2023 updated MASCC/ESMO consensus recommendations: controlling nausea and vomiting with chemotherapy of low or minimal emetic potential

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Abstract

Purpose: Review the literature to update the MASCC guidelines from 2016 for controlling nausea and vomiting with systemic cancer treatment of low and minimal emetic potential.

Methods: A working group performed a systematic literature review using Medline, Embase, and Scopus databases between June 2015 and January 2023 of the management of antiemetic prophylaxis for anticancer therapy of low or minimal emetic potential. A consensus committee reviewed recommendations and required a consensus of 67% or greater and a change in outcome of at least 10%.

Results: Of 293 papers identified, 15 had information about managing systemic cancer treatment regimens of low or minimal emetic potential and/or compliance with previous management recommendations. No new evidence was reported that would change the current MASCC recommendations. No antiemetic prophylaxis is recommended for minimal emetic

potential therapy, and single agents recommended for low emetic potential chemotherapy for acute emesis, but no prophylaxis is recommended for delayed emesis. Commonly, rescue medication includes antiemetics prescribed for the next higher level of emesis.

Conclusion: There is insufficient data to change the current guidelines. Future studies should seek to more accurately determine the risk of emesis with LEC beyond the emetogenicity of the chemotherapy to include patient-related risk assessment.

Keywords: Guidelines; Nausea; Vomiting; Chemotherapy; Low emetogenicity; Minimal emetogenicity

Introduction

The major predictor used to determine whether a patient will experience nausea and/or vomiting after receiving systemic therapy for cancer has been the emetic potential of the therapy. With drugs classified as having minimal emetic potential, the risk is < 10%, while those classified as low emetogenic potential (LEC) had a risk of emesis of 10 to 30% if no antiemetics are given [1, 2].

Many oral agents fit into these categories, and many of the new targeted and immunotherapies have been classified as having minimal risk of emesis or LEC [3, 4]. However, there are many agents where there is a lack of data to be able to classify their emetogenicity, and more research is needed that specifically documents the risk of nausea and vomiting over time.

Comparing recent updated guidelines of ASCO and NCCN with 2016 MASCC/ESMO guidelines shows no change in the recommendations of no prophylactic antiemetics for systemic anticancer agents with minimal risk. For low-risk regimens, ASCO recommends single-agent 5HT3 receptor antagonists or steroids. In contrast, NCCN and MASCC/ESMO also include other single agents, such as dopamine antagonists for acute emesis but no additional prophylaxis for delayed emesis [3, 5].

This paper reviews the recent literature to update the previous MASCC guidelines of 2016 for controlling nausea and vomiting with systemic cancer treatment of minimal emetic potential and LEC [6].

Methods

Searches were performed in the Medline, Embase, and Scopus databases, for papers published between June 1, 2015, and June 2022 and then extended to January 2023. The search terms were cancer AND antiemetics AND low OR minimal emetogenicity AND cancer chemotherapy, and filters restricting papers to humans, English language, and adults 19 + years. Papers must report new information management of antiemetics for cancer therapy of low to minimal risk or/and compliance with management guidelines. To mitigate the risk of bias, two reviewers (IO and RCS) assessed the full-text papers and identified the relevant papers for the review, which were shared with the seven members of the working group who analyzed the content of the manuscripts to enable recommendations to be made. The systematic literature review followed the PRISMA guidelines for reporting [7].

The recommendations were presented to the whole consensus committee, which discussed, modified, and finally approved the recommendations.

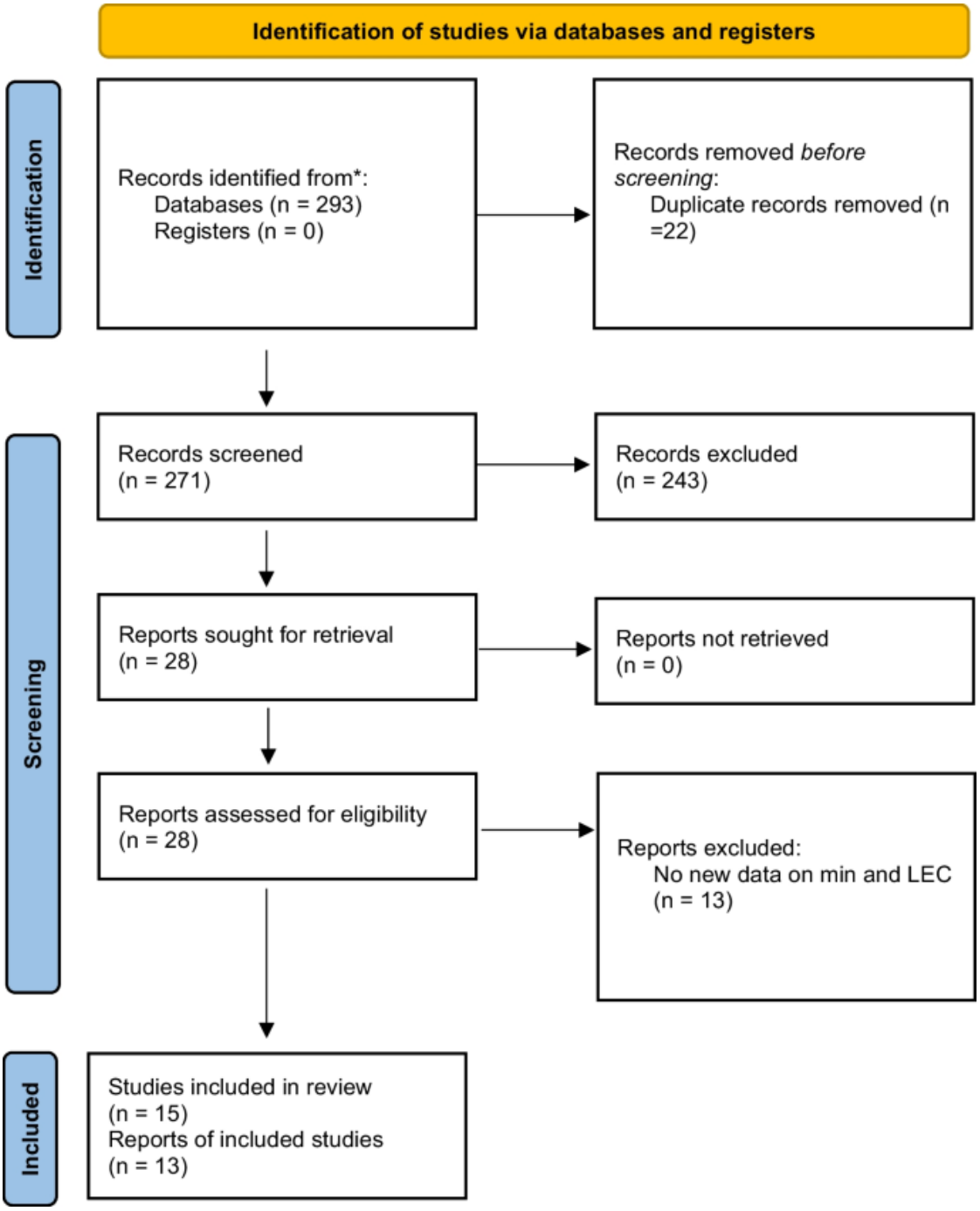

Fig. 1. PRISMA flow diagram

Results

Of 293 papers identified from the three databases, 15 were judged relevant with information about the management of systemic cancer treatment regimens of low or minimal emetic potential and/or compliance with previous management recommendations (Fig. 1). No new evidence was reported that would change the current MASCC recommendations for the management of systemic cancer treatment of low or minimal emetic potential.

However, several issues were raised because it was clear that some patients were being overtreated, usually with regimens recommended for moderately emetogenic chemotherapy. Such regimens are also employed to rescue those patients who experienced emesis despite receiving guideline approve antiemetics. Other patients experienced emesis and were therefore undertreated despite complying with recommendations [8, 9]. This led to a discussion about identifying higher-risk patients and what treatment they should receive.

Recommendations

Prevention of acute nausea and vomiting in patients receiving low emetogenic chemotherapy

A single antiemetic agent, such as dexamethasone, a 5-HT3 receptor antagonist, or a dopamine receptor antagonist, such as metoclopramide, may be considered for prophylaxis in patients receiving chemotherapy of low emetic risk.

Level of evidence: II.

Grade of recommendation: B

Prevention of acute nausea and vomiting in patients receiving minimally emetogenic chemotherapy

No antiemetic should be routinely administered before chemotherapy to patients without a history of nausea and vomiting.

Level of evidence: IV.

Grade of recommendation: D

Prevention of delayed nausea and vomiting in patients receiving low or minimally emetogenic chemotherapy

No antiemetic should be administered for the prevention of delayed nausea and vomiting induced by low or minimal emetogenic chemotherapy.

Level of evidence: IV.

Grade of recommendation: D

Discussion

Although few studies have provided evidence for strategies for managing antiemesis with regimens of low and minimal emetic potential and, therefore, no change in the antiemetic recommendations, several recent studies report on compliance with current guidelines, which highlight the real-world antiemetic usage in these groups.

Major causes of overuse of antiemetics occurred with LEC where two antiemetic agents, often a 5-hydroxytryptamine type 3 receptor antagonist (5HT3RA) and a steroid, were used when the recommendation was just for a single agent, and in the minimal emetic potential where single agents or a 5HT3RA and steroid were used where no prophylactic antiemetics were recommended [9,10,11,12]. Under-usage usually occurred where steroids were omitted in patients receiving low emetic potential chemotherapy [13]. Concordance with guidelines can change as guidelines are updated, as occurred with low emetic risk chemotherapy when the ASCO guidelines changed between 2006 and 2017, allowing 5HT3 receptor antagonists, and concordance in a Japanese study increased from 5.9 to 57.9% reflecting this change [13].

Studies have had mixed outcomes regarding whether guideline compliance affects chemotherapy-induced nausea and vomiting (CINV) outcomes. An international review and, more recently, Kandasamy et al., in an Indian study, found that clinicians' guideline adherence was greater when the antiemetics used in practice complied with antiemetic guidelines. Also, the CINV outcomes were better [14, 15]. However, Caracuel et al., in a study from Spain, and Nikbakht et al. from Iran could not show that antiemetic guideline adherence reduced CINV [10, 12]. Indeed, though, cost-effectiveness increased from reducing the overuse of antiemetics [9].

Can guideline adherence be improved? Araz M et al., surveying the Turkish Oncology Group, did not find any characteristic of the practitioners, age, gender, experience, or academic status which predicted adherence to guidelines for low acute or delayed emetic chemotherapy [16]. Active education was proposed to increase guideline adherence. Paradoxically, education increased the improper prescribing of 5HT3RA for the prophylaxis of low emetic chemotherapy in an Italian study [17]. In contrast, Grunberg et al. on reviewing barriers to implementation of antiemetic guidelines concluded that the use of a local opinion leader or an in-house education program only had a short-term impact on practice [18]. Similarly, the ASCO Choosing Wisely guidelines only had a short-term impact on antiemetic prescribing except in the low-risk intravenous group, where it was more prolonged, but not in the antiemetic usage in the minimal-risk group [8]. Affronti et al., however, found that standardized order sets for the antiemetics with audit feedback significantly improved compliance in patients with glioma [19].

A major focus of recent studies is whether in determining antiemetic usage other risk factors than the emetogenicity of the chemotherapy should be considered. This has been the case with the selection of specific antiemetics. For example, in treating pancreatic cancer, steroid exposure may need to be minimized to avoid the development of diabetes [20]. In choosing a suitable regimen, salvaging low- and minimal-risk regimens has involved moving to the drug recommended for the next higher level of emesis [21]. There are successful salvage regimens for low emetic chemotherapy both in the acute and delayed phase, which spare steroids by using palonosetron. This suggests that this single agent could be used for low-emetic chemotherapy when steroid sparing is desirable [22, 23]. Likewise, olanzapine has been shown to be effective in patients with refractory LEC [24].

A significant advancement in reducing the overuse or underuse of antiemetics with low and minimal risk. Chemotherapy would be the ability to predict the risk of emesis in individual patients more accurately. This may entail adding personal risk factors to the emetic risk of the chemotherapy. Dranitsaris and Petrella published a prediction tool for identifying patients at high risk for nausea and vomiting after chemotherapy analyzing multiple factors, but their application is complex in routine practice and, as it is different for acute and delayed emesis, it is even less practical [25, 26]. A prospective Japanese study of 222 patients undergoing LEC showed, in a multivariate analysis, that a prior history of nausea and receiving chemotherapy other than taxanes were independent risk factors associated with nausea and vomiting [27]. This study did not show younger age or sex to be a risk factor.

In a study of 95 patients, 26.3% received LEC, and 40% of those experienced nausea. We need to better identify those patients with a risk of nausea and achieve better control in LEC patients. The patient characteristics which increased the risk of nausea in this study were being female, having an age of less than 60 years, and having a history of motion sickness or morning sickness [28]. Investigators in clinical trials should report levels of nausea and vomiting even when grade 1 or 2 to ascertain the level of prophylactic antiemetics to be prescribed more accurately.

Conclusions

There is insufficient data to change the guidelines for controlling nausea and vomiting with chemotherapy of low or minimal emetic potential. No prophylactic antiemetics are recommended for patients receiving chemotherapy of minimal emetic potential. Single agents are recommended for acute emesis but not to prevent delayed emesis with chemotherapy of low emetic potential. More data should be collected on the emetogenicity of new agents, particularly oral targeted therapies and immunotherapy. Future studies should seek to more accurately determine the risk of emesis with LEC beyond the emetogenicity of the chemotherapy to include patient-related risk assessment.

Contributions

The initial draft was written by IO and all authors revised it critically for its intellectual content.

All authors reached agreement on the recommendations, are accountable for the accuracy and integrity of the work, and have approved the version to be published.

Conflict of interest

Schwartzberg COI: Consultant, Helsinn, GlaxoSmithKline, Pfizer.

The other authors have no relevant financial or non-financial interests to declare.

Data Availability

All data supporting the findings of this study are available within the paper and its publicly available references.

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