Nausea and vomiting in day case anaesthesia: risk score, prophylaxis and rescue therapy

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Who is at risk for PONV?

Estimating an individual’s baseline risk for PONV can indicate who will most likely benefit from prophylactic antiemetic therapy.

In adults, only a few baseline risk factors have consistently been shown to be independent predictors for PONV [1, 2]. The most important patient-specific predictors of increased risk are female gender, non-smoking and a history of PONV or motion sickness. In addition, general anaesthesia with volatile anaesthetics or nitrous oxide, and the use of postoperative opioids are important anaesthesia-related predictors. The emetogenic effect of inhalational anaesthetics and opioids appears to be dose related - longer procedures, with concomitantly longer anaesthesia times and increased postoperative opioid consumption, are associated with an increased incidence of PONV. Conversely, many factors that are associated with or commonly believed to increase the patient’s risk are, in fact, not independent predictors. For example, type of surgery is not generally useful in predicting the incidence of PONV [3]. While several studies have identified a number of surgical procedures as independent predictors, those results were generally not consistent across studies. An exception may be laparoscopic cholecystectomies or laparoscopic hysterectomies that have been reported to be independent predictors in several independent studies. Data on other factors such as obesity, anxiety, and neuromuscular blockade suggest that they have no significant clinical influence on PONV.

Unfortunately, none of the patient- or anaesthesia-related risk factors are sufficiently sensitive or specific enough to adequately predict PONV risk in adults [3]. For example, although a history of PONV is undoubtedly a risk factor for future PONV, the sensitivity is surprisingly only about 50%, that is, only 50% of patients who develop PONV will be correctly identified beforehand if a history of PONV is used as a single predictor. Thus, several risk models have been developed using multiple risk factors. For adults undergoing general inhalational anaesthesia, the simplified risk models of Apfel et al and Koivuranta et al have been shown to have good predictive characteristics in a variety of situations (Figure 1) [2, 4, 5].

The simplified risk score of Apfel et al includes four independent predictors: female gender, non-smoking status, history of PONV or motion sickness, and planned usage of postoperative IV opioids [4]. When 0, 1, 2, 3 or 4 of these predictors are present, the patient’s risk is approximately 10%, 20%, 40%, 60% or 80%, respectively. While the true incidences in various patient populations might deviate from these predicted risks - for example, for patients undergoing short ambulatory procedures, a simplified risk model allows clinicians to make a reasonable and practical estimate of an individual adult’s risk for PONV.

What is unique about postoperative nausea and postoperative vomiting in day case anaesthesia?

According to the Society for Ambulatory Surgery (SAMBA), 65% of all surgical procedures are now done on an outpatient basis. A shift from inpatient procedures to ambulatory surgery began in the 1980s and continues to this day. Until recently, anaesthesiologists have focused the majority of their analgesic and anti-emetic strategies on patient care up to the point of patient discharge. This failure to plan ahead is reflected in the growing documentation of patients’ experiences with nausea and vomiting after patients have left the hospital. Nausea and vomiting in ambulatory surgery patients following discharge becomes particularly dangerous because they no longer have immediate access to fast-onset intravenous anti-emetics while potentially being unable to tolerate oral medications. However, there has been relatively little research to date examining the problem of post-discharge nausea and vomiting (PDNV), an outcome that we predict to be occurring more frequently with increased application of day case anaesthesia care.
Although significant research on the prevention of postoperative nausea and vomiting has been performed in the last 20 years, the research shows the incidence of PDNV to be still surprisingly high. A systematic review from 2002 reported an incidence of 17% for nausea (range 0-55%) and 8% for vomiting (range 0-16%) after outpatient surgery [6]. One prospective multicenter survey reported an even higher incidence of nausea and vomiting after ambulatory surgery. Nausea occurred in 48% of the patients on postoperative day 1 and 8% on postoperative day 7. Vomiting occurred in a smaller proportion of the patients: 12% on postoperative day 1 and 1% on postoperative day 7. Nearly half of all patients who did not have PONV in the hospital experienced nausea and/or vomiting on post-discharge days 1 to 3 [7]. In a recent multicenter cohort study on 2170 patients, we measured the incidence, established risk factors, and developed a prediction model for PDNV. After being discharged from the hospital, 37% of patients experienced nausea, 13% severe nausea, 12% vomiting, and 5% severe vomiting.

The incidences of nausea and vomiting in the recovery room are much lower than after discharge, indicating that substantially more patients suffer from nausea or vomiting after discharge than in the recovery room. Therefore, this phenomenon is usually not witnessed by the surgical or anaesthesia team covering the peri-operative treatment in the hospital setting. Additionally, PONV can delay discharge from postanaesthesia care units and is one of the leading causes of unexpected hospital admission after planned ambulatory surgery [7]. Not surprisingly, PDNV adversely affects patient recovery and possibly influences the cost effectiveness of day case surgical procedures.

**What can I do to prevent PONV?**

Use of prophylactic anti-emetics should be based on a valid assessment of an individual patient’s risk for PONV or postoperative vomiting. More specifically, anti-emetic prophylaxis should primarily be used when an individual patient’s baseline risk multiplied by the relative risk reduction resulting from prophylaxis produces a clinically meaningful decrease in the risk of PONV (absolute risk reduction). In general, prophylaxis in a patient already at low risk for PONV will not produce a clinically meaningful decrease in PONV incidence. On the other hand, even a small decrease in PONV risk might be clinically desirable for patients where vomiting can cause significant medical harm; for instance, in a patient with a wired jaw or increased intracranial pressure, or following gastric or oesophageal surgery.

Of the identified PONV risk factors, only a few can be directly addressed by the anaesthesiologist: use of volatile anaesthetics, nitrous oxide and opioids. Avoiding these emetogenic agents should be the first line approach to prevent PONV in patients at high baseline risk,
or clinical risk, for PONV (Figure 1). For instance, use of a local or regional peripheral anaesthetic technique instead of general anaesthesia may be the most effective way to prevent PONV [8]. However, if general anaesthesia is needed in patients at high risk for PONV, avoiding both volatile anaesthetics and nitrous oxide by using a ‘total intravenous technique’ with propofol and air can reduce a patient’s baseline risk by about 30% [9]. This means that if a patient’s baseline risk is 80%, TIVA will reduce the risk by 24% \((0.80 \times 0.30 = 0.24)\).

In other words, if TIVA is consistently used in patients predicted to have a baseline PONV risk of 80%, it will on average prevent PONV in about 24% (or 1 out of 4) of such patients. If however, TIVA is consistently used in patients with a predicted baseline risk of only 20%, it will reduce the risk only by 6\% \((0.20 \times 0.30 = 0.06)\), or only in about 1 out of 17 patients. Thus, it is really the baseline risk that critically determines whether antiemetic prevention will significantly decrease PONV.

As pointed out above, using TIVA alone would still leave about one out of two high risk patients with PONV (80% baseline risk minus a 24\% absolute risk reduction = 56\%). Clearly, additional anti-emetic strategies are needed, which is the reason why a multimodal approach is generally favoured in patients at high or very high risk. Again, PONV should be recognized as a major concern for at risk patients undergoing day case anaesthesia. As patients no longer have immediate access to healthcare after discharge, anti-emetics should be long-lasting and have limited side effects.

The most commonly used antiemetic agents for the prevention of PONV (in the United States) are the serotonin (5HT3)-antagonists, such as ondansetron, dolasetron, granisetron and palonosetron [9]. Serotonin-antagonists are highly specific, have no sedative side effects and are generally believed to be very safe. However, serotonin-antagonists can also lead to QT-prolongation. Serious arrhythmias reported after dolasetron usage have lead the Canadian health authority to issue a black box warning for dolasetron, even though the QT prolongation after inhalational anaesthesia is significantly longer. Nevertheless, it is worth noting that palonosetron, a novel serotonin-antagonist whose main advantage is probably the half life of 40 h, is unique in this class as it does not have any effect on the QT interval [10]. Furthermore, in contrast to other serotonin antagonists, palonosetron has been shown to be effective in the prevention of delayed chemotherapy-induced nausea and vomiting (CINV), possibly due to its unique anti-emetic mechanisms or its considerable 40-h half life [10]. These properties are promising for specifically preventing nausea and vomiting in ambulatory anaesthesia, but well designed prospective studies will be required before firm recommendations can be made.

The scopolamine patch seems to provide reasonable protection against nausea and vomiting and remains active for up to 72 h [11]. Dry mouth and blurred vision are possible side-effects. Confusion may be another side-effect but is not supported by the literature. In fact, in a study that reported confusion as a side-effect, the incidences of confusion in the scopolamine and placebo groups were similar, and scopolamine was not associated with an increased incidence of side-effects in a well designed study of a 620 relatively young and healthy female outpatients [11]. One reason for this may be that the studies preferentially included young and healthy patients who may be less susceptible to confusion compared with elderly patients, so well-designed, randomized controlled trials may be needed to clarify whether the scopolamine patch may selectively increase postoperative confusion in elderly patients.

The latest anti-emetic is the neurokinin (NK1)-receptor antagonist aprepitant. While its efficacy is well known in the chemotherapy literature, it has also been demonstrated to be effective for prevention of PONV. Specifically, it is at least as effective as ondansetron against nausea, but much more effective against vomiting [12]. This is especially relevant for patients where vomiting might pose a medical risk (wired jaws, abdominal surgery, etc.). Other neurokinin antagonists such as rolapitant and casopitant are currently under investigation. Because of the longer duration of action of palonosetron, aprepitant and the scopolamine patch, [13] these drugs may prove to be particularly useful for post-discharge nausea and vomiting (PDNV). However, studies specifically targeting PDNV are needed before making recommendations.

A dose of 0.625 or 1.25 mg droperidol has been shown to be equally effective as 4 mg ondansetron [9] but reports of severe cardiac arrhythmias have led the FDA to issue a black box warning that in effect limits its use to rescue treatment when other drugs have failed, and requires ECG monitoring for at least 6 h. Recent investigations have shown that droperidol prolongs the QT interval, but again, these effects are generally smaller than those from a general anaesthetic itself [14]. There are also several reports of akathisia or anxiety associated with low doses of droperidol, but most studies have not reported these or any other side-effects [14].

An effective alternative to a 5-HT3 antagonist or droperidol is dexamethasone 4 mg. Given at the beginning of the procedure, it appears to be equally effective as ondansetron 4 mg or droperidol 1.25 mg, but without an increased incidence of side-effects (Figure 2) [9]. Another alternative is metoclopramide. While it has previously been established that the standard dose of 10 mg is ineffective, a recent dose-response study from Wallenborn et al suggests that 25 mg is the minimally effective dose. Because there was a trend of the
50 mg data to have better coverage the next morning, it may be appropriate to give 25 mg intra-operatively IV and either a second 25 mg IV or an equipotent oral dose before discharge [15]. However, an important contra-indication of metoclopramide is that it can exacerbate Parkinsonian symptoms and, therefore, should not be used in patients with Parkinson’s disease [16].

The limited efficacy of a single anti-emetic has prompted numerous studies of prophylaxis and rescue treatment using a combination of anti-emetics. The most successful study was conducted by Scuderi et al, where they were able to eliminate postoperative vomiting before discharge using a multimodal approach [17]. These impressive results triggered our International Multi-center Protocol to Assess the benefits of single and combined antiemetic interventions in a randomized Controlled clinical Trial (IMPACT) to investigate the benefits of ondansetron 4 mg, droperidol 1.25 mg, dexamethasone 4 mg, propofol (instead of volatile anaesthetics), air (instead of nitrous oxide) and remifentanil (instead of fentanyl). The critical findings in this large multicenter study of over 5,000 patients were that ondansetron, dexamethasone, droperidol or TIVA each reduced PONV incidence by about 25-30%, and that combining any of these drugs leads to additive effects (not synergistic nor antagonistic) [9]. Furthermore, the relative risk reduction for each single intervention was independent of all risk factors and, therefore, from the patient’s baseline risk.

Thus, interventions produce the greatest absolute risk reduction in patients most likely to experience PONV. As a corollary, the first antiemetic used for a patient leads to the largest absolute reduction, and each subsequently used antiemetic leads to a smaller absolute additional effect (Table 1) [9].
What do I do if my patient experiences PONV?

All available drug interventions can only reduce but not eliminate the risk of PDNV so there is still a need for effective rescue treatment. For the treatment of PONV in the recovery room, intravenous ondansetron is the most commonly used medication. While thousands of studies have investigated anti-emetics for the prevention of PONV, very few have studied the efficacy of rescue treatment. The most prominent study of rescue treatment is by Kovac et al, in which patients were re-dosed with 4 mg rescue ondansetron to treat PONV in the PACU despite previous prophylaxis with ondansetron 4 mg. In this setting, 4 mg of rescue ondansetron was apparently no more effective than placebo [18]. As might be expected, it appears that rescue medication is unlikely to be effective if it targets the same receptor class previously blocked by prophylactic medication. This conclusion is supported by a study from Candiotti et al and by a retrospective database analysis from Habib et al [19, 20]. In addition, the relatively short half-life (4 h) of intravenous ondansetron suggests a limited effectiveness for the post-discharge period. Therefore, as long as the patient is in the recovery room a long-lasting 5HT₃ antagonist such as palonosetron 0.075 mg is likely to be the better option.

Patients with prior PONV in the recovery room might benefit from a scopolamine patch applied before discharge. However, it may require several hours before significant plasma levels have been reached and the full anti-emetic properties have developed. Rectal application of prochlorperazine or promethazine suppositories are other alternatives, but no studies support their effectiveness for the treatment of PDNV, and both drugs have sedation as a significant side effect, which may not necessarily improve patient satisfaction with postoperative recovery. Alternatively, non-pharmacological interventions such as acupressure stimulation of the P6 may be another approach that could be taught to the patient before discharge.

Conclusion

Patients at low baseline PONV risk rarely benefit from prophylaxis, patients at moderate risk may benefit from a single anti-emetic strategy, and patients at high or very high risk should receive two or more prophylactic interventions to prevent PONV [1]. Finally, when a patient requires rescue medication, it should target a different receptor class than other PONV medications recently given.
Key learning points

- A patient’s risk for PONV is best predicted by a simplified risk score using independent predictors.
- The incidences of nausea and vomiting in the recovery room are much lower than after discharge, indicating that substantially more patients suffer from nausea and/or vomiting after discharge than in the recovery room.
- A PONV prophylaxis strategy should be tailored based on a valid assessment of an individual patient’s baseline risk. Patients at greatest risk will experience the greatest absolute risk reduction from interventions and antiemetic prophylaxis should primarily be used when an individual patient stands to benefit from a clinically meaningful decrease in the risk of PONV.
- A multimodal approach is generally favoured in patients at high or very high risk, so avoiding or reducing exposure to inhaled anaesthetics and opioids in addition to prophylactic anti-emetics. For day case anaesthesia patients, anti-emetics should have a long duration of action and have limited side effects.
- Palonosetron, aprepitant and the scopolamine patch may prove to be particularly useful.
- When a patient requires rescue medication after developing nausea or vomiting, it should target a different receptor class than other PONV medications recently given.

References


