Review Article

Role of general anesthetic agents in postoperative nausea and vomiting: A review of literature

ABSTRACT

Postoperative nausea and vomiting (PONV) is considered to be the most unpleasant experience associated with surgery and is believed to be one of the most common reasons for poor patient satisfaction in the postoperative period. It also results in prolonged hospitalization and increased use of resources such as intravenous fluids and drug supplements along with prolonged medical attention, all of which have psychological and financial implications. In addition to this, PONV can result in aspiration, laryngospasm, dehydration, electrolyte disturbances, gastric bleeding, increased intracranial pressure, increased intraocular pressure, and wound dehiscence particularly when the surgical intervention is performed through an intraoral approach. It is a well-known fact that there are many etiological factors as well as predisposing factors for PONV. Hence, this review is intended to evaluate as an individual factor what the role was played by the anesthetic agents used for GA in the incidence of PONV.

Keywords: General anesthesia, postoperative nausea and vomiting, surgery

INTRODUCTION

It is a well-known fact that postoperative nausea and vomiting (PONV) is a common sequela following surgical intervention performed in the oral and maxillofacial region, particularly via intraoral approach under general anesthesia. It is considered to be an unpleasant experience associated with surgery and is believed to be the most common reason for poor patient satisfaction in the postoperative period.[1] Clinically, patients would appear pale and diaphoretic in response due to the sensation of nausea. As a result of anxiety, there would be tachycardia and tachypnea. Active vomiting can stimulate a sympathetic response leading to hypertension and tachycardia. The Valsalva associated with active vomiting can lead to bradycardia and leads to increased intrathoracic pressure and intracranial pressure which can be detrimental to patients in the postoperative period. PONV can result in aspiration, laryngospasm, dehydration, electrolyte disturbances, gastric bleeding, increased intracranial pressure, increased intraocular pressure, and wound dehiscence.[1]

Few predisposing factors are put forth to be associated with PONV. These include previous history of nausea and vomiting, gastrointestinal tract disorders, the duration and type of

Shilpa Sunil Khanna, Muqthadir Siddiqui Mohammed Abdul[1], Urooj Fatima[2], Harshitha Garlapati[3], Mohd Abdul Qayyum[4], Sunil Kumar Gulia[5]

Department of Oral and Maxillofacial Surgery, Sri Ramakrishna Dental College and Hospital, Coimbatore, Tamil Nadu, [3]General Dentist, Narayana Dental College and Hospital, Nellore, Andhra Pradesh, [4]General Dentist, Pro Dent Advanced Dental Care, Hyderabad, Telangana, [5]Department of Oral and Maxillofacial Surgery, SGT University, Jhajjar, Haryana, India, [1]Department of Paediatric Dentistry, Ministry of Health, King Khaled Hospital, Riyadh, [2]Skin and Laser Care Centre, Dr. Sulaiman Al Habib Hospital, Riyadh, Saudi Arabia

Address for correspondence: Dr. Shilpa Sunil Khanna, Department of Oral and Maxillofacial Surgery, Sri Ramakrishna Dental College and Hospital, Coimbatore, Tamil Nadu, India.
E-mail: khannashilpa03@gmail.com

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anesthetic used, and the type of surgical access adopted.[2] PONV is influenced by multiple factors which are related to the patient, surgery, and pre-, intra-, and postoperative anesthesia factors.[3] The reason for PONV is multifactorial. It is assumed to be arising from the chemoreceptor trigger zone (CTZ) in the brainstem, from opiate-induced, direct effects on the gastrointestinal (GI) tract and other anesthetics as well as in the vestibular system through movement and from the sensitization of this system by agents commonly used in anesthesiology. Type and location of surgery play a role as well, and ocular and tympanic surgery and intracranial, abdominal, and gynecological surgeries pose an increased risk for PONV.[4,5]

Previous studies have shown that pediatric patients exhibit only vomiting due to difficulties in eliciting nausea at a young age. PONV is noticed in 13%–42% of all pediatric patients undergoing surgical interventions under GA. A peak incidence of 34%–51% is noticed in the 6–16 year age group. Prior to puberty, gender differences for postoperative vomiting have not been identified.[6] Literature shows that general anesthesia is associated with an 11-fold increased risk of PONV, which is frequently caused by the emetic properties of volatile anesthetics and the opioids administered.[7] In addition to this, literature shows that the type of surgery is an independent risk factor for PONV.[4] Surgical interventions involving the maxillofacial region, eyes, oropharynx, and auditory system have been shown to have a higher prevalence of PONV.[2]

A literature search was done on Medline and relevant articles were chosen. In this article, we present evidence regarding the risk factors, prophylaxis, and treatment of PONV based on the existing literature using data from randomized controlled trials, systematic reviews, logistic regression analyses, and expert opinion.

Anesthetic factors

Since the anesthesiologist employs more than one drug during an anesthetic procedure, it is difficult to sort out the effects of an individual drug on the incidence of PONV. The incidence of PONV is reported to occur around 8% to 92% and varies according to type and duration of the surgical procedure, age, gender and smoking status of the patient, use of opioids, and anesthetic technique.[8] The pathophysiology of PONV is complex as it involves various pathways and receptors. There are five primary afferent pathways involved in stimulating vomiting which include the CTZ, the vagal mucosal pathway in the GI system, neuronal pathways from the vestibular system, reflex afferent pathways from the cerebral cortex, and the midbrain afferents.[9] Stimulation of one of these afferent pathways can activate the sensation of vomiting via cholinergic, dopaminergic, histaminergic, or serotonergic receptors.[1,9] The multifactorial etiology of PONV necessitates the need to investigate whether the anesthetic agents used in general anesthesia play a role in PONV.

Nitrous oxide

Studies have shown that there was a significant decrease in postoperative emesis in clinical scenarios where nitrous oxide was avoided in patients undergoing laparoscopic procedures. Two meta-analyses have demonstrated that avoiding nitrous oxide can reduce PONV risk.[10,11] Three mechanisms have been put forth as contributing factors to the increased incidence of postoperative emesis associated with nitrous oxide.[12] Due to stimulation of sympathetic nervous system with catecholamine release, middle ear pressure changes result in traction of the membrane of round window and consequent stimulation of the vestibular system and Increased abdominal distension as a result of exchange of nitrous oxide and nitrogen in gas introduced into GI tract during mask ventilation.[13-15] Previous studies show that nitrous oxide does not play a role in the incidence of PONV particularly in adults when halogenated inhalation agents are used.[12] However, nitrous oxide can increase the incidence of PONV in children when used with propofol.[16]

A recent study evaluated the inclusion of nitrous oxide in the gas mixture and it is implicated in PONV taking duration of exposure as a criterion. They concluded that there exists a relation between the duration of exposure to nitrous oxide and the incidence of PONV. This duration-related effect may be via disturbance of methionine and folate metabolism. There was no existing clinically significant effect of nitrous oxide on the risk of PONV for less than an hour of exposure. Hence, nitrous oxide-related PONV should not be seen as an impediment to its use in minor or ambulatory surgery.[17] A recent study retrospectively reviewed the records of 372 patients who underwent surgical interventions in the oral and maxillofacial region to determine the incidence and ascertain the risk factors of PONV. They concluded that a longer duration of anesthesia was associated with an increased risk of PONV.[2,9] Another study supported this concept and reported that a duration of surgery greater than 60 min increases a patient's risk of experiencing both PON and POV and that a 30-min increase in surgical time predicts a 60% increase in the risk of PONV.[18]

Inhalational agents

Previous studies show that ether and cyclopropane play a role in the higher incidence of PONV as a result of increase in endogenous catecholamines. Sevoflurane, enflurane, desflurane, and halothane are considered to be associated with

a lesser degree of PONV.[19] Based on the available literature, it can be advocated that the effect of volatile anesthetics on PONV is dose dependent and is predominantly noticed in the first 2–6 h following surgery. Volatile anesthetics can be considered as the major cause of early PONV and they have minimal impact on delayed PONV.[20] A retrospective cross-sectional analytic survey revealed that a higher prevalence of PONV was noticed with the use of volatile general anesthetics.[21]

Propofol

Numerous studies have shown that propofol results in a lesser incidence of PONV when compared to other intravenous agents even in pediatric patients.[22] Even though some studies have speculated that propofol has a specific antiemetic effect, there is a lack of evidence pertaining to the effect of propofol on the emetic center or CTZ. Studies show that propofol when used alone as an intravenous agent is associated with a lesser incidence of PONV.[16] Ostman *et al*. advocated that the antiemetic effect of propofol may not be attributed to lipid emulsion used to solubilize the drug.[23] Borgeat *et al*. reported that propofol does not have vagolytic properties.[24] In a study by Hammas *et al*., propofol reduced the intensity of PONV after oral intake of ipecacuanha syrup, which releases 5-hydroxytryptamine. It is concluded that propofol may have a serotonin antagonistic effect.[25] Propofol decreased synaptic transmission in the olfactory cortex in an animal study, suggesting a decrease in the release of excitatory amino acids such as glutamate and aspartate, which may be related to its antiemetic activity.[26]

Ketamine

Previous studies have shown that ketamine used for induction resulted in a higher incidence of PONV compared to a patient receiving barbiturates with nitrous oxide. It is advocated that the emetic effect of ketamine is secondary to endogenous catecholamine release.[27] A recent study evaluated the effect of ketamine as an adjunct to a fentanyl-based IV patient-controlled analgesia (IV-PCA) on PONV. It concluded that ketamine did not reduce the incidence of PONV and exerted a negative influence on the severity of nausea. However, it was able to reduce postoperative fentanyl consumption in patients at high risk of PONV.[28] Another study demonstrated that a low-dose administration of ketamine during anesthesia induction improves the extubation time but has no effect on postoperative pain, nausea and vomiting, and perioperative additional analgesic requirements.[29]

Opioids

It is advocated that opioids cause PONV through stimulation of opioid receptors located in CTZ. However, the role of intraoperative opioids in the incidence of PONV is minimal.[3] A recent study evaluated the factors associated with postoperative nausea vomiting following oral and maxillofacial surgery during the first 24–48 h following the surgical intervention. They concluded that the occurrence of PONV after oral and maxillofacial surgery was found to be more strongly associated with patients who used opioids.[2] The prevalence of PONV in pstients who underwent maxillary and/or mandibular osteotomies reveals a higher prevalence of PONV as a result of the use of volatile general anesthetics and postoperative opioid analgesics.[23] In addition to this, studies have shown that there is no difference among different opioids in the incidence of PONV.[30] The incidence of analgesic-induced PONV is reduced with the development of potent NSAIDs. Intraoperative ketorolac has shown to be as effective as morphine and propofol in reducing postoperative pain as is associated with a lesser incidence of PONV.[31]

The drug used for the treatment of postoperative nausea and vomiting and its site of action and the review of previous studies are shown in Tables 1 and 2 respectively.

MANAGEMENT

Previously, a study evaluated the role of prophylactic antiemetic and its effects in the management of postoperative

Table 1: The drug used for the treatment of postoperative nausea and vomiting and its site of action

Drug used for PONV	Site of action
Palonosetron	Selective serotonin 5-HT3 receptor antagonist. Acts by inhibition of 5-HT3 receptor both centrally and peripherally
Ondansetron	Selective serotonin 5-HT3 receptor antagonist and peripherally
Clonidine	Alpha 2 adrenergic agonist
Dexamethasone	Interact with serotonin and receptor proteins tachykinin NK1 and NK2, alpha-adrenaline

PONV: Postoperative nausea and vomiting

Table 2: The review of previous studies

Previous studies	Inference
Medeiros AF *et al.* (2016) Ostman PL *et al.* (1990)	PONV incidence increases with the use of volatile general anesthetics and postoperative opioid analgesics
Abdolahi M *et al.* (2013) Thompson GE *et al.* (1973)	PONV incidence increases with the use of ketamine
Islam S (2004))	PONV incidence increases with the use of ether and cyclopropane
Stark RD *et al.* (1985) Watcha MF *et al.* (1991) Hammas B *et al.* (1998)	PONV incidence decreases with the use of propofol
Silva AC *et al.* (2006) Islam S (2004))	PONV incidence decreases with the use of sevoflurane, enflurane, desflurane, and halothane
Peyton PJ *et al.* (2004) Watcha MF *et al.* (1992)	PONV incidence not related with the use of nitrous oxide
Tramèr M *et al.* (1997) *et al*., (1996)	PONV incidence increases with the use of nitrous oxide

PONV: Postoperative nausea and vomiting

nausea and vomiting following maxillofacial surgery. It concluded that in moderate, high, and very high-risk patients, the benefits of prophylaxis for PONV outweigh the risks, side effects, and cost of antiemetic medications and are preferable to giving no prophylaxis.[32] Palonosetron is a newer antiemetic with a half-life of 40 h. Literature shows that it can be safely used in patients with cardiac impairment.[33] A meta-analysis revealed that palonosetron is safe and more effective than ondansetron or ramosetron in preventing early and late PONV.[34] Another recent study compared the efficacy of ondansetron and clonidine in the prevention of postoperative pain and nausea and vomiting after orthognathic surgeries and concluded that ondansetron with dexamethasone premedication was more effective in controlling PONV after orthognathic surgery compared to clonidine with dexamethasone group.[35] A combination of prophylactic antiemetic drugs with different mechanisms of action should be administered to patients with moderate to high risk of developing PONV. With the existing evidence in literature, clinicians should intervene in PONV as early as possible since it can be cost-effective to the patients and enhance their comfort levels in the postoperative phase.[36]

CONCLUSION

Based on the existing literature, there are numerous factors associated with the risk of PONV in the form of age, gender, history of motion sickness or postoperative vomiting, and the type of surgical intervention. Based on this review of literature, it is understood that the anesthetic agents have a little or no effect on the incidence of PONV. However, the duration of surgery definitely plays a key role in the incidence of PONV. Potent nonopioid analgesics like ketorolac should be considered to control pain instead of opioid analgesics. Proper antiemetic therapy should be administered in the preoperative period to avoid deleterious effects of PONV in the postoperative period whenever required.

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Conflicts of interest

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REFERENCES

1. Dobbeleir M, De Coster J, Coucke W, Politis C. Postoperative nausea and vomiting after oral and maxillofacial surgery: A prospective study. Int J Oral Maxillofac Surg 2018;47:721-5.
2. Albuquerque AF, Queiroz SI, Germano AR, da Silva JS. Factors associated to post-operative nausea and vomiting following oral and maxillofacial surgery: A prospective study. Oral Maxillofac Surg 2017;21:49-54.
3. Shaikh SI, Nagarekha D, Hegade G, Marutheesh M. Postoperative nausea and vomiting: A simple yet complex problem. Anesth Essays Res 2016;10:388-96.
4. Friedberg BL. Postoperative nausea and vomiting with plastic surgery: A practical advisory to etiology, impact, and treatment. Plast Reconstr Surg 2018;142:608e-9.
5. 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.
6. Habib AS, Gan TJ. Evidence-based management of postoperative nausea and vomiting: A review. Can J Anaesth 2004;51:326-41.
7. Thompson HJ. The management of post-operative nausea and vomiting. J Adv Nurs 1999;29:1130-6.
8. Alexander M, Krishnan B, Yuvraj V. Prophylactic antiemetics in oral and maxillofacial surgery: A requiem? J Oral Maxillofac Surg 2009;67:1873-7.
9. Apipan B, Rummasak D, Wongsirichat N. Postoperative nausea and vomiting after general anesthesia for oral and maxillofacial surgery. J Dent Anesth Pain Med 2016;16:273-81.
10. Tramèr M, Moore A, McQuay H. Meta-analytic comparison of prophylactic antiemetic efficacy for postoperative nausea and vomiting: Propofol anaesthesia vs omitting nitrous oxide vs total IV omitting nitrous oxide vs total iv anaesthesia with propofol. Br J Anaesth 1997;78:2561-9.
11. Tramèr M, Moore A, McQuay H. Omitting nitrous oxide in general anaesthesia: Meta-analysis of intraoperative awareness and postoperative emesis in randomized controlled trials. Br J Anaesth 1996;76:186-93.
12. Watcha MF, White PF. Postoperative nausea and vomiting. Its etiology, treatment, and prevention. Anesthesiology 1992;77:162-84.
13. Jenkins LC, Lahay D. Central mechanisms of vomiting related to catecholamine response: Anaesthetic implication. Can Anaesth Soc J 1971;18:434-41.
14. Perreault L, Normandin N, Plamondon L, Blain R, Rousseau P, Girard M, *et al.* Middle ear pressure variations during nitrous oxide and oxygen anaesthesia. Can Anaesth Soc J 1982;29:428-34.
15. Eger EI 2nd, Saidman LJ. Hazards of nitrous oxide anesthesia in bowel obstruction and pneumothorax. Anesthesiology 1965;26:61-6.
16. Watcha MF, Simeon RM, White PF, Stevens JL. Effect of propofol on the incidence of postoperative vomiting after strabismus surgery in pediatric outpatients. Anesthesiology 1991;75:204-9.
17. Peyton PJ, Wu CY. Nitrous oxide-related postoperative nausea and vomiting depends on duration of exposure. Anesthesiology 2014;120:1137-45.
18. Phillips C, Brookes CD, Rich J, Arbon J, Turvey TA. Post operative nausea and vomiting following orthognathic surgery. J Oral Maxillofac Surg 2015;44:745-51.
19. Islam S, Jain P. Post-operative nausea and vomiting (PONV). Indian J Anaesth 2004;48:253.
20. Apfel CC, Kranke P, Katz MH, Goepfert C, Papenfuss T, Rauch S, *et al.* Volatile anaesthetics may be the main cause of early but not delayed postoperative vomiting: A randomized controlled trial of factorial design. Br J Anaesth 2002;88:659-68.
21. Silva AC, O'Ryan F, Poor DB. Postoperative nausea and vomiting (PONV) after orthognathic surgery: A retrospective study and literature review. J Oral Maxillofac Surg 2006;64:1385-97.
22. Stark RD, Binks SM, Dutka VN, O'Cooner KM, Arustein MJ, Glen JB. A reviw of the safety and tolerance of propofol. Postgrad Med J 1985;61:152-6.
23. Ostman PL, Faure E, Glosten B, Kemen M, Robert MK, Bedwell S. Is the antiemetic effect of the emulsion formulation of propofol due to the lipid emulsion? Anesth Analg 1990;71:536-40.
24. Borgeat A, Wilder-Smith OH, Saiah M, Rifat K. Subhypnotic doses of propofol possess direct antiemetic properties. Anesth Analg 1992;74:539-41.

25. Hammas B, Hvarfner A, Thörn SE, Wattwil M. Effects of propofol on ipecacuanha-induced nausea and vomiting. Acta Anaesthesiol Scand 1998;42:447-51.
26. Collins GG. Effects of the anesthetic 2,6-diisopropylphenol on synaptic transmission in the rat olfactory cortex slice. Br J Pharmacol 1988;95:939-49.
27. Thompson GE, Remington MJ, Millman BS, Bridenbaugh LD. Experiences with outpatient anesthesia. Anesth Analg 1973;52:881-7.
28. Song JW, Shim JK, Song Y, Yang SY, Park SJ, Kwak YL. Effect of ketamine as an adjunct to intravenous patient-controlled analgesia, in patients at high risk of postoperative nausea and vomiting undergoing lumbar spinal surgery. Br J Anaesth 2013;111:630-5.
29. Abdolahi M, Soltani HA, Montazeri K, Soleymani B. Preemptive low-dose of ketamine does not effective on anesthetic consumption, perioperative analgesic requirement and postoperative pain, nausea and vomiting in painful ophthalmic surgery. J Res Med Sci 2013;18:583-7.
30. Gan TJ, Diemunsch P, Habib AS, Kovac A, Kranke P, Meyer TA, *et al.* Consensus guidelines for the management of postoperative nausea and vomiting. Anesth Analg 2014;118:85-113.
31. Buckley MM, Brogden RN. Ketorolac. A review of its pharmacodynamic and pharmacokinetic properties, and therapeutic potential. Drugs 1990;39:86-109.
32. Kovac AL. The prophylactic treatment of postoperative nausea and vomiting in oral and maxillofacial surgery. J Oral Maxillofac Surg 2005;63:1531-5.
33. Schwartzberg LS, Marks SM, Gabrail NY, Geller RB, Kish J. Real-world effectiveness of palonosetron-based antiemetic regimens: Preventing chemotherapy-induced nausea and vomiting. J Comp Eff Res 2019;8:657-70.
34. Dawood A, Saeed N, Abbasali D, Hossein D. Comparison of prophylactic effects of intravenous metoclopramide and ondansetron on postoperative nausea and vomiting after maxillofacial surgery. IESRJ 2017;3:47-50.
35. Samieirad S, Sharifian-Attar A, Eshghpour M, Mianbandi V, Shadkam E, Hosseini-Abrishami M, *et al.* Comparison of Ondansetron versus Clonidine efficacy for prevention of postoperative pain, nausea and vomiting after orthognathic surgeries: A triple blind randomized controlled trial. Med Oral Patol Oral Cir Bucal 2018;23:e767-76.
36. Dewinter G, Staelens W, Veef E, Teunkens A, Van de Velde M, Rex S. Simplified algorithm for the prevention of postoperative nausea and vomiting: A before-and-after study. Br J Anaesth 2018;120:156-63.