tropisetron (Navoban) alone and in combination with dexamethasone in the prevention of chemotherapy-induced emesis: the Nordic experience. Semin Oncol 21(5 Suppl 9):20–26
74. Sorbe BG, Berglind AM, Andersson H et al (1998) A study evaluating the efficacy and tolerability of tropisetron in combination with dexamethasone in the prevention of delayed platinum-induced nausea and emesis. Cancer 83(5):1022–1032
75. Sorbe BG, Högberg T, Glimelius B et al (1994) A randomized, multicenter study comparing the efficacy and tolerability of tropisetron, a new 5-HT3 receptor antagonist, with a metoclopramide-containing antiemetic cocktail in the prevention of cisplatin-induced emesis. Cancer 73(2):445–454
76. Saito Y, Takekuma Y, Takeshita T, Sugawara M (2021) Impact of reducing day 1 dexamethasone dose in anthracycline-containing regimens on acute gastrointestinal symptoms associated with breast cancer treatment. Sci Rep 11(1):23298
77. Tamura K, Aiba K, Saeki T et al (2015) Testing the effectiveness of antiemetic guidelines: results of a prospective registry by the CINV Study Group of Japan. Int J Clin Oncol 20(5):855–865
78. Tan EH, Ang PT, Khoo KS (1994) Control of emesis by intravenous granisetron in breast cancer patients treated with 5-FU, epirubicin and cyclophosphamide. Support Care Cancer 2(3):197–200
79. Vardy J, Chiew KS, Galica J, Pond GR, Tannock IF (2006) Side effects associated with the use of dexamethasone for prophylaxis of delayed emesis after moderately emetogenic chemotherapy. Br J Cancer 94(7):1011–1015
80. Fujiwara S, Terai Y, Tsunetoh S, Sasaki H, Kanemura M, Ohmichi M (2015) Palonosetron versus granisetron in combination with aprepitant for the prevention of chemotherapy-induced nausea and vomiting in patients with gynecologic cancer. J Gynecol Oncol 26(4):311–319
81. Trifilio S, Welles C, Seeger K et al (2017) Olanzapine reduces chemotherapy-induced nausea and vomiting compared with aprepitant in myeloma patients receiving high-dose melphalan before stem cell transplantation: a retrospective study. Clin Lymphoma Myeloma Leuk 17(9):584–589
82. Tsuji Y, Baba H, Takeda K et al (2017) Chemotherapy-induced nausea and vomiting (CINV) in 190 colorectal cancer patients: a prospective registration study by the CINV study group of Japan. Expert Opin Pharmacother 18(8):753–758
83. Ohnishi S, Watari H, Kanno M et al (2017) Additive effect of rikkunshito, an herbal medicine, on chemotherapy-induced nausea, vomiting, and anorexia in uterine cervical or corpus cancer patients treated with cisplatin and paclitaxel: results of a randomized phase II study (JORTC KMP-02). J Gynecol Oncol 28(5):e44
84. Sun Y, Zheng Y, Yang X et al (2021) Incidence of chemotherapy-induced nausea and vomiting among cancer patients receiving moderately to highly emetogenic chemotherapy in cancer centers in Sichuan. China J Cancer Res Clin Oncol 147(9):2701–2708