Chemotherapy-Induced Nausea and Vomiting (CINV): Strategies for Optimizing Oncology Nursing Care

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Educational Objectives

• Describe the primary pathways that result in CINV
• Identify appropriate therapeutic options to address specific types of CINV
• Utilize educational tactics to help patients improve CINV outcomes
Breast Cancer Case Study

• 58 y/o female presents to oncology clinic after mastectomy with lymph node dissection. She had a 2.3cm ductal carcinoma of the L breast with 2 positive axillary nodes. Her tumor is HER2 negative, ER/PR +.

• PET/CT scan and MRI brain are negative for metastases.

• She is a married mother of 2 grown children and she has a 3-year-old grandson whom she watches 2 days a week to help her daughter with childcare expenses.
Breast Cancer Case Study cont.

• PMH: minor HTN, thyroid cancer in her 20’s, post thyroidectomy
• PSH: she smoked 1 PPD for 15 years, quit at age 30, and drinks socially, about one drink per week
• She is depressed about diagnosis, anxious about side effects of chemotherapy including nausea and hair loss
• Also concerned about her ability to care for her grandson 2 days a week (Thursdays and Fridays)
Breast Cancer Case Study cont.

<table>
<thead>
<tr>
<th>Patient will receive three sequential chemotherapy regimens</th>
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<tbody>
<tr>
<td><strong>Initial treatment</strong></td>
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<tr>
<td>Dose dense doxorubicin (60mg/m²) with cyclophosphamide</td>
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<tr>
<td>(600mg/m²) every 2 weeks for 4 cycles</td>
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Scope of the Problem: Chemotherapy-Induced Nausea and Vomiting (CINV)

- CINV is among the most common, unpleasant, and feared side effects of chemotherapy.
- Approximately 70% - 80% of all patients who receive chemotherapy experience nausea or vomiting.
- CINV can be prevented in 70% - 80% of patients with the application of evidence-based treatment guidelines.

Poorly Controlled CINV

• Leads to:
  – Weight loss (or gain)
  – Life threatening complications: dehydration, electrolyte imbalances, GI perforation, bleeds, aspiration
  – Decrease in quality of life
  – Anticipatory CINV

Reported Negative Impact of CINV on Daily Activities

- Eating Meals: 47%
- Household Tasks: 35%
- Running Errands: 33%
- Time with Friends: 33%
- Work/Employment: 23%
- Caring for Others: 19%
- Taking medications: 12%

CINV
Risk Factors
Factors Contributing to CINV: Chemotherapy

Emetogenic Potential of Agents

<table>
<thead>
<tr>
<th>Emetogenic Potential</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>High</td>
<td>&gt;90%</td>
</tr>
<tr>
<td>Moderate</td>
<td>30% - 90%</td>
</tr>
<tr>
<td>Low</td>
<td>10% - 30%</td>
</tr>
<tr>
<td>Minimal</td>
<td>&lt;10%</td>
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High Emetogenic Chemotherapy (HEC) >90% Without Antiemetics

- AC combination
  - Doxorubicin or epirubicin with cyclophosphamide
- Cisplatin (any dose)
- Carmustine >250 mg/m²
- Cyclophosphamide ≥1,500 mg/m²

- Dacarbazine
- Doxorubicin ≥60mg/m²
- Epirubicin >90mg/m²
- Ifosfamide >2g/m² per dose
- Mechlorethamine
- Streptozotocin

Moderate Emetogenic Chemotherapy (MEC) 30% – 90% Without Antiemetics

- Aldesleukin >12-15 million IU/m²
- Amifostine >300mg/m²
- Arsenic trioxide
- Azacitidine
- Bendamustine
- Busulfan
- Carboplatin*
- Carmustine* ≤250mg/m²
- Clofarabine
- Cytarabine >200 gm/m²
- Cyclophosphamide <1,500 mg/m²
- Dactinomycin*
- Daunirubicin*
- Doxorubicin* <60mg/m²
- Epirubicin* <90mg/m²
- Idarubicin
- Ifosfamide* <2000mg/m²
- Interferon alfa ≥10 million IU/m²
- Irinotecan*
- Melphalan
- Methotrexate* ≥250mg/m²
- Oxaliplatin
- Temozolomide

*May be highly emetogenic in certain patients

Factors Contributing to CINV: Patient

- Female$^{1,2}$
- Age <50 years$^2$
- History of low alcohol intake (<1.5oz/day)$^{1,2}$
- History of prior CINV$^{1,2}$
- History of motion sickness$^2$
- History of morning sickness$^2$
- Anxiety$^3$

Breast Cancer Case Study

- Risk factors for our patient:
  - AC regimen, high risk chemotherapy
  - Female
  - Over age 50, though not much
  - Anxiety

- What are her social barriers and issues?
  - Active lifestyle
  - Cares for grandson
The Pathophysiology of CINV

• A complex interaction involving receptors and neurotransmitters located in
  – Brain stem
  – Gastrointestinal tract
  – Cortical and limbic systems

The Pathophysiology of CINV: GI Enteric Nervous System/Peripheral

- Vagal and sympathetic: Visceral pathways
- Receptors in close proximity to the enteroendocrine cells of the GI mucosa and proximal small intestine
- Stimulated by direct mucosal or blood borne mechanisms
- Afferent impulse terminates in the NTS
- Primarily mediated by 5-HT3 and NK-1
- Vagal: Dependent pathway is primary mechanism for acute CINV

Neurotransmitters Involved in Vomiting

How will we prevent CINV in our patient?
Goals of Treatment

- Prevention, rather than reaction, is key
- Minimize CINV by using optimal medications
- Choose regimen that will minimize side effects of the antiemetics in each particular patient
- Have rescue medications on hand at home
Acute first 24 hours
- Mediated primarily by serotonin
- Related to emetogenic potential of the regimen
- Intensity peaks at 5 - 6 hours
- Pharmacological management is primary strategy

Delayed 24 hours to 7 days
- Substance P plays the primary role
- Effective management of acute CINV will reduce the severity
- More common with long half-life
- Cisplatin is the most common drug with peak intensity at 48 - 72 hours

Anticipatory – Occurs before drug administration
- Experiential; more difficult to control, ongoing
- Nausea is more common than vomiting
- Effective treatment of acute and delayed CINV is key

Refractory and breakthrough
- Ongoing; may be a result of underlying processes
Breast Cancer Case Study cont.

• What antiemetic regimen will be right for our patient receiving dose dense AC?
  – Following the guidelines, NCCN

• What prescriptions should she have at home for CINV?
History of Antiemetics


*NK₁ receptor antagonists approved with steroids and 5-HT₃ RA


Phenothiazines

High-dose metoclopramide with or without steroids

5-HT₃ receptor antagonists

Ondansetron 1991
Granisetron 1993

Steroids

Palonosetron 2003
Granisetron Transdermal 2008

Aprepitant Oral 2003
Fosaprepitant IV 2008

NK₁ receptor antagonists

Netupitant/Palonosetron PO 2014

Rolapitant 2015
### Classes of Agents for CINV Prevention

<table>
<thead>
<tr>
<th>5-HT3 RA</th>
<th>NK-1 RA</th>
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<tbody>
<tr>
<td>– Dolasetron</td>
<td>– Aprepitant</td>
</tr>
<tr>
<td>– Granisetron</td>
<td>– Fosaprepitant</td>
</tr>
<tr>
<td>– Ondansetron</td>
<td>– Netupitant</td>
</tr>
<tr>
<td>– Palonosetron</td>
<td>• combination tab with palonosetron</td>
</tr>
<tr>
<td></td>
<td>– Rolapitant</td>
</tr>
<tr>
<td></td>
<td>• approved Sept. 2015</td>
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Other Classes of Agents for CINV

• Corticosteroids: dexamethasone is most used
• Metoclopromide
• Benzodiazepines: lorazepam, alprazolam, midazolam
• Dopamine RAs: prochlorperazine, haloperidol
• Cannabinoids: dronabinol, nabilone
Newer Agents: Netupitant/Palonosetron (NEPA)

- First combined tablet of an NK-1 RA netupitant (300mg) with oral 5-HT3 RA palonosetron (0.5mg)
  - One capsule taken 1 hour prior to chemotherapy (with or without food)
- 3 large trials looked at NEPA + dex in highly and moderately emetogenic chemotherapy regimen vs oral palonosetron + dex
  - NEPA + dex showed improvement in CR* in treating CINV over oral palonosetron + dex

* CR = complete response

Newer Agents: NEPA (continued)

• Safety study
  – NEPA + dex vs. oral palonosetron + dex + aprepitant
  – Comparable safety profile in both arms
• Offers a different route for potential convenience for the patient as well as infusion suite
• NEPA is a tablet and CYP 3A4 inhibitor so should be used cautiously with other drugs metabolized this way.
  – Dexamethasone is example, should reduce the dose of dex when given with NEPA

Newly Approved Agent: Rolapitant

• Oral NK-1 RA approved Sept. 2015 by FDA for treatment of CINV
  – 180-hr half-life (7.5 days)
• TRIaled with IV granisetron/dex vs granisetron/dex alone
  – Found to be superior in arm with the rolapitánt
• Does not inhibit CYP 3A4 pathway, so good to avoid drug-drug interactions
• May be good for multiday regimens as well given long half-life

Old Drug, New Use: Olanzapine

- Used as atypical antipsychotic, but exhibits antiemetic properties
- Targets multiple receptors: dopaminergic, serotonergic, adrenergic, histaminergic, muscarinic
- Trialed and found to be comparable in the prophylactic and breakthrough settings
- Some side effects of somnolence, hypotension, constipation, dizziness, fatigue, dyspepsia and restlessness
  - None were grade 3 or 4 toxicities

CINV Guidelines

- Guidelines are based on evidence, formulated by experts who review clinical trials
- NCCN, ASCO, MASCC/ESMO, ONS
- Inadequate treatment of CINV leads to higher healthcare costs and patient suffering
- Adherence to guidelines leads to better outcomes for CINV

### NCCN Guidelines for HEC

**Option A**
- NK-1 RA (aprepitant tri-pack or fosaprepitant)
- 5-HT3 RA (dolasetron/granisetron/ondansetron/palonosetron)
- Dexamethasone 12mg PO/IV day 1
  - Dexamethasone 8mg day 2-4

**Option B**
- Netupitant/palonosetron tablet day 1
- Dexamethasone 12mg PO/IV day 1
  - Dexamethasone 8mg day 2-4

**Option C**
- Olanzapine 10mg day 1-4
- Palonosetron IV
- Dexamethasone 20mg IV day 1
Breast Cancer Case Study cont.

• Want to be sure she is receiving NK-1 RA + 5-HT3 RA + Dex
  – Oral regimen versus IV regimen?
  – Long acting NK-1 RA and/or long acting 5-HT3 RA
  – Dex taper per guidelines, or not?

• Want to be sure she has something at home for breakthrough CINV

• How will we assess if our antiemetic treatment is effective?

• What possible side effects could she have from the antiemetics?
### Patient Barriers and Misconceptions to CINV treatment

<table>
<thead>
<tr>
<th>CINV is part of treatment; don’t want to be a complainer</th>
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<tbody>
<tr>
<td>Don’t want to be perceived as weak; need to be strong</td>
</tr>
<tr>
<td>Do not want to take more medications; fear side effects</td>
</tr>
<tr>
<td>Feared cost</td>
</tr>
<tr>
<td>Communication barriers with the oncology provider</td>
</tr>
<tr>
<td>Fear healthcare provider may withhold chemotherapy</td>
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<tr>
<td>CINV means treatment is working</td>
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Provider Barriers and Misconceptions to CINV treatment

| Underestimation of CINV, especially delayed |
| Communication with the patient |
| Feared cost to patient |
| Fear of side effects of antiemetics to the patient |
| CINV treatment might interfere with other medications |
| Limit number of medications |
| CINV may be phenotypic marker for response |

How can nurses ensure patient gets correct antiemetics?

• Know the patient and risk factors
• Be knowledgeable on guidelines and available medications
• Develop protocols
  – Standard order sets on EMR
• Consider use of tools to assess CINV or diaries

Patient Education Techniques

• Oncology nurses are best poised to educate patients about CINV
• Clear written instructions on how to take prophylactic and as needed antiemetics
• Using diaries or phone calls to document CINV between office visits
• Be sure that patient has appropriate contact information to the office
• Educate on when is appropriate to call office about N/V

Key Clinical Take-Aways

- CINV continues to be an important aspect of supportive oncology care that, when not well controlled, has significant consequences
- Understanding pathways will help guide treatment options
- Following evidence-based guidelines is critical to optimal management of CINV
- Several medications and combinations are available for use
- There continues to be active research looking into new medications and pathways to prevent and treat CINV