Supportive Care for Patients With Cancer

Barriers in Achieving a Balance Between Optimizing Outcomes and Minimizing Side Effects With Chemotherapy-Induced Nausea and Vomiting

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Conflicts of Interest

Teresa Scardino has acted as a speaker for Heron Therapeutics (formerly A.P. Pharma)

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Learning Objective

Apply current evidence regarding drug management of chemotherapy-induced nausea and vomiting to the advanced practitioner role

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In terms of chemotherapy-induced nausea and vomiting (CINV), the most distressing and poorly controlled manifestation is:

A. Acute vomiting
B. Acute nausea
C. Delayed vomiting
D. Delayed nausea

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CINV Subtypes

- **Acute:** Occurring within 24 hr
- **Delayed:** Occurring between 24 hr and 5 days
- **Breakthrough:** Occurring despite prophylactic treatment
- **Anticipatory:** Triggered by taste, odor, memories, visions, or anxiety related to chemotherapy
- **Refractory:** Occurring during subsequent cycles when antiemetics have failed in earlier cycles

Gill, P., et al. (2006). *Oncology*, 1482-1496.

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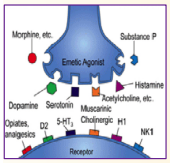
Pathophysiology

Brainstem Vomiting Center
- Area postrema
  - Chemoreceptor trigger zone (CTZ)
- Nucleus tractus solitarius
- Dorsal motor nucleus of the vagus nerve

- **Substance P/neurokinin$_1$ (NK$_1$) receptors**
- Serotonin/5-HT$_3$ receptors

GI Vagal Afferent Nerve Fibers
- **Serotonin/5-HT$_3$ receptors**
- Substance P/NK$_1$ receptors



Aziz, F., (2012). *Ann Palliat Med*, 1(2), 130-136 (left); www.nomex.com (right).

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CINV Assessment Tool

MASCC Antiemesis Tool

- If and how much CINV
- Developed in 2004 by nurses, physicians, and pharmacists
- Validated
- Easy to use

http://www.mascc.org/mat

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Personal Risk Factors

- Female
- Patient age (under 55 years old)
- History of light alcohol use
- History of previous CINV
- History of nausea and vomiting during pregnancy
- History of motion sickness
- Anxiety or depression
- Anticipation of CINV
- Gastroparesis among patients with upper GI tract tumors

Gill, P., et al. (2006). *Oncology,* 1482-1496.

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Adverse Effects of CINV

- Dehydration
- Malnutrition
- Electrolyte abnormalities
- Decreased functional status
- Withdrawal from treatment
- Can lead to anticipatory nausea, which can be refractory to treatment
- Increased costs
  - *Additional antiemetics
  - *ER visits
  - *Unscheduled office visits
  - *Hospitalizations

Haiderali, A., et al. (2011). *Support Care Cancer, 19,* 843-851.

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Ms. L is a 28-year-old woman with newly diagnosed stage IIa, classic Hodgkin lymphoma who will start standard ABVD (doxorubicin, bleomycin, vinblastine, dacarbazine) in the infusion center tomorrow. Prior to writing her chemotherapy orders, you review your initial consult note and recall that she suffered significant morning sickness during her pregnancy and also has motion sickness during car rides. She is extremely anxious about suffering nausea and vomiting with chemotherapy.

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Which preventive CINV medications would you order prior to starting ABVD?

A. Because ABVD is a low emetogenic (LEC) regimen, you order an oral agent (i.e., a 5-HT_3 receptor antagonist, dexamethasone, prochlorperazine or metoclopramide ± lorazepam and ± an H2 blocker or a PPI).
B. ABVD is a highly emetogenic chemotherapy (HEC) regimen, so you prescribe fosaprepitant 150 mg IVPB, dexamethasone 12 mg IVPB, and palonosetron 250 µg (0.25 mg) IVPB.
C. ABVD is considered a moderately emetogenic chemotherapy (MEC) regimen, so you order dexamethasone and a 5-HT_3 antagonist.

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Evidence-Based Guidelines for the Prevention of CINV

- Most relevant guidelines
  - MASCC (2013)
  - NCCN (2014)
  - ASCO (2012)
- All stratify emetogenicity of chemo agents
- All recommend prevention approaches based on risk stratification

MASCC Antiemetic Guidelines 2013, www.mascc.org; NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), Antiemesis 2014, www.nccn.org; ASCO Antiemesis Guidelines 2012, www.asco.org.

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Emetogenic Potential of Chemotherapy Agents

High (HEC), ≥ 90%

- Cisplatin
- Dacarbazine
- Cyclophosphamide (> 1,500 mg/m^2)
- Carmustine (> 250 mg/m^2)
- ABVD
- MOPP/COPP/BEACOPP
- CBV
- VIP
- BEP
- AC

Moderate (MEC), 30%–90%

- Carboplatin
- Methotrexate
- Doxorubicin
- Docetaxel
- Paclitaxel
- Etoposide
- Ifosfamide
- Cyclophosphamide (≤ 1,500 mg/m^2)
- CHOP/CHOP-R

Basch, E., et al. (2011). *J Clin Oncol*, 29, Abstract 4189.

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Emetogenic Potential of Chemotherapy Agents

Low (LEC), 10%–30%

- Bortezomib
- Cytarabine ≤ 1,000 mg/m^2
- Docetaxel
- Etoposide
- Methotrexate ≤ 1 g
- Paclitaxel
- Temsirolimus
- Topotecan
- Vorinostat

Minimal, < 10%

- Bevacizumab
- Bleomycin
- Busulfan
- Fludarabine
- Rituximab
- Vinblastine
- Vincristine
- Vinorelbine

Basch, E, et al. (2011). *J Clin Oncol*, 29, Abstract 4189.

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NCCN Guidelines: Acute Emesis Prevention

EMESIS RISK GROUP	ANTIEMETICS
HEC	5-HT$_3$ RA* + dexamethasone + NK1 RA, ± lorazepam, H2B, PPI *or* Olanzapine + palonosetron + dexamethasone, ± lorazepam, H2, PPI
MEC	5-HT$_3$ RA* + dexamethasone ± NK1 RA, ± lorazepam, H2, PPI *or* Olanzapine + palonosetron + dexamethasone, ± lorazepam, H2, PPI
LEC	Dexamethasone or metoclopramide or prochlorperazine *or* 5-HT$_3$ RA, ± lorazepam, H2, PPI
Minimal	No routine prophylaxis

*Palonosetron preferred
RA = receptor antagonist; PPI = proton pump inhibitor

Adapted from NCCN. (2014). NCCN Clinical Practical Guidelines in Oncology (NCCN Guidelines®), Antiemesis. Version 1.2014.

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NCCN Guidelines: Delayed Emesis Prevention

EMESIS RISK GROUP	ANTIEMETICS
HEC	5-HT_3 RA* + dexamethasone + NK1 RA, ± lorazepam, H2, PPI *or* Olanzapine-containing regimen
MEC	5-HT_3 RA or dexamethasone *or* NK1 RA, ± dexamethasone ± lorazepam, H2, PPI *or* olanzapine-containing regimen
LEC	Use breakthrough treatment guidelines
Minimal	No routine prophylaxis

*Palonosetron preferred

Adapted from NCCN. (2014). NCCN Clinical Practical Guidelines in Oncology (NCCN Guidelines®), Antiemesis. Version 1.2014.

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NCCN Guidelines for Breakthrough CINV

- Difficult situation as ongoing CINV is challenging to reverse and prevention is easier
- Around the clock rather than prn antiemetics
- Curtailed regimen
  - Oral, IV, rectal, nasal spray, patch
  - Multiple agents
  - Alternating schedules
  - Alternating routes
- Metoclopramide, olanzapine, scopolamine patch, corticosteroids, lorazepam, PPI, H2 blockers, dronabinol

NCCN. (2014). NCCN Clinical Practical Guidelines in Oncology (NCCN Guidelines®), Antiemesis. Version 1.2014.

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NCCN Guidelines for Anticipatory CINV

- 20% of patients will experience anticipatory CINV when proper prevention of CINV is implemented
- Anxiolytics
  - Lorazepam
  - Alprazolam

NCCN. (2014). NCCN Clinical Practical Guidelines in Oncology (NCCN Guidelines®), Antiemesis. Version 1.2014.

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Multiday Emetogenic Chemotherapy Regimens

- At risk based on the emetogenic potential of the individual chemo agents and their sequence
- Difficult to recommend a specific regimen for each day
- Depends on specific regimen and emetogenic potential of the last agent given
- In general a combination of 5-HT_3 antagonist with dexamethasone daily has been the standard treatment
- NK-1 antagonist may be used with HEC with a significant risk of developing delayed nausea

NCCN. (2014). NCCN Clinical Practical Guidelines in Oncology (NCCN Guidelines®), Antiemesis. Version 1.2014.

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Comparing and Contrasting Guidelines

- NCCN added alternative with olanzapine-containing regimen for HEC/MEC, acute, and delayed CINV
- NCCN guidelines recommend using aprepitant for MEC (based on evidence), but the others do not due to limited evidence
- NCCN gives the option to add on lorazepam, H2, or PPI in the acute and delayed phases

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INSPIRE Study

- Measured antiemetic guidelines consistency and incidence of CINV
- 1,295 patients enrolled
- Guidelines-consistent prophylaxis was ~ 57%
- For HEC, guidelines consistency increased from ~ 29% to 90% with corticosteroids on days 2−4
- For MEC, guidelines consistency increased from ~ 73% to 99% with NK-1 RA
- Over 5 days post-chemotherapy, the incidence of no CINV was significantly higher in the guidelines-consistent group
- Concluded that increased adherence to antiemetic guidelines significantly reduces CINV after HEC/MEC

Gilmore, J., et al. (2014). *J Oncol Pract*. http://dx.doi.org/10.1200/JOP.2012.000816

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Barriers to Treatment

- Inaccurate provider perception of CINV
  - 75% underestimated incidence
- Poor HCP adherence to published guidelines on CINV management
- Poor patient adherence
- Patient financials
- Patient extent of health-care coverage

Grunberg, S., et al. (2004). *Cancer, 100*, 2261-2268.

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Conclusion

- Role of the advanced practitioner in optimizing treatment of CINV
  - Enhancing practitioner education
  - Guideline adherence
  - Accurate assessment of physical, psychosocial, and financial needs of the patient
  - Multidisciplinary collaboration with clinicians
  - Patient and family education

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Final Thought

The most significant cost of inadequately controlled CINV is patient suffering.

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