J Anesth (2001) 15:223–232

Journal of
Anesthesia

Review

Current prevention and treatment of postoperative nausea and vomiting with 5-hydroxytryptamine type 3 receptor antagonists: a review

Yoshitaka Fujii and Hidenori Toyooka

Department of Anesthesiology, University of Tsukuba Institue of Clinical Medicine, 2-1-1 Amakubo, Tsukuba, Ibaraki 305-8576, Japan

Key words Complications · Nausea · Vomiting · Antiemetics · 5-HT_3 receptor antagonists

Introduction

Postoperative nausea and vomiting (PONV) are distressing and frequent adverse events of anesthesia and surgery, with a remarkably high incidence after gynecological surgery and after pediatric strabismus surgery [1,2]. The etiology of PONV is complex and is dependent on a variety of factors, including patient demographics, type of surgery, anesthetic technique, and postoperative care [3]. Pharmacological approaches (antihistamines, butyrophenones, dopamine receptor antagonists) have been investigated for the prevention and treatment of PONV, but undesirable side effects, such as excessive sedation, hypotension, dry mouth, dysphoria, restlessness, and extrapyramidal symptoms have been noted [4]. Ondansetron is one of a new class of antiemetic agents known as hydroxytryptamine type 3 (5-HT_3) receptor antagonists, and is suitable for the prophylaxis of nausea and vomiting induced by antineoplastic drugs [5]. Since the first report by Lesser and Lip [6] that ondansetron is effective for the control of PONV after gynecological surgery under general anesthesia, a number of investigations have evaluated the efficacy and safety of 5-HT_3 receptor antagonists (ondansetron, granisetron, tropisetron, dolasetron, ramosetron) for the prevention and treatment of PONV. The 5-HT_3 receptor antagonists commonly lack the sedative, dysphoric, and extrapyramidal effects associated with non-5-HT_3 receptor antagonists such as droperidol and metoclopramide [4]. The precise mechanism by which 5-HT_3 receptor antagonists prevent PONV is not known. The purpose of this article is to review the current prevention and treatment of PONV with 5-HT_3 receptor antagonists. A Medline search from 1990 to 2000 was performed, and search terms included PONV, antiemetics, 5-HT_3 receptor antagonists, ondansetron, granisetron, tropisetron, dolasetron, and ramosetron. Consideration was given to the choice of 5-HT_3 receptor antagonists for the prevention and treatment of PONV which were available at the time the article was written.

Address correspondence to: Y. Fujii
Received: December 20, 2000 / Accepted: April 24, 2001

Ondansetron (Table 1)

In a randomized, double-blind, placebo-controlled trial, ondansetron given orally and intravenously (i.v.) was effective for the prevention and treatment of PONV in women undergoing general anesthesia for gynecological surgery [6,7]. Kenny et al. [8] have evaluated the efficacy of oral ondansetron at three different doses (1, 8, and 16 mg) and placebo administered every 8 h, and have demonstrated that ondansetron 8 mg given orally is the minimum effective dose for the prevention of PONV after gynecological surgery. Two studies comparing ondansetron 1, 4, and 8 mg with placebo administered i.v. before the induction of anesthesia have determined that ondansetron 4 mg is the optimal prophylactic dose for the control of PONV in female patients undergoing gynecological surgery under general anesthesia [9,10]. In ambulatory male and female outpatients, the optimal dose of ondansetron for the treatment of PONV appears to be 4 mg [11–13]. Patients with a positive history of motion sickness and/or previous postoperative emesis experience a greater incidence of PONV [3]. In this population, ondansetron 4 mg cannot entirely prevent PONV during the first 24 h after anesthesia [14]. Several investigations have compared the prophylactic antiemetic efficacy of ondansetron

Table 1. Ondansetron

Reference	Type of surgery (no. of patients)	Regimen (dose, route)	Emesis-free (rate)	Comments (efficacy)
Prevention			24h after anesthesia	
Lesser and Lip. [6]	Gynecological (84 females)	Ondansetron (16 mg, PO) Placebo	71% 33%	Ondansetron > placebo
Kenny et al. [8]	Gynecological (982 females)	Ondansetron (1, 8, 16 mg, PO) Placebo	56%, 70%, 75% 55%	Ondansetron 16 mg = 8 mg > 1 mg = placebo
McKenzie et al. [10]	Gynecological (544 females)	Ondansetron (1, 4, 8 mg, IV) Placebo	62%, 76%, 77% 46%	Ondansetron 8 mg = 4 mg > 1 mg = placebo
DuPen et al. [11]	Ambulatory (447 males, 53 females)	Ondansetron (1, 4, 8 mg, IV) Placebo	41%, 47%, 47% 15%	Ondansetron 8 mg = 4 mg > 1 mg = Placebo
Alon and Himmelseher [15]	Gynecological (66 females)	Ondansetron (8 mg, IV) Droperidol (1.25 mg, IV) Metoclopramide (10 mg, IV)	87% 55% 45%	Ondansetron > droperidol = metoclopramide
Raphael and Norton [16]	Gynecological (123 females)	Ondansetron (4 mg, IV) Metoclopramide (10 mg, IV)	82% 47%	Ondansetron > metoclopramide
Desilva et al. [20]	Gynecological (360 females)	Ondansetron (4 mg, IV) Droperidol (1.25 mg, IV) Perphenazine (5 mg, IV) Metoclopramide (10 mg, IV) Placebo	63% 76% 70% 50% 43%	Ondansetron = droperidol = perphenazine > placebo = metoclopramide
Rose et al. [21]	Strabismus repair (90 children)	Ondansetron (0.15 mg·kg^{-1}, IV) Metoclopramide (0.25 mg·kg^{-1}, IV) Placebo	70% 47% 33%	Ondansetron > placebo = metoclopramide
Furst and Rodarte [23]	Tonsillectomy (256 children)	Ondansetron (0.15 mg·kg^{-1}, IV) Droperidol (0.075 mg·kg^{-1}, IV) Metoclopramide (0.5 mg·kg^{-1}, IV) Placebo	73% 38% 42% 38%	Ondansetron > droperidol = metoclopramide = placebo
Watcha et al. [26]	Ambulatory (130 children)	Ondansetron (0.01, 0.05, 0.1 mg·kg^{-1}, IV) Placebo	85%, 81%, 47% 42%	Ondansetron 0.1 mg·kg^{-1} = 0.05 mg·kg^{-1} > 0.01 mg·kg^{-1} = placebo
Rose et al. [30]	Tonsillectomy (136 children)	Ondansetron (0.075, 0.15 mg·kg^{-1}, PO) Placebo	85%, 64% 62%	Ondansetron 0.15 mg·kg^{-1} > 0.075 mg·kg^{-1} = placebo
Treatment			24 h after administration	
Diemunsch et al. [34]	Gynecological and other (64 males, 682 females)	Ondansetron (4 mg, IV) Metoclopramide (10 mg, IV)	59% 41%	Ondansetron > metoclopramide
Khalil et al. [35]	Ambulatory (375 children)	Ondansetron (0.1 mg·kg^{-1}, IV) Placebo	53% 17%	Ondansetron > placebo

with other commonly used and well established antiemetics, i.e., droperidol and metoclopramide, in patients undergoing general anesthesia for dilatation and curettage or gynecological laparoscopic surgery, and have shown that preoperative prophylactic administration of ondansetron 4 mg is superior to droperidol 1.25 mg or metoclopramide 10 mg [15–17]. However, in patients undergoing hip and knee replacements and femoral resections and receiving a standardized combined epidural and general anesthetic, no difference in the incidence of PONV was observed between ondansetron (4 mg) and droperidol (1.25 mg) groups [18]. Steinbrook et al. [19] have reported that droperidol 0.625 mg plus metoclopramide 10 mg administered i.v. after induction of anesthesia is more effective than ondansetron 4 mg for the prevention of PONV after laparoscopic cholecystectomy. Desilva et al. [20] have compared the prophylactic antiemetic efficacy of ondansetron 4 mg, droperidol 1.25 mg, perphenazine 5 mg, and metoclopramide 10 mg, compared with placebo, in patients undergoing gynecologic surgery, and have demonstrated that ondansetron, droperidol, and perphenazine are comparable for the prophylaxis against PONV. In children undergoing ambulatory surgery with an increased risk of postoperative vomiting (POV) (i.e., strabismus repair, tonsillectomy, dental surgery), ondansetron 0.1–0.15 $mg \cdot kg^{-1}$, administered i.v. after anesthetic induction and prior to surgery, reduces the incidence and severity of POV [21–25], and is a better prophylactic antiemetic than droperidol 0.05–0.075 $mg \cdot kg^{-1}$ or metoclopramide 0.25–0.5 $mg \cdot kg^{-1}$ [21,22–25]. A dose-response study comparing ondansetron at a dose of 0.01, 0.05, or 0.1 $mg \cdot kg^{-1}$ with placebo has demonstrated that ondansetron 0.05 $mg \cdot kg^{-1}$ is as effective as 0.1 $mg \cdot kg^{-1}$ for the prevention of POV [26]. Splinter and Rhine [27] have shown that ondansetron 0.15 $mg \cdot kg^{-1}$, compared with 0.05 $mg \cdot kg^{-1}$, is an effective prophylactic antiemetic. However, ondansetron 0.15 $mg \cdot kg^{-1}$ does not reduce the incidence of POV in children undergoing resective neurosurgical procedures, a group that is at a high risk of POV [28]. Prophylactic therapy with ondansetron 0.1 $mg \cdot kg^{-1}$ given orally decreases the incidence of POV after pediatric tonsillectomy [29]. Oral ondansetron 0.075 $mg \cdot kg^{-1}$ is not effective for the prevention of POV in children undergoing tonsillectomy [30]. Most studies have evaluated the efficacy of ondansetron as a prophylactic antiemetic administered i.v. immediately before the induction of anesthesia [6–18]. Two investigations have evaluated the effect of the timing of this drug administration on its efficacy as a prophylactic antiemetic [31,32]. Both studies have demonstrated that ondansetron is more effective for preventing PONV, for reducing rescue antiemetics, and for improving patient satisfaction when administered at the completion of versus prior to the surgery. In the treatment of established PONV, i.v. ondansetron 4 mg appears to be the optimal dose, and it is more effective than metoclopramide 10 mg in adults [33,34]. For children, ondansetron 0.1 $mg \cdot kg^{-1}$ administered i.v. is effective for the treatment of POV [35].

Granisetron (Table 2)

Numerous clinical studies have shown that prophylactic granisetron administered i.v. or orally reduces the incidence of PONV in adults undergoing gynecologic surgery [36–38], and reduces the incidence of POV in children undergoing strabismus surgery, tonsillectomy, or dental surgical procedures [39,40]. Wilson et al. [41] have compared three doses (0.1, 1, and 3 mg) of i.v. granisetron to placebo for the prevention of PONV during 0–24 h after anesthesia, and have determined the minimum effective prophylactic dose to be 1 mg in adult patients. Munro et al. [42] have reported that oral granisetron, at a dose of 0.02 $mg \cdot kg^{-1}$, provides effective prophylaxis against POV in pediatric patients. However, in other investigations, i.v. granisetron 0.04 $mg \cdot kg^{-1}$ appears to be the minimum effective dose for adults [43] and for children [44]. In comparative studies, the antiemetic efficacy of granisetron is superior to the traditional antiemetic regimens, droperidol and metoclopramide, for the prophylactic treatment of PONV. It was found that i.v. granisetron 0.04 $mg \cdot kg^{-1}$ was more effective than droperidol 1.25 mg or metoclopramide 10 mg for the prevention of PONV after gynecologic surgery [36,45]. Two studies comparing the effectiveness of granisetron, droperidol, and metoclopramide for the control of PONV in female patients with a history of motion sickness and/or previous PONV at increased risk for developing emesis [3] have demonstrated that granisetron is the most efficacious against PONV [46,47]. Granisetron 0.04 $mg \cdot kg^{-1}$ administered i.v. is a better antiemetic than droperidol 0.05 $mg \cdot kg^{-1}$ or metoclopramide 0.25 $mg \cdot kg^{-1}$ in the reduction of POV after pediatric strabismus repair or tonsillectomy [48,49]. For the treatment of established PONV, Taylor et al. [50] have compared the antiemetic efficacy of granisetron 0.1, 1, and 3 mg with that of placebo administered i.v. in patients undergoing various types of surgery, and have shown that granisetron is more effective than placebo in all groups.

Tropisetron (Table 3)

In a randomized, double-blind, placebo-controlled study, the prophylactic antiemetic tropisetron, administered at a dose of 5 mg i.v., effectively reduced the incidence of PONV after gynecologic surgery [51,52].

Table 2. Granisetron

Reference	Type of surgery (no. of patients)	Regimen (dose, route)	Emesis-free (rate)	Comments (efficacy)
Prevention			24 h after anesthesia	
Fujii et al. [36]	Gynecological (60 females)	Granisetron (3 mg, IV) Metoclopramide (10 mg, IV) Placebo	95% 60% 60%	Granisetron > placebo = metoclopramide
Fujii et al. [38]	Gynecological (120 females)	Granisetron (1, 2, 4 mg, PO) Placebo	63%, 90%, 90% 53%	Granisetron 4 mg = 2 mg > 1 mg = placebo
Cieslak et al. [40]	Ambulatory (97 children)	Granisetron (0.01, 0,04 mg·kg^{-1}, IV) Placebo	64%, 91% 58%	Granisetron 0.04 mg·kg^{-1} > 0.01 mg·kg^{-1} = placebo
Wilson et al. [41]	Gynecological and other (20 males, 507 females)	Granisetron (0.1, 1, 3 mg, IV) Placebo	27%, 49%, 42% 18%	Granisetron 3 mg = 1 mg > 0.1 mg = placebo
Fujii et al. [45]	Gynecological (60 females)	Granisetron (0.04 mg·kg^{-1}, IV) Drope1ridol (1.25 mg, IV) Placebo	92% 64% 56%	Granisetron > placebo = droperidol
Fujii et al. [48]	Strabismus repair tonsillectomy (100 children)	Granisetron (0.04 mg·kg^{-1}, IV) Droperidol (0.05 mg·kg^{-1}, IV) Metoclopramide (0.25 mg·kg^{-1}, IV) Placebo	88% 76% 68% 60%	Granisetron > placebo = droperidol = metoclopramide
Treatment			24 h after administration	
Taylor et al. [50]	Gynecological and other	Granisetron (0.1, 1, 3 mg, IV) Placebo	38%, 46%, 49% 20%	Granisetron 3 mg = 1 mg = 0.1 mg > placebo

Table 3. Tropisetron

Reference	Type of surgery (no. of patients)	Regimen (dose, route)	Emesis-free (rate)	Comments (efficacy)
Prevention			24 h after anesthesia	
Zomers et al. [51]	Gynecological (69 females)	Tropisetron (5 mg, IV) Placebo	74% 41%	Tropisetron > placebo
Capouet et al. [53]	Gynecological (385 females)	Tropisetron (0.5, 2, 5 mg, IV) Placebo	69%, 74%, 70% 56%	Tropisetron 5 mg = 2 mg > 0.5 mg = placebo
Chan et al. [54]	Breast (148 females)	Tropisetron (2, 5 mg, IV) Placebo	38%, 69% 17%	Tropisetron 5 mg > 2 mg = placebo
Ang et al. [55]	Tonsillectomy (48 children)	Tropisetron (0.1 mg·kg^{-1}, IV) Placebo	35% 71%	Tropisetron > placebo
Purhonen et al. [56]	Gynecological (150 females)	Tropisetron (5 mg, IV) Droperidol (1.25 mg, IV) Placebo	81% (48 h after anesthesia) 55% (48 h after anesthesia) 43% (48 h after anesthesia)	Tropisetron > droperidol = placebo
Naguib et al. [58]	Laparoscopic cholecystectomy (24 males, 108 females)	Tropisetron (5 mg, IV) Ondansetron (4 mg, IV) Granisetron (3 mg, IV) Metoclopramide (10 mg, IV) Placebo	48% 66% 52% 29% 28%	Tropisetron = ondansetron = granisetron > metoclopramide = placebo
Treatment			24 h after administration	
Alon et al. [59]	Gynecological and other (25 males, 289 females)	Tropisetron (0.5, 2, 5 mg, IV) Placebo	52%, 58%, 60% 29%	Tropisetron 5 mg = 2 mg = 0.5 mg > placebo

Capouet et al. [53] have compared the efficacy of tropisetron at three different doses (0.5, 2, and 5 mg) with the effect of placebo administered i.v. before the induction of anesthesia, and have determined that tropisetron 2 mg is the optimal dose for the prevention of PONV in women undergoing gynecologic surgery. However, in female patients undergoing breast surgery, tropisetron 5 mg was more effective than tropisetron 2 mg for prophylaxis against PONV [54]. For children, tropisetron 0.1 mg·kg^{-1} administered i.v. after tracheal intubation prior to surgery reduced the incidence of POV after tonsillectomy [55]. Two studies comparing the antiemetic efficacy of tropisetron 5 mg and droperidol 1.25 mg for the prevention of PONV in female patients undergoing gynecologic surgery or laparoscopic cholecystectomy have demonstrated that tropisetron effectively prevents vomiting, but not nausea, and have shown that droperidol fails to prevent PONV, and shows a higher incidence of drowsiness [56,57]. Naguib et al. [58] have evaluated the effectiveness of ondansetron 4 mg, granisetron 3 mg, and tropisetron 5 mg, compared with placebo, for the prevention of PONV after laparoscopic cholecystectomy, and demonstrated no difference in the number of patients who were emesis-free during 24 h after anesthesia among the ondansetron, granisetron, and tropisetron groups. In the treatment of established PONV, Alon et al. [59] have compared the efficacy and tolerability of three doses (0.5, 2, and 5 mg) of i.v. tropisetron, and have determined that tropisetron 2 mg is the optimal dose.

Dolasetron (Table 4)

In clinical trials, dolasetron, administered i.v. and orally, has been evaluated for the prevention and treatment of PONV. Graczyk et al. [60] have compared the efficacy and safety of i.v. dolasetron at three different doses (12.5, 25, and 50 mg) for the prevention of PONV after outpatient laparoscopic gynecologic surgery, and have determined that dolasetron 12.5 mg is the minimum effective dose. The 12.5 mg dose of dolasetron administered i.v. was also effective for the treatment of established PONV [61]. Prophylactic oral dolasetron 50–100 mg reduces the incidence of PONV in female patients undergoing gynecologic surgery [62,63]. Frighetto et al. [64] have reported that dolasetron 50 mg and droperidol 1.25 mg, given intraoperatively, are more cost-effective than no prophylaxis (i.e., rescue therapy) for PONV in ambulatory gynecologic surgery. When given at the induction of anesthesia, dolasetron 50 mg and ondansetron 4 mg were comparable for the prophylaxis of PONV [65].

Table 4. Dolasetron

Reference	Type of surgery (no. of patients)	Regimen (dose, route)	Emesis-free (rate)	Comments (efficacy)
Prevention			24 h after anesthesia	
Graczyk et al. [60]	Gynecological (635 females)	Dolasetron (12.5, 25, 50 mg, IV) Placebo	50%, 52%, 56% 31%	Dolasetron 50 mg = 25 mg = 12.5 mg > placebo
Diemunsch et al. [63]	Gynecological (789 females)	Dolasetron (25, 50, 100, 200 mg, PO) Placebo	45%, 57%, 51%, 47% 35%	Dolasetron 200 mg = 100 mg = 50 mg > placebo = dolasetron 25 mg
Korttila et al. [65]	Gynecological and other (30 males, 484 females)	Dolasetron (25, 50 mg, IV) Ondansetron (4 mg, IV) Placebo	51%, 71% 64% 49%	Dolasetron 50 mg = ondansetron 4 mg > dolasetron 25 mg = placebo
Treatment			24 h after administration	
Kovac et al. [61]	Gynecological and other (86 males, 414 females)	Dolasetron (12.5, 25, 50, 100 mg, IV) Placebo	35%, 28%, 29%, 29% 11%	Dolasetron 100 mg = 50 mg = 25 mg = 12.5 mg > placebo

Ramosetron (Table 5)

Two studies have compared the efficacy of ramosetron 0.3 mg and granisetron 2.5 mg administered i.v. at the end of surgery for the prevention of PONV in female patients undergoing gynecologic surgery, or laparoscopic cholecystectomy [66,67]. In these investigations, the antiemetic efficacy of ramosetron was similar to that of granisetron for the prevention of PONV during 0–24 h after anesthesia, and ramosetron was more effective than granisetron for increasing the number of patients who were emesis-free during 24–48 h after anesthesia. A dose-ranging study comparing three different doses (0.15, 0.3, and 0.6 mg) of ramosetron with the effect of placebo, given at the completion of the surgical procedure, has found the minimum effective dose of ramosetron to be 0.3 mg for prophylaxis against PONV after gynecologic surgery [68].

Combinations (Table 6)

Dexamethasone decreases chemotherapy-induced emesis when added to an antiemetic regimen [69]. McKenzie et al. [70] and Lopes-Olaondo et al. [71] have compared the antiemetic efficacy of ondansetron 4 mg plus dexamethasone 8 mg with that of ondansetron 4 mg alone administered i.v. after the induction of anesthesia in women undergoing gynecologic surgery, and have demonstrated that combined ondansetron and dexamethasone is more effective than ondansetron as a sole antiemetic for the prevention of PONV. In two studies that have evaluated the effectiveness of granisetron 0.04 mg·kg^{-1} in combination with dexamethasone 8 mg (adults) or 4 mg (children) for prophylaxis against PONV, it was shown that the granisetron/dexamethasone combination was highly efficacious [72,73]. Because antiemetics have different sites of action, the combination of two antiemetics may be more effective than one drug alone. McKenzie et al. [74] first reported that the prophylactic efficacy of combined ondansetron 4 mg and droperidol 1.25 mg administered i.v. immediately after the induction of anesthesia was superior to that of droperidol alone for the prevention of PONV in women having tubal banding. In patients undergoing abdominal surgery, ondansetron 4 mg plus droperidol 2.5 mg was more effective than either antiemetic alone for the control of PONV [75]. Similarly, the granisetron/droperidol combination improves the antiemetic effect. A prophylactic combination of granisetron 2.5 mg and droperidol 1.25 mg was more effective than either antiemetic alone for prophylaxis against PONV after gynecologic surgery, without any clinically serious adverse effects [76]. Overall, better results can be obtained by

Table 5. Ramosetron

Reference	Type of surgery (no. of patients)	Regimen (dose, route)	Emesis-free (rate)	Comments (efficacy)
Prevention			24–48 h after anesthesia	
Fujii et al. [66]	Gynecological (120 females)	Granisetron (2.5 mg, IV)	70%	Ramosetron > granisetron
		Ramosetron (0.3 mg, IV)	92%	*Emesis-free during 24 h after anesthesia, ramosetron (90%) = granisetron (85%)
Fujii et al. [68]	Gynecological (120 females)	Ramosetron (0.15, 0.3, 0.6 mg, IV)	53%, 90%, 93%	Ramosetron 0.3 mg = 0.6 mg > 0.15 mg = placebo
		Placebo	50%	

Table 6. Combinations

Reference	Type of surgery (no. of patients)	Regimen (dose, route)	Emesis-free (rate)	Comments (efficacy)
Prevention			24 h after anesthesia	
McKenzie et al. [70]	Gynecological (89 females)	Ondansetron (4 mg, IV) + dexamethasone (8 mg, IV)	52%	Ondansetron + dexamethasone > ondansetron
		Ondansetron (4 mg, IV)	38%	
McKenzie et al. [74]	Gynecological (120 females)	Ondansetron (4 mg, IV) + droperidol (1.25 mg, IV)	92%	Ondansetron + droperidol > droperidol
		Droperidol (1.25 mg, IV)	78%	
Pueyo et al. [75]	Gynecological and other (100 females)	Ondansetron (4 mg, IV) + droperidol (2.5 + 1.25 mg, IV)	92% (48 h after anesthesia)	Ondansetron + droperidol > ondansetron = droperidol = Placebo
		Ondansetron (4 mg, IV)	56% (48 h after anesthesia)	
		Droperidol (2.5 + 1.25 mg, IV)	60% (48 h after anesthesia)	*Droperidol 1.25 mg (2nd dose) administered 12 h after 1st dose
		Placebo	28% (48 h after anesthesia)	
Fujii et al. [72]	Gynecological (90 females)	Granisetron (0.04 mg·kg^{-1}, IV) + dexamethasone (8 mg, IV)	96%	Granisetron + dexamethasone > granisetron
		Granisetron (0.04 mg·kg^{-1}, IV)	80%	
Fujii et al. [76]	Gynecological (150 females)	Granisetron (2.5 mg, IV) + droperidol (1.25 mg, IV)	96%	Granisetron + droperidol > granisetron > droperidol
		Granisetron (2.5 mg, IV)	84%	
		Droperidol (1.25 mg, IV)	54%	

using a combination of antiemetics acting at different emetogenic receptors.

Cost-effectiveness

Several investigations have criticized new antiemetics, such as the 5-HT_3 receptor antagonists, because of their high cost (i.e., more than ¥10 000 per surgical procedure in Japan) [77,78]. The 5-HT_3 receptor antagonists are much more expensive than other, traditional, antiemetics, such as droperidol and metoclopramide (i.e., less than ¥1000 per surgical procedure in Japan). At present, prophylactic therapy with 5-HT_3 receptor antagonists for PONV is not approved by the health insurance system in Japan. This higher cost may delay the widespread employment of 5-HT_3 receptor antagonists as antiemetics. However, the use of the traditional antiemetics, droperidol and metoclopramide, has been limited because these drugs occasionally cause undesirable adverse effects, including excessive sedation and extrapyramidal signs [4]. The choice of antiemetics should not be limited to these costs, but should also take into consideration patient preference and satisfaction.

Conclusion

Although specific antiemetic agents have become available in recent years, PONV remains a "big little problem". In patients at high risk for PONV, we need to consider the prophylactic use of antiemetic drugs. A number of investigations have shown that 5-HT_3 receptor antagonists are better antiemetics than other commonly used and well established antiemetics, such as droperidol and metoclopramide, for the prevention and treatment of PONV. The prophylactic antiemetic efficacies of ondansetron, granisetron, tropisetron, and dolasetron are comparable. Ramosetron is effective for the long-term prevention of PONV. Combinations of 5-HT_3 receptor antagonists (ondansetron, granisetron) with dexamethasone or droperidol improve their efficacy for prophylaxis against PONV. Further studies are required to compare the efficacy and safety of 5-HT_3 receptor antagonists used as antiemetics in patients undergoing various types of surgery. Knowledge of all available antiemetic drugs is necessary to successfully manage PONV.

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