Nouveautés en prévention des nausées et vomissements post-opératoires

Dr Jean-Luc Demeere
BAAS
27-02-2015
NOUVEAUTES

• 1. The big « little problem »: be conscious!
• 2. Multimodal approach
• 3. Risk factors and guidelines
• 4. Consensus in prevention: new medication
• 5. Guidelines and practice: decision support is a necessity!
Perioperative nausea and emesis pose problems for patients undergoing all types of procedures requiring anesthesia or sedation. Particular groups of patients have been identified as being at higher risk, i.e., those with predisposing factors to prolonged gastric emptying (e.g., obstetric, bowel obstruction, or diabetic), those with recent food or liquid intake, those with inadequate protective mechanisms (e.g., hiatal hernia, nasogastric tube in place, or anesthetized upper airway), or those undergoing nausea-producing procedures, such as laparoscopy. As the authors of the accompanying articles (1,2) have pointed out, previous pharmacologic efforts to diminish the incidence and/or reduce the risk of emesis have included administering antihistaminics, anticholinergics, and dopamine antagonists. Sometimes narcotic-based anesthetic techniques are avoided. Physical maneuvers have included imposing various “nothing per or” regimens, preanesthetic suctioning of gastric contents, application of cricoid cartilage pressure, avoiding inflation of the stomach during ventilation by mask, and ingestion of antacid solutions. None of the above, alone or in combination, have been entirely successful in mitigating the distressing occurrence of emesis and its potential sequelae.

The predisposing factors mentioned above are more common within the inpatient population. However, as the number of acceptable surgical procedures increases in the field of ambulatory anesthesia, the need to find more effective alternatives to the options now available becomes more urgent. The potential cost savings of performing these procedures on an ambulatory basis may be negated by an unanticipated postoperative admission for intractable nausea (3). In addition, although intractable nausea is distressing, possibly dehydrating, and not easily manageable at home, the expense of a hospital stay is disproportionate to the actual morbidity of nausea for most healthy outpatients. Thus the therapy of last resort, hospitalization, is ultimately unsatisfactory for the patient, the anesthesiologist, and the surgeon.

Even lesser degrees of postoperative nausea are often perceived as failures of therapy, rather than as an unavoidable consequence of the perioperative experience. In most instances, the latter is in fact the case because of imperfect treatment options. When queried about previous anesthetic experiences, many patients are heard to lament about the distressing nausea after a prior procedure and beg to be spared that experience again. During preoperative evaluations for subsequent anesthetics, such patients are often assured that the latest available antiemetic medications will be administered and that a nauseasparing anesthetic technique will be used. However, anesthesia providers cannot be sure that such a goal will be realized with the antiemetic treatment alternatives now available.

A potential new entry into the antiemetic pharmacopeia is ondansetron, of the class of selective 5-hydroxytryptamine subtype 3 (5-HT3) receptor antagonists, which lack effects at cholinergic, adrenergic, dopaminergic, or histaminergic receptors (4). Ondansetron (1,2,3,9-tetrahydro-9-methyl-3-[2-methyl-1Himidazol]-1-methyl]-4H-carbazol-4-one, monohydrochloride, dihydrate) is structurally related to serotonin. 5-HT3 receptors are located both peripherally (vagal nerve terminals) and centrally (chemoreceptor trigger zone). The antiemetic properties of ondansetron may be mediated peripherally, centrally, or both.

Ondansetron has been studied in relation to cancer chemotherapy-induced emesis (5,6), which is associated with serotonin release from small intestine enterochromaffin cells and urinary excretion of serotonin metabolites. Presumably, the release of serotonin stimulates vagal afferent 5-HT3 receptors and/or the central vomiting reflex. In experimental animal studies, cisplatin-induced emesis can be prevented by section of the abdominal vagus and greater splanchnic nerve, or by pretreatment with either a serotonin synthesis inhibitor or a 5-HT3 receptor antagonist. In normal volunteers, ondansetron has little effect on lower esophageal sphincter pressure, esophageal or gastric motility, or small bowel transit time. By 5-HT3 selectivity, the undesirable side effects of using
1. Consequences of PONV

Update on the management of postoperative nausea and vomiting. Curr Opin Anesthesiol 2014; 27: 605-609

- Electrolyte imbalances
- Dehydration
- Aspiration
- Suture dehiscence
- Esophageal rupture
- Subcutaneous emphysema

Incidence: 30% et 80% in high-risk patients

- 0.18% of all patients: intractable PONV
  - Delay in discharge
  - Unexpected hospital admission
  - Healthcare cost
2. Pathophysiology

- Vomiting Center (brain stem)
  - Chemoreceptor trigger zone
  - Mediastinum
  - Vestibular
  - Visual
  - GI

- Higher cortical centres
  - Memory, fear, anticipation

- Chemoreceptor Trigger Zone (area Prostema-4th ventricle)

- Stomach
  - Small intestine

- Labyrinths

- Sensory input (pain, smell, sight)

- Anaesthetics
  - Opioids

- Surgery

Neuronal pathways

Factors which can cause PONV

PONV
Antiemetics

Sensory input (pain, smell, sight)

Higher cortical centres

Memory, fear, anticipation

Histamine antagonists
Muscarinic antagonists
Dopamine antagonists
Cannabinoids

Benzodiazepines

Chemoreceptor Trigger Zone (area postrema, 4th ventricle)

Vomiting Centre (medulla)

Vomiting Reflex

Anaesthetics
Opioids

Sphincter modulators

5HT3 antagonists

Stomach Small intestine

Labyrinths

Surgery

Gastroprokinetic agents

Factors which can cause PONV

Sites of action of drugs

Neuronal pathways

Dr. Demeere Jean-Luc
3. Consensus guidelines for the management of postoperative nausea and vomiting.


- Anesth Analg. 2014 Jan;118(1):85-113

Erratum in
A Simplified Risk Score for Predicting Postoperative Nausea and Vomiting

Conclusions from Cross-validations between Two Centers

Christian C. Apfel, M.D.,* Esa Läärä, Ph.D.,† Merja Koivuranta, M.D., Ph.D.,‡ Clemens-A. Greim, M.D.,§ Norbert Roewer, M.D.‖

Table 3. Incidence of Postoperative Nausea and Vomiting in Both Centers According to the Predictors or the Type of Operation

<table>
<thead>
<tr>
<th></th>
<th>Oulu</th>
<th>Wuerzburg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>63 (58–68)</td>
<td>47 (44–50)</td>
</tr>
<tr>
<td>Male</td>
<td>38 (30–46)</td>
<td>20 (18–22)</td>
</tr>
<tr>
<td>History of motion sickness or PONV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>66 (61–72)</td>
<td>57 (53–62)</td>
</tr>
<tr>
<td>No</td>
<td>44 (38–50)</td>
<td>25 (23–27)</td>
</tr>
<tr>
<td>Nonsmoker</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>62 (57–66)</td>
<td>36 (33–38)</td>
</tr>
<tr>
<td>No</td>
<td>38 (29–46)</td>
<td>21 (17–24)</td>
</tr>
<tr>
<td>Use of postoperative opioids</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>59 (55–64)</td>
<td>37 (31–43)</td>
</tr>
<tr>
<td>No</td>
<td>39 (29–49)</td>
<td>31 (29–33)</td>
</tr>
<tr>
<td>Type of surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orthopedic</td>
<td>52 (32–71)</td>
<td>33 (27–40)</td>
</tr>
<tr>
<td>Ophthalmology</td>
<td>33 (19–47)</td>
<td>28 (23–33)</td>
</tr>
<tr>
<td>Otolarygology</td>
<td>49 (37–62)</td>
<td>27 (24–30)</td>
</tr>
<tr>
<td>Laparoscopy</td>
<td>57 (49–64)</td>
<td>38 (24–51)</td>
</tr>
<tr>
<td>Laparotomy</td>
<td>75 (65–85)</td>
<td>34 (26–42)</td>
</tr>
<tr>
<td>Other</td>
<td>55 (46–63)</td>
<td>38 (34–42)</td>
</tr>
</tbody>
</table>

Data are presented as percent of patients with PONV (95% confidence interval).
PONV = postoperative nausea and vomiting.
### Table 1

<table>
<thead>
<tr>
<th>Evidence</th>
<th>Risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive overall</td>
<td>Female sex (B1)</td>
</tr>
<tr>
<td></td>
<td>History of PONV or motion sickness (B1)</td>
</tr>
<tr>
<td></td>
<td>Nonsmoking (B1)</td>
</tr>
<tr>
<td></td>
<td>Younger age (B1)</td>
</tr>
<tr>
<td></td>
<td>General versus regional anesthesia (A1)</td>
</tr>
<tr>
<td></td>
<td>Use of volatile anesthetics and nitrous oxide (A1)</td>
</tr>
<tr>
<td></td>
<td>Postoperative opioids (A1)</td>
</tr>
<tr>
<td></td>
<td>Duration of anesthesia (B1)</td>
</tr>
<tr>
<td></td>
<td>Type of surgery (cholecystectomy, laparoscopic, gynecological) (B1)</td>
</tr>
<tr>
<td>Conflicting</td>
<td>ASA physical status (B1)</td>
</tr>
<tr>
<td></td>
<td>Menstrual cycle (B1)</td>
</tr>
<tr>
<td></td>
<td>Level of anesthetist’s experience (B1)</td>
</tr>
<tr>
<td></td>
<td>Muscle relaxant antagonists (A2)</td>
</tr>
<tr>
<td>Disproven or of limited clinical relevance</td>
<td>BMI (B1)</td>
</tr>
<tr>
<td></td>
<td>Anxiety (B1)</td>
</tr>
<tr>
<td></td>
<td>Nasogastric tube (A1)</td>
</tr>
<tr>
<td></td>
<td>Supplemental oxygen (A1)</td>
</tr>
<tr>
<td></td>
<td>Perioperative fasting (A2)</td>
</tr>
<tr>
<td></td>
<td>Migraine (B1)</td>
</tr>
</tbody>
</table>

PONV = postoperative nausea and vomiting; BMI = body mass index; MS = motion sickness.

*Consensus Guidelines for the Management of Postoperative Nausea and Vomiting*

Gan, Tong J.; Diemunsch, Pierre; Habib, Ashraf S.; Kovac, Anthony; Kranke, Peter; Meyer, Tricia A.; Watcha, Mehroo; Chung, Frances; Angus, Shane; Apfel, Christian C.; Bergese, Sergio D.; Candioti, Keith A.; Chan, Matthew TV; Davis, Peter J.; Hooper, Vallire D.; Lagoo-Deenadayalan, Sandhya; Myles, Paul; Nezat, Greg; Philip, Beverly K.; Tramer, Martin R. Anesthesia & Analgesia. 118(1):85-113, January 2014. doi: 10.1213/ANE.0000000000000002

Table 1. Risk Factors for PONV in Adults
3. Risk scoring systems and incidence

• Apfel et al.: simplified risk score*
  – Number of patients: 2,722
  – Risk factors
    • Female
    • History PONV/ motion sickness
    • Non-smoking
    • Postop opioids

  – Simplified risk score**

    • 0 risk factors => 10% PONV
    • 1 risk factor  => 21% PONV
    • 2 risk factors => 39% PONV
    • 3 risk factors => 61% PONV
    • 4 risk factors => 79% PONV


*** Aaron Skolinck et Al : Curr Opin Anesthesiol 2014, 27: 605-609
Figure 3

Consensus Guidelines for the Management of Postoperative Nausea and Vomiting

Gan, Tong J.; Diemunsch, Pierre; Habib, Ashraf S.; Kovac, Anthony; Kranke, Peter; Meyer, Tricia A.; Watcha, Mehernoor; Chung, Frances; Angus, Shane; Apfel, Christian C.; Bergese, Sergio D.; Candiotti, Keith A.; Chan, Matthew TV; Davis, Peter J.; Hooper, Vallire D.; Lagoo-Deenadayalan, Sandhya; Myles, Paul; Nezat, Greg; Philip, Beverly K.; Tramèr, Martin R.
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Figure 3. Simplified risk score for POV in Children. Simplified risk score from Eberhart et al.48 to predict the risk for POV in children. When 0, 1, 2, 3, or 4 of the depicted independent predictors are present, the corresponding risk for PONV is approximately 10%, 10%, 30%, 50%, or 70%, respectively. POV = postoperative vomiting; PONV = postoperative nausea and vomiting.
3. Who is at risk for postdischarge nausea and vomiting after ambulatory surgery? PDNV


• Results: The overall incidence of PDNV was 37%. Logistic regression analysis of the development dataset (n = 1,913) identified five independent predictors (odds ratio; 95% CI): female gender (1.54; 1.22 to 1.94), age less than 50 yr (2.17; 1.75 to 2.69), history of nausea and/or vomiting after previous anesthesia (1.50; 1.19 to 1.88), opioid administration in the postanesthesia care unit (1.93; 1.53 to 2.43), and nausea in the postanesthesia care unit (3.14; 2.44–4.04). In the validation dataset (n = 257), zero, one, two, three, four, and five of these factors were associated with a PDNV incidence of 7%, 20%, 28%, 53%, 60%, and 89%, respectively, and an area under the receiver operating characteristic curve of 0.72 (0.69 to 0.73).
A Factorial Trial of Six Interventions for the Prevention of Postoperative Nausea and Vomiting

Christian C. Apfel, M.D., Kari Korttila, F.R.C.A., Ph.D., Mona Abdalla, Ph.D., Heinz Kerger, M.D., H. Turan, M.D., Ina Vedder, M.D., Carmen Zernak, M.D., Klaus Danner, M.D., Ritva Jokela, M.D., Ph.D., Stuart J. Pocock, Ph.D., Stefan Trenkler, M.D., Markus Kredel, M.D., Andreas Biedler, M.D., Daniel I. Sessler, M.D., and Norbert Roewer, M.D., for the IMPACT Investigators*

Ondansetron, dexamethasone, and droperidol each reduced the risk of postoperative nausea and vomiting by about 26 percent. Propofol reduced the risk by 19 percent, and nitrogen by 12 percent; the risk reduction with both of these agents (i.e., total intravenous anesthesia) was thus similar to that observed with each of the antiemetics. All the interventions acted independently of one another and independently of the patients' baseline risk. Consequently, the relative risks associated with the combined interventions could be estimated by multiplying the relative risks associated with each intervention. Absolute risk reduction, though, was a critical function of patients’ baseline risk.
**Figure 2. Incidence of Postoperative Nausea and Vomiting Associated with the Various Combinations of Antiemetic Drugs.**

The data shown represent outcomes in 5161 patients. Solid circles represent the average value for each number of prophylactic antiemetics, and open symbols the incidence for each antiemetic or combination of antiemetics. Ond denotes ondansetron, Dex dexamethasone, and Dro droperidol. I bars represent 95 percent confidence intervals.


Consensus Guidelines for the Management of Postoperative Nausea and Vomiting

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doi: 10.1213/ANE.0000000000000002

Figure 4. Algorithm for management of postoperative nausea and vomiting. PONV = postoperative nausea and vomiting.
# Table 3

## Consensus Guidelines for the Management of Postoperative Nausea and Vomiting

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Dose</th>
<th>Evidence</th>
<th>Timing</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aprepitant</td>
<td>40 mg per os</td>
<td>A2&lt;sup&gt;113,115&lt;/sup&gt;</td>
<td>At induction</td>
<td>A2&lt;sup&gt;113&lt;/sup&gt;</td>
</tr>
<tr>
<td>Casopitant</td>
<td>150 mg per os</td>
<td>A3&lt;sup&gt;117,118&lt;/sup&gt;</td>
<td>At induction</td>
<td>A1&lt;sup&gt;226&lt;/sup&gt;</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>4–5 mg IV</td>
<td>A1&lt;sup&gt;121&lt;/sup&gt;</td>
<td>At induction</td>
<td>A1&lt;sup&gt;233–254&lt;/sup&gt;</td>
</tr>
<tr>
<td>Dimenhydrinate</td>
<td>1 mg/kg IV</td>
<td>A1&lt;sup&gt;152–154&lt;/sup&gt;</td>
<td>End of surgery; timing may not affect efficacy</td>
<td>A2&lt;sup&gt;83&lt;/sup&gt;</td>
</tr>
<tr>
<td>Dolasetron</td>
<td>12.5 mg IV</td>
<td>A2&lt;sup&gt;94,85&lt;/sup&gt;</td>
<td>End of surgery</td>
<td>A1&lt;sup&gt;138,139&lt;/sup&gt;</td>
</tr>
<tr>
<td>Droperidol&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.625–1.25 mg IV</td>
<td>A2&lt;sup&gt;223,224&lt;/sup&gt;</td>
<td>End of surgery</td>
<td>A1&lt;sup&gt;140&lt;/sup&gt;</td>
</tr>
<tr>
<td>Ephedrine</td>
<td>0.5 mg/kg IM</td>
<td>A1&lt;sup&gt;91–93&lt;/sup&gt;</td>
<td>End of surgery</td>
<td>A2&lt;sup&gt;106–110&lt;/sup&gt;</td>
</tr>
<tr>
<td>Granisetron</td>
<td>0.35–3 mg IV</td>
<td>A1&lt;sup&gt;1146&lt;/sup&gt;</td>
<td>End of surgery</td>
<td>A1&lt;sup&gt;107&lt;/sup&gt;</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>0.5–2 mg IM/IV</td>
<td>A2&lt;sup&gt;137&lt;/sup&gt;</td>
<td>End of surgery</td>
<td>A2&lt;sup&gt;105,106&lt;/sup&gt;</td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>40 mg IV</td>
<td>A2&lt;sup&gt;140&lt;/sup&gt;</td>
<td>End of surgery</td>
<td>A2&lt;sup&gt;106,106&lt;/sup&gt;</td>
</tr>
<tr>
<td>Ondansetron</td>
<td>4 mg IV, 8 mg ODT</td>
<td>A1&lt;sup&gt;174,75&lt;/sup&gt;</td>
<td>End of surgery</td>
<td>A2&lt;sup&gt;105,108&lt;/sup&gt;</td>
</tr>
<tr>
<td>Palonosetron</td>
<td>0.075 mg IV</td>
<td>A2&lt;sup&gt;1162&lt;/sup&gt;</td>
<td>End of surgery</td>
<td>A2&lt;sup&gt;102&lt;/sup&gt;</td>
</tr>
<tr>
<td>Perphenazine</td>
<td>5 mg IV</td>
<td>A2&lt;sup&gt;119&lt;/sup&gt;</td>
<td>End of surgery</td>
<td>A2&lt;sup&gt;102&lt;/sup&gt;</td>
</tr>
<tr>
<td>Promethazine</td>
<td>6.25 - 12.5 mg IV</td>
<td>A2&lt;sup&gt;222,256&lt;/sup&gt;</td>
<td>End of surgery</td>
<td>A2&lt;sup&gt;102&lt;/sup&gt;</td>
</tr>
<tr>
<td>Ramosetron</td>
<td>0.3 mg IV</td>
<td>A2&lt;sup&gt;102&lt;/sup&gt;</td>
<td>End of surgery</td>
<td>A2&lt;sup&gt;102&lt;/sup&gt;</td>
</tr>
<tr>
<td>Rolapitant</td>
<td>70–200 mg per os</td>
<td>A2&lt;sup&gt;102&lt;/sup&gt;</td>
<td>End of surgery</td>
<td>A2&lt;sup&gt;102&lt;/sup&gt;</td>
</tr>
<tr>
<td>Scopolamine</td>
<td>Transdermal patch</td>
<td>A1&lt;sup&gt;157,158&lt;/sup&gt;</td>
<td>Prior evening or 2 h before surgery</td>
<td>A1&lt;sup&gt;157&lt;/sup&gt;</td>
</tr>
<tr>
<td>Tropisetron</td>
<td>2 mg IV</td>
<td>A1&lt;sup&gt;197&lt;/sup&gt;</td>
<td>End of surgery</td>
<td>Expert opinion</td>
</tr>
</tbody>
</table>

These recommendations are evidence-based, and not all the drugs have an FDA indication for PONV. Drugs are listed alphabetically.

<sup>a</sup>See FDA Black box warning.
4. Serotonin receptor antagonists

• **Ondansetron** (Zofran®, Avessa®)
  – Anti-vomiting > anti-nausea
  – End of surgery => most effective
  – 4 - 8 mg IV adults
  – 50 -100 microg/kg IV children
  – NNT 5 - 6
  – Side effects: Headache, dizziness, flushing, liver enzymes elevated

• **Tropisetron** (Novaban®)
  – 2 - 5 mg IV
  – NNT nausea 6.7
  – NNT vomiting 5

• **Granisetron** (Kytril®)
  – 0.35 - 3 mg (most 1 mg, lower doses recent study)
  – Treatment established P.O.N.V. : 0.1 mg
  – Belgium: chemo- and radiotherapie N & V
4. Droperidol

- Dihydrobenzperidol™ / DHB
- 1.25 mg more cost-effective than Ondansetron 4 mg
- NNT 4 - 7
- 0.625 - 1.25 - 1.5 - 2.5 mg IV adults
- 10 - 15 microg/kg IV children
- Most effective end of surgery
- Also effective with Morphine-PCIA
  - NNT N:5.1 ; V: 3.1
  - 15 - 50 microg/mg morphine
- Side effects: sedation and drowsiness (less at doses 0.625/1.25mg)
4. Steroids

- **Dexamethasone** *(Acidexam™)*
  - Effective in chemotherapy emesis as well as in PONV prophylaxis
  - **Mechanism of action??**
    - Central inhibition PG synthesis?
    - Decrease 5-HT3 turnover CNS or changes permeability 5-HT3?
    - Liberation Endorphines?
  - 5 - 10 mg IV in adults
  - 150 microg/kg IV children
  - Most effective when administered prior to induction
  - Particularly effective LATE PONV
  - No adverse effects at doses used
Methylprednisolone vs. dexamethasone in the prevention of post-operative nausea and vomiting: a prospective, randomised, double-blind, placebo-controlled trial

M. Weren and J. L. Demeere

**Table II**

Incidence of PONV

<table>
<thead>
<tr>
<th></th>
<th>Dexamethasone (n = 38)</th>
<th>Methylprednisolone (n = 40)</th>
<th>Placebo (n = 40)</th>
<th>p value methylprednisolone vs. placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early nausea</td>
<td>7 (18, 8-34)</td>
<td>4 (10, 3-24)</td>
<td>7 (18, 7-33)</td>
<td>0.289</td>
</tr>
<tr>
<td>Early retch</td>
<td>5 (13, 4-12)</td>
<td>1 (3, 0-13)</td>
<td>5 (13, 4-27)</td>
<td>0.1</td>
</tr>
<tr>
<td>Early vomiting</td>
<td>4 (11, 3-25)</td>
<td>2 (5, 1-17)</td>
<td>6 (15, 6-30)</td>
<td>0.132</td>
</tr>
<tr>
<td>Early PONV</td>
<td>7 (18, 8-34)</td>
<td>4 (10, 3-24)</td>
<td>7 (18, 7-33)</td>
<td>0.259</td>
</tr>
<tr>
<td>Late nausea</td>
<td>11 (29, 15-46)</td>
<td>5 (13, 4-27)</td>
<td>14 (35, 21-52)</td>
<td>0.017</td>
</tr>
<tr>
<td>Late retch</td>
<td>8 (21, 10-37)</td>
<td>3 (8, 2-20)</td>
<td>11 (28, 15-44)</td>
<td>0.018</td>
</tr>
<tr>
<td>Late vomiting</td>
<td>5 (13, 4-12)</td>
<td>3 (8, 2-20)</td>
<td>8 (20, 9-34)</td>
<td>0.096</td>
</tr>
<tr>
<td>Late PONV</td>
<td>11 (29, 15-46)</td>
<td>6 (15, 6-30)</td>
<td>14 (35, 21-52)</td>
<td>0.045</td>
</tr>
</tbody>
</table>

All data are presented as number of patients (% of total, 95% CI).
4. Methylprednisolone 125mg

- PONV ↓ 30% during the first 24h
  - Reduced activity of phospholipase A2
  - Blocking (selectively) (COX)2-MRNA
  - Negligible effect on COX1
  - Satisfaction score 🎉

- Parecoxib: no effect

Randomised controlled trial of the effect of oral premedication with dexamethasone on hyperglycaemic response to abdominal hysterectomy
Leopold H.J. Eberhart, Jürgen Graf, Astrid M. Morin, Thomas Stief, Matthias Kalder, Ralph Lattermann and Thomas Schricker

Conclusion Amounts of dexamethasone frequently used for prophylaxis of post-operative nausea and vomiting can cause short-lasting hyperglycaemia in the post-operative period, but no relevant alterations in fat metabolism. Thus, the benefits of administering corticosteroids should be weighed against the potential side-effects of short-lasting hyperglycaemia.

Eur J Anaesthesiol 2011;28:000–000
4. Corticoids: PONV PREVENTION in paediatric anaesthesia

• Over the age of 2 years
  – Tropisetron: 0.05-0.1 mg.kg up to 2 mg
  – Dexamethasone: 150 µg/kg (up to 5mg)

• DHB: «impressive» extrapyramidal side effects ⇒C.I.
• Metoclopramide: C.I.

• «It may be preferable to use dexamethasone as the first line drug for prevention of PONV and to keep the setrons as a back-up drug for treatment of PONV»

**Table 5**

**Consensus Guidelines for the Management of Postoperative Nausea and Vomiting**

Gan, Tong J.; Diemunsch, Pierre; Habib, Ashraf S.; Kovac, Anthony; Kranke, Peter; Meyer, Tricia A.; Watcha, Mehernoor; Chung, Frances; Angus, Shane; Apfel, Christian C.; Bergese, Sergio D.; Candiotti, Keith A.; Chan, Matthew TV; Davis, Peter J.; Hooper, Vallire D.; Lagoo-Deenadayalan, Sandhya; Myles, Paul; Nezat, Greg; Philip, Beverly K.; Tramèr, Martin R.

doi: 10.1213/ANE.0000000000000002

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dexamethasone</td>
<td>150 mcg/kg up to 5 mg</td>
<td>A1⁹³²</td>
</tr>
<tr>
<td>Dimenhydrinate</td>
<td>0.5 mg/kg up to 25 mg</td>
<td>A1⁵⁴</td>
</tr>
<tr>
<td>Dolasetron</td>
<td>350 mcg/kg up to 12.5 mg</td>
<td>A2⁸³³</td>
</tr>
<tr>
<td>Droperidol⁶</td>
<td>10–15 mcg/kg up to 1.25 mg</td>
<td>A1⁸⁴⁰</td>
</tr>
<tr>
<td>Granisetron</td>
<td>40 mcg/kg up to 0.6 mg</td>
<td>A²⁸³⁴</td>
</tr>
<tr>
<td>Ondansetron⁷</td>
<td>50–100 mcg/kg up to 4 mg</td>
<td>A¹³³⁵</td>
</tr>
<tr>
<td>Tropisetron</td>
<td>0.1 mg/kg up to 2 mg</td>
<td>A¹³⁹⁷</td>
</tr>
</tbody>
</table>

These recommendations are evidence based, and not all the drugs have an FDA indication for PONV. Drugs are listed alphabetically.

⁶See FDA black box warning. Recommended doses 10 to 15 mcg/kg.
⁷Approved for POV in pediatric patients aged 1 month and older.

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**Table 5. Antiemetic Doses for Prophylaxis of POV in Children**
Table 4

Consensus Guidelines for the Management of Postoperative Nausea and Vomiting

Gan, Tong J.; Diemunsch, Pierre; Habib, Ashraf S.; Kovac, Anthony; Kranke, Peter; Meyer, Tricia A.; Watcha, Mehrenoor; Chung, Frances; Angus, Shane; Apfel, Christian C.; Bergese, Sergio D.; Candioti, Keith A.; Chan, Matthew TV; Davis, Peter J.; Hooper, Vallire D.; Lagoo-Deenadayalan, Sandhya; Myles, Paul; Nezat, Greg; Philip, Beverly K.; Tramèr, Martin R.
doi: 10.1213/ANE.000000000000225

<table>
<thead>
<tr>
<th>Adults</th>
<th></th>
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<tbody>
<tr>
<td>Droperidol + dexamethasone&lt;sup&gt;47&lt;/sup&gt; (A1)</td>
<td></td>
</tr>
<tr>
<td>5-HT&lt;sub&gt;3&lt;/sub&gt; receptor antagonist + dexamethasone&lt;sup&gt;47,120,189,192,327,474,120,189,192&lt;/sup&gt; (A1)</td>
<td></td>
</tr>
<tr>
<td>5-HT&lt;sub&gt;3&lt;/sub&gt; receptor antagonist + droperidol&lt;sup&gt;47,140,188,257&lt;/sup&gt; (A1)</td>
<td></td>
</tr>
<tr>
<td>5-HT&lt;sub&gt;3&lt;/sub&gt; receptor antagonist + dexamethasone + droperidol (A2)</td>
<td></td>
</tr>
<tr>
<td>Ondansetron + casopitant&lt;sup&gt;118,117,117,118&lt;/sup&gt; or TDS&lt;sup&gt;187&lt;/sup&gt; (A1)</td>
<td></td>
</tr>
</tbody>
</table>

Combinations in children

| Ondansetron, 0.05 mg/kg, + dexamethasone, 0.015 mg/kg<sup>328,329</sup> (A1) |  |
| Ondansetron, 0.1 mg/kg, + droperidol, 0.015 mg/kg<sup>330</sup> (A1) |  |
| Tropisetron, 0.1 mg/kg, + dexamethasone, 0.5 mg/kg<sup>331</sup>(A1) |  |

See Table 5 for dose ranges for children.
Alizapride (litican®): rescue

**Droperidol, alizapride and metoclopramide in the prevention and treatment of post-operative emetic sequelae.**
Kauste A, Tuominen M, Heikkinen H, Gordin A, Korttila K.

**Alizapride in prevention of postoperative nausea and vomiting.**
Booij LH, Rachmat S, Bulder ER.

**[Clinical use of antiemetic drugs for prevention and therapy of postoperative nausea and vomiting**
Saur P, Kazmaier S, Buhre W, Neumann P.

**The benefits and risks of different therapies in preventing postoperative nausea and vomiting in patients undergoing thyroid surgery.**
Fujii Y.
Double-blind comparison of alizapride, droperidol and ondansetron in the treatment of post-operative nausea.

Stienstra R¹, Samhan YM, el-Mofty M, de Bont LE, Bovill JG. Eur J Anaesthesiol. 1997 May;14(3):290-4

• It is concluded that alizapride 100 mg, droperidol 1 mg and ondansetron 8 mg intravenously are equally effective in the treatment of PONV after gynaecological procedures and that the newer drugs alizapride and ondansetron offer no advantage over droperidol.
5. Ongoing Provision of Individual Clinician Performance Data Improves Practice Behavior

doi: 10.1213/ANE.0b013e3181dd5899

Figure 1. Sample demonstrating layout and content of an individual provider report.
5. Decision support increases guideline adherence for prescribing postoperative nausea and vomiting prophylaxis


Figure 1. Week by week analysis of all high risk patients. The bars show the percentage of high risk patients receiving postoperative nausea and vomiting prophylaxis prescribed.
5. Decision support increases guideline adherence for prescribing postoperative nausea and vomiting prophylaxis

• In conclusion, an electronic DS system using patient-specific automated reminders significantly improved the guideline adherence for the prescription of PONV prophylaxis. Moreover, the mandatory data entry of risk factors for PONV improved identification of patients at high risk for PONV. After deactivating the DS system, the effect on guideline adherence disappeared completely
6. Conclusion

1. Quality depends on patient’s perception
2. PONV is the big problem
3. PDCA, education can be used in anesthesia
4. Guidelines
5. Measurements
6. DHB, dexamethasone, 5 HT inhibitors are by evidence, preventive and curative drugs for PONV
7. Guidelines and daily practice?
Thank you!
First anaesthesia: Boston: Morton: 16 oct 1846