EDITORIAL VIEW

Postoperative nausea and vomiting (PONV): A cause for concern

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SUMMARY

Postoperative nausea and vomiting (PONV) has been a cause for concern, not only for the anesthesiologist but also for the patients. It is troublesome and may cause many untoward physiological consequences. Various authors have studied risk factors associated with it and management strategies, but the results have been confusing. Many new drugs have been developed for preventing and treating PONV, including ondansetron and palonosetron, and the research for the more effective and safe anti-emetic drug continues. This editorial compliments an original article being published in this issue of 'Anesthesia, Pain & Intensive Care' on the same topic.

Key words: Postoperative nausea and vomiting; PONV; Ambulatory surgery; Ondansetron; Palonosetron; Prevention; Prophylaxis

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Postoperative nausea and vomiting (PONV) is a cause for concern, not only for the anesthesiologist but regarded as the most undesirable morbidity by the patients as well.[1] PONV is a debilitating morbidity that may have serious consequences including *dehydration, electrolyte imbalance* (resultant cardiac arrhythmias), *wound dehiscence, and post-surgical haemmorhage*. The indirect effects include delayed discharge from the PACU, unplanned hospital admissions in day stay surgery, longer hospital stay for inpatients and adds to the overall cost of the operation.

Parra-Sanches et a**l**[2] reported an incidence of PONV in ambulatory surgery as 37% during hospitalization, 42% on the first postoperative morning and 49%.by the third postoperative morning. Patients with PONV spent one hour longer in the postanesthesia care unit than patients without PONV. Nursing time spent was significantly greater with an increase in total cost of postoperative recovery. The nuisance and recall value of PONV is such that patients have expressed their willingness to pay for the treatment of PONV.[1]

There has been extensive research regarding the etiology, prophylaxis and treatment of PONV. It has been suggested that the etiology of PONV is multifactorial. They identified patient, anesthesia, and surgery related risk factors.[3,4] The search for the 'independent prediction risk factors' for PONV has lead researchers to devise 'PONV prediction scoring systems. Apfel et al devised a simplified 0-4 point score for four independent risk predictors. The female patient, young age, history of PONV or travel sickness and high risk surgery were identified.[4] The estimated probability of PONV was 10%, 21%, 39%, and 78% with 0, 1, 2, 3, and 4 risk factors, respectively.[4] A large prospective multicenter study of 2,170 adults under general anesthesia in ambulatory settings in the United States between 2007 and 2008 assessed post discharge nausea and vomiting (PDNV) from discharge until the end of the second postoperative day. It found that about one in four patients suffered from PONV, and identified five independent predictors i.e. female gender, age less than 50 years, history of nausea and/or vomiting after previous anesthesia, opioid administration in the postanesthesia care unit and occurrence of nausea in the postanesthesia care unit. The estimated probability of PDNV was 7%, 20%, 28%, 53%, 60%, and 89% with 0, 1, 2, 3, 4 and 5 risk factors, respectively.[5] The authors suggests that PDNV affects a substantial number of patients after ambulatory surgery and their recently validated simplified risk score system will help identify patients who would benefit from long-

acting prophylactic antiemetics at discharge from the ambulatory care center.[4,5] However, it is of note that PDNV has not been well studied in the literature perhaps due to logistics involved in a day-stay patient follow-up seriously limits tracking of patients for PONV at home. This area deserves more attention.

Other researchers identified young, female, non smoker, with a history of PONV and travel sickness undergoing a surgical procedure likely to last more than 60 minutes, as independent PONV predictors.[6] Both the scoring systems predicted between 7-89% independent predictors for PONV.[4,6] Van Den Bosch et al validated these two PONV prediction scoring systems.[7] Combining these two systems, female gender, history of PONV and motion sickness, postoperative use of opioids, non- smokers, duration of surgery > 60 minutes and age < 60 years emerged as an independent predictors for PONV.

In a systematic review of prospective studies (n > 500 patients) Apfel et al[8] analysed 22 studies and found similar most reliable independent predictors of PONV. More importantly, the review discouraged the use of widely held beliefs about certain factors such as *preoperative fasting, menstrual cycle*, and the *type of surgery* as the predictors of PONV since no or insufficient evidence is available to substantiate it. Similarly, *obesity* has not been shown to be an independent risk factor for high incidence of PONV.[9]

Preoperative prolonged fasting and consequent dehydration and hypovolaemia is believed to be responsible for increased incidence of PONV. In a recently published systematic review of prospective randomised controlled trials, Apfel at al[10] concluded that IV crystalloids were associated with a lower incidence of several PONV outcomes but a number of PONV outcomes failed to reach statistical significance, perhaps due to the lack of power. Supplemental IV crystalloids were shown to have reduced postoperative nausea (PON) in early, late and overall perioperative phase. The incidence of postoperative vomiting (POV) in early and late phases remains unaffected by the supplemental IV fluid administration although overall risk of POV was reduced.

The authors recommended studies sufficiently powered for the less frequent outcomes (e.g. POV) to ascertain the value of supplemental IV fluid administration routinely. It can be, however, suggested that a judicious use of IV fluid administration (to cover preoperative fasting), avoidance of known emetic agents and early resumption of clear oral fluids may help reduce the unnecessary incidence for patient discomfort and hence PONV.

There is a no excuse for us as an anesthesiologist not to take appropriate active measures to prevent this debilitating morbidity since the PONV predictors / risk factors are identified, validated and widely published. In reality, the patient factors are hard to modify or controllable. Nevertheless, anesthetic factors should be modified and a 'PONV free' anesthesia technique may be tailored for an individual patient with high predictors. The debate is still alive whether or not to administer prophylactic antiemetics in every patient of 'zero' score that carries a risk of 7%-10% PONV.[3-5]

Traditionally, the words '*prevention'* or '*prophylaxis'* are used and aim for adequate anticipated PONV management. Habib and Gan have not advocated prophylaxis for patients at low risk for PONV;[3] however, they recommended prophylaxis for patients at moderate risk for PONV, using a single antiemetic or a combination of two agents. Even more important recommendation is to adopt **a** 'multimodal approach' incorporating steps to keep the baseline risk of PONV low and consider double and triple antiemetic combinations for patients at high risk for PONV.[4]

Since there are multiple inputs for nausea and vomiting, the drug therapies are specific to receptor antagonism, which include antihistamines, anti-dopamine, anticholinergic, and 5-Hydroxytryptamine [5-HT3] receptor antagonists, that are widely used as monotherapy or in combination. Dexamethasone and now Neurokinin 1 (NK-1 RA) - a substance P receptor antagonist, have been added to the antiPONV armamentarium. Substance P, a regulatory neuropeptide, binds to neurokinin-1 (NK1) receptors and is competitively inhibitsed by the NK-1 receptor antagonist. Preoperative administration of aprepitant (a neurokinin-1 antagonist) is effective in reducing both vomiting and nausea for up to 48 h after surgery.[11,12] Pre-hydration with oral carbohydrate containing clear fluids up to 2 h before surgery also reduces PONV.[13] In the 24-h postoperative period, 40 mg aprepitant may be superior to ondansetron in reducing PONV. Recommendation varies regarding prophylactic us of anti-emetics or whether to use monotherapy aor a combination of drugs. Double and triple antiemetic combinations were recommended for patients at high risk for PONV. [14-16]

The prophylactic antiemetic should not be repeated if PONV occurs within 6 hours after the end of surgery. Instead, antiemetic drug acting at a different receptor should be used. Dexamethasone and transdermal scopolamine may not be an appropriate choice if an emetic episode occurs more than 6 h after surgery. There is increasing evidence that the combination of several potentially beneficial factors (multimodal approach)

may lead to an improved outcome. The optimum cost-effective approach to the management of PONV will differ between an ambulatory centre and an inpatient hospital setting.[3] Dexamethasone is widely used as one of the main single dose antiemetic in current anaesthetic practice. The right dose of dexamethasone for PONV prevention has been studied and a 4-5 mg dexamethasone seems to be as effective as 8-10 mg as a single drug or as a combination therapy. These findings do support the current recommendation of the SAMBA (Society of Ambulatory Anesthesia) guidelines for PONV that favors the 4-5 mg dose regimen of systemic dexamethasone.[17-20] Combination anti-emetics may be equally effective. However, for economy, cost and apparent safety, dexamethasone at a dose of 4 mg is an attractive first-line agent for prophylaxis against postoperative nausea and vomiting.[19,20]

SAMBA guidelines recommend the identification of the primary risk factors for PONV in adults and postoperative vomiting (POV) in children. The SAMBA experts panel also recommended to establish factors that reduce the baseline risks for PONV in addition to determine the most effective anti-emetic monotherapy and combination therapy regimens for PONV/POV prophylaxis. The panel of experts recommended use of pharmacologic and non-pharmacologic approaches and emphasise to ascertain the optimal approach of treatment of PONV with or without PONV prophylaxis and determine the optimal dosing and timing of antiemetic prophylaxis. Cost evaluation, justification and creation of an algorithm for patients at high risk of PONV with effective treatment strategies is also recommended.

A planned multimodal algorithm starting in the preoperative area can significantly reduce the incidence of PONV.[21] Proper risk assessment, risk reduction, and targeted therapy while matching the number of risk with the number of anti-emetics administered. In authors opinion, most patients present with at least one Apfel criteria risk factor, authors' preference is to start with a minimum of two anti-emetics i.e. dexamethasone 4 mg soon after induction and ondansetron 4 mg 20 min before the end of surgery. They recommended addition of other groups of anti-emetics depending on other risk factors. However the efficacy of the multimodal technique in preventing PDNV cannot be confirmed with the available evidence. Serotonin antagonists palonosetron is an effective, long-acting antiemetic.[21,22]

The PONV prevention strategy must include a careful history taking to identify patient factors, recognising surgical factors, and avoiding use of any agent which has known emetic properties. Employing a meticulous technique for hand mask ventilation (without inflating stomach) and avoiding emesis inducing drugs for general anesthesia and pain management may help in reducing if not eliminating completely the occurrence of PONV. Avoiding general anesthesia and sole use of regional techniques and peripheral nerve blockade may preclude PONV from the list of complications. However, hypotension induced vomiting as a result of intrathecal or epidural analgesia may continue in the postoperative phase, if not adequately treated.

Propofol based total Intravenous anesthesia (TIVA) may be employed to avoid administration of volatiles and nitrous oxide. Managing pain with multimodal techniques and drugs like local anesthetics, Paracetamol and non-steroidal, provide an opportunity to use lowest possible dose of opioids. Adequate intravenous hydration with crystalloids and colloids and administration of 100% oxygen during and post anesthesia recovery phase may reduce the incidence of PONV.

New drugs are being constantly developed, but with a variable blessing. Palonosetron is one such drug and it has been shown by Shadangi BK et al in this issue to be more effective than ondansetron in reducing nausea, but almost equally effective in prevention of PONV.[23]

REFERENCES

1. Gan TJ, Sloan F, Dear GL, El-Moalem HE, Lubarsky DA. How much are patients willing to pay to avoid postoperative nausea and vomiting? Anesth Analg 2001;92:393-400 [Medline] [Free Full Article]
2. Parra-Sanchez I, Abdallah R, You J, et al. A time-motion Economic Analysis of Postoperative Nausea and Vomiting in Ambulatory Surgery. Can J Anaesth. April 2012;59(4):366-75. [Medline] doi: 10.1007/s12630-011-9660-x.
3. Habib AS, Gan TJ. Evidence-based management of postoperative nausea and vomiting: a review. Can J Anaesth. 2004 Apr;51(4):326-41. [Medline]
4. Apfel CC, Läärä E, Koivuranta M, Greim CA, Roewer N. A simplified risk score for predicting postoperative nausea and vomiting. Anesthesiology 1999;91:693–700. [Medline] [Free Full Article]
5 - Apfel CC, Philip BK, Cakmakkaya OS, Shilling A, Shi YY, Leslie JB, et al. Who Is at Risk For Postdischarge nausea and Vomiting After Ambulatory Surgery? Anesthesiology 2012 Sep;117(3):475-86. [Medline] [Free Full Article] [Free Full Article]
6- Koivuranta M, Laara E, Snare L, Alahuhta S. A survey of postoperative nausea and vomiting. Anaesthesia 1997;52:443-449 [Medline]
7- Van Der Bosch JE, Kalkman CJ, Vergouwe Y, Van Klei WA, Bonsel GJ, Grobbee DE, Moons KG. Assessing the applicability of scoring systems for predicting postoperative nausea and vomiting. Anaesthesia 2005;60:323-331 [Medline]
8- Apfel CC, Heidrich FM, Jukar-Rao S, Jalota L, Hornuss C, Whelan RP, et al. Evidence-based analysis of risk factors for postoperative nausea and vomiting. Br J Anaesth. 2012 Nov;109(5):742-53. [Medline] doi: 10.1093/bja/aes276
9- Kranke P, Apfel CC, Papenfuss T, Rauch S, Löbmann U, Rübsam B, et al. An increased body mass index is no risk factor for postoperative nausea and vomiting; A systematic review. Acta Anaesthesiol Scand. 2001 Feb;45(2):160-6. [Medline]
10- Apfel CC, Meyer A, Orhan-Sungur M, Jalota L, Whelan RP, Jukar-Rao S. Supplemental intravenous crystalloids for the prevention of postoperative nausea and vomiting: quantitative review. Br J Anaesthesia 2012 Jun;108(6):893-902. [Medline]
11 Diemunsch P, Gan TJ, Philip BK, Girao MJ, Eberhart L, Irwin MG, et al. Single-dose aprepitant vs ondansetron for the prevention of postoperative nausea and vomiting: a randomized, double-blind phase III trial in patients undergoing open abdominal surgery. Br J Anaesth 2007;99:202–11 [Medline]
12 Gan TJ, Apfel CC, Kovac A, Philip BK, Singla N, Minkowitz H, et al. A randomized, double-blind comparison of the NK1 antagonist, aprepitant, versus ondansetron for the prevention of postoperative nausea and vomiting. Anesth Analg 2007;104:1082–9 [Medline] [Free Full Article]
13 Jensen K, Kehlet H, Lund CM. Post-operative recovery profile after laparoscopic cholecystectomy: a prospective, observational study of a multimodal anaesthetic regime. Acta Anaesthesiol Scand 2007;51:464–71 [Medline]
14- Diemunsch P, Apfel C, Gan TJ, Candiotti K, Philip BK, Chelly J, et al. Preventing postoperative nausea and vomiting: post hoc analysis of pooled data from two randomized active-controlled trials of aprepitant. Curr Med Res Opin 2007;23:2559-65 [Medline]
15- Scuderi PE, James RL, Harris L, Mims GR. Antiemetic prophylaxis does not improve outcomes after outpatient surgery when compared to symptomatic treatment. Anesthesiology 1999;90:360–71. [Medline] [Free Full Article]
16- Gan TJ, Meyer T, Apfel CC, Chung F, Davis PJ, Eubanks S, et al. Consensus Guidelines for Managing Postoperative Nausea and Vomiting. Anesth Analg 2003;97:62–71 [Medline] [Free Full Article]
17- De Oliveira GS Jr, Castro-Alves LJ, Ahmad S, Kendall MC, McCarthy RJ. Dexamethasone to Prevent Postoperative Nausea and Vomiting: An Updated Meta-Analysis of Randomized Controlled Trials. Anesth Analg 2013;116:58–74 [Medline] [Free Full Article] doi: 10.1213/ANE.0b013e31826f0a0a.
18- Henzi I, Walder B, Tramer MR. Dexamethasone for the Prevention of Postoperative Nausea and Vomiting: A Quantitative Systematic Review. Anesth Analg 2000;90:186–94 [Medline] [Free Full Article]
19- 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. N Engl J Med 2004; 350:2441-2451 [Medline] [Free PMC Article]
20- Gan TJ,. Meyer TA,. Apfel CC, Chung F, Davis PJ, Habib AS, et al. Society for Ambulatory Anesthesia (SAMBA) Guidelines for the Management of Postoperative Nausea and Vomiting. Anesth Analg 2007;105;6:1615–28 [Medline] [Free Full Article]
21- Chandrakantan A, Glass P. S. A. Multimodal therapies for postoperative nausea and vomiting, and pain. Br J Anaesthesia 107 (S1): i27–i40 (2011)
22. Apfel CC, Kranke P, Eberhart LHJ, Roos A, Roewer N. Comparison of predictive models for postoperative nausea and vomiting. Br J Anaesthesia 2002; 88: 234–40. [Medline]
23. Shadangi BK, Agrawal J, Pandey R, Kumar A, Jain S. Mittal R and Chorasia. A prospective, randomized, double-blind, comparative study of the efficacy of intravenous ondansetron and palonosetron for prevention of postoperative nausea and vomiting. Anaesth Pain & Intensive Care 2013;17(1):55-58

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