An analysis of the management and incidence of postoperative nausea and vomiting

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Keywords
Evidence-based practice; Outcomes; Patient safety; Pharmacology; Post-anaesthetic care; Quality of care

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An analysis of the management and incidence of postoperative nausea and vomiting

Brooke Szachnowicz, Jayne Pawasauskas and Todd Brothers

Abstract

Background: Postoperative nausea and vomiting significantly increases recovery time, reduces patient satisfaction, and increases time to discharge. Consensus guidelines for the management of postoperative nausea and vomiting highlight effective methods for prophylaxis and treatment. Implications of adherence to these guidelines include both improved patient outcomes and reduced healthcare costs.

Objective: This study aimed to assess the incidence, contributing factors, and current prescribing practices for prophylaxis and treatment of postoperative nausea and vomiting.

Methods: Electronic medical records were assessed for adult patients who had an elective gastrointestinal or gynaecologic surgical procedure over a one-year period. Patient demographics and perioperative data were collected to assess risk factors and the incidence of postoperative nausea and vomiting. The appropriateness of prophylaxis and treatment was assessed according to current guidelines.

Results: The incidence of postoperative nausea and vomiting was consistent with previously noted findings. The average time spent under anaesthesia was significantly higher in patients who experienced postoperative nausea and vomiting. Appropriate evidence-based rescue therapy was administered in a minority of the cohort experiencing postoperative nausea and vomiting.

Conclusion: There is substantial opportunity for provider education and adherence to best prescribing practices. Enhanced adherence to evidence-based rescue therapy prescribing may improve patient outcomes and satisfaction.

Keywords

Evidence-based practice / Patient safety / Outcomes / Pharmacology / Post-anaesthetic care / Quality of care

Introduction and literature review

Postoperative nausea and vomiting (PONV) significantly increases recovery time, reduces patient satisfaction, and increases time to hospital discharge (Pace et al 2014). PONV has been reported to be the second most common postoperative complaint following pain and is ranked by patients in the top five most undesirable outcomes of surgery (Dzwonczyk et al 2012, Shaikh et al 2016). The occurrence of PONV has been associated with additional negative clinical outcomes including bleeding, aspiration, dehydration, and airway obstruction, all of which prolong recovery times (Matthews 2017). Consensus guidelines for the management of PONV highlight effective methods for both prophylaxis and treatment (Gan et al 2014). Numerous strategies may reduce the incidence of PONV, including recognition of patients at increased risk, administering prophylactic therapies when necessary, and identifying those in need of rescue therapy.

The first step in avoidance of PONV is to identify patients who are at an increased risk. There is current literature support identifying perioperative and patient-related factors that increase a patient’s risk of developing PONV (Apfel et al 2012). Perioperative risk factors of developing PONV include surgical type, length of exposure of anaesthetic administration, use of particular anaesthetic agents such as noxious inhalants, use of

Table 1 highlights the Apfel Risk Factor Assessment Tool, a validated scoring tool that was constructed as a result of a cross-validation study of two prospective cohort analyses (Apfel et al 1999). Application of the Apfel scoring tool uses patient and perioperative risk factors to estimate the likelihood of developing PONV. The current consensus guidelines for the management of PONV recommend the use of this scoring tool and outline the prophylactic approach recommended for each Apfel risk score (Gan et al 2014). Table 2 highlights each Apfel score with the corresponding PONV incidence and number of recommended prophylactic approaches. For example, patients with an Apfel risk score of 3 have a 60% incidence of PONV and should receive between one and two prophylactic approaches. By identifying patients at a medium or high risk of PONV, meaning an Apfel risk score of at least 2, the application of prophylactic treatments may reduce the need for rescue therapy postoperatively (Apfel et al 1999). Due to an unnecessary risk of adverse effects, prophylactic therapy is not recommended for low-risk patients unless emesis is a direct medical risk or concern, such as in patients with a wired jaw or increased intracranial pressure.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Apfel Risk Factor Assessment Tool</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk factor</td>
<td>Points</td>
</tr>
<tr>
<td>Female gender</td>
<td>1</td>
</tr>
<tr>
<td>History of PONV</td>
<td>1</td>
</tr>
<tr>
<td>Nonsmoker</td>
<td>1</td>
</tr>
<tr>
<td>Postoperative opioid use</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>0–4</td>
</tr>
</tbody>
</table>

PONV: postoperative nausea and vomiting.
Source: Apfel et al (1999)

Table 2 | Prophylaxis based on Apfel risk score

<table>
<thead>
<tr>
<th>Risk score</th>
<th>Risk category</th>
<th>PONV incidence (%)</th>
<th>Number of prophylactic approaches recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Low</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>Low</td>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>Medium</td>
<td>40</td>
<td>1–2</td>
</tr>
<tr>
<td>3</td>
<td>Medium</td>
<td>60</td>
<td>1–2</td>
</tr>
<tr>
<td>4</td>
<td>High</td>
<td>80%</td>
<td>3–</td>
</tr>
</tbody>
</table>

PONV: postoperative nausea and vomiting.
Source: Gan et al (2014)

The primary objective of this study was to retrospectively assess the incidence, contributing factors, and treatment of PONV. Current prescribing practices and their accordance to recent evidence-based guidelines regarding both prophylaxis and treatment of PONV were assessed. The secondary objective of this study was to determine the proportion of recently discharged postoperative patients who returned to the hospital presenting with post-discharge nausea and vomiting (PDNV).

**Methods**

**Study population**

In this retrospective cohort study, records were screened for adult patients undergoing an elective gastrointestinal or genitourinary surgical procedure performed at Kent Hospital, a medium-sized community teaching hospital in Rhode Island, over a one-year period. Patients undergoing these procedures were identified using Current Procedural Terminology codes. Procedures accepted for analysis included any form of cholecystectomy, hysterectomy, or hernia repair, not limited by either open or laparoscopic procedures. These procedures were selected to capture as many PONV cases as possible, as they are associated with increased risk (Greene et al 2015). The included cohort population consisted of patients 18 years of age or older who had been admitted to any inpatient medicine unit following their surgical procedure. Patients admitted to the intensive care unit, labour and delivery unit, or patients receiving hospice or palliative care were excluded from the study. Medical records with incomplete medication administration documentation were also excluded from the analysis.

**Data collection and analysis**

Data collection from electronic medical records was performed by the primary author and confirmed by the co-authors of this paper. Using these records, patient demographics were first assessed to determine individual Apfel risk scores, which included age, sex, tobacco use, and personal history of PONV. Perioperative data were collected, including procedure type; length of time receiving anaesthesia; preoperative, intraoperative, and postoperative medication administration; post-anaesthesia care unit (PACU) length of stay; and incidence of PONV. Lastly, records were assessed for hospital re-presentations due to complaints of PDNV. Data cleaning was performed in regard to erroneous data as well as outliers for continuous variables. Chi-square tests and logistic regression analyses including...
standard errors of the mean were used to determine the significance of differences in variables between the cohort that experienced PONV and the cohort that did not. Mann–Whitney tests were used to determine the significance of differences in continuous variables, with an a priori significance level of 0.05. Statistical tests were performed using SPSS, version 26 (IBM Corporation, Armonk, NY). The hospital’s Institutional Review Board approved this study.

Results

One hundred and sixty-one records met inclusion criteria (Figure 1). The final sample population was predominantly female (85%) and reported as nonsmokers (79%). The incidence of inpatient PONV in the total sample was 31.1%. The average age of the sample experiencing PONV was 46.8 years (±13.67) and (96%) female. There were no statistically significant differences in age, gender, hospital length of stay, PACU length of stay, or return to the hospital with PDNV between cohorts. The median number of prophylactic approaches used in patients who experienced PONV was higher than in those patients who did not (3.04 ± 0.11 versus 2.72 ± 0.07, p = 0.014). This appropriately correlated with higher average Apfel risk scores in the PONV cohort compared to the non-PONV cohort (2.72 ± 0.07 versus 2.43 ± 0.07, p = 0.03). This same correlation was also observed when adjusting Apfel risk scores by adding one point to the score for patients with unknown PONV histories (3.72 ± 0.07 versus 3.43 ± 0.07, p = 0.025). The average exposure time (minutes) of inhaled anaesthesia were significantly higher in patients who experienced PONV than in patients who did not (135.38 ± 6.2 versus 119.96 ± 3.97, p = 0.027) (Table 3). Of the 161 total studied patients, 12 presented to the ED complaining of nausea and vomiting following hospital discharge. Lastly, appropriate administration of PONV rescue therapy, in accordance with best practice guidelines, was observed in 38% of PONV cases. Inappropriate administration of rescue therapy was defined as patients receiving a second dose of the same antiemetic agent within 6h of administration of the prophylactic dose.

Discussion

The mechanism of PONV is multifactorial. Afferent stimulation from several physiologic areas including the pharynx, gastrointestinal tract, and chemoreceptor

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**Figure 1** Population identification. CPT: Current Procedural Terminology

**Table 3** Results.

<table>
<thead>
<tr>
<th>Variable</th>
<th>PONV cohort</th>
<th>No PONV cohort</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years ± SEM)</td>
<td>46.8 ± 1.93</td>
<td>51.9 ± 1.38</td>
<td>0.084</td>
</tr>
<tr>
<td>Gender (% female)</td>
<td>96%</td>
<td>79%</td>
<td>0.004</td>
</tr>
<tr>
<td>Length of Stay (days)</td>
<td>1.44 ± 0.135</td>
<td>1.36 ± 0.064</td>
<td>0.791</td>
</tr>
<tr>
<td>PACU length of stay (min)</td>
<td>77.5 ± 5.10</td>
<td>75.7 ± 3.92</td>
<td>0.436</td>
</tr>
<tr>
<td>Return to hospital</td>
<td>8</td>
<td>6</td>
<td>0.249</td>
</tr>
<tr>
<td>Apfel Risk Score</td>
<td>2.72 ± 0.07</td>
<td>2.43 ± 0.07</td>
<td>0.030</td>
</tr>
<tr>
<td>Apfel score adjusted (+1)</td>
<td>3.72 ± 0.07</td>
<td>3.43 ± 0.07</td>
<td>0.025</td>
</tr>
<tr>
<td>No. of prophylactic</td>
<td>3.04 ± 0.11</td>
<td>2.72 ± 0.07</td>
<td>0.014</td>
</tr>
<tr>
<td>approaches</td>
<td>135.38 ± 6.20</td>
<td>119.96 ± 3.97</td>
<td>0.027</td>
</tr>
</tbody>
</table>

PACU: post-anaesthesia care unit; PONV: postoperative nausea and vomiting
trigger zone (CTZ), located in the area postrema, can affect the central vomiting centre. The activation of histaminergic, serotonergic, dopaminergic, muscarinic, opioid, and neurokinin receptors is all implicated in the stimulation of the CTZ (Chatterjee et al 2011). Blockade of these receptors is the primary mechanism of most antiemetic drugs. Figure 2 outlines numerous antiemetics and their location of action. The choice of prophylactic therapy should be based upon patient preference, level of PONV risk, relevant patient conditions, and cost (Gan et al 2014). Adverse effects of certain antiemetic medications must also be considered in each patient case. For example, dexamethasone is associated with reduced wound healing, and droperidol may lengthen the QT interval, increasing the risk of arrhythmia. Combination prophylactic therapy with pharmacologic agents utilising different mechanisms of action is preferred over monotherapy in patients deemed moderate to high PONV risk.

Aside from antiemetic agents, avoidance of volatile anaesthetics, nitrous oxide, general anaesthesia, and opioids when possible has also been shown to reduce the risk of PONV (Oderda et al 2019, Shaikh et al 2016). Cholecystectomy, laparoscopy, and gynaecological procedures have shown to significantly increase the risk of PONV (Apfel et al 2012). The emetogenicity of these procedures may be due to vagal stimulation as well as stretching and peritoneal irritation (Miller 2009). In regard to patient-specific risk factors, smoking has shown to be protective for PONV due to the gradual desensitisation of the CTZ (Shaikh et al 2016). Given this information, there is a multitude of prophylactic measures available to reduce the incidence of PONV.

This study aimed to evaluate the incidence of PONV, identify contributing risk factors, and determine prescribing practices in relation to evidence-based practice guidelines. The incidence of PONV observed in this study, 31.1%, is consistent with most other findings previously noted (Watcha & White 1992). This suggests that the sample population may have been demographically similar to those previously studied and may have also received similar therapies.

The Apfel risk score solely assesses independent risk factors and utilisation of this tool has been shown to significantly reduce the incidence of PONV (Apfel et al 1999, Pierre et al 2002). As anticipated with published findings, our study demonstrated that patients with higher Apfel risk scores were more likely to experience PONV. One barrier that we encountered in this assessment was reduced documentation in the electronic medical record in regard to patient history of PONV. To account for a lack of complete patient charting, one additional point was assigned to the risk score for each patient with an unknown PONV history. Patients with higher adjusted Apfel risk scores were found to have a higher incidence of PONV, suggesting that this adjustment was non-contributory to the overall risk. Also, time under anaesthesia was found to be a significant risk factor for the incidence of PONV, confirming findings from previous studies (Apfel et al 2012, Sinclair et al 1999) that suggest shorter, less intensive procedures are commonly associated with a reduced PONV risk.

As previously stated, a higher Apfel risk score correlates to an increased need for prophylaxis. Our study identified the number of prophylactic approaches utilised in patients to be appropriate, in regard to their Apfel risk score, in the large majority of cases. However, patients receiving more prophylactic approaches were found to have a higher incidence of PONV. Previous studies assessing the incidence of PONV in a similar cohort have also found high rates of PONV despite antiemetic prophylaxis (Shiraishi-Zapata et al 2020). This may be

Knowing the modifiable risks of PONV such as opioid administration, volatile anaesthetic use, pain, and time under anaesthesia, it is in the patient’s best interest to avoid these practices whenever possible. A completely opioid and volatile anaesthetic-free procedure under general anaesthesia is not feasible. Using total intravenous anaesthesia (TIVA) rather than inhaled anaesthetics is one approach to reducing PONV risk (Gan et al 2014). However, TIVA requires the use of an intravenous sedative, such as propofol, in combination with an intravenous opioid, such as fentanyl. On the contrary, using non-opioid analgesia such as intraoperative ketorolac may also be a preferred approach (Gan et al 2014). However, inhaled anaesthetics would likely be used in this scenario and the increased PONV risk of opioid use must be balanced with the increased PONV risk of pain. Opioids may be necessary to manage pain in certain circumstances and using scheduled analgesia rather than on an as-needed basis is preferred.

Most significantly, we identified a large disparity between observed rescue therapy prescribing and appropriate prescribing according to the current treatment guidelines. Appropriate evidence-based rescue therapy was administered in only 38% of the cohort, indicating that the majority of patients received a second dose of the same antiemetic agent within 6h of administration of the prophylactic dose. This is considered inappropriate because evidence suggests that administration of a second dose of the same antiemetic is highly unlikely to be effective if the first agent administered did not prevent PONV (Gan et al 2014, Kovac et al 1999). For example, if a corticosteroid such as dexamethasone was given intraoperatively for prophylaxis and the patient was to experience PONV shortly after in the PACU, a 5HT-3 antagonist such as ondansetron would be an appropriate rescue therapy option because of its different mechanism of action. This observation of inappropriate rescue therapy prescribing identifies a substantial opportunity for provider education and adherence to best practices. Further, this low adherence to rescue therapy guidelines may have played a role in the PDNV observed. The incidence of patient return to the hospital with PDNV may be reduced if the treatment of PONV is optimised.

Studies have demonstrated difficulties with adherence to evidence-based guidelines in the preventative management of PONV (Dusart et al 2019); however, aside from this study, there is little data on the adherence to evidence-based guidelines in regard to rescue treatment of PONV. Solicitation of provider feedback is known to be beneficial in educating prescribers on PONV prevention and treatment (Greene et al 2015). Implementation of an institutional protocol that is inclusive of appropriate rescue therapy prescribing is another option to increasing compliance with evidence-based guidelines. Staff communication regarding best prescribing practices is of importance. Prescriber compliance can be measured using data from the electronic medical record and feedback in regard to the prescriber’s clinical performance may be insightful. Pharmacists should also be involved in the medication verification process in ensuring that rescue therapy adheres to best practices. Perioperative pharmacy is a growing specialty that has the potential to optimise therapy in this area. Perioperative pharmacists can be utilised for providing medication information as well as drug therapy management including perioperative order review (Bickham et al 2019).

Finally, the effective prevention and management of PONV is a financially relevant concern. Although this study did not assess cost, it has been previously well-described that the prevention of PONV has the ability to ameliorate healthcare expenditure outcomes (Dzwonczyk et al 2012). PONV prophylaxis has been reported to reduce hospital expenses in comparison to the costs of PONV treatment and readmission (Dzwonczyk et al 2012). In a retrospective chart review of surgical cases, one facility’s net profit increased linearly with increased PONV prophylaxis administration (Dzwonczyk et al 2012). Furthermore, researchers noted administering prophylaxis to all surgical patients yielded an estimated hospital net profit of $140,866 (just over £105,000) during the two-year study period, whereas administering prophylaxis to patients with at least three risk factors resulted in a net profit of $105,650, a 25% decrease (Dzwonczyk et al 2012). This reduction in profit may be attributed to the increased expenses incurred due to rescue therapy and readmissions.

**Limitations**

Limitations of this study include a lack of complete patient charting and a lack of patient information available outside of the electronic medical record due to its retrospective nature. This could have potentially led to errors in the calculation of each patient’s Apfel risk score; however, we were able to account for this by correcting the risk score for patients with certain unknown baseline characteristics.

**Future research**

Future studies assessing the impact of evidence-based PONV prophylaxis and particularly rescue therapy prescribing on the incidence of PDNV would be insightful. This study found that 24% of patients experiencing PONV returned to the hospital with PDNV. Implications of this include reduced patient outcomes and satisfaction as
well as increased costs of care. Further, utilising the postoperative quality of recovery (QoR-40) score to assess patient preparedness for discharge from the PACU can offer insight into the impact of this prescribing on patient perception of recovery. Studies have found that PONV is a common patient concern prior to surgery and that patients want to know the risk of PONV in regard to anaesthesia (Royston & Cox 2003). Another potential area for future research is the investigation of patient informed consent in regard to their understanding of risk level for PONV, anaesthesia, and analgesia choices. Future directions to examine at-risk patients may include implementation of pharmacogenomic data, use of machine learning systems and artificial intelligence to guide treatment algorithms, and use of novel pharmacotherapeutic agents.

Conclusion

PONV contributes to poorer clinical and economic outcomes; therefore, improvement in both prevention and management strategies is paramount. The complexity of the condition requires practical management with application of best practices. Clinical and economic PONV outcomes can be achieved with accurate identification of risk factors and deployment of effective treatment options. Utilising a proactive approach remains fundamental to reduce its incidence. Enhanced adherence to current guidelines in regard to rescue therapy prescribing may be vital in improving patient outcomes. Prescriber education remains essential to support the use of risk scoring tools, effective prophylactic approaches, and appropriate rescue therapies.

Key phrases

- Clinical and economic PONV outcomes can be achieved with accurate identification of risk factors and deployment of effective, evidence-based prophylaxis and rescue therapy treatment options.
- Utilising a proactive approach remains fundamental to reducing PONV incidence, subsequently limiting both complications and therapy-related costs.
- Prescriber education remains essential to support the use of risk scoring tools, effective prophylactic approaches, and appropriate rescue therapies.
- Enhanced adherence to current guidelines in regard to rescue therapy prescribing may be vital in improving patient outcomes.

Key terms

- Postoperative Nausea and Vomiting Outcomes, Anaesthesia, Incidence, Risk Factors.

Declarations

Competing Interests

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: Pawauskas is a consultant for Mallinckrodt Pharmaceuticals and Heron Therapeutics and is a member of Speakers’ Bureau for Mallinckrodt Pharmaceuticals.

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References

Apfel CC, Kranke P, Katz MH, et al 2002 Volatile anaesthetics may be the main cause of early but not delayed postoperative vomiting: a randomized controlled trial of factorial design British Journal of Anaesthesia 88 (5) 659–668
Apfel CC, Lääärä E, Koivuranta M, et al 1999 A simplified risk score for predicting postoperative nausea and vomiting: conclusions from cross-validations between two centers Anesthesiology 91 (3) 693–700
Chatterjee S, Rudra A, Sengupta S 2011 Current concepts in the management of postoperative nausea and vomiting Anesthesiology Research and Practice 2011 748031
Dusart CC, Lois FJ, Steyaert AH 2019 The observance of evidence-based guidelines for the prevention of postoperative nausea and vomiting is difficult in daily practice of an academic hospital – a retrospective cohort study Acta Anaesthesiologica Belgica 70 53–60
Dzwonczyk R, Weaver TE, Puente EG, et al 2012 Postoperative nausea and vomiting prophylaxis from an economic point of view American Journal of Therapeutics 19 (1) 11–15
Gan TJ, Diemunsch P, Habib AS, et al 2014 Consensus guidelines for the management of postoperative nausea and vomiting Anesthesia and Analgesia 118 (1) 85–113
Greene NH, Norstedt PA, Nair BG, et al 2015 Systematic postoperative nausea prophylaxis feedback improves clinical performance in anaesthesiology residents Journal of Education in Perioperative Medicine 17 (3) 301
Leslie K, Myles PS, Chan MT, et al 2008 Risk factors for severe postoperative nausea and vomiting in a randomized trial of
nitrous oxide-based vs nitrous oxide-free anaesthesia
British Journal of Anaesthesia 101 (4) 498–505
Mannix K 2006 Palliation of nausea and vomiting in malignancy Clinical Medicine 6 (2) 144–147
Miller RD (Eds) 2009 Miller’s Anesthesia 7th ed Philadelphia, PA, Churchill Livingstone/Elsevier
Moon YE 2014 Postoperative nausea and vomiting Korean Journal of Anesthesiology 67 (3) 164–170
Pace NL, Carlisle J, Eberhart LHJ, et al 2014 Prediction models for the risk of postoperative nausea and vomiting Cochrane Database of Systematic Reviews 9 CD011318
Pierre S, Benais H, Pouymayou J 2002 Apfel’s simplified score may favourably predict the risk of postoperative nausea and vomiting Canadian Journal of Anaesthesia 49 (3) 237–242
Roberts GW, Bekker TB, Carlsen HH, et al 2005 Postoperative nausea and vomiting are strongly influenced by postoperative opioid use in a dose-related manner Anesthesia and Analgesia 101 (5) 1343–1348
Royston D, Cox F 2003 Anesthesia: the patient’s point of view The Lancet 362 (9396) 1648–1658
Sinclair DR, Chung F, Mezei G 1999 Can postoperative nausea and vomiting be predicted? Anesthesiology 91 (1) 109–118
Visser K, Hassink EA, Bonsel GJ, et al 2001 Randomized controlled trial of total intravenous anesthesia with propofol versus inhalation anesthesia with isoflurane-nitrous oxide: postoperative nausea with vomiting and economic analysis Anesthesiology 95 (3) 616–626
Watcha MF, White PF 1992 Postoperative nausea and vomiting: its etiology, treatment, and prevention Anesthesiology 77 182–184