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EDITORIAL

Prevention of postoperative nausea and vomiting: new insights for patient care

Prevenção de náusea e vômito no pós-operatório: novos pontos de vista no cuidado do paciente

Postoperative Nausea and Vomiting (PONV) remains a common complication following anesthesia and surgery, causing patient dissatisfaction and significant discomfort.[1] Although PONV is seldom related to a life-threatening condition, it is consistently considered as one of the most undesirable side effects related to surgery and anesthesia. Previous studies have indicated that the estimated incidence of PONV is approximately 30% in the general surgical population and up to 80% in high-risk patients.[2] Increased medical costs, longer stay in the postanesthesia care unit, prolonged hospitalization, and hospital readmission are strongly associated with PONV.[3]

Despite PONV being the focus of a plethora of clinical studies on its prevention and treatment, its optimal management is still a complex and challenging process. There are several antiemetics available to prevent and manage PONV, displaying varying pharmacokinetics, efficacy and side-effects.[4] Thus, the potential benefit of an antiemetic drug needs to be balanced with the side-effects profile and its cost, depending on the clinical context. Very recently, a new consensus statement was published,[5] presenting a comprehensive and evidence-based set of guidelines for the care of PONV in both adult and pediatric patients. These guidelines provided recommendation on how to identify high-risk patients, manage baseline PONV risk factors, main strategies for prophylaxis and rescue treatments. Additionally, these updated guidelines provided some insights into the most recent evidence for newer drugs and recommendations for the institutional implementation of a PONV protocol, general multimodal PONV prophylaxis, and PONV management as part of enhanced recovery pathways.[5]

In this issue of the *Brazilian Journal of Anesthesiology*, six interesting studies provide some new insights into PONV risk factors and prophylaxis. There are well-known risk factors for the development of PONV, including patient-related factors, anesthetic technique, use of volatile anesthetics, use of nitrous oxide, duration of anesthesia, opioid administration, and type of surgery.[6] Surprisingly, there is a lack of information about the main risk factors for PONV in the obstetric population. Perioperative nausea and vomiting seem to be frequent in obstetric patients and pharmacological effects of antiemetics to the fetus and newborn are not well established. Hence, Guimarães et al.[7] performed an interesting and well-designed observational study, combining both prospective and retrospective data, and investigating potential risk factors for nausea and vomiting after cesarean section. Authors enrolled pregnant women who had a cesarean section under spinal anesthesia and received a combination of dexamethasone and ondansetron during the surgical procedure. Two hundred and fifty patients were ultimately included and analyzed. The incidence of PONV was relatively low as compared to previous data, perhaps in consequence of an effective prophylaxis protocol applied to all patients. Notably, maternal age under 25 years and intraoperative nausea were the main risk factors for PONV after cesarean section under spinal anesthesia. Unexpectedly, absence of self-reported nausea during the first gestational trimester was also an important risk factor for PONV. Of note, lower dose of spinal bupivacaine and higher spinal morphine dose (<13 mg and >80 μg, respectively), history of motion sickness and lower gestational age were also relatively weak risk factors for PONV in patients undergoing cesarean section.

Previous studies have demonstrated that Total Intravenous Anesthesia (TIVA) is effective in reducing the incidence of PONV. Amiri et al.[8] performed a randomized

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controlled trial comparing TIVA versus inhalation anesthesia on the incidence of PONV in 105 patients undergoing abdominal surgery. In this study, authors have shown once again that TIVA, as compared to inhalational-based anesthesia (isoflurane and fentanyl), significantly reduced the incidence of postoperative nausea and decrease the need for antiemetic rescue medication after surgery. Importantly, some relevant limitations of the present study should be pointed out. Firstly, this was a fairly small clinical trial and blinding was limited. Moreover, different opioids were used in both arms (fentanyl versus remifentanil), compromising further conclusions. Finally, there was no description of a well-established protocol of antiemetics intraoperatively, potentially increasing the overall incidence of PONV in both groups. Although this study displays several concerns and limitations, it still corroborates previous findings by showing that TIVA is effective in reducing the incidence of PONV in numerous surgical scenarios and may be indicated or preferred in patients displaying a higher risk for PONV.

Currently, 5-HT_3 receptor antagonists are the first choice for PONV prophylaxis, especially considering their effectiveness, safety, and favorable side-effects profile as they lack the sedative, dysphoric and extrapyramidal side effects of other drugs.[5] Ondansetron was the initial 5-HT_3 receptor antagonist used clinically, it was the most commonly studied and its antiemetic efficacy is well established. Therefore, Ondansetron is considered a ''gold standard'' in PONV management.[4,5] However, more recently, newer and more selective 5-HT_3 receptor antagonists have emerged, namely ramosetron, granisetron, tropisetron, and palonosetron. In this issue of BJAN, two small but exciting clinical trials investigated the potential benefits of palonosetron in preventing the development of PONV.[9,10] As a second-generation 5-HT_3 receptor antagonist, palonosetron has a prolonged 40-hour half-life, allosteric binding and receptor internalization, combining both 5-HT_3 and Neurokinin-1 (NK1) receptor inhibition. Fonseca et al.[9] investigated the effects of palonosetron, ondansetron and dexamethasone or dexamethasone alone in the prevention of PONV in patients undergoing laparoscopic cholecystectomy under TIVA. Authors showed that palonosetron was more effective than ondansetron and/or dexamethasone in preventing PONV following laparoscopic cholecystectomy. Srivastava et al.[10] designed a randomized controlled trial, comparing the combination palonosetron-dexamethasone or ondansetron-dexamethasone for prevention of PONV in adult patients undergoing middle ear surgery. This randomized clinical trial enrolled 64 patients who received the prophylactic medication before anesthesia induction. Authors concluded that the association of palonosetron instead of ondansetron with dexamethasone was significantly superior in preventing PONV after middle ear surgery. Although previous studies have already indicated that palonosetron is more effective than other 5-HT_3 receptor antagonists in reducing the incidence of PONV,[5] these two new studies provided relevant additional data about the effectiveness and safety of this antiemetic drug in reducing PONV in high-risk patients.

Several neurotransmitters and their receptors play a role in the mechanisms underlying nausea and vomiting related to anesthesia and surgery, including serotonin, acetylcholine, histamine, opioids, dopamine, and substance P, explaining the different potential prevention and treatment modalities available for PONV. More recently, NK1 receptor antagonists have received significant attention as effective prophylactic antiemetics in the surgical setting.[4,5] Murakami et al.[11] performed a systematic review investigating the effects of NK1 receptor antagonists against PONV, especially aprepitant and fosaprepitant. In this systematic review, 18 studies were ultimately included into the final analysis. Although some limitations could be pointed out, this meta-analysis has overall demonstrated that NK1 receptor antagonists, especially aprepitant and fosaprepitant, were more effective than 5-HT_3 receptor antagonists for preventing postoperative vomiting and delaying the time to first vomiting episode after surgery. However, given the significant data heterogeneity, more studies are still warranted to further increase the available evidence on the effectiveness and safety of NK1 receptor antagonists in preventing PONV.

Considering that antiemetic drugs are only partially effective in preventing PONV and display some important side effects, it is tempting to investigate the effectiveness of alternative nonpharmacological strategies in preventing and managing nausea and vomiting after surgery. There is previous moderate evidence that some acupuncture strategies may present comparable benefits as antiemetics in preventing PONV.[12] Therefore, Miranda et al.[13] investigated if acupuncture is effective in reducing the incidence of PONV following laparoscopic cholecystectomy. In this trial, sixty-eight adult women were randomly assigned to receive auriculoacupuncture or no intervention and further evaluated for the incidence of nausea and vomiting after laparoscopic cholecystectomy. Authors showed that auriculoacupuncture was effective in reducing the incidence of PONV in this population. Notably, this study displays some important limitations. Firstly, it is a single center study with a small sample size. Additionally, and most importantly, authors did not implement any additional prophylaxis for PONV unless metoclopramide and the overall incidence of PONV was approximately 60%, significantly higher than recent studies where well-established strategies were implemented before the end of surgery.[4,5] Therefore, new studies are still warranted to further investigate the role of acupuncture in preventing PONV.

In summary, PONV is still a significant challenge faced every day by anesthesiologists everywhere. Despite many pharmacological and nonpharmacological options for prophylaxis and different anesthetic techniques with good evidence for prevention, there remain few options for management after it has manifested, especially in those patients who have already received adequate prophylaxis. The six studies published here aimed to present new insights into the main risk factors and potential strategies to reduce PONV incidence. These studies overall have demonstrated that seeking novel pathways for implementing evidence-based and possibly multimodal interventions to improve clinical outcomes such as PONV is pivotal in the surgical setting.

Conflicts of interest

The author declares no conflicts of interest.

References

1. Myles PS, Williams DL, Hendrata M, et al. Patient satisfaction after anaesthesia and surgery: results of a prospective survey of 10,811 patients. Br J Anaesth. 2000;84:6–10.
2. Apfel CC, Läärä E, Koivuranta M, et al. A simplified risk score for predicting postoperative nausea and vomiting: conclusions from cross-validations between two centers. Anesthesiology. 1999;91:693–700.
3. Wiesmann T, Kranke P, Eberhart L. Postoperative nausea and vomiting – a narrative review of pathophysiology, pharmacotherapy and clinical management strategies. Expert Opin Pharmacother. 2015;16:1069–77.
4. Tateosian VS, Champagne K, Gan TJ. What is new in the battle against postoperative nausea and vomiting? Best Pract Res Clin Anaesthesiol. 2018;32:137–48.
5. Gan TJ, Belani KG, Bergese S, et al. Fourth Consensus Guidelines for the Management of Postoperative Nausea and Vomiting. Anesth Analg. 2020;131:411–48.
6. Apfel CC, Heidrich FM, Jukar-Rao S, et al. Evidence-based analysis of risk factors for postoperative nausea and vomiting. Br J Anaesth. 2012;109:742–53.
7. Guimarães GM, da Silva HB, Ashmawi HA. Risk factors for postcaesarean nausea and vomiting: a prospective prognostic study. Rev Bras Anestesiol. 2020;70:457–63.
8. Amiri AA, Karvandian K, Ashouri M, et al. Comparison of postoperative nausea and vomiting with intravenous versus inhalational anesthesia in laparotomic abdominal surgery; a randomized clinical trial. Rev Bras Anestesiol. 2020;70:471–6.
9. Fonseca NM, Pedrosa LR, Melo N, et al. Effect of palonosetron, ondansetron and dexamethasone or dexamethasone for prevention of postoperative nausea and vomiting in video cholecystectomy with total venous anesthesia with propofol-remifentanil – randomized clinical trial. Rev Bras Anestesiol. 2020;70:464–70.
10. Srivastava VK, Khan S, Agrawal S, et al. Comparison of palonosetron-dexamethasone and ondansetron-dexamethasone for prevention of postoperative nausea and vomiting in middle ear surgery: a randomized clinical trial. Rev Bras Anestesiol. 2020;70:477–83. http://dx.doi.org/10.1016/j.bjane.2020.08.001.
11. Murakami C, Kakuta N, Satomi S, et al. Neurokinin-1 receptor antagonists for postoperative nausea and vomiting: a systematic review and meta-analysis. Rev Bras Anestesiol. 2020;70:508–19. http://dx.doi.org/10.1016/j.bjan.2020.04.005.
12. Fu C, Wu T, Shu Q, et al. Acupuncture therapy on postoperative nausea and vomiting in abdominal operation: a Bayesian network meta-analysis. Medicine (Baltimore). 2020;99:e20301.
13. Miranda LE, Filho LF, de Siqueira AC, et al. Effect of acupuncture on the prevention of nausea and vomiting after laparoscopic cholecystectomy: a randomized clinical trial. Rev Bras Anestesiol. 2020;70:484–90. http://dx.doi.org/10.1016/j.bjan.2019.08.001.

André P. Schmidt [a,b,c,d,e]

[a] *Hospital de Clínicas de Porto Alegre (HCPA), Serviço de Anestesia e Medicina Perioperatória, Porto Alegre, RS, Brazil*

[b] *Universidade Federal do Rio Grande do Sul (UFRGS), Instituto de Ciências Básicas da Saúde (ICBS), Departamento de Bioquímica, Porto Alegre, RS, Brazil*

[c] *Universidade Federal de Ciências da Saúde de Porto Alegre (UFCSPA), Santa Casa de Porto Alegre, Serviço de Anestesia, Porto Alegre, RS, Brazil*

[d] *Hospital Nossa Senhora da Conceição, Serviço de Anestesia, Porto Alegre, RS, Brazil*

[e] *Universidade Federal do Rio Grande do Sul (UFRGS), Faculdade de Medicina, Programa de Pós-graduação em Ciências Pneumológicas, Porto Alegre, RS, Brazil*

E-mail: aschmidt@ufrgs.br