Abstract:

Background: Nausea and vomiting are a common clinical symptom in the advanced cancer patient. Pharmacologic management is important. Evidence for drug choices and guidelines are needed to help clinicians manage nausea and vomiting in this population.

Methods: Evidence from a systematic review published in 2010, initial MASCC guidelines developed from a systematic review of literature to 2015, and a new systematic review of randomized trials published between 2015 and February 2, 2021, was combined to establish a new guideline.

Results: A search of the literature between 2015 and February 2, 2021, revealed 257 abstracts of which there was one systematic review and 4 randomized trials which were used to modify the guideline. The new guideline is as follows: First Line: Metoclopramide (II) multiple small RCTs including a placebo-controlled trial, haloperidol (II) multiple non-placebo-controlled RCTs, high consensus. Second line: Methotrimeprazine (II) 1 well-powered non-placebo-controlled RCT, olanzapine (II) 1 placebo-controlled pilot RCT, high consensus. Third line: Tropisetron (II) large unblinded lower quality non-placebo-controlled RCT, levosulpiride (II) 1 blinded non-placebo-controlled pilot RCT, high consensus.

Discussion: Haloperidol, metoclopramide, methotrimeprazine, olanzapine tropisetron, and levosulpiride have been antiemetics used in randomized trials with antiemetic activity demonstrated. There are only three placebo-controlled randomized trials we could find in our literature review. Placebo responses varied significantly between two randomized trials. More randomized placebo-controlled trials with either metoclopramide or haloperidol rescue are needed to clarify antiemetic choices in advanced cancer.

Conclusion: First-line antiemetics for nausea and vomiting in advanced cancer are metoclopramide and haloperidol, and second-line medications are methotrimeprazine and olanzapine.
Guideline Statements:
Metoclopramide is first-line antiemetic
Level of evidence – II; Grade of recommendation – A; Guideline – Recommendation

Haloperidol is a first-line antiemetic
Level of evidence – II; Grade of recommendation – A; Guideline – Recommendation

Methotrimeprazine is a second-line antiemetic
Level of evidence – II; Grade of recommendation – B; Guideline – Recommendation

Olanzapine is a second-line antiemetic
Level of evidence – II; Grade of recommendation – B; Guideline – Recommendation

Levosulpiride is a third-line antiemetic
Level of evidence – III; Grade of recommendation – B; Guideline – Suggested use

Tropisetron is a third-line antiemetic
Level of evidence – II; Grade of recommendation – B; Guideline – Suggested use

Levels of Evidence and Grading/Categories of Guidelines:

Level I: Evidence obtained from meta-analysis of multiple, well-designed, controlled studies; randomized trials with low false-positive and false-negative errors (high power).
Level II: Evidence obtained from at least one-well designed experimental study; randomized trials with high false-positive and/or false-negative errors (low power).
Level III: Evidence obtained from well-designed, quasi-experimental studies, such as nonrandomized, controlled single-group, pretest-posttest comparison, cohort, time, or matched case-control series.
Level IV: Evidence obtained from well-designed, non-experimental studies, such as comparative and correlational descriptive and case studies.
Level V: Evidence obtained from case reports and clinical examples.

Grade A: Evidence of type I or consistent findings from multiple studies of type II, III, or IV
Grade B: Evidence of types II, III, or IV and findings are generally consistent
Grade C: Evidence of types II, III, or IV and findings are inconsistent
Grade D: Little or no systematic empirical evidence

Recommendation: Reserved for guidelines that are based on Level I or Level II evidence.
Suggestion: Used for guidelines that are based on Level III, Level IV, and Level V evidence; this implies panel consensus on the interpretation of this evidence.
**No guideline possible:** Used when there is insufficient evidence on which to base a guideline; this implies (1) that there is little or no evidence regarding the practice in question, or (2) that the panel lacks consensus on the interpretation of existing evidence.