Chapter 28
Antiemetic Agents

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Contents

Introduction

Fifty-two percent of all surgical patients will experience postoperative nausea and vomiting (PONV) when no antiemetics are used. Risk factors include female sex, nonsmoker, having a history of motion sickness, or PONV. Anesthetic risk factors include not receiving a total intravenous anesthetic (TIVA), receiving opioids,

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A.D. Kaye et al. (eds.), *Essentials of Pharmacology for Anesthesia, Pain Medicine, and Critical Care*, DOI 10.1007/978-1-4614-8948-1_28,

exposure to nitrous oxide, and the length of the anesthetic. Class/type of antiemetic or not using a triggering anesthetic technique was associated with the same decrease in PONV, and to each was attributed a 26 % decrease in PONV [1]. Additionally, patients are willing to pay between $56 and $100 out of pocket to receive an antiemetic that is completely effective [2]. Neostigmine has been found to be a triggering agent at a dose above 2.5 mg in some studies, but other studies have failed to show any correlation between neostigmine and PONV [3]. A recent meta-analysis showed that inhaled isopropyl alcohol was more effective than placebo, but less effective than standard antiemetics [4].

The chemoreceptor trigger zone is located outside the blood-brain barrier in the medulla and is responsible for beginning the emesis process. Lesions of the area do not prevent emesis due to vagal stimulation or motion [5]. The CTZ is rich in chemical receptors, and antagonists to these receptors have become the mainstay of PONV prevention. While not well studied, PONV in diabetic patients with gastroparesis can be treated with metoclopramide.

Drug Class and Mechanism of Action

Serotonin Receptor Antagonists *(see Fig. 28.1)*

Serotonin released from enterochromaffin cells of the small intestinal mucosa binds to the 5-hydroxytryptamine type 3 (5-HT_3) in the CTZ. Most of the 5-HT3 blockers (ondansetron, granisetron) competitively antagonize these receptors and receptors in the gut [6]. The newest 5-HT3 antagonist (palonosetron) allosterically binds and causes downregulation of this type of serotonin receptor, possibly contributing to its long half-life [7]. It may also inhibit the emetic response caused by substance P, a characteristic shared by the NK1 receptor antagonists [8]. In a recent study, it was shown to be as effective as other 5-HT3 blockers plus dexamethasone and more effective than the others alone [9].

Corticosteroids

Dexamethasone and other corticosteroids stabilize liposomal membranes and interfere with the synthesis of prostaglandins [10].

Anticholinergics

Scopolamine

While there are many anticholinergic agents, only scopolamine is used in the prevention of PONV by inhibiting the binding of acetylcholine in the vestibular

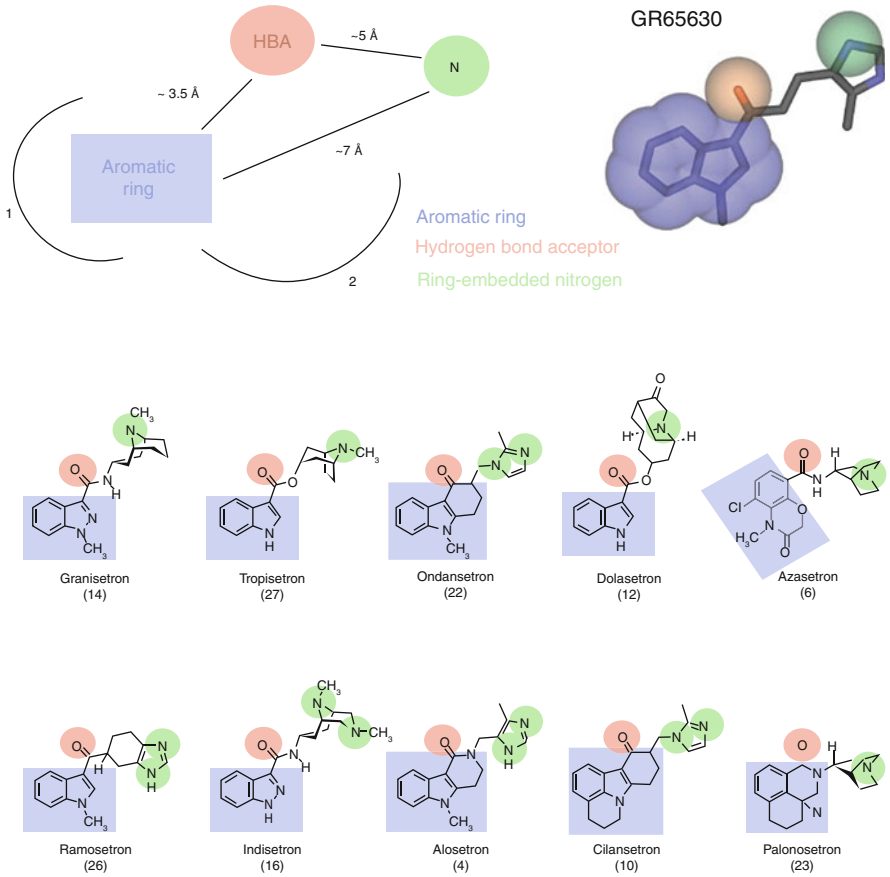


Fig. 28.1 5-hydroxytryptamine3 (5-HT3) receptor antagonists Thompson [22]

system [11] and the cortex and pons [12]. It is available in IV or transdermal formulations. It has been shown to be effective across a wide range of surgery times as a preventative agent as opposed to a rescue medication. Additionally, patients receiving this antiemetic reported much higher satisfaction scores than those in other treatment groups despite a high incidence of side effects [13].

Substance P Receptor (NK1) Antagonists

Aprepitant has been found to be more effective than ondansetron at preventing PONV in the perioperative period [14]. It has been found to exert its effects via a final, more common pathway of the emetic centers after crossing the blood-brain barrier [15]. In fact, there were no improved outcomes when scopolamine and aprepitant were combined [16]. However, it has not led to complete abolishment of nausea, so other mechanisms may be involved.

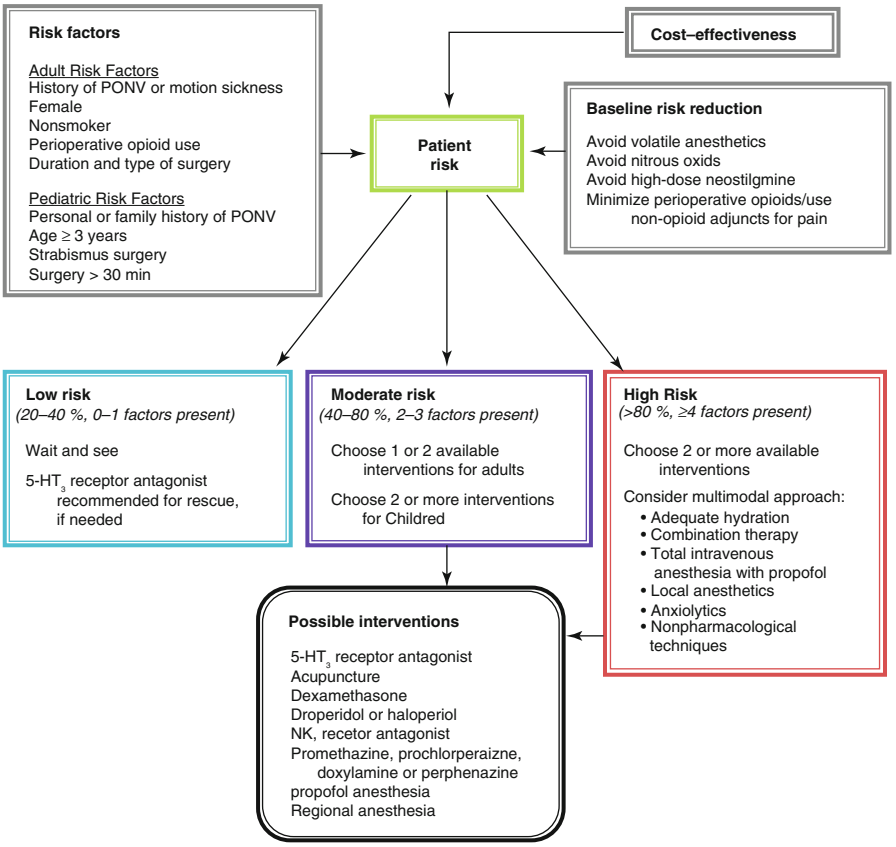


Fig. 28.2 A clinical decision algorithm for the prevention and treatment of postoperative nausea and vomiting (PONV) Le and Gan [18]

Dopamine Antagonists

Droperidol and promethazine block the effects of dopamine on the CTZ, and promethazine has additional histamine-blocking properties [17].

Indications/Clinical Pearls

- Le and Gan have developed an algorithm for the prevention of PONV based on risk factors. Risk factors include female sex, nonsmoker, having a history of motion sickness or PONV, and the use of opioids. For 0–1 risk factors, no antiemetics are recommended. For 2–3 risk factors, give one or two antiemetics, and if four or more risk factors are present, consider two or more antiemetics. TIVA can be used in place of one antiemetic [18] (See Fig. 28.2).

- As mentioned, alcohol has been shown to be effective in the clinical setting. Owing to its parasympathetic mediation, nausea can be rapidly treated successfully with two alcohol pads in each nostril with four deep breaths through the nose. The mechanism is believed to be the noxious smell creating a sympathetic overdrive response, and it should be seen within 30 s to a minute.

Dosing Options [17]

Ondansetron should be given in 4 mg doses. Dexamethasone should be administered at a dose of 8 mg [17] and it should be given at least 2 h prior to the end of surgery [19]. Scopolamine transdermal patch (1.5 mg) should be applied the night before surgery and removed 24 h after surgery. Aprepitant should be given in a dose of 40 mg [14]. Droperidol should be administered in a dose of 0.625 mg.

Drug Interactions (Package Inserts)

Ondansetron should not be given with apomorphine or any agent that prolongs QTc. Dexamethasone has no interaction with commonly used operating room drugs. Scopolamine levels may be increased by ipratropium, magnesium sulfate, and droperidol. Aprepitant may increase the levels of corticosteroids. Droperidol should not be given with MAO inhibitors or other agents that prolong the QTc.

Side Effects/Black Box Warnings

Headaches and constipation are the most common side effects associated with ondansetron, and it has a black box warning for QTc prolongation, most commonly associated with high doses. Dexamethasone has many side effects, but rarely are any of them a concern with a single injection with the exception of perineal burning after rapid IV injection [20]. Aprepitant is associated with fatigue, constipation, weakness, and hiccups. Droperidol was issued a block box warning for prolonged QT syndrome. However, this is rarely seen in the low doses used to prevent PONV [21].

Summary

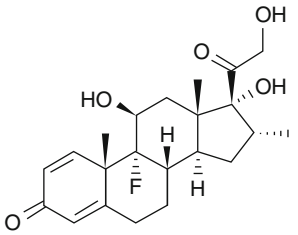
PONV is a frequent problem that rarely leads to hospital admission. Most of the antiemetics today are inexpensive and have a very favorable side effect profile. All classes of antiemetics have been shown to be somewhat efficacious, but much of the

data is contradictory given the complex nature of PONV. Nausea and emesis are multifactorial, and, therefore, no one agent is likely to prevent PONV in all patients. A large number of patients need to be studied to best sort out individual variables. Identifying patients who are at high risk and giving appropriate preventative antiemetics can decrease PACU stays and increase patient comfort.

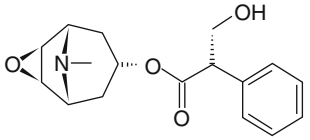
Disclosure The opinions expressed in this manuscript are the opinions of the author and do not necessarily reflect the opinions of the US Air Force, Army, or government.

Chemical Structures

Chemical Structure
28.1 Dexamethasone



Chemical Structure
28.2 Scopolamine



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