MEDICAL SCIENCE MONITOR

PRODUCT INVESTIGATIONS

e-ISSN 1643-3750
© Med Sci Monit, 2013; 19: 993-1000
DOI: 10.12659/MSM.889597

Received: 2013.07.22
Accepted: 2013.08.29
Published: 2013.11.14

Prophylaxis of intra- and postoperative nausea and vomiting in patients during cesarean section in spinal anesthesia

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ACDEF 1 Matthias Voigt
ABC 1,2 Christian W. Fröhlich
ABCD 1 Christiane Hüttel
D 3 Peter Kranke
B 1 Jan Mennen
B 1 Oliver Boessneck
D 4 Christian Lenz
DE 2 Thalia Erbes
BD 1 Jürgen Ernst
ACDE 1 Heinz Kerger

1 Evangelian Deaconry Hospital, Freiburg, Germany
2 University Hospital of Freiburg, Freiburg, Germany
3 University Hospital of Würzburg, Würzburg, Germany
4 University Hospital of Mannheim, Mannheim, Germany

Corresponding Author: Matthias Voigt, e-mail: voigt-m-fr@t-online.de
Source of support: Departmental sources

Background: This paper describes a randomized prospective study conducted in 308 patients undergoing caesarean section in spinal anaesthesia at a single hospital between 2010 and 2012 to find a suitable anti-emetic strategy for these patients.

Material/Methods: Spinal anesthesia was performed in left prone position, at L3/L4 with hyperbaric 0.5% Bupivacaine according to a cc/cm body height ratio. There were no opioids given peri-operatively. The patients received either no prophylaxis (Group I) or tropisetron and metoclopramide (Group II) or dimenhydrinate and dexamethasone (Group III), or tropisetron as a single medication (Group IV). The primary outcome was nausea and/or vomiting (NV) in the intraoperative, early (0–2 h) or late (2–24 h) postoperative period.
Multivariate statistical analysis was conducted with a regression analysis and a backward elimination of factors without significant correlation.

Results: All prophylactic agents significantly reduced NV incidence intraoperatively. Relative risk reduction for NV by prophylaxis was most effective (59.5%) in Group II (tropisetron and metoclopramide). In Group III (dimenhydrinate and dexamethasone), NV risk was reduced by 29.9% and by 28.7% in Group IV (tropisetron mono-therapy). The incidence of NV in the early (0–2 h) and the late (2–24 h) postoperative period was low all over (7.8%), but the relative risk reduction of NV in the early postoperative period was 54.1% (Group IV), 45.1% (Group III), and 34.8% (Group II), respectively. In the late postoperative period, there was no significant difference between the 4 groups.

Conclusions: We recommend a prophylactic medication with tropisetron 2 mg and metoclopramide 20 mg for patients during caesarean section. These agents are safe, reasonably priced, and highly efficient in preventing nausea and vomiting.

Key words: intraoperative nausea and vomiting • PONV • caesarean section • anti-emetic prophylaxis

Full-text PDF: http://www.medscimonit.com/download/index/idArt/889597

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

Background

Caesarean section in spinal anesthesia has become increasingly popular in recent years and is now a commonly performed surgical procedure. Regional anesthesia is performed in 80% of anesthetized patients compared to 20% who receive general anesthesia [1,2]. While consciousness allows the patient to enjoy the early intimate contact with the newborn child (bonding), the procedure may be associated with various important problems [3]. Arterial hypotension and headache, insufficient or abundant anesthesia, and psychologic distress may be some of the adverse effects of regional anesthesia for caesarean section [4,5].

A common problem in caesarean section is intra- and postoperative nausea and vomiting under regional anesthesia [6–8]. NV can happen during and after the birth and may affect the well-being of mother and family [9]. The well-being of patients may be severely compromised [10]; 72% of patients are afraid of NV [11] and 71% feel significant discomfort [12]. Critical anesthesiological complications such as airway obstruction, aspiration pneumonitis, and wound dehiscence are rare and mainly related to postoperative nausea and vomiting in general surgical patients [13,14]. In addition to postoperative pain, NV is one of the most frequent anesthesiological complications. Previous reports and our observations suggest both nausea and vomiting as a frequent phenomenon, with incidences up to 80% [5,9,15,16].

Necessary therapeutic measures, the use of personnel, and room and material resources represent an enormous economic burden and are being closely monitored by health system administrators [17]. Due to the complex pathophysiology, the treatment and prophylaxis of NV is difficult. To keep the costs low, alternative treatments like acupressure and acupuncture are used [8,18–20]. The pharmacological interventions available include a wide range of drug medication, including dopamine and serotonin receptor antagonists, corticosteroids, antihistamines, sedatives, and anticholinergic drugs [9,16,21].

The major risk factor for nausea and vomiting during or after spinal anesthesia in cesarean section is arterial hypotension due to the blockade of the sympathetic nerve system [9]. NV may be influenced by hormonal changes during pregnancy, which alter the sphincter tone of the esophagus and the stomach and the activity of the small bowel and esophagus, as well as adverse effects of uterotonic drugs, intraoperative manipulation of the uterus, and/or psychological distress aggravated by insufficient or excessive anesthesia [22–24].

Previous studies have addressed the efficiency of different anti-emetics in terms of reduction of PONV risk in cesarean section patients, mostly using only 1 agent [9,21]. In a recently published study, we were able to find a multimodal prophylactic regimen for breast surgical procedures [25]. There are several studies in spinal anesthesia indicating that multimodal prophylaxis is preferable to prevent NV, especially in caesarean section [5,9,21].

The goal of the present study was to investigate multimodal pharmacological approaches with tropisetron and metoclopramide (Group II) and dimenhydrinate and dexamethasone (Group III) compared to a mono therapy with tropisetron (Group IV) *versus* no prophylaxis (Group I) to prevent NV intra- and postoperatively in patients undergoing cesarean section under spinal anesthesia.

Material and Methods

For statistical analysis, we created 4 groups:
Group I: No prophylactic agents;
Group II: Tropisetron 2 mg + Metoclopramide 20 mg prophylactically;
Group III: Dimenhydrinate 31 mg and Dexamethasone 4 mg prophylactically;
Group IV: Tropisetron 2 mg prophylactically.

The antiemetic efficacy of the 4 different treatments was evaluated in 308 patients undergoing cesarean section. We included 308 patients scheduled for cesarean section as a planned or non-urgent procedure. Not included were procedures using epidural anesthesia, emergency procedures and procedures using general anesthesia, systemically ill patients, parturients affected with gestosis, HELLP syndrome, and known allergies to the planned medication. Also excluded were patients under the age of 18.

After obtaining approval from the Institutional Review Board (Evangelian Deaconry Hospital Freiburg, Germany) and written informed patient consent, patients were randomly assigned to 1 of the 4 groups.

All patients were given premedication with midazolame 3.75 mg orally 1 hour before transfer to the operating theatre. Spinal anesthesia (SPA) was induced in left lateral position between L3/L4 with 0.5% hyperbaric bupivacaine. Dosage depended on the body height. Body height 150 cm resulted in 1.8 ml bupivacaine 0.5%; every 5 cm additional body height resulted in an additional 0.2 ml bupivacaine dosage. No opioids were used. After successful puncture, patients were brought in prone position, a Foley catheter was applied and the operating table was brought into a 20° left lateral position to circumvent vena cava compression syndrome. When the anesthetic effect reached the TH 4/5 segment, patients were kept in an anti-Trendelenburg position to stop further ascent. Systolic blood pressure was

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

kept at a minimum of 100 mmHg with 2 ml doses of cafedrin-theodrenalin diluted 1:10. Cesarean section was carried out in standard surgical technique in all patients. After full development of the child, the anti-emetic prophylaxis was applied according to randomization. Further medication was oxytocin (3 units bolus, and 10 units in 500 cc 0.9% NaCl), antibiotic prophylaxis (1.5 g Uracid or 2 g Cefazolin in case of allergy to Penicillin). Postoperative pain management was carried out with piritramide and pethidine boluses. Events of nausea and/or vomiting were recorded in a special questionnaire 2 and 24 h postoperatively.

Data recorded consisted of: date of operation, age, ASA, duration of anesthesia and operative procedure, medication taken at home, intraoperative medication, level of SPA, NV risk factors, type of NV prophylaxis given, intraoperative complications, intraoperative NV according to the numeric rating scale (NRS) with 0 representing no NV and 10 the worst possible NV event, intraoperative fluid management, postoperative opioids, onset and degree of NV in minutes after the end of the operation and medication given, other postoperative complications, and overall patient satisfaction.

The primary outcome in this study was the incidence of nausea, emesis, or both during the operation and in the early (0–2 h) or late (2–24 h) postoperative period. Trained investigators recorded the number of episodes and the time of occurrence. In all intervals, patients scored the NV experience on a scale comparable to the numeric rating scale (NRS), where 0 represented no NV and 10 the worst possible NV event.

Patients were randomly assigned preoperatively to 1 of 4 groups with sealed opaque envelopes that were opened by the anesthetist before induction of anesthesia. Randomization resulted in 76 patients in Group I (no prophylaxis given), 82 patients in Group II (prophylactic agents Tropisetron and Metoclopramide), 79 patients in Group III (prophylactic agents Dimenhydrinate and Dexamethasone), and 71 patients in Group IV (prophylactic agent Tropisetron).

Anti-emetic therapy of patients exhibiting PONV in the early and late postoperative period (0–2 h and 2–24 h) was left to the discretion of the physician responsible for the ward, where all agents except the ones already used for anti-emetic prophylaxis could be taken into account.

Statistical analysis

To assess the individual risk of the patients and the risk reduction through the anti-emetic prophylaxis, a multivariate statistical analysis was performed. The variables considered (eg, duration of the operation, events of hypotension) were used to build a statistical model with SAS/STAT (SAS Institute Inc., Cary, NC). During multiple steps, all factors with $p>0.05$ were removed. The remaining factors significantly affected the observed endpoint, which was the incidence of nausea and vomiting. The degree of association of the considered factors and the endpoint were determined using odds ratios. Results were considered statistically significant at $p<0.05$.

Results

There were 308 patients who underwent randomization to 1 of the 4 groups: 76 patients in Group I (no prophylaxis given), 82 patients in Group II (prophylactic agents Tropisetron and Metoclopramide), 79 patients in Group III (prophylactic agents Dimenhydrinate and Dexamethasone), and 71 patients in Group IV (prophylactic agent Tropisetron).

Outcome data were complete for all 308 patients: 100% of the patients were female, 90.3% were non-smokers, 23.4% had a history of nausea and vomiting or motion sickness, and 56.8% received postoperative opioids. Intraoperative hypotension was recorded in 46.15% and all patients had a dermatome level TH4/5. There were no significant differences between groups (Table1).

Groups were investigated regarding nausea and vomiting intraoperatively and postoperatively in the early (0–2 h) and late (2–24 h) postoperative period. The incidences of nausea and vomiting were summarized because the incidence of vomiting was rare and statistically non-significant.

Overall 165 (53.6%) patients out of 308 experienced intra- or postoperative nausea and vomiting (Table 2).

There were significant differences in incidence of NV between groups (Figure 1).

Group II had the lowest incidence of intraoperative NV (26.8%) and Groups III and IV showed no significant differences. The relative incidence of IONV was 46.8% (Group 3) and 46.5% (Group 4).

Group I had the highest rate of patients experiencing IONV (64.5%) (Tables 2 and 3).

Compared to Group I (no medication), all prophylactic medication (Groups II, III, and IV) led to a significantly lower rate of IONV. Group II had the most effective prophylactic medication. The effect of medication of Group III and Group IV are roughly similar (an odds ratio of 1 means equality) (Table 4).

The difference between Group II and III and Group II and IV was also significant. The odds ratios (OR) of 0.42 and 0.42

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

Table 1. Patient characteristics, no influence on outcome, tested by Chi-Square independence test.

Group	Age	Non-smoker %	PONV/ motion sickness %	Length of surgery min.	Postop opioids %	Introp hypote-nsion %	Piri-tramid mg	Pethidin mg	Brad-ycadia <50/min.	Oxytocin 3 I.E.	Oxytocin 10 I.E.	Derm-atome
I none (n=76)	33	86.8	27.6	27.5	50	47.4	15.0	37.5	1.3	92.1	93.8	TH 4/5
TM (n=82)	33	91.5	20.7	26.5	68.3	45.1	15.0	25.0	6.1	93.6	92.7	TH 4/5
III DD (n=79)	31	91.1	22.8	25.0	58.2	45.8	15.0	50.0	5.1	93.7	96.2	TH 4/5
IV T (n=71)	33	91.5	22.5	26.0	50.7	46.5	15.0	25.0	2.8	94.4	94.4	TH 4/5
p value	0.75	0.72	0.78	0.74	0.70	0.99	0.83	0.76	0.99	0.96	0.72	

Table 2. Overall outcome of 308 patients intra- and postoperative in the early (0–2 h) and late (2–24 h) period, incidence of Nausea and/or vomiting.

Group	Intraop	Early (0–2 h)	Late (2–24 h)	Total (intra-24 h)
I none (n=76)	49 (64.5%)	7 (9.2%)	1 (1%)	57 (74.7%)
II TM(n=82)	22 (26.8%)	5 (6.1%)	1 (1%)	28 (33.9%)
III DD (n=79)	37 (46.8%)	4 (5.1%)	1 (1%)	42 (52.9%)
IV T (n=71)	33 (46.5%)	3 (4.2%)	2 (3%)	38 (53.7%)

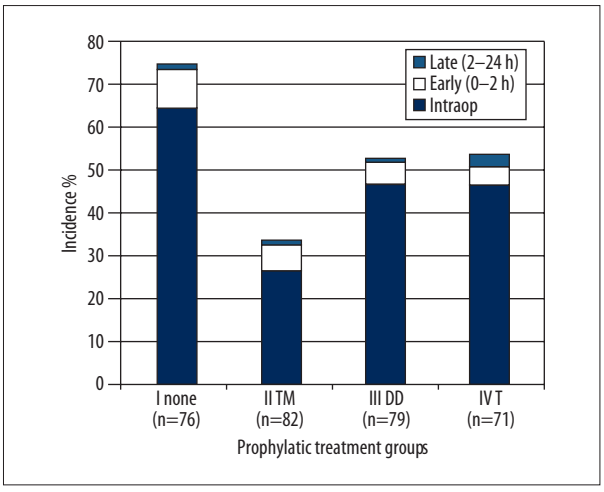

Figure 1. Reduction of PONV in treatment groups (group II and III) compared to control group without prophylactic treatment (group I).

emphasize the significantly lower incidence of IONV in Group II compared to Group III and Group IV.

In detail the results for intra and postoperative nausea and vomiting separately are mentioned.

Intraoperative nausea and vomiting

Patients without any prophylaxis given experienced the most nausea intraoperatively (63.2%). Every prophylaxis given significantly lowered the incidence of nausea intraoperatively. The most effective prophylactic medication against intraoperative nausea was a combination of tropisetron and metoclopramide (25.6%) (Group II).

Intraoperative vomiting was also highest in Group I (15.8%) and was significantly lower in Group II (3.7%), Group III (8.9%), and Group IV (1.4%).

Postoperative nausea and vomiting

In the early postoperative period (0–2 h) the incidence of nausea was highest in the non-treated group I (9.2%), and was lowered by prophylaxis in Group II (6.1%), Group III (5.1%), and group IV (4.2%). Differences were marginally significant.

There were no differences in the incidence of nausea in the late postoperative period (2–24 h) between groups (1% in Groups I–III, and 3% in Group IV).

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

Table 3. Intraoperative Nausea and Vomiting (IONV) and type of medication.

		Intraoperative Nausa and Vomiting (IONV)		
		No	Yes	Total
Group I: No prophylaxis	Incidence	27.0	49.0	76.0
	%	35.5	64.5	100.0
Group II: Tropisetrone + Metoclopramid	Incidence	60.0	22.0	82.0
	%	73.2	26.8	100.0
Group III: Dimenhydrinate + Dexamethasone	Incidence	42.0	37.0	79.0
	%	53.2	46.8	100.0
Group IV: Tropisetrone	Incidence	38.0	33.0	71.0
	%	53.5	46.5	100.0

Table 4. Odds ratios: comparison of groups in pairs and p-values of chi-square test.

Design	Group		Odds ratio	Lower KI	Upper KI	p-value Chi²-test
1	Group I	Group II	4.95	2.51	9.75	0.000
2	Group I	Group III	2.06	1.08	3.93	0.027
3	Group I	Group IV	2.09	1.08	4.05	0.028
4	Group II	Group III	0.42	0.22	0.80	0.008
5	Group II	Group IV	0.42	0.22	0.83	0.012
6	Group III	Group IV	1.01	0.53	1.93	0.965

Postoperative vomiting was rare: 3% in Group I and none of the patients in the treatment groups experienced vomiting postoperatively.

The major influence from a statistical point of view seems to have been the type of medication given. The medication in Group II is preferable to medication of Groups III and IV.

There are no statistical differences between the effect of medication of Groups III and IV.

The other risk factors additionally investigated did not show any significant differences. There was no risk factor that influenced all groups.

The median of symptom strength among the symptomatic patients was 5.5 and the mean number of episodes was 1.5.

Discussion

The aim of this study was to find a highly efficient anti-emetic regimen and anesthetic procedure to reduce the incidence of intra- and postoperative nausea and vomiting in 308 female patients exposed to cesarean section surgery under spinal anaesthesia. The study was conducted on the background that an optimal perioperative patient comfort is of outstanding interest and NV with an average incidence of 30% is rated as one of the most undesirable events in the context of surgery and anesthesia [26–28].

Therefore, every attempt should be made, especially in the context of birth, to avoid this complication, which is not only an unpleasant adverse effect, but also may cause severe complications such as wound dehiscence, dehydration, aspiration, or pneumothorax [13,14].

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

We compared combinations (tropisetron/metoclopramide and dimenhydrinate/dexamethasone) and a single-drug regimen (tropisetron) of known and effective drugs against no prophylaxis to find the best prophylactic treatment for intraoperative and postoperative nausea and vomiting. All anti-emetic agents used in this study have been previously extensively investigated and their efficacy in terms of NV reduction has been proven [29–35].

In our patients, intraoperative nausea and vomiting was the main problem (60% in the untreated group). Postoperative events of nausea and vomiting were low (9%) even in the untreated group. This finding agrees with results of other investigations, which showed the main onsets of discomfort during the procedure, with incidences of up to 80% [15]. Causes for the high incidence of NV may be intraoperative hypotension, reduced cardiac output due to vena cava compression, uterotonic drugs such as oxytocin and particularly Methergine, exteriorization and manipulation of the uterus, intestines, and peritoneum, as well as psychological distress, although underlying pathomechanisms are not fully understood in all details [24,36,37].

In addition, pregnant women *per se* have a predisposition for NV – 20% of pregnant women have emesis gravidarum and 10% have hyperemesis gravidarum, perhaps due to high levels of HCG, obesitas, reduced gastroesophageal tone, and psychological changes [38].

Prophylactic agents

Tropisetron was one of the prophylactic anti-emetic agents used in this study. It belongs to the group of 5-HT3- or serotonin antagonists acting in the chemoreceptive trigger zone [39]. These substances block the vagal stimulated emetogen effect of serotonin. Efficacy of serotonin antagonists in prevention and therapy of PONV has been extensively proven in numerous investigations [30]. Primarily developed for the treatment of chemotherapy-induced nausea and vomiting, they now play an important role in modern anesthesia. They are considered as relatively safe – single-dose adverse effects are mostly limited to headache, tachycardia, and sedation [29]. According to the investigations of Apfel and others, serotonin antagonists are primarily used as second- or third-line drugs in preventing or treating PONV [32,40]. The relative expensiveness of these drugs may limit general use, considering increasing economic constraints in most health care systems [40,41].

Dexamethasone was also used as an anti-emetic in this study. Eberhart et al. showed that dexamethasone is as effective as other established anti-emetic drugs in PONV prophylaxis and therapy [42]. This was confirmed by the multi-center trial of Apfel et al, which demonstrated that the anti-emetic effects of dexamethasone, droperidol, and ondansetron are comparable [32]. The underlying mechanism of action is not entirely clear and needs further investigation [43]. Dexamethasone has a delayed onset of action, but a long-lasting effect [44]. In addition, it is known to lower surgery-induced inflammation [45]. No severe adverse effects are known with this drug and it is reasonably priced [42]. Dexamethasone is also well established in the context of chemotherapy induced nausea and vomiting [46,47]; low doses provide a sufficient anti-emetic effect [45].

Dimenhydrinate was another anti-emetic agent used in this study and belongs to the group of antihistamines acting on histamine receptors in the chemoreceptor trigger zone [40,48]. It is, for example, very successfully used for the treatment of motion sickness [49,50]. Its efficacy has also been proven in the context of PONV prophylaxis and therapy, although with fewer studies. Its use in anesthesia so far appears to be less frequent, although it is safe and reasonably priced [40,51]. One major drawback may be sedation caused by this agent [50].

Metoclopramide antagonizes dopamine effects in the chemoreceptor trigger zone in the brainstem. Adverse effects include sedation and in some cases agitation and extrapyramidal effects. Drugs of these group may be problematic due to the profile of adverse effects, which include not only sedation, but also Parkinson symptoms (tremor, rigor, akinesis) [34] and severe arrhythmias (torsade de pointes), which is why droperidol, one of the oldest and best established anti-emetics and also used in the context of PONV, was withdrawn from the German market, but subsequently relaunched [29]. Several investigations have shown the efficacy of metoclopramide in terms of PONV prophylaxis and therapy when it is used in high doses or in combination with other antiemetic drugs like corticoids [52].

Numerous investigations have shown that both metoclopramide and tropisetron may reduce intra- and postoperative nausea and vomiting in parturients with spinal anesthesia, dexamethasone reduces intraoperative nausea and vomiting, and antihistamines reduce postoperative nausea and vomiting, although data for the latter group of substances are comparatively sparse [5,21].

Previous studies in other surgical procedures, such as the multicenter trial of Apfel et al. in 2004, have also shown that anti-emetics in combination add their individual contribution to NV reduction and, therefore, are preferable, particularly in high-risk patients [31,48,53]. Apfel et al. demonstrated that in a combination of anti-emetics, each drug has an additional proportional effect, which means that a double or triple combination is twice or three times as effective as a single drug. Comparison of ondansetron, dexamethasone, and droperidol, for example, shows a step-wise NV risk reduction of 30% by each individual drug [48], which, however, was assessed in the context of general anesthesia.

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

In this study, we chose 2 anti-emetic combinations (tropisetron/metoclopramide and dimenhydrinate/dexamethasone) and a single-drug regimen consisting of tropisetron in comparison to no prophylaxis. With the combination dimenhydrinate/dexamethasone, we had an excellent anti-emetic experience in a previous investigation with patients undergoing elective breast surgery under general anesthesia. On the other hand, preliminary investigations have shown that tropisetron and/or metoclopramide have a good anti-emetic effect in parturient patients with spinal anesthesia. Previous experiences have also shown that these drugs were in part randomly used and, therefore, not in a controlled, firmly-established prophylaxis.

In our study, double prophylaxis with metoclopramide/tropisetron was most effective regimen and reduced nausea to 25.6% intraoperatively and to 6.1% 1–2 h and 1% 2–24 h postoperatively. Vomiting was 3.66% lower intraoperatively. In contrast, dimenhydrinate/dexamethasone prophylaxis significantly decreased the incidence of nausea intraoperatively to 44.2% and 1–2 hrs postoperatively to 5.06% and to 1% 2–24 h postoperatively, and was just as effective as the single prophylaxis with tropisetron (45.07% intraoperatively, 4.23% 0–2 h postoperatively, 3% 2–24 h, and 1.41% intraoperatively).

In the postoperative period, there was no significant difference in nausea between the treatment groups. Vomiting, in contrast to nausea, is rare intra- and postoperatively, and was lowered by approximately the same extent in the untreated group as in the treated groups.

Why are the different anti-emetic regimes so different in their effects? One aspect to be considered is the surgical procedure itself, which is associated with an exteriorization of the uterus and often manipulation of the peritoneum and bowel, thus irritating receptors (e.g., 5-HT3 and 5-HT4 type) and the vagal nerve system, thus causing nausea and vomiting [54]. In contrast to dexamethasone and dimenhydrinate, both tropisetron and metoclopramide have a direct and pronounced effect on the bowel and the upper gastrointestinal system, respectively [30,49].

Tropisetron interacts with 5-HT3 and 5-HT4 receptors in the bowel, thus influencing motility and preventing serotonin-mediated nausea and vomiting (e.g., induced by surgical manipulation of the bowel and intestines) [11,30]. Metoclopramide increases forward motility of the upper gastrointestinal system, thus preventing reflux and regurgitation, but also interacts with 5 HT3 and 5 HT4 receptors as tropisetron and may additionally reduce nausea and vomiting by this mechanism [43,55]. Both agents interact via receptors at the chemoreceptor trigger zone, thus accentuating their anti-emetic effect [11,43].

Unfortunately, in most cases anti-emetic medication is given as a treatment, so the patients and their family are exposed to the unpleasant experience of intraoperative NV or PONV. Our results suggest that prophylaxis as applied in this study can certainly reduce the onset of intraoperative NV and PONV and the associated discomfort. Both the mono- and combination therapy with well-known and safe drugs are efficient ways of doing this.

In terms of costs and adverse effect profile, the anti-emetic combination of tropisetron and metoclopramide appears to be superior and preferable. Except for sedation, no substantial adverse effect was observed in any of our patients. Current costs for metoclopramide/tropisetron prophylaxis are in a range of 0.15–0.8 Euros in our hospital, compared to for example, 0.25/1.2 Euros for dexamethasone/dimenhydrinate. Prices, however, may vary in different hospitals.

Although a triple anti-emetic prophylaxis may have further decreased NV and PONV incidence in this study, we did not test this due to increasing risk of significant adverse effects and is advised only in extremely high-risk patients.

Conclusions

Our investigation in 308 patients experiencing cesarean section under spinal anaesthesia shows that intra- and postoperative nausea and vomiting can be significantly reduced by an anti-emetic prophylaxis combination of tropisetron 2 mg and metoclopramide 20 mg.

Therefore, this safe and reasonably priced combination should be preferred for use in preventing intraoperative NV and PONV in cesarean section patients under spinal anaesthesia.

Disclosure

None of the authors have any financial relationships with commercial companies involved with a product in this study.

References:

1. Bowring J, Fraser N, Vause S, Heazell AE: Is regional anaesthesia better than general anaesthesia for caesarean section? J Obstet Gynaecol, 2006; 26(5): 433–34
2. Jenkins JG, Khan MM: Anaesthesia for Caesarean section: a survey in a UK region from 1992 to 2002. Anaesthesia, 2003; 58(11): 1114–18
3. Ratcliffe FM, Evans JM: Neonatal wellbeing after elective caesarean delivery with general, spinal, and epidural anaesthesia. Eur J Anaesthesiol, 1993; 10(3): 175–81
4. Tarkkila PJ, Kaukinen S: Complications during spinal anesthesia: a prospective study. Reg Anesth, 1991; 16(2): 101–6

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

5. Habib AS, George RB, McKeen DM et al: Antiemetics added to phenylephrine infusion during cesarean delivery: a randomized controlled trial. Obstet Gynecol, 2013; 121(3): 615–23
6. Santos A, Datta S: Prophylactic use of droperidol for control of nausea and vomiting during spinal anesthesia for cesarean section. Anesth Analg, 1984; 63(1): 85–87
7. Lussos SA, Bader AM, Thornhill ML, Datta S: The antiemetic efficacy and safety of prophylactic metoclopramide for elective cesarean delivery during spinal anesthesia. Reg Anesth, 1992; 17(3): 126–30
8. Harmon D, Ryan M, Kelly A, Bowen M: Acupressure and prevention of nausea and vomiting during and after spinal anaesthesia for caesarean section. Br J Anaesth, 2000; 84(4): 463–67
9. Balki M, Carvalho JC: Intraoperative nausea and vomiting during cesarean section under regional anesthesia. Int J Obstet Anesth, 2005; 14(3): 230–41
10. Macario A, Weinger M, Carney S, Kim A: Which clinical anesthesia outcomes are important to avoid? The perspective of patients. Anesth Analg, 1999; 89(3): 652–58
11. Scholz J, Hennes HJ, Steinfath M et al: Tropisetron or ondansetron compared with placebo for prevention of postoperative nausea and vomiting. Eur J Anaesthesiol, 1998; 15(6): 676–85
12. Unkel W, Peters J: [Postoperative nausea and emesis: mechanisms and treatment]. Anasthesiol Intensivmed Notfallmed Schmerzther, 1998; 33(9): 533–44
13. Schumann R, Polaner DM: Massive subcutaneous emphysema and sudden airway compromise after postoperative vomiting. Anesth Analg, 1999; 89(3): 796–97
14. Bremner WG, Kumar CM: Delayed surgical emphysema, pneumomediastinum and bilateral pneumothoraces after postoperative vomiting. Br J Anaesth, 1993; 71(2): 296–97
15. Abouleish EI, Rashid S, Haque S et al: Ondansetron versus placebo for the control of nausea and vomiting during Caesarean section under spinal anaesthesia. Anaesthesia, 1999; 54(5): 479–82
16. Mishriky BM, Habib AS: Metoclopramide for nausea and vomiting prophylaxis during and after Caesarean delivery: a systematic review and meta-analysis. Br J Anaesth, 2012; 108(3): 374–83
17. Watcha MF: The cost-effective management of postoperative nausea and vomiting. Anesthesiology, 2000; 92(4): 931–33
18. Stein DJ, Birnbach DJ, Danzer BI et al: Acupressure versus intravenous metoclopramide to prevent nausea and vomiting during spinal anesthesia for cesarean section. Anesth Analg, 1997; 84(2): 342–45
19. Duggal KN, Douglas MJ, Peteru EA, Merrick PM: Acupressure for intrathecal narcotic-induced nausea and vomiting after caesarean section. Int J Obstet Anesth, 1998; 7(4): 231–36
20. Dundee JW, Ghaly RG, Bill KM et al: Effect of stimulation of the P6 antiemetic point on postoperative nausea and vomiting. Br J Anaesth, 1989; 63(5): 612–18
21. Griffiths JD, Gyte GM, Paranjothy S et al: Interventions for preventing nausea and vomiting in women undergoing regional anaesthesia for caesarean section. Cochrane Database Syst Rev, 2012; 9: CD007579
22. Broussard CN, Richter JE: Nausea and vomiting of pregnancy. Gastroenterol Clin North Am, 1998; 27(1): 123–51
23. Koch KL, Frissora CL: Nausea and vomiting during pregnancy. Gastroenterol Clin North Am, 2003; 32(1): 201–34, vi
24. Wahab MA, Karantzis P, Eccersley PS et al: A randomised, controlled study of uterine exteriorisation and repair at caesarean section. Br J Obstet Gynaecol, 1999; 106(9): 913–16
25. Voigt M, Frohlich CW, Waschke KF et al: Prophylaxis of postoperative nausea and vomiting in elective breast surgery. J Clin Anesth, 2011; 23(6): 461–68
26. Cohen MM, Duncan PG, DeBoer DP, Tweed WA: The postoperative interview: assessing risk factors for nausea and vomiting. Anesth Analg, 1994; 78(1): 7–16
27. Koivuranta M, Laara E, Snare L, Alahuhta S: A survey of postoperative nausea and vomiting. Anaesthesia, 1997; 52(5): 443–49
28. Palazzo M, Evans R: Logistic regression analysis of fixed patient factors for postoperative sickness: a model for risk assessment. Br J Anaesth, 1993; 70(2): 135–40
29. Tramer MR, Reynolds DJ, Moore RA, McQuay HJ: Efficacy, dose-response, and safety of ondansetron in prevention of postoperative nausea and vomiting: a quantitative systematic review of randomized placebo-controlled trials. Anesthesiology, 1997; 87(6): 1277–89
30. Carlisle JB, Stevenson CA: Drugs for preventing postoperative nausea and vomiting. Cochrane Database Syst Rev, 2006; 3: CD004125
31. Eberhart LH, Mauch M, Morin AM et al: Impact of a multimodal anti-emetic prophylaxis on patient satisfaction in high-risk patients for postoperative nausea and vomiting. Anaesthesia, 2002; 57(10): 1022–27
32. Apfel CC, Kranke P, Piper S et al: [Nausea and vomiting in the postoperative phase. Expert- and evidence-based recommendations for prophylaxis and therapy]. Anaesthesist, 2007; 56(11): 1170–80
33. Culebras X, Corpataux JB, Gaggero G, Tramer MR: The antiemetic efficacy of droperidol added to morphine patient-controlled analgesia: a randomized, controlled, multicenter dose-finding study. Anesth Analg, 2003; 97(3): 816–21
34. Foster PN, Stickle BR, Laurence AS: Akathisia following low-dose droperidol for antiemesis in day-case patients. Anaesthesia, 1996; 51(5): 491–94
35. Lim BS, Pavy TJ, Lumsden G: The antiemetic and dysphoric effects of droperidol in the day surgery patient. Anaesth Intensive Care, 1999; 27(4): 371–74
36. Cooke RD, Comyn DJ, Ball RW: Prevention of postoperative nausea and vomiting by domperidone: A double-blind randomized study using domperidone, metoclopramide and a placebo. S Afr Med J, 1979; 56(21): 827–29
37. de Groot AN, van Dongen PW, Vree TB et al: Ergot alkaloids. Current status and review of clinical pharmacology and therapeutic use compared with other oxytocics in obstetrics and gynaecology. Drugs, 1998; 56(4): 523–35
38. Uhl B: Nausea und Emesis. Gynäkologie und Geburtshilfe Compact. Stuttgart: Thieme Verlag, 2009; 98–102 [in German]
39. Lang IM: Noxious stimulation of emesis. Dig Dis Sci, 1999; 44(8 Suppl.): 58–63S
40. Kranke P, Schuster F, Eberhart LH: Recent advances, trends and economic considerations in the risk assessment, prevention and treatment of postoperative nausea and vomiting. Expert Opin Pharmacother, 2007; 8(18): 3217–35
41. Tramer MR: [Postoperative nausea and vomiting]. Anaesthesist, 2007; 56(7): 679–85
42. Eberhart LH, Morin AM, Georgieff M: [Dexamethasone for prophylaxis of postoperative nausea and vomiting. A meta-analysis of randomized controlled studies]. Anaesthesist, 2000; 49(8): 713–20
43. Henzi I, Walder B, Tramer MR: Metoclopramide in the prevention of postoperative nausea and vomiting: a quantitative systematic review of randomized, placebo-controlled studies. Br J Anaesth, 1999; 83(5): 761–71
44. Henzi I, Walder B, Tramer MR: Dexamethasone for the prevention of postoperative nausea and vomiting: a quantitative systematic review. Anesth Analg, 2000; 90(1): 186–94
45. Wang JJ, Ho ST, Lee SC et al: The use of dexamethasone for preventing postoperative nausea and vomiting in females undergoing thyroidectomy: a dose-ranging study. Anesth Analg, 2000; 91(6): 1404–7
46. Naeim A, Dy SM, Lorenz KA et al: Evidence-based recommendations for cancer nausea and vomiting. J Clin Oncol, 2008; 26(23): 3903–10
47. Lohr L: Chemotherapy-induced nausea and vomiting. Cancer J, 2008; 14(2): 85–93
48. Apfel CC, Korttila K, Abdalla M et al: A factorial trial of six interventions for the prevention of postoperative nausea and vomiting. N Engl J Med, 2004; 350(24): 2441–51
49. Muth ER, Jokerst M, Stern RM, Koch KL: Effects of dimenhydrinate on gastric tachyarrhythmia and symptoms of vection-induced motion sickness. Aviat Space Environ Med, 1995; 66(11): 1041–45
50. Seibel K, Schaffler K, Reitmeir P, Golly I: A randomised, placebo-controlled study comparing two formulations of dimenhydrinate with respect to efficacy in motion sickness and sedation. Arzneimittelforschung, 2002; 52(7): 529–36
51. Vener DF, Carr AS, Sikich N et al: Dimenhydrinate decreases vomiting after strabismus surgery in children. Anesth Analg, 1996; 82(4): 728–31
52. Wallenborn J, Gelbrich G, Bulst D et al: Prevention of postoperative nausea and vomiting by metoclopramide combined with dexamethasone: randomised double blind multicentre trial. BMJ, 2006; 333(7563): 324
53. Scuderi PE, James RL, Harris L, Mims GR III: Multimodal antiemetic management prevents early postoperative vomiting after outpatient laparoscopy. Anesth Analg, 2000; 91(6): 1408–14
54. Habib AS: A review of the impact of phenylephrine administration on maternal hemodynamics and maternal and neonatal outcomes in women undergoing cesarean delivery under spinal anesthesia. Anesth Analg, 2012; 114(2): 377–90
55. Apfel CC, Kranke P, Katz MH 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(5): 659–68

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]