The PONV Problem

The PONV Problem:
Frequent – Predictable – Evaluable –
Expensive – Dissatisfying – Avoidable

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PONV “Terminology”

• Air the diced carrots
• Bart - Boot - Blow - Brack
• Bark at the moon
• Blow foam, chunks, or bile
• Bring it up for a vote
• Burpin’ solid
• Call Uncle Earl or Ralph
• Call Europe
• Call up the beasties
• Chumming
• Chunder and Chunks
• Clean house
• Core dump
• Drive the porcelain bus
• Drive the Buick
• Emit with a food fountain
• Empty your bucket
• Fertilize the carpet
• Groul at the ground
• Hurl - Hack - Heave - Huey
• Liquid laugh or yawn
• Lunch re-run
• Laugh at the carpet
• Make an inventory
• Make a pavement pizza
• Private exorcism (AKA LB)
• Produce the liquid laugh
• Puke - Spew - Retch - Urp
• Park the tiger
• Protein spill
• Shout at your shoes
• Sick-up and spew
• Technicolour yaw
• Toss your cookies
• Vomit or Un-eat

Have we solved the PONV “little big problem”?

3 decades of clinical trials
Risk Stratification
Multiple combination therapies
Guidelines & Updated Guidelines
“Breakthrough medications”
“Break-the-Bank Expenses”

Incidence of PONV/PDNV/OIE

• Overall range: 25% to 30%
• High-risk patients: 70% to 80%
• Outpatient range: 20% to 80%, depending on the patient population
• 35% to 67% of patients may experience PDNV
• PONV may persist for 5 days after surgery
• Opioid-induced emesis (OIE): 10% to 60%
• No 1 or No 2 adverse outcome following routine outpatient surgery!

Many Patients Experience PONV Beyond the PACU

Many Patients Experience PONV Beyond the PACU

Overall: 41% had PONV and ... of patients who experienced PONV, nearly 80% initially did so in the PACU and/or within 48 hours after discharge.

Study Design: Data from a study examining patients’ experiences with PONV following discharge from outpatient surgery centers. Incidence of PONV was measured in the recovery room, by telephone the day after discharge, and by a questionnaire 5 days after surgery. Patients who experienced PONV during PACU stay also completed questionnaires 5 days after surgery. Patients who initially experienced PONV continued to experience PONV for up to 5 days after PACU discharge.

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PONV Remains a Problem Despite Current Therapies

<table>
<thead>
<tr>
<th>Overall</th>
<th>Up to 30% for all surgeries and patient populations.¹ ²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outpatient</td>
<td>About 40% of patients with PONV treated at outpatient surgery centers.⁴</td>
</tr>
<tr>
<td>Breakthrough</td>
<td>More than 30% of patients with PONV were receiving prophylactic antiemetics.³</td>
</tr>
</tbody>
</table>

— No significant differences among ondansetron, dexamethasone, and droperidol


PONV vs PDNV: Under-Recognized Problem

Prospective Study of 2175 Outpatients in 12 USA Centers

Conclusion: The results of this 12-center multicenter cohort study showed a substantial incidence of PDNV in the US.... Clinical trials that address this patient population with a long acting antiemetic strategy are needed

What does failure to prevent PONV actually cost?

Patient Risk
Patient discomfort
Patient dissatisfaction
Economic burden

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"You know, sometimes I sort of enjoy this herd mentality."
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Potential Consequences of PONV

- Medical Consequences of PONV
  - Can cause electrolyte abnormalities and dehydration\(^1\)
  - Can cause tension on suture lines\(^1\)
  - Venous hypertension\(^2\)
  - Can cause hematomas (increased bleeding) beneath surgical flaps, vascular anastomosis, aneurysm clipping, etc\(^1\)
  - Can place the patient at risk for pulmonary aspiration of vomit if airway reflexes are depressed from lingering effects of anesthetic and analgesic drugs\(^1,2\) (esp increased risk with jaw wired closed)
- Practical Consequences of PONV
  - Delayed Discharge after out-patient surgery\(^2\)
  - Unanticipated hospital admission\(^1\)

\(^1\) Golembiewski J, et al. Am J Health-System Pharm; Vol 62 Jun, 2005

PONV: #1 Patient Problem

Emesis is the postoperative outcome least preferred by patients

<table>
<thead>
<tr>
<th>Rank</th>
<th>Postoperative Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Vomiting</td>
</tr>
<tr>
<td>2</td>
<td>Gagging on endotracheal tube</td>
</tr>
<tr>
<td>3</td>
<td>Incisional pain</td>
</tr>
<tr>
<td>4</td>
<td>Nausea</td>
</tr>
<tr>
<td>5</td>
<td>Recall without pain</td>
</tr>
<tr>
<td>6</td>
<td>Residual weakness</td>
</tr>
<tr>
<td>7</td>
<td>Shivering</td>
</tr>
<tr>
<td>8</td>
<td>Sore throat</td>
</tr>
<tr>
<td>9</td>
<td>Somnolence</td>
</tr>
</tbody>
</table>

Data from a survey of adult patients (N=153) conducted at Stanford University Medical Center. Patients were eligible if they were scheduled to undergo surgery at the center. Patients were asked to rank-order 10 possible postoperative outcomes from most to least desirable. \(P<0.01\).

Cost Components in PONV Episodes

Cost Components for an Episode of Emesis (% total median management cost per patient)

- PACU nurses 78%
- Personnel 83%
- Antiemetic cost 3%
- Materials* 0.2%
- PACU admission 10%
- PACU delay 4%
- Hospital admission 10%

*Per item of basin, gloves, paper, linen, and gown


PONV Incurs Higher Cost$

- In a study conducted in 2000, PONV was associated with increased cost*:
  - A single episode of *emesis* costs an average of $305
  - A single episode of *nausea* costs an average of $82
- PONV is a major factor limiting early discharge of ambulatory surgical patients (1st or 2nd all major studies)
- PONV is a leading cause of unanticipated hospital admissions (24% primary reason)
- Preventing PONV can be cost-effective

* PACU personnel costs are biggest component: NOT PHARMACEUTICALS

Hill RP et al. Anesthesiology. 2000;92:958-967

Clinical Application of PONV Global Risk Assessment

- Opportunity to improve overall incidence by looking at individual patients
  - Patients who have risk factors are more likely to experience PONV\(^1\)
- Consider looking beyond the recovery room to assess PONV after surgery
  - PONV often does not start in recovery room, but begins later\(^2\)
- Incorporate PONV risk assessment into each case
- Consider 3 categories of risk:\(^3\)
  - Patient characteristics
  - Surgical procedure
  - Anesthesia

\(^1\) Falke CD et al. Anesthesiology. 1996;84:765-705.
\(^3\) Kinjo A. Jpn J. 2005;2:71-723.

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Why do patients develop PONV?

PONV Risk Prediction Tool?

Risk Factors for PONV

PONV Risk Factors

- **Patient related**: 1-7
  - Female gender
  - History of PONV and/or motion sickness
  - Nonsmokers
  - Younger age
  - Anxiety
  - Underlying disease (e.g., GI obstruction, neuromuscular disorders, gastric hypomotility)

PONV Risk Factors (cont)

- **Surgery related**: 1-5
  - Duration of surgery
  - Operative procedure (e.g., gynecologic, laparoscopic, eye, plastic, abdominal)

- **Anesthesia related**: 1-3, 6-8
  - Volatile anesthetics
  - General anesthesia
  - Duration of anesthesia
  - Postoperative opioids
  - Muscle relaxant antagonists (e.g., neostigmine)

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PONV Risk Factors (cont)

- Most predictive\(^1-3\)
  - Female gender
  - Nonsmokers
  - History of PONV/motion sickness
  - Postoperative opioid analgesics

- Multiple (≥3) risk factors\(^2\)
  - 60%–80% of patients may experience PONV

Comparison of predictive models for PONV

- Apfel
- Koivuranta
- Palazzo
- Sinclair

Most predictive\(^1-3\)
- Female gender
- Nonsmokers
- History of PONV/motion sickness
- Postoperative opioid analgesics

Multiple (≥3) risk factors\(^2\)
- 60%–80% of patients may experience PONV

“A risk score to predict the probability of postoperative vomiting in adults.”

1137 ENT patients split into an evaluation set (533) and a validation set (584)

POV Risk (probability) = \( \frac{1}{1 + e^{-z}} \)

Where: \( z = (\text{no}=0, \text{yes}=1) \)
- 1.28*(female gender)
- 0.029*(age)
- 0.74*(smoking)
- 0.63*(history motion sickness or PONV)
- 0.26*(duration)
- 0.92

SAMBA Algorithm Factors for PONV

<table>
<thead>
<tr>
<th>Adult Risk Factors</th>
<th>Children Risk Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Related</td>
<td>Environmental</td>
</tr>
<tr>
<td>History of PONV or Motion Sickness</td>
<td>Postop Opioids</td>
</tr>
<tr>
<td>Female Gender</td>
<td>Emetogenic surgery (type &amp; duration)</td>
</tr>
<tr>
<td>Non-Smoker</td>
<td>History of PONV or relative with PONV</td>
</tr>
</tbody>
</table>

Simplified Risk Score to Predict PONV in Adults\(^1\)

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female Gender</td>
<td>1</td>
</tr>
<tr>
<td>Non-Smoker</td>
<td>1</td>
</tr>
<tr>
<td>History of PONV**</td>
<td>1</td>
</tr>
<tr>
<td>Postoperative Opioids</td>
<td>1</td>
</tr>
</tbody>
</table>

Sum = 0, 1, 2, 3, 4

Percent Risk for PONV

- 0 Risk Factor: 0%
- 1 Risk Factor: 20%
- 2 Risk Factors: 60%
- 3 Risk Factors: 80%

Where are we in the development and implementation of “best practices” PONV guidelines?

** or motion sickness?

For example (YELLOW BOX), if a patient is a “female” “non-smoker” she has 2 risk factors and there is a 40% chance of her experiencing PONV

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PONV Patient-At-Risk “Game Plan”

Strategies to Reduce Baseline PONV Risk

- Avoidance of general anesthesia by the use of regional anesthesia (RCT)
- Use of propofol for induction and maintenance of anesthesia (RCT/SR)
- Avoidance of nitrous oxide (RCT/SR)
- Avoidance of volatile anesthetics (RCT)
- Minimization of intraoperative and postoperative opioids (RCT/SR)
- Minimization of neostigmine (SR)
- Adequate hydration (RCT)


Guidelines for Antiemetic Prophylaxis for PONV

ASA 2002
- Prophylaxis with 1 or more:
  - 5-HT3 RA
  - Droperidol
  - Dexamethasone
  - Metoclopramide
  - Scopolamine
- Give adequate IV hydration
- Use total IV anesthesia
- If patient fails in PACU, then administer another category of agent

ASPA 2006
- Prophylaxis with 1 or more:
  - 5-HT3 RA
  - Droperidol
  - Dexamethasone
  - Metoclopramide
- Give adequate IV hydration
- Use total IV anesthesia
- If patient fails in PACU, then administer another category of agent

SAMBA 2007
- Assess patient risk
- Reduce baseline risk factors
- Prophylaxis with 1 or 2 interventions for patients at moderate risk
  - 5-HT3 RA
  - Droperidol
  - Dexamethasone
  - Metoclopramide
  - Scopolamine
  - Ephedrine
  - High-risk multimodal approach
- If patient fails, then administer another category of agent

PONV Antiemetics

Receptor Site Affinity

<table>
<thead>
<tr>
<th>Drug</th>
<th>FDA Approved</th>
<th>Serotonin</th>
<th>Dopamine</th>
<th>Histamine</th>
<th>Muscarinic</th>
<th>Neurokinin</th>
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<tbody>
<tr>
<td>Prochlorperazine</td>
<td>+</td>
<td>**</td>
<td>**</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Haloperidol</td>
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<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Droperidol</td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Scopolamine</td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Dimenhydrinate</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Promethazine</td>
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<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Aprepitant</td>
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<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Granisetron</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Ondansetron</td>
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<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Palonosetron</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Dolasetron</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Aprepitant</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
</tbody>
</table>

Dexamethasone
Antagonist of prostaglandins and release of endorphins

PONV Treatment Team

The Consensus Guidelines for the management of PONV was written by a multi-disciplinary panel that included such clinicians as...

SAMBA Treatment Algorithm Options for PONV

<table>
<thead>
<tr>
<th>Level of Risk</th>
<th>Daily nausea (D)</th>
<th>Post-op nausea (P)</th>
<th>Total nausea (D+P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>1 or 2 interventions for adults</td>
<td>1 or 2 interventions for children</td>
<td>1 or 2 interventions for children</td>
</tr>
<tr>
<td>Medium</td>
<td>&gt; 2 interventions</td>
<td>&gt; 2 interventions</td>
<td>&gt; 2 interventions</td>
</tr>
<tr>
<td>High</td>
<td>&gt; 2 interventions</td>
<td>&gt; 2 interventions</td>
<td>&gt; 2 interventions</td>
</tr>
</tbody>
</table>

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SAMBA Treatment Algorithm Options for PONV

- If prophylaxis fails or was not received, use antiemetic from different class than prophylaxis agent
- Readministration only if >6 hours after PACU; do not readminister dexamethasone or scopolamine
- Use dexamethasone in children only if other therapy has failed and patient is being admitted to hospital
- Some of the drugs may not have been studied or approved by the FDA for use in children

SAMBA Treatment Algorithm Options for PONV

- No specific pharmacologic superiority

Selecting “Best Shot” PONV/PDNV Drugs?

Increasing the Number of Antiemetics Reduces the Incidence of PONV (n=5161 patients at high risk for PONV)

Estimated Incidence of PONV as a function of Baseline Risk

Assumption: Each Intervention Reduces risk by 26%

Despite multiple combinations with current drugs, we fail...yes, we fail!

Estimated PONV incidence as a function of baseline risk, assuming each intervention reduces relative risk by 26%

Table:

<table>
<thead>
<tr>
<th>Number of interventions</th>
<th>Baseline risk (no intervention)</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>10%</td>
<td>7%</td>
<td>5%</td>
<td>4%</td>
<td>3%</td>
<td></td>
</tr>
<tr>
<td>20%</td>
<td>15%</td>
<td>11%</td>
<td>8%</td>
<td>6%</td>
<td></td>
</tr>
<tr>
<td>40%</td>
<td>29%</td>
<td>22%</td>
<td>16%</td>
<td>12%</td>
<td></td>
</tr>
<tr>
<td>60%</td>
<td>44%</td>
<td>33%</td>
<td>24%</td>
<td>18%</td>
<td></td>
</tr>
<tr>
<td>80%</td>
<td>59%</td>
<td>44%</td>
<td>32%</td>
<td>24%</td>
<td></td>
</tr>
</tbody>
</table>

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Selecting the Ideal Antiemetic? Pathway?
The Numbers are In. We Are Failing ;-;

PONV Summary and Conclusions

- **PONV**: Ranked as most undesirable consequence of surgery
  - 30% overall incidence
  - PONV incidence increases with each additional risk factor, thus underscoring need for assessment and preventative intervention
- Risk assessment helps identify patients who would benefit from prophylactic antiemetics
- Effective PONV prevention strategy incorporates risk assessment that reflects its multifactorial etiology
- Global risk assessment includes evaluation of:
  - Patient-related characteristics
  - Surgery-related characteristics
  - Anesthesia-related characteristics

PONV Summary and Conclusions (cont)

- Understanding of emetic pathways continues to evolve
  - Peripheral versus central emetogenic triggers
  - Peripheral versus central neurotransmitter/receptor pathways
- Involvement of different emetic neurotransmitter pathways may impact treatment strategies
  - Source of emetic stimuli impacts effectiveness of pharmacologic antiemetic intervention
  - Multiple receptor approach probably logical and effective
- Ideal combination unproven: Consider 5-HT3 + steroid + droperidol/haloperidol + SCOP + "special needs" + techniques
- New pharmacology 5HT3 antagonist palonosetron
- First substance P/NK 1 antagonist now available for prevention of troublesome PONV and PDNV: Aprepitant 40 mg

SCOAP PONV Challenge

Risk stratification can and should be done.
Prevention measures should be implemented.
Outcome benefits should be producible and measurable.
Benefits should include patient satisfaction and reduced costs.
The PONV initiative should be widely applicable.

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