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EDUCATIONAL OBJECTIVES

This presentation will provide a comprehensive overview of postoperative nausea and vomiting (PONV). After this lecture the clinician should be able to:

1. Understand limitations and difficulties of PONV risk factor assessment,
2. Assess patient risk for PONV by using a simplified risk score,
3. Understand that a patient's predicted baseline PONV risk determines the level of predicted benefit from prophylactic therapy,
4. Realize that the effectiveness of a single antiemetic is limited, and
5. Apply a risk-dependent approach to prevent PONV.

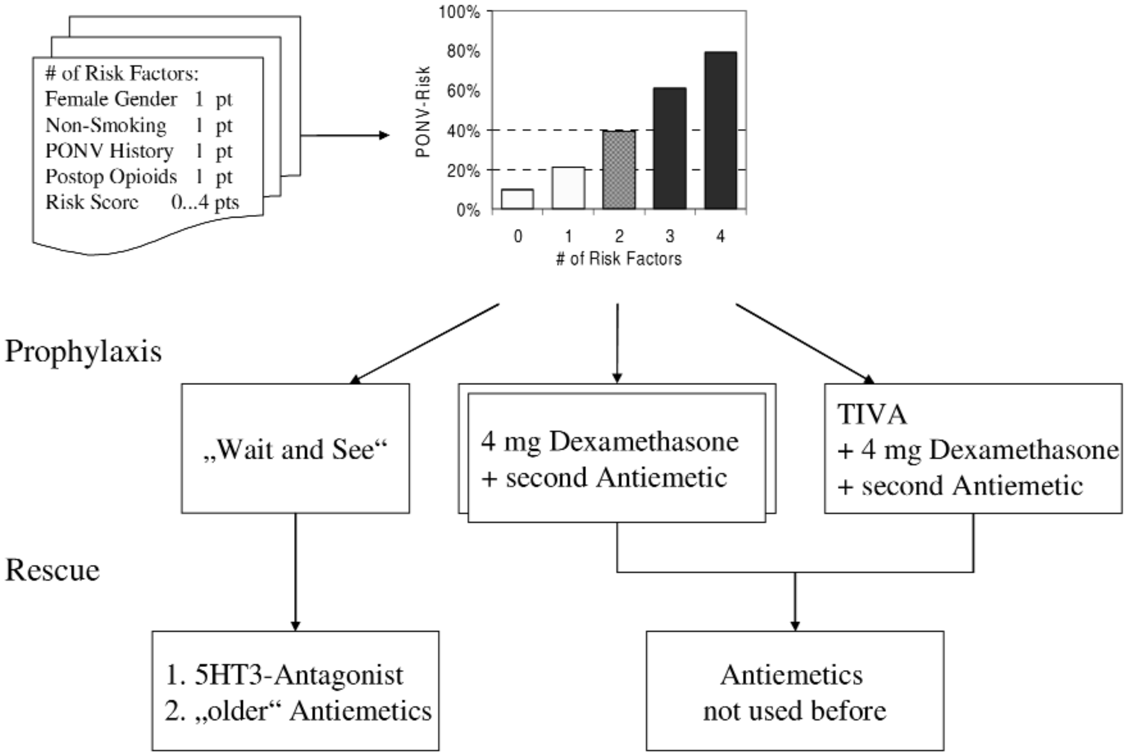
WHO IS AT RISK FOR PONV?

Estimating an individual's baseline risk for PONV can indicate who is most likely to benefit from prophylactic antiemetic therapy.

In adults, only a few baseline risk factors have consistently been shown to be independent predictors for PONV [1-7]. 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. However, many factors that are commonly believed to increase risk are not in fact independent predictors. Factors such as obesity, anxiety, the use of antagonizing neuromuscular block antagonists and the type of surgery are not generally useful in predicting the incidence of PONV [2,7-9].

Unfortunately, no single patient-related or anaesthesia-related risk factor is sufficiently sensitive or specific to adequately predict PONV risk in adults [7]. Several risk models have therefore been developed. The simplified models of Apfel et al. and Koivuranta et al. have been shown to have good predictive characteristics for adults undergoing general inhalational anaesthesia in a variety of situations (see figure 1) [2,4,5,10]. The simplified score of Apfel et al. includes four risk factors: female gender, non-smoking status, history of PONV or motion sickness, and need for postoperative intravenous opioids [4]. When 0, 1, 2, 3, or 4 risk factors are present; the patient's risk is approximately 10%, 20%, 40%, 60%, or 80% respectively. While the true incidence in various patient populations might deviate from these predicted risks (e.g. patients undergoing short ambulatory procedures) a simplified risk model such as this allows clinicians to make a reasonable and practical estimate of an individual adult's risk for PONV.

FIGURE 1. SIMPLIFIED RISK SCORE FROM APFEL ET AL TO PREDICT PATIENT RISK OF PONV [4].



When 0, 1, 2, 3, or 4 of the depicted independent predictors are present, the corresponding risk for PONV is approximately 10%, 20%, 40%, 60% or 80%. The suggested selection of antiemetics can be adjusted to clinical circumstances and needs [1].

For children, publications have cited a variety of risk factors thought to be associated with PONV. However, supporting evidence has been meagre. More recently, Eberhart et al applied multivariate analysis to a large series of paediatric patients to identify PONV risk factors [11]. Four factors were independent predictors: duration of surgery ≥ 30 min, age ≥ 3 years, strabismus surgery, and a history of relatives with POV (postoperative vomiting) or PONV. Eberhart demonstrated that the risk for POV was 9%, 10%, 30%, 55% and 70% when 0, 1, 2, 3, or 4 of these independent predictors were present.

WHAT CAN I DO TO PREVENT PONV?

The use of prophylactic antiemetics should be based on a valid assessment of an individual patient’s risk for PONV or POV. More specifically, antiemetic 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 some patients. In situations 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) then PONV prophylaxis might be desirable even if it results in only a small decrease in PONV risk.

Only a few of the identified PONV risk factors can be directly addressed by the anaesthetist; the use of volatile anaesthetics, nitrous oxide and opioids. Avoiding these emetogenic agents is one approach to prevent PONV in patients at high baseline risk, or clinical risk, of PONV. For instance, use of a local or regional peripheral anaesthetic technique instead of general anaesthesia can be considered [12]. 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% [13]. This means that if a patient’s baseline risk is 80%, TIVA will reduce the risk by 24% (0.80 x 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 in 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 x 0.30 = 0.06), or about 1 in 17 patients. Thus, it is really the baseline risk that determines whether an antiemetic can lead to a relatively significant decrease in PONV.

However, in patients predicted to have a very high baseline risk of PONV, a TIVA would still leave about every second patient with actual PONV (80% baseline risk minus a 24% absolute risk reduction = 56%). Clearly, additional antiemetic strategies are needed. The most commonly used antiemetic agents (in the United States) are the serotonin ($5HT_3$)-antagonists, i.e. ondansetron, dolasetron or granisetron. A new drug on the market is palonosetron, which is the only serotonin antagonist on the market that has shown effectiveness and received approval for delayed chemotherapy-induced nausea and vomiting. A recent study by White, Scuderi and colleagues has shown it is also effective for PONV. An even more recent development is the neurokinine (NK_1)-receptor antagonist aprepitant. A study by Gan et al. suggests it is as effective against nausea as ondansetron but much more effective against vomiting [ASA abstracts 2005]. Palonosetron, aprepitant and the scopolamine patch seem to have extended duration of actions, which make these drugs especially useful for post discharge nausea and vomiting (PDNV) [14].

A dose of 0.625 or 1.25 mg droperidol has been shown to be equally effective as 4 mg ondansetron [13,15]. 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 hours. Recent investigations have shown that droperidol has minor but short term effects on QT prolongation. However, these effects are no worse than those from a general anaesthetic itself [16,17]. There are also reports of akathisia or anxiety associated with low doses of droperidol. However, most studies have not reported these or any other side effects, so the extent of any such effects remains unclear [18].

A cost effective alternative to a $5\text{-}HT_3$ antagonist or droperidol is 4 mg dexamethasone. Given at the beginning of the procedure it appears to be equal in effectiveness to 4 mg ondansetron or 1.25 mg droperidol, but without an increased incidence of side-effects [13]. Another alternative is metoclopramide. Whilst it is already well-established that the standard dose of 10 mg is ineffective, a recent dose-response study suggests that 25 mg may in fact be the minimally effective dose, and that 50 mg provides a better 24 hour coverage [19].

The limited efficacy of a single antiemetic has prompted numerous studies of prophylaxis and/or rescue treatment using a combination of antiemetics. The most successful study was conducted by Scuderi et al, where they were able to eliminate postoperative vomiting before discharge using a multimodal approach [20]. These impressive results triggered an ***I***nternational ***M***ulti-centre ***P***rotocol to ***A***ssess the benefits of single and combined antiemetic interventions in a randomized ***C***ontrolled clinical ***T***rial (IMPACT) to investigate the benefits of ondansetron, droperidol, dexamethasone, propofol (instead of volatile anaesthetics), air (instead of nitrous oxide) and remifentanil (instead of fentanyl). The critical findings were that a) ondansetron, dexamethasone, droperidol or TIVA each reduced relative PONV incidence by about 25 to 30 %, and b) that combining any of theses drugs leads to additive effects (not synergistic or antagonistic) [13]. The relative risk reduction for each single intervention is therefore apparently independent over a wide range of absolute risks. 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 [13].

In conclusion, patients at low baseline PONV risk rarely benefit from prophylaxis, patients at moderate risk may benefit from a single antiemetic strategy, and patients at high or very high risk should receive two or more prophylactic intervention to prevent PONV [1].

Further information is available at www.ponv.org

If you have any further questions then I can be contacted at apfel@ponv.org

REFERENCES

1. Apfel CC, Roewer N. Risk assessment of postoperative nausea and vomiting. Int Anesthesiol Clin 2003;41(4):13-32.
2. Koivuranta M, Laara E, Snare L, Alahuhta S. A survey of postoperative nausea and vomiting. Anaesthesia 1997;52:443-449.
3. Sinclair DR, Chung F, Mezei G. Can postoperative nausea and vomiting be predicted? Anesthesiology 1999;91(1):109-118.
4. Apfel CC, Laara E, Koivuranta M, Greim CA, Roewer N. A simplified risk score for predicting postoperative nausea and vomiting: Conclusions from cross-validations between two centers. Anesthesiology 1999;91(3):693-700.
5. Pierre S, Benais H, Pouymayou J. Apfel's simplified score may favourably predict the risk of postoperative nausea and vomiting. Canadian Journal of Anesthesia 2002;49(3):237-42.
6. Stadler M, Bardiau F, Seidel L, Albert A, Boogaerts JG. Difference in risk factors for postoperative nausea and vomiting. Anesthesiology 2003;98(1):46-52.
7. Apfel CC, Kranke P, Eberhart LH. Comparison of surgical site and patient's history with a simplified risk score for the prediction of postoperative nausea and vomiting. Anaesthesia 2004;59(11):1078-82.
8. Kranke P, Apfel CC, Papenfuss T, Rauch S, Lobmann U, Rubsam B, et al. An increased body mass index is no risk factor for postoperative nausea and vomiting. A systematic review and results of original data. Acta Anaesthesiologica Scandinavica 2001;45(2):160-166.
9. Van den Bosch JE, Moons KG, Bonsel GJ, Kalkman CJ. Does measurement of preoperative anxiety have added value for predicting postoperative nausea and vomiting? Anesth Analg 2005;100(5):1525-32.
10. van den Bosch JE, Kalkman CJ, Vergouwe Y, Van Klei WA, Bonsel GJ, Grobbee DE, et al. Assessing the applicability of scoring systems for predicting postoperative nausea and vomiting. Anaesthesia 2005;60(4):323-31.
11. Eberhart LH, Geldner G, Kranke P, Morin AM, Schauffelen A, Treiber H, et al. The development and validation of a risk score to predict the probability of postoperative vomiting in pediatric patients. Anesth Analg 2004;99(6):1630-7.
12. Friedberg BL. Propofol-ketamine technique: dissociative anesthesia for office surgery (a 5-year review of 1264 cases). Journal of Clinical Anesthesia 1999;23(1):70-75.
13. Apfel CC, Korttila K, Abdalla M, Kerger H, Turan A, Vedder I, et al. A factorial trial of six interventions for the prevention of postoperative nausea and vomiting. New England Journal of Medicine 2004;350(24):2441-51.
14. Kranke P, Morin AM, Roewer N, Wulf H, Eberhart LH. The efficacy and safety of transdermal scopolamine for the prevention of postoperative nausea and vomiting: a quantitative systematic review. Anesth Analg 2002;95(1):133-143.
15. Fortney JT, Gan TJ, Graczyk S, Wetchler B, Melson T, Khalil S, et al. A comparison of the efficacy, safety, and patient satisfaction of ondansetron versus droperidol as antiemetics for elective outpatient surgical procedures. S3A-409 and S3A-410 Study Groups. Anesthesia and Analgesia 1998;86(4):731-738.
16. Charbit B, Albaladejo P, Funck-Brentano C, Legrand M, Samain E, Marty J. Prolongation of QTc interval after postoperative nausea and vomiting treatment by droperidol or ondansetron. Anesthesiology 2005;102(6):1094-100.
17. White PF, Song D, Abrao J, Klein KW, Navarette B. Effect of low-dose droperidol on the QT interval during and after general anesthesia: a placebo-controlled study. Anesthesiology 2005;102(6):1101-5.
18. Lim BS, Pavy TJ, Lumsden G. The antiemetic and dysphoric effects of droperidol in the day surgery patient. Anaesth Intensive Care 1999;27(4):371-4.
19. Wallenborn J, Gelbrich G, Bulst D, Behrends K, Wallenborn H, Rohrbach A, et al. Prevention of postoperative nausea and vomiting by metoclopramide combined with dexamethasone: randomised double blind multicentre trial. British Medical Journal 2006;333:324-8.
20. Scuderi PE, James RL, Harris L, Mims GR, III. Multimodal antiemetic management prevents early postoperative vomiting after outpatient laparoscopy. Anesthesia and Analgesia 2000;91(6):1408-1414.