

# Incidence of intraoperative nausea and vomiting during spinal anaesthesia for Caesarean section in two Cape Town state hospitals

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**Background:** Intraoperative nausea and vomiting (IONV) during spinal anaesthesia (SA) for Caesarean section (CS) is unpleasant and may interfere with surgery. The incidence of IONV during elective CS was studied, as well as the influence of ethnicity on this outcome.

**Methods:** A total of 258 healthy term patients undergoing SA for elective CS were recruited to this prospective observational study conducted at two Cape Town Level 2 hospitals. Standard practice was employed for SA for CS at the University of Cape Town: 2 ml hyperbaric bupivacaine plus 10 µg fentanyl at the L3/4 interspace, and 15 mL/kg crystalloid coload. Spinal hypotension was managed with phenylephrine boluses according to a standard protocol. Nausea and/or vomiting were treated by restoration of blood pressure, and metoclopramide. Intraoperative complaints of nausea, and vomiting, were noted. Patients were also interviewed postoperatively as to any experience of intraoperative or previous history of nausea.

**Results:** Of the 258 patients enrolled in the audit, 112 (43.4%) were non-African and 146 (56.6%) were Black African patients. The overall incidence (95% CI) of nausea was 0.32 (0.27–0.38), with 20% occurring prior to and 11% after the delivery. The overall incidence of vomiting was 0.07 (0.05–0.11), with 3.2% occurring prior to and 3.8% after delivery. The incidence of nausea and/or vomiting was 0.33 (0.28 – 0.40). Black Africans experienced significantly less nausea than non-African patients (36/145 [24.8%] vs. 47/112 [42.0%] respectively,  $p = 0.004$ ). There was no significant difference in the incidence of vomiting (10/145 [6.8%] vs. 8/112 [7.1%] respectively). The odds of experiencing intraoperative nausea for patients with any blood pressure value < 70% of baseline were 2.46 (95% CI 1.40–4.33).

**Conclusions:** Though in keeping with international standards, the clinically significant incidence of nausea and/or vomiting of 33% requires adjustments to the management protocol for spinal hypotension. The inclusion of ethnicity as a risk factor for nausea during SA for CS should be considered.

**Keywords:** Caesarean section, ethnicity, intraoperative, nausea and vomiting, spinal anaesthesia

## Introduction

Intraoperative nausea and vomiting (IONV) causes distress to the patient and may interfere with the surgery. The incidence of IONV during spinal anaesthesia (SA) for Caesarean section (CS) is dependent on the anaesthesia technique used, together with preventative and therapeutic measures employed by the anaesthetist.<sup>1</sup> There is little research on the incidence of IONV during SA for CS within the South African population. In a recent study it was shown that postoperative nausea and vomiting (PONV) in Black South African (African) patients undergoing general anaesthesia (GA) is significantly lower than in the remainder of the multi-ethnic South African population (non-African).<sup>2</sup> Clinical experience suggests that the incidence of nausea and vomiting during SA for CS is low in African patients. The primary outcome of this study was thus an assessment of the incidence of nausea and vomiting, and the secondary outcome was a comparison of the incidence of these symptoms between African and non-African patients during SA for CS.

## Methods

A prospective observational study was conducted at Mowbray Maternity Hospital and New Somerset Hospital, after approval had been obtained from the Human Research Ethics Committee of the University of Cape Town. Healthy, term patients undergoing elective SA for CS during daylight hours were studied, during the period August 2014–February 2015. Exclusion criteria were three previous Caesarean sections, previous major abdominal surgery, anti-emetics administered prior to CS, preoperative or

intraoperative systemic opioid administration, known adverse reaction to metoclopramide, conversion to general anaesthesia, pre-eclampsia or other causes of severe hypertension, and the use of ergometrine.

Cefazolin (1–2 g) or, if the patient was allergic to penicillin, clindamycin (600 mg), was given over a minimum time period of 5 minutes, and at least 10 minutes prior to induction of SA. If nausea or vomiting occurred as a result of administration, it was noted separately. Preoperatively, systolic blood pressure (SBP) was measured twice with the patient in the left lateral position, and the mean value calculated. The target for treatment of hypotension was 80% of this value. The procedure included the standard practice for SA for CS at the University of Cape Town, i.e. 2 ml intrathecal hyperbaric bupivacaine plus 10 µg fentanyl, 15 ml/kg rapid crystalloid coload via a freely running infusion into an 18G cannula. The patient was positioned supine, with 20 degrees left lateral tilt. Dermatome block height was assessed by temperature sensitivity as assessed by ethyl chloride spray. Blood pressure was measured every minute for the entire procedure. The initial vasopressor used was phenylephrine 50 µg, given in response to a 20% decrease in SBP. A 30% decrease in SBP was treated with 100 µg of phenylephrine. This was repeated every minute until the target SBP was achieved (within 20% of baseline value). If the heart rate decreased to less than 55 beats per minute in association with hypotension (SBP decreased by 30% from baseline), ephedrine 10 mg was administered, followed by atropine 0.25–0.5 mg if bradycardia persisted.

Ephedrine was also administered if there was a poor response to two consecutive doses of phenylephrine. Nausea and vomiting were treated with intravenous phenylephrine to restore blood pressure, and metoclopramide 10 mg. Oxytocin 3 IU was given over 60 seconds, after clamping of the cord.

The following data were collected by the attending anaesthetist: patient age, booking weight, gestational age, gravity, parity, and number of previous Caesarean sections. Also recorded was the lowest systolic blood pressure (SBP) during the procedure, the highest level of the spinal block, total fluid volume administered, and the total dose of phenylephrine, ephedrine, atropine and metoclopramide. The total blood loss was estimated by measurement in a graded suction bottle and inspection of swabs. Whether or not the uterus was exteriorised was also noted. Episodes of nausea and vomiting were noted, and whether these events occurred prior to, or after, delivery. Other adverse events, as well as duration of surgery, were recorded at completion of the case.

Interviews were conducted after the operation and consent requested at this time for participation in the study. This was done in order to exclude potential suggestion bias introduced by explaining the study objectives prior to surgery. The following direct questions were asked: 'What race do you classify yourself?', 'Have you ever experienced motion sickness or postoperative nausea and vomiting?', and 'Did you experience nausea during this operation?'

### Statistical analysis

Sample size calculation for the primary outcome was based on a clinical estimate of an incidence of nausea and/or vomiting of 25% overall, with an absolute accuracy of  $\pm 6\%$ . This required 184 patients. Sub-group analysis was planned a priori. With an expected proportion of African/non-African patients of 66/33%, and an expected incidence of nausea and/or vomiting of 15% amongst Black Africans and 35% in non-Africans, allowing for 90% power and  $p < 0.05$ , 156 Black African and 78 non-African patients were required. In the time available for the conduction of the audit, 143 Black African and 112 non-African parturients were studied.

Individual categorical variables were summarised with frequency and percentage frequency distributions and illustrated using bar

charts. Continuous variables were summarised using means and standard deviations or medians and interquartile ranges. Associations between categorical variables were summarised in two-way frequency tables and tested for statistical significance using a chi-square test. Observed  $p$ -values are quoted.  $P$ -values smaller than 0.05 were considered to be statistically significant. The joint associations between the predictor variables and the presence/absence of nausea/vomiting were modelled using a logistic regression model. The exponentiated coefficients of this model are estimated on adjusted odds ratios. Multinomial logistic regression models were used to estimate the association between predictor variables and the three-level categorical outcomes. These models are equivalent to parallel binary logistic models where the relative odds of each of the categories compared with a chosen reference category are estimated. We chose 'none' as the reference category.

### Results

Two hundred and fifty-eight patients were recruited (146 Black South Africans and 112 multi-ethnic [non-African] parturients). There were no patients excluded from recruitment. One patient was excluded from the analysis because of erroneous recruitment (three previous Caesarean sections). Patient demographic data and baseline haemodynamic values were similar in the two groups (Table 1). Patient age ranged between 18 and 44 years, and all were American Society of Anaesthesiologists Class I or II.

#### Primary outcome: incidence of IONV during SA for CS

The overall incidence of nausea was 0.323, 95% CI 0.27–0.38, with 20% occurring prior to delivery of the baby and 11% after the delivery. The overall incidence of vomiting was 0.0698, 95% CI 0.05–0.11, with 3.1% prior to delivery and 3.8% after the delivery. The combined incidence of nausea and vomiting was 0.333, 95% CI 0.28–0.40.

#### Secondary outcome: between-group comparison

There was a significant difference ( $p = 0.004$ ) in the incidence of nausea between African and non-African patients (36/145 [24.8%] vs. 47/112 [42.0%],  $p = 0.004$ ; odds ratio [95% CI] = 0.47 [0.27–0.82]). There was also a significant difference ( $p = 0.012$ ) in the incidence of nausea and vomiting (combined) between African and non-African patients (38/146 [26%] vs. 48/112 [42%],

Table 1: Patient demographic data, and relevant data pertaining to spinal anaesthesia

Factor	African	Non-African	$p$ -value
Number	146	112	
Age (years)	29.8	30.4	NS
Parity	2.6	2.9	NS
Number of previous Caesarean sections	1.15	1.19	NS
Weight (kg)	83.2	79.2	NS
Smoker (yes/no)	8 (5.5%)	40 (35.7%)	< 0.001
History of motion sickness (yes/no)	17 (11.6%)	12 (10.7%)	NS
Hypotension (% patients with SBP $\leq$ 70% baseline)	65 (44%)	48 (42.9%)	NS
Baseline heart rate	89	87	NS
Exteriorisation of uterus	26 (17.8%)	9 (8%)	0.023
Duration of operation (minutes)	45	43	NS
Highest dermatomal level of block (mode)	T3 (C5–T7)	T3 (T1–T7)	NS

Notes: Statistical significance was defined as  $p < 0.05$ . NS = not significant.

$p = 0.012$ ). There was no significant difference between the groups in respect of the incidence of vomiting: African patients 10/145 (6.8%) and non-African patients 8/112 (7.1%).

In addition, logistic regression showed a correlation between hypotension (SBP  $\leq$  70% baseline) and IONV. There was no association between IONV and baseline heart rate, incidence of smoking, history of motion sickness, or exteriorisation of the uterus.

## Discussion

This study showed an overall incidence of nausea of 32% during SA for CS. There was also a significantly lower incidence in African patients than in the non-African group. The incidence of vomiting was low (18/258 [7%]), and not significantly different between the groups.

There are few studies measuring the incidence of intraoperative nausea and vomiting (IONV). Therefore, the incidence of IONV is often taken from the placebo groups of studies examining the effect of antiemetic preventative measures. Some review articles do quote the incidence of intraoperative nausea and vomiting (IONV) during SA for CS, but most of these have also included postoperative nausea and vomiting (PONV). Previous studies have reported varying incidences of nausea, ranging from 6.7% to 60%,<sup>3-5</sup> and vomiting (12% to 58%).<sup>1,5</sup>

Many factors, anaesthetic and non-anaesthetic, contribute to the incidence of nausea and vomiting during Caesarean section. The anaesthetic risks are hypotension, the use of neuraxial and IV opioids, and an increase in vagal activity. The non-anaesthetic factors include manipulation and exteriorisation of the uterus, vigorous movement of the patient, and the use of uterotonic agents such as oxytocin.<sup>1</sup>

In a review of the incidence of nausea and vomiting during SA for CS, it was suggested that hypotension, baseline heart rate, spinal dermatomal level, a history of non-smoking, or history of motion sickness increases the risk of nausea and vomiting, either intra- or postoperatively.<sup>1</sup> However, using logistic regression, we showed that heart rate, smoking and a history of motion sickness did not significantly increase this risk. It remains controversial whether exteriorisation of the uterus increases the risk of IONV.<sup>6</sup> We found in the present audit that although there was an increased incidence of vomiting in patients in whom the uterus was exteriorised, this was prior to delivery, and hence prior to exteriorisation of the uterus.

In our study, the only factor known to be associated with IONV, along with ethnicity, was hypotension. Many studies have shown a correlation between blood pressure control and IONV. A decrease in blood pressure of  $> 30\%$  below baseline has been found to increase the risk of IONV to 60%.<sup>7</sup> The incidence of IONV increases in proportion to the percentage decrease from baseline blood pressure. Ngan Kee *et al.* found the incidence of IONV to be 4%, 14%, and 40% with targets, as a percentage of baseline systolic blood pressure, of 100%, 90%, and 80% respectively.<sup>8</sup> Hypotension may be compounded by aortocaval compression during SA for CS, particularly if lateral tilt is not adequately applied.<sup>9</sup> In the present study, the odds of experiencing nausea with a minimum-recorded SBP less than 70% of baseline were 2.46 times higher than those in whom SBP was always higher than 70% of the baseline value. There was no difference in the incidence of hypotension between our two groups, and no difference in oxytocin use.

Some of the causes of IONV can be manipulated and controlled, but certain patients may be particularly susceptible. This requires early identification and possibly the use of pharmacological prophylaxis. A recent Cochrane review of interventions for prevention of nausea and vomiting in women undergoing regional anaesthesia for CS showed that many agents were effective in preventing IONV, keeping with the multifactorial pathogenesis of the condition. The best agents were 5-HT<sub>3</sub> antagonists, dopamine antagonists and sedatives. They also found that there was little evidence that combinations of treatments were superior to single agents.<sup>3</sup> These medications are not without their risks, which may include agitation, extrapyramidal symptoms and arrhythmias.<sup>10</sup> In our study, we used metoclopramide 10 mg as treatment of vomiting or reported nausea. Only 7.7% of our patients received this intervention. This percentage was in keeping with the incidence of intraoperative vomiting.

There was a significantly higher incidence of nausea in the non-African group of patients in this study, despite the higher number of smokers in this group (smoking is known to be protective against PONV).<sup>11</sup> It has been shown that nausea and vomiting of pregnancy is more common in western and Asian populations than in African, Eskimo and Native Americans.<sup>12</sup> A Canadian study examining the racial differences in the incidence of nausea and vomiting of pregnancy showed that Asian and Black women were less likely to report these symptoms than Caucasians. This difference in the reporting of symptoms was attributed to cultural or genetic factors.<sup>13</sup> A study investigating racial differences in response to chemotherapy found the African-American population have a lower incidence of nausea and vomiting than Caucasian patients.<sup>14</sup> It has been the perception amongst South African anaesthesiologists that Black South African patients have a decreased incidence of PONV after general anaesthesia. A prospective observational study performed in KwaZulu-Natal (KZN) measured the incidence of PONV in patients undergoing general anaesthesia, and showed a significant difference between Black South African (African) patients (27%) as opposed to multi-ethnic (non-African) patients (45%).<sup>2</sup> It is postulated that the isoenzyme variation in the hepatic P-450 cytochrome system is a potential factor in the precipitation of nausea and vomiting. Patients who have a CYP2E1 poor-metaboliser phenotype may be at a greater risk for the development of PONV. This allele has not been identified in the KZN black population and this may explain the lower incidence of PONV.<sup>15</sup> With regard to intraoperative nausea and vomiting during SA for CS, this mechanism does not apply. Other centrally mediated mechanisms may be involved.

There are certain limitations to this study. We did not use a visual analogue score (VAS) and thus the binary response of 'yes' or 'no' did not allow for the identification of different levels of nausea. Patient responses may also have been affected by confirmation bias. In addition, nausea is under-reported, and the absence of formally trained interpreters meant that the African patients might not have fully understood the meaning of the word nausea.

Nausea and vomiting remain unpleasant symptoms during SA for CS. We therefore regarded it as important to establish the incidence of these side effects in our population, using a standardised SA technique. The intention was to introduce interventions to reduce the incidence of IONV, and improve patient experience of the birth and bonding process. This study found the incidence of nausea and/or vomiting during SA for CS

to be 33% in the South African population. Black South Africans had a significantly lower incidence of intraoperative nausea. The only other factor contributing to an increased incidence of IONV was hypotension. However, in keeping with international standards, the clinically significant incidence of nausea and/or vomiting of 33% requires adjustments to our management protocol for spinal hypotension. The inclusion of ethnicity as a risk factor for nausea during SA for CS should be considered.

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