

Prevention of Emetic Episodes During Cesarean Delivery Performed Under Regional Anesthesia in Parturients

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Abstract: Nausea, retching, and vomiting are common in parturients undergoing cesarean delivery performed under regional anesthesia. These emetic episodes are distressing to the parturient and disturbing to the surgeon. Numerous antiemetics have been studied for the prevention of these emetic episodes in parturients scheduled for cesarean delivery. Traditional antiemetics, including butyrophenones (e.g., droperidol), benzamide (e.g., metoclopramide), and anticholinergics (e.g., glycopyrrolate), are used for the control of these emetic episodes. Non-traditional antiemetics, propofol and dexamethasone, are available for the prevention of these emetic episodes. Serotonin receptor antagonists, ondansetron and granisetron, are more effective than traditional antiemetics for the prophylaxis against these emetic episodes.

None of the available antiemetics are entirely effective, perhaps because most of them act through the blockade on one type of receptor. There is a possibility that combined antiemetics with different sites of activity would be more effective than one drug alone for the prevention of these emetic episodes. Antiemetic therapy with combined granisetron and dexamethasone or combined propofol and dexamethasone is highly effective for the prevention of these emetic episodes in parturients scheduled for cesarean delivery. Non-pharmacological technique includes acupressure at P6 (Nei-Kuwan) point. Overall, these pharmacological and non-pharmacological therapy reduces emetic episodes in parturients undergoing regional anesthesia for cesarean delivery.

The clinician must weight the benefit of using pharmacological and non-pharmacological techniques for nausea, retching, and vomiting in parturients undergoing cesarean delivery performed under regional anesthesia.

Keywords: Complications, nausea, vomiting, antiemetics, cesarean delivery, parturients.

INTRODUCTION

Cesarean delivery under regional anesthesia has become increasingly popular over the past decade, due to increased patient acceptability, improved fetal condition at birth and greater maternal safety [1,2]. When used for cesarean delivery, combined spinal-epidural (CSE) anesthesia offers several advantages over epidural and single-shot spinal techniques [3]. This technique brings together the rapid-onset, dense anesthesia induced by the spinal component and the potential for continuing anesthesia or analgesia using the epidural route [4].

Nausea, retching, and vomiting during regional anesthesia for cesarean delivery are common occurrences, especially when the uterus is exteriorized [5,6]. These symptoms are distressing and uncomfortable for the parturient and may interfere with the surgical procedure. Patients who experience these symptoms consume more resources and require additional health care professional time than do those in whom these complications are avoided [7]. The overall incidence of nausea, retching, and vomiting during regional anesthesia for cesarean delivery is extremely variable, up to 80%, in patients receiving no pharmacological antiemetics [8]. Numerous antiemetics have been studied for the prevention and treatment of these emetic symptoms. These drugs

include butyrophenones, benzamides, anticholinergics, corticosteroids, propofol, and serotonin receptor antagonists. All of which have been associated with varying degrees of success [5,6,8-32].

In this review, MEDLINE and EMBASE searches from January, 1980 to March, 2006 were performed, and search terms included complications, nausea, retching, vomiting, antiemetics, surgery, cesarean delivery, and parturient. Consideration was given to the choice of antiemetics for the prevention of emetic episodes during cesarean delivery in parturients which were available at the time the article was written.

RISK FACTORS FOR NAUSEA, RETCHING, AND VOMITING DURING REGIONAL ANESTHESIA FOR CESAREAN DELIVERY

Nausea, retching, and vomiting during regional anesthesia for cesarean delivery have a complex and multifactorial etiology [33-49]. These emetic symptoms are influenced by maternal hypotension [33]. This hypotension leads to cerebral hypoperfusion and brainstem ischemia that activates the circulatory, respiratory and vomiting centers in the medulla [34]. It also leads to gut ischemia and release of emetogenic substances such as serotonin from the intestine [7]. Untreated severe hypotension poses serious risks to both mother in the form of unconsciousness, pulmonary aspiration, apnea or even cardiac arrest, and baby leading to impaired placental perfusion causing hypoxia, fetal acidosis, and neurological injury [7]. Lateral uterine displacement and prehydration are commonly used to prevent hypotension but these have

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limited efficacy and a vasopressor drug is often required [35,36].

In general, a number of factors, including age, gender, smoking habit, history of motion sickness and/or previous postoperative emesis, pain, operative procedure, and anesthetic technique, are all considered to affect the occurrence of nausea, retching, and vomiting [37]. Pioneer studies described a decreasing incidence of emetic symptoms among men with increasing age and an insignificant decrease among women until 80 years [38]. Female patients have 3 times greater incidence of emetic symptoms than males, due to increased gonadotropin, estrogen, and plasma progesterone levels during their menstrual cycles [39]. Cigarette smoking confers protection against emetic symptoms, due to the presence of an antiemetic substance in tobacco smoke [40], and thus the incidence of emetic symptoms appears to be less in smokers than in non-smokers [41]. Patients with a history of motion sickness and/or previous postoperative emesis are at increased risk for developing emetic symptoms, due to a low threshold for vomiting p [37,42].

Surgical stimuli that is responsible for nausea, retching, and vomiting during cesarean delivery performed under regional anesthesia include exteriorization of the uterus, intra-abdominal manipulation or exploration and peritoneal traction during closure. These operative procedures produce visceral pain that is mediated by unmyelinated C-fibers [43,44]. Visceral pain is a potent stimulus for emetic symptoms during regional anesthesia [43]. Handling of abdominal viscera stimulates sensory vagal fibers and induces emesis by activating the vomiting center [43]. To reduce visceral pain, adding opioids (morphine, fentanyl) to intrathecal or epidural local anesthetic for cesarean delivery increased the incidence of emetic episodes postoperatively but not intraoperatively [45-47].

Anesthetic-related factors are preanesthetic medication and anesthetic technique [37]. Premedication with opioids (morphine, fentanyl) increases the incidence of emetic symptoms by stimulating central nervous system opioid receptors

[48]. Sympathetic block secondary to regional anesthesia results in nausea and vomiting induced by gastrointestinal hyperactivity due to relative overactivity of the vagus. The efficacy of the vagolytic agent, glycopyrrolate, to reduce the incidence and severity of nausea has been shown in patients performed under regional anesthesia [37]. Opioids are used with local anesthetic solution to intensify the regional block, to improve the quality of intraoperative analgesia, and to provide postoperative pain relief [7]. However, intrathecal and epidural opioids produce side effects, including nausea, retching, and vomiting [49]. Direct stimulation of the chemoreceptor trigger zone (CTZ) occurs as a result of cephalad spread of the drug in the cerebrospinal fluid (CSF) to the brainstem, secondary to vascular uptake and delivery to the vomiting center and the CTZ, and to modulation of afferent input at the area postrema [37]. Nausea, retching, and vomiting are also common adverse events of opioids administered intravenously during regional anesthesia [37].

TRADITIONAL ANTIEMETICS

Traditional antiemetics used for nausea, retching, and vomiting during regional anesthesia for cesarean delivery in parturients include butyrophenones (e.g., droperidol), benzamides (e.g., metoclopramide), and anticholinergics (e.g., glycopyrrolate) (Table 1). Butyrophenones possess antiemetic activity as a result of their antagonistic properties at the dopamine receptors [50]. Benzamides have both central (CTZ and area postrema vomiting centers) and peripheral (gastrointestinal tract) antiemetic actions, by blocking dopaminergic receptors, and increase esophageal sphincter tone and promote gastric motility, thereby preventing the delayed gastric emptying produced by the opioid analgesics [51]. Anticholinergics are potent inhibitors of muscarinic and cholinergic central nervous system emetic receptors in the cerebral cortex and pons [52].

Droperidol is the most popular and effective drug in the prevention and treatment of nausea, retching, and vomiting during cesarean delivery performed under regional anesthesia for 2 decades. In a randomized, double-blind, placebo-

Table 1. Traditional Antiemetics

Reference	No. of Patients	Regimen (Dose, Route)	Emetic Episodes (Rate, Intraoperatively)	Comments (Efficacy, <i>P</i> Values)
Santos <i>et al.</i> [5]	50 parturients	Droperidol (2.5 mg, IV) Placebo	12% (nausea) 40% (nausea)	Droperidol > Placebo (<i>P</i> = 0.024)
Mandel <i>et al.</i> [9]	128 parturients	Droperidol (0.5 mg, IV) Placebo	13% (nausea) 41% (nausea)	Droperidol > Placebo (<i>P</i> = 0.001)
Fujii <i>et al.</i> [10]	120 parturients	Granisetron (3 mg, IV) Droperidol (1.25 mg, IV) Metoclopramide (10 mg, IV) Placebo	13% 17% 20% 60%	Granisetron = Droperidol = Metoclopramide > Placebo (all <i>P</i> = 0.001 versus Placebo)
Chestnut <i>et al.</i> [11]	67 parturients	Metoclopramide (0.15 mg/kg, IV) Placebo	12% (nausea) 0% (vomiting) 36% (nausea) 15% (vomiting)	Metoclopramide > Placebo (<i>P</i> = 0.026)
Chestnut <i>et al.</i> [12]	81 parturients	Droperidol (0.5 mg, IV) Metoclopramide (15 mg, IV)	20% (nausea) 5% (vomiting) 30% (nausea) 3% (vomiting)	Droperidol = Metoclopramide (<i>P</i> = 0.333)
Ure <i>et al.</i> [13]	49 parturients	Glycopyrrolate (200 mcg, IV) Placebo	42% (nausea) 68% (nausea)	Glycopyrrolate > Placebo (<i>P</i> = 0.03)

controlled trial, droperidol 2.5 mg administered intravenously prophylactically during spinal anesthesia for cesarean delivery reduces the incidence in nausea from 40% to 12% when compared to placebo (saline) [5]. Similarly, Mandell *et al.* found the antiemetic efficacy of droperidol 0.5 mg in parturients undergoing epidural anesthesia for cesarean delivery [9]. Fujii *et al.* compared droperidol 1.25 mg with placebo (saline) in patients scheduled for cesarean delivery during spinal anesthesia. They demonstrated that droperidol is effective for the prophylaxis against emetic episodes [10]. When used at large doses (more than 2.5 mg), droperidol may cause undesirable adverse effects, including drowsiness, dysphoria, restlessness, and extrapyramidal signs [55]. Recently, the US Food and Drug Administration (FDA) issued adverse events warning about droperidol because of its dysrhythmogenic effects, such as prolonged QT syndrome [53]. However, after carefully evaluating all of the reports submitted to the FDA, Hobib *et al.* concluded that in none of the cases in which arrhythmias occurred after small doses of droperidol (less than 1.25 mg) was there evidence of a cause-and-effect relationship [54].

Metoclopramide is an antiemetic used widely in clinical practice [37]. Two studies focused on the effectiveness of metoclopramide administered intravenously immediately after the umbilical was clamped for the prophylaxis against nausea and vomiting during regional anesthesia for cesarean delivery. Chestnut *et al.* demonstrated that metoclopramide 0.15 mg/kg reduced the incidence of intraoperative nausea from 36% to 12% and vomiting from 15% to 0% in parturients undergoing cesarean delivery [11]. Lussos *et al.* evaluated the efficacy and safety of prophylactic metoclopramide for cesarean delivery during spinal anesthesia. They concluded that metoclopramide 10 mg administered intravenously before induction of spinal anesthesia appeared to be

antiemetic effect [6]. Fujii *et al.* and Chestnut *et al.* found metoclopramide 10-15 mg to be as effective as droperidol 0.5-1.25 mg for preventing nausea and vomiting during regional anesthesia for cesarean delivery [10,12]. Metoclopramide has relatively few adverse effects when used in low doses (0.1-0.2 mg/kg). Higher doses (more than 0.2 mg/kg) of metoclopramide is associated with extrapyramidal reactions, such as akathisia and motor restlessness [37].

Glycopyrolate 0.2 mg administered intravenously before induction of spinal anesthesia for cesarean delivery reduces the incidence and severity of nausea, but not affect the occurrence of vomiting [13]. Transdermal scopolamine is effective for preventing nausea and vomiting following cesarean delivery in patients receiving epidural morphine for postoperative analgesia [14]. However, there were no reports investigating scopolamine antiemetic therapy during regional anesthesia for cesarean delivery in parturients. Scopolamine produces undesirable adverse effects, such as dry mouth, sedation, restlessness, and occasionally central cholinergic syndrome [37].

NON-TRADITIONAL ANTIEMETICS

The currently available non-traditional antiemetics for the prevention of nausea, retching, and vomiting in parturients undergoing cesarean delivery under regional anesthesia are propofol and dexamethasone (Table 2).

Propofol, a rapid-onset, short acting intravenous agent, has become popular for induction and maintenance of anesthesia [55]. Propofol possesses direct antiemetic properties [56], which is not a result of the lipid emulsion in the formulation of propofol [56]. The exact mechanism by which propofol acts as an antiemetic is unknown, but propofol is not considered to have vagolytic properties [57]. In an experi-

Table 2. Non-Traditional Antiemetics

Reference	No. of Patients	Regimen (Dose, Route)	Emetic Episodes (Rate, Intraoperatively)	Comments (Efficacy, P Values)
Numazaki <i>et al.</i> [15]	60 parturients	Propofol (1.0 mg/kg/h, IV) Placebo	23% 63%	Propofol > Placebo ($P = 0.002$)
Fujii <i>et al.</i> [16]	80 parturients	Propofol (2.0 mg/kg/h, IV) Propofol (1.0 mg/kg/h, IV) Propofol (0.5 mg/kg/h, IV) Placebo	20% 20% 55% 60%	Propofol 2.0 mg/kg/h = Propofol 1.0 mg/kg/h > Propofol 0.5 mg/kg/h = Placebo (both $P = 0.01$: Propofol 2.0 • 1.0 mg/kg/h versus Placebo, $P = 0.5$: Propofol 0.5 mg/kg/h versus Placebo)
Numazaki <i>et al.</i> [17]	100 parturients	Propofol (1.0 mg/kg/h, IV) Droperidol (1.25 mg, IV) Metoclopramide (10 mg, IV) Placebo	20% 20% 22% 60%	Propofol = Droperidol = Metoclopramide > Placebo (both $P = 0.004$: Propofol • Droperidol versus Placebo, $P = 0.01$: Metoclopramide versus Placebo)
Shi <i>et al.</i> [18]	50 parturients	Propofol (10 mg, IV) Placebo	24% (nausea) 16% (vomiting) 40% (nausea) 20% (vomiting)	Propofol = Placebo ($P = 0.225$)
Wang <i>et al.</i> [20]	180 parturients	Dexamethasone (10 mg, IV) Dexamethasone (5 mg, IV) Dexamethasone (2.5 mg, IV) Placebo	18% (postoperatively) 18% (postoperatively) 25% (postoperatively) 50% (postoperatively)	Dexamethasone 10 mg = Dexamethasone 5 mg > Dexamethasone 2.5 mg = Placebo (both $P = 0.01$: Dexamethasone 10 • 5 mg versus Placebo, $P = 0.063$: Dexamethasone 2.5 mg versus Placebo)

mental rat model, there is a possibility that the antiemetic property of propofol is associated with the reduced levels of serotonin in the area postrema and the CSF [58]. Numazaki *et al.* evaluated the efficacy of propofol for the prevention of nausea and vomiting during spinal anesthesia for cesarean delivery in parturients. They concluded that propofol at a subhypnotic dose (1.0 mg/kg/h) was effective for reducing the incidence of emetic episodes from 63% to 23% [15]. Fujii *et al.* compared three doses (0.5 mg/kg/h, 1.0 mg/kg/h, and 2.0 mg/kg/h) of propofol to placebo for the prophylaxis against intraoperative nausea, retching, and vomiting, and determined the minimum effective dose to be 1.0 mg/kg/h in patients undergoing spinal anesthesia for cesarean delivery (16). Numazaki *et al.* showed prophylactic antiemetic efficacy of propofol at a subhypnotic dose (1.0 mg/kg/h), droperidol 1.25 mg, and metoclopramide 10 mg to be comparable in parturients undergoing cesarean delivery [17]. Three investigations did not find any patients being sedated [15-17]. However, in other work, a bolus injection of low-dose propofol (10 mg) did not reduce the incidence of emetic episodes during spinal anesthesia for cesarean delivery. It was hypothesized that lack of antiemetic effect was due to the short duration of a propofol bolus administration before the onset of emesis and/or that the dose of propofol used was insufficient [18].

Dexamethasone is an inexpensive and effective antiemetic drug, with minimal side effects after a single-dose administration [59]. The exact mechanism of the antiemetic action of dexamethasone is not known, but there have been several suggestions, such as central or peripheral inhibition of the production or secretion of serotonin, central inhibition of the synthesis of prostaglandins, or changes in the permeability of the blood-brain barrier to serum proteins [59,60]. In three studies, dexamethasone 5-8 mg is effective for the prophylaxis against postoperative nausea and vomiting after epidural or spinal morphine for cesarean delivery in parturients [19-21]. Efficacy and safety of dexamethasone as an antiemetic have been reported [59], but its role in the prevention and treatment of intraoperative nausea, retching, and vomiting in patients during regional anesthesia for cesarean delivery has not gained wide acceptance because of its pharmacokinetic properties and delayed onset of action [59,60].

SEROTONIN RECEPTOR ANTAGONISTS

Serotonin receptor antagonists (ondansetron, granisetron) are highly effective for nausea, retching, and vomiting during regional anesthesia for cesarean delivery in parturients [22-26] (Table 3). Their actions involve both central and peripheral mechanisms in the control of emetic symptoms.

Table 3. Serotonin Receptor Antagonists

Reference	No. of Patients	Regimen (Dose, Route)	Emetic Episodes (Rate, Intraoperatively)	Comments (Efficacy, <i>P</i> Values)
Abouleish <i>et al.</i> [8]	74 parturients	Ondansetron (4 mg, IV)	36%	Ondansetron > Placebo (<i>P</i> = 0.028)
		Placebo	58%	
Fujii <i>et al.</i> [10]	120 parturients	Granisetron (3 mg, IV)	13%	Granisetron = Droperidol = Metoclopramide > Placebo (all <i>P</i> = 0.001 versus Placebo)
		Droperidol (1.25 mg, IV)	17%	
		Metoclopramide (10 mg, IV)	20%	
		Placebo	60%	
Pan <i>et al.</i> [22]	164 parturients	Ondansetron (4 mg, IV)	24% (nausea) 13% (vomiting)	Ondansetron > Metoclopramide = Placebo (nausea) (<i>P</i> = 0.001: Ondansetron versus Placebo, <i>P</i> = 0.151: Metoclopramide versus Placebo) Ondansetron = Metoclopramide = Placebo (vomiting) (<i>P</i> = 0.125: Ondansetron versus Placebo, <i>P</i> = 0.315: Metoclopramide versus Placebo)
		Metoclopramide (10 mg, IV)	43% (nausea) 16% (vomiting)	
		Placebo	56% (nausea) 25% (vomiting)	
Pan <i>et al.</i> [23]	48 parturients	Ondansetron (8 mg, IV)	31%	Ondansetron = Droperidol > Placebo (<i>P</i> = 0.033: Ondansetron versus Placebo, <i>P</i> = 0.013: Droperidol versus Placebo)
		Droperidol (0.625 mg, IV)	25%	
		Placebo	69%	
Fujii <i>et al.</i> [25]	100 parturients	Granisetron (80 mcg/kg, IV)	12%	Granisetron 80 mcg/kg = Granisetron 40 mcg/kg > Granisetron 20 mcg/kg = Placebo (both <i>P</i> = 0.001: Granisetron 80•40 mcg/kg versus Placebo, <i>P</i> = 0.39: Granisetron 20 mcg/kg versus Placebo)
		Granisetron (40 mcg/kg, IV)	16%	
		Granisetron (20 mcg/kg, IV)	52%	
		Placebo	64%	
Fujii <i>et al.</i> [26]	120 parturients	Granisetron (3 mg, IV)	13%	Granisetron = Droperidol = Metoclopramide > Placebo (all <i>P</i> = 0.001 versus Placebo)
		Droperidol (1.25 mg, IV)	17%	
		Metoclopramide (10 mg, IV)	20%	
		Placebo	63%	

Centrally, they bind competitively and selectively to serotonin receptors in the CTZ of the central nervous system. In addition to this central effect, they also block receptors in the gastrointestinal tract, which prevents the action of serotonin and inhibits emetic syndrome [61].

In a randomized, double-blind, placebo-controlled trial, ondansetron 4 mg administered intravenously after umbilical-cord clamping is effective for the prevention of nausea and vomiting during cesarean delivery under spinal anesthesia in parturients [8]. Pan *et al.* compared the prophylactic antiemetic efficacy of ondansetron with traditional antiemetics (droperidol, metoclopramide) in patients undergoing epidural anesthesia for cesarean delivery [22,23]. Prophylactic ondansetron 4 mg was more effective than metoclopramide 10 mg in the prevention of nausea (24% versus 43%) and is equally effective in the prevention of vomiting (13% versus 16%) [22]. They found no difference in the incidence of intraoperative emetic symptoms between patients receiving ondansetron 4 mg (31%) and those receiving droperidol 0.625 mg (25%) [23]. Prophylactic ondansetron 8 mg administered intravenously is effective in reducing the frequency and severity of nausea and vomiting after cesarean delivery in patients given intrathecal sufentanil-morphine [24].

Three studies have shown that prophylactic granisetron administered intravenously after clamping of the umbilical cord reduces the incidence of nausea and vomiting in parturients undergoing spinal anesthesia for cesarean delivery [25,26]. Fujii *et al.* compared three doses (20 mcg/kg, 40 mcg/kg, and 80 mcg/kg) of granisetron to placebo for the prevention of intraoperative emetic symptoms, and determined the minimum effective dose to be 40 mcg/kg [25]. In a comparative study, granisetron 40 mcg/kg was as effective as traditional antiemetics, droperidol 1.25 mg and metoclopramide 10 mg, for the prevention of nausea and vomiting during spinal anesthesia for cesarean delivery [26].

Other serotonin receptor antagonists (tropisetron, dolasetron, and ramosetron) are effective for the prevention of postoperative nausea and vomiting after gynecological surgery [62-64]. However, the use of these serotonin antagonists has not been reported in parturients undergoing regional anesthesia for cesarean delivery.

Serotonin receptor antagonists are generally well tolerated with few adverse effects. Because they have no affinity for dopaminergic receptors, muscarinic cholinergic receptors, and histamine receptors, they are not associated with sedation and/or anticholinergic effects [37]. Headache is the most commonly reported adverse events in clinical trials of serotonin receptor antagonists for emetic symptoms during cesarean delivery under spinal anesthesia [22,23,26]. Ex-

trapyrnidial reactions have been reported in patients receiving ondansetron performed under general anesthesia [65,66], but there have been no reports in parturients during regional anesthesia for cesarean delivery.

COMBINATION ANTIEMETIC THERAPY

None of the currently available antiemetic is entirely effective, perhaps because most of them act through the blockade of one type of receptor [67]. Therefore, it is possible that a combination of antiemetics with different sites of activity would more effective than one drug alone. In a clinical trial comparing the efficacy of granisetron 3 mg plus dexamethasone 8 mg with granisetron 3 mg alone, when administered after clamping the umbilical cord, for the prophylaxis against emetic episodes during cesarean delivery under spinal anesthesia. Consequently, prophylactic use of combined granisetron and dexamethasone is more effective than granisetron alone in reducing the incidence of intraoperative emetic episodes without clinically important adverse events [27]. The mechanism by which dexamethasone enhances the antiemetic efficacy of granisetron is not known, but is attributable to the hypothesis that corticosteroids may reduce levels of serotonin in neural tissue by depleting its precursor tryptophan; anti-inflammatory properties of corticosteroids may prevent the release of serotonin in the gut; dexamethasone may potentiate the main effect of other antiemetics by sensitizing the pharmacological receptor [68-70]. In another study, Fujii *et al.* demonstrated that adding dexamethasone 8 mg to propofol at a subhypnotic dose (1.0 mg/kg/h) increased antiemetic efficacy in patients undergoing spinal anesthesia for cesarean delivery, and found an improvement in its efficacy of 15% [28]. The exact mechanism by which dexamethasone increases the effectiveness of propofol as an antiemetic is unknown. Thus, antiemetic therapy with combined granisetron and dexamethasone or combined propofol and dexamethasone is highly effective for the prevention of nausea, retching, and vomiting during regional anesthesia for cesarean delivery [27,28] (Table 4). While, Kocamanoglu *et al.* found no difference in antiemetic efficacy in patients receiving granisetron alone and combined with droperidol and dexamethasone for the prevention of postoperative nausea and vomiting after general anesthesia for cesarean delivery [29]. Unfortunately, they did not evaluate the efficacy of combination antiemetic therapy for reducing emetic episodes during cesarean delivery performed under regional anesthesia.

NON-PHARMACOLOGICAL THERAPY

Acupressure, a non-invasive variation of acupuncture, has been reported as a potential non-pharmacological therapy

Table 4. Combination Antiemetic Therapy

Reference	No. of Patients	Regimen (Dose, Route)	Emetic Episodes (Rate, Intraoperatively)	Comments (Efficacy, <i>P</i> Values)
Fujii <i>et al.</i> [27]	120 parturients	Granisetron (3 mg, IV)	18%	Granisetron+Dexamethasone > Granisetron (<i>P</i> = 0.008)
		Graniseron (3 mg, IV) +Dexamethasone (8 mg, IV)	4%	
Fujii <i>et al.</i> [28]	120 parturients	Propofol (1.0 mg/kg/h, IV)	20%	Propofol+Dexamethasone > Propofol (<i>P</i> = 0.012)
		Propofol (1.0 mg/kg/h, IV) +Dexamethasone (8 mg, IV)	5%	

Table 5. Non-Pharmacological Therapy

Reference	No. of Patients	Regimen (Dose, Route)	Emetic Episodes (Rate, Intraoperatively)	Comments (Efficacy)
Harmon <i>et al.</i> [30]	94 parturients	Acupressure	14% (nausea) 8% (vomiting)	Acupressure > Placebo ($P = 0.018$)
		Placebo	36% (nausea) 17% (vomiting)	
Stein <i>et al.</i> [31]	75 parturients	Acupressure	24%	Acupressure = Metoclopramide > Placebo (both $P = 0.001$ versus Placebo)
		Metoclopramide (10 mg, IV)	16%	
		Placebo	76%	
Ho <i>et al.</i> [32]	110 parturients	Acupressure	64% (nausea) 22% (vomiting)	Acupressure = Placebo ($P = 0.416$)
		Placebo	71% (nausea) 27% (vomiting)	

for the prevention of emetic episodes. In acupressure, manual stimulation is applied, whereas in acupuncture the skin is pierced with a needle. Most published articles indicate the efficacy of acupressure and acupuncture at the P6 (Nei-Kuwan) point located between the flexor tendons three fingerbreadths below the hand-wrist crease [71]. The mechanism by which acupuncture and acupressure prevent emetic episodes is unknown, but it is postulated that these techniques may mediate the release of beta-endorphin in CSF, potentiating the endogenous antiemetic action of mu-receptor [72]. The serotonergic and norepinephrinergic fibers may also be activated, and the antiemetic effects of these methods may be explained by changes in serotonin transmission [31]. Three studies evaluating the effectiveness of acupressure for the prevention of nausea and vomiting during spinal anesthesia for cesarean delivery in parturients [30-32] (Table 5). Harmon *et al.* showed that application of acupressure at P6 point using a band (Sea band™, Sea Band UK Ltd, Leicestershire, UK) during cesarean delivery decreased the incidence of nausea from 36% to 14% and vomiting from 17% to 8%, compared with placebo [30]. Stein *et al.* demonstrated that acupressure at P6 point and metoclopramide 10 mg were comparable and both were more effective than placebo for the prevention of emetic episodes during cesarean delivery [31]. In contrast, Ho *et al.* showed that prophylactic use of acupressure on the P6 acupoint failed to prevent nausea and vomiting during spinal anesthesia for cesarean delivery [32].

TREATMENT

Management of nausea, retching, and vomiting during regional anesthesia for cesarean delivery essentially depends on the prophylaxis. If the prophylactic pharmacological and non-pharmacological therapy fails, treatment would be required for emetic episodes during cesarean delivery. However, there have been no available data to support the efficacy of any antiemetic as rescue medication for intraoperative nausea, retching, and vomiting during cesarean delivery in parturients.

GUIDELINES

In the prevention of nausea, retching, and vomiting during cesarean delivery performed under regional anesthesia in parturients, the first step is to reduce the risk factors, including maternal hypotension, patient characteristics, surgical procedure, and anesthetic technique. Particularly, lateral uterine displacement, prehydration, and vasopressor drugs are used to avoid the maternal hypotension. Second, prophylactic

lactic drugs for these emetic episodes should be considered for use as monotherapy. Because of cost considerations, traditional and non-traditional antiemetics are commonly considered for first-line prophylactic drugs. If there are concerns about adverse effects of these antiemetics, serotonin receptor antagonists can instead be administered. Combination antiemetic therapy may lead to an improved outcome. Third, in patients who had experienced drug-induced allergy, acupressure at P6 (Nei-Kuwan) point, as a non-pharmacological technique, should be considered.

CONCLUSIONS

Most of published trials indicate an improved antiemetic prophylaxis in parturients during cesarean delivery under regional anesthesia when risk factors for emetic episodes would be avoided and/or effective antiemetic therapy would be performed. Traditional antiemetics (droperidol, metoclopramide, glycopyrrolate), non-traditional antiemetics (propofol, dexamethasone), and serotonin receptor antagonists (ondansetron, granisetron) have been studied for the prevention of intraoperative nausea, retching, and vomiting. Serotonin receptor antagonists are more effective than traditional antiemetics, but these drugs are not entirely effective, perhaps because most of them act through the blockade on one type of receptor. Antiemetic therapy with combined granisetron and dexamethasone or combined propofol and dexamethasone is highly effective for the prevention of these emetic episodes in parturients scheduled for cesarean delivery. Non-pharmacological technique includes acupressure at P6 (Nei-Kuwan) point. Overall, these pharmacological and non-pharmacological therapy reduces emetic episodes in parturients undergoing regional anesthesia for cesarean delivery.

The clinician must weight the benefit of using pharmacological and non-pharmacological techniques for nausea, retching, and vomiting in parturients undergoing cesarean delivery performed under regional anesthesia.

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