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Being older as a risk factor for vomiting in those undergoing spinal anesthesia

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ABSTRACT

Purpose: To explore the effect of older age (≥ 65 years) as a risk factor for nausea and vomiting in the context of spinal anesthesia by assessing patient-, surgery- and anesthesia-related variables.
Methods: This is an observation study using a survey instrument in a tertiary general hospital. Patients scheduled to undergo surgery with spinal anesthesia were surveyed by questionnaire and record review to prospectively and consecutively study all patients consenting to spinal anesthesia for surgery during the intraoperative and 24-hour postoperative periods. Risk factors were examined via univariate and multivariate analysis.
Results: Of the 903 patients (69.7% were men) scheduled to undergo surgery with spinal anesthesia, 421 of them (46.6%) were older than 65 years of age. During the intraoperative and postoperative 24-hour observation period, 87 patients (28.1%) experienced nausea and 55 (17.7%) vomited. The incidence of nausea did not differ between elderly (≥ 65 years) and nonelderly patients. However, being elderly was a risk factor for vomiting (24.7% vs. 15.6%, $p < 0.0001$). After adjustment, being elderly was an independent risk factor for vomiting (adjusted odds ratio = 1.84, 95% confidence interval 1.26–2.68).
Conclusion: In patients undergoing spinal anesthesia, the proportion of those complaining of nausea does not differ between elderly and non-elderly patients, but older patients do have a higher risk for vomiting.

1. Introduction

Although nausea and vomiting are not lethal, they are troublesome outcomes of surgery to both patients and caregivers. They can cause significant morbidity and even reverse the gain of using modern fast track anesthesia by delaying discharge or resulting in unexpected admission.[1,2] Nausea and vomiting are thought to be multifactorial in origin, resulting from a combination of factors related to the patient, anesthesia, and surgery. Over the last 20 years, several robust prediction models of postoperative nausea and vomiting (PONV), postoperative nausea (PON), and postoperative vomiting (POV) have been established for patients undergoing general or regional anesthesia.[3–6] However, considering the quite different technique, population and pharmacodynamic effect of the two types of anesthesia, we suspect that patient-, surgery- and anesthesia-related factors may differ vastly between the two. In addition, nausea and vomiting induced by regional anesthesia should be investigated for both the first postoperative 24 hours and the intraoperative period.[7] Therefore, the predictive model for nausea and vomiting should be separated.

A meta-analysis of randomized controlled trials by Liu and colleagues[8] analyzed regional anesthesia by whether it was central neuraxial block or peripheral nerve block, reporting that central neuraxial block was not associated with reduced nausea. Spinal anesthesia remains a fundamental part of the modern practice of central neuraxial block because of its proven high success rate, predictability, high patient satisfaction, and low complication rate. In previous predictive models of nausea and vomiting induced by spinal anesthesia, the observation periods were only intraoperative or until the end of the stay in the postanesthesia care unit (PACU)[9,10]; in addition, they were not long enough (more than 24 hours), as suggested by Apfel.[7] Patient-related risk factors for patients undergoing spinal anesthesia, such as smoking status, motion sickness, or obesity, have not been sufficiently investigated. Additionally, studies differ in their construction; in one, 12% of the material was combined with inhalational general anesthesia, potentially skewing results.[9]

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A history of previous PONV has been found to be an important predictor of PONV[11] and may be strongly associated with other risk factors for PONV. Clinically, anesthesiologists pay more attention to these patients to prevent PONV as those who have experienced PONV tend to request that anesthesiologists take measures to prevent it in subsequent surgeries.[12] The incidence of PONV in patients who previously underwent surgery may be greatly influenced by the biological and psychological effect of their previous anesthesia experience.[13,14] However, some studies have classified those patients with no previous anesthesia experience (around 15%–20% of the study population) as not experiencing nausea or vomiting after an operation when in fact their true risk of previous PONV history is unknown.[3–6] No PON or POV predictive model exists for patients receiving anesthesia for the first time.

The purpose of this study was to explore whether age ($\geq$ 65 years) was a risk factor for nausea and vomiting in the context of spinal anesthesia by assessing patient-, surgery- and anesthesia-related variables. We also sought to identify the risk factors for nausea and vomiting using logistic regression models.

2. Methods

The study was approved by the Institutional Review Board of Kaohsiung Veterans General Hospital, and written informed consent was given by all patients enrolled. During the study period, patients older than 14 years who received spinal anesthesia with 0.5% hyperbaric bupivacaine only were included. We excluded outpatients, patients who received general anesthesia, had communication difficulties, were transferred to an intensive care unit, were pregnant, or had known allergies to the medication (bupivacaine) used in the study. A total of 903 patients were enrolled. None received prophylactic antiemetic treatment. One of the researchers interviewed patients to determine preoperative patient characteristics including age, body height, body weight, sex, motion sickness, smoking status, history of migraine, American Society of Anesthesiologists (ASA) physical status (ASA 1:Healthy patient without organic, biochemical, or psychiatric disease; ASA 2:A patient with mild systemic disease, e.g., mild asthma or well-controlled hypertension. No significant impact on daily activity. Unlikely to have an impact on anesthesia and surgery; ASA 3: Significant or severe systemic disease that limits normal activity, e.g., renal failure on dialysis or class 2 congestive heart failure. Significant impact on daily activity. Probable impact on anesthesia and surgery; ASA 4: Severe disease that is a constant threat to life or requires intensive therapy, e.g., acute myocardial infarction, respiratory failure requiring mechanical ventilation. Serious limitation of daily activity. Major impact on anesthesia and surgery; ASA 5: Moribund patient who is equally likely to die in the next 24 hours with or without surgery; ASA 6: Brain-dead organ donor; "E" added to the classification indicates emergency surgery.), and preoperative anxiety. Patients rated the severity of anxiety using a four-point verbal rating scale (0 = none, 1 = mild, 2 = moderate, 3 = severe).

Lumbar puncture was performed between L2 and L5, with the patient in the lateral position. Using the paramedian approach, a 25-gauge needle (Becton Dickinson, Madrid, Spain) was inserted into the subarachnoid space, with the bevel parallel to the dural fibers. When free flow of cerebrospinal fluid was obtained, 2.0–3.0 ml of 0.5% hyperbaric bupivacaine (AstraZeneca AB, Södertälje, Sweden) without additives was administered. Delayed supine position was defined as keeping the lateral position for 5 minutes after the induction of spinal anesthesia. Peak sensory block level was evaluated with alcohol sponge padding every 10 minutes until the maximum level was reached. Sedation was achieved using intravenous injection of midazolam. Bradycardia (heart rate $<$ 50 beats minute^{-1}) was treated by intravenous administration of 0.5–1.0 mg atropine. Hypotension (systolic blood pressure 20% below baseline)[15] was managed by increased intravenous fluid supplementation or intravenous injection of ephedrine (5 mg) or both. Blood pressure was measured when the patient arrived at the operating room and at least every 5 minutes thereafter, and electrocardiographic data and arterial oxyhemoglobin saturation (SpO_2) were continuously monitored and recorded during the entire procedure.

After induction of spinal anesthesia, the presence and severity of nausea, retching, or vomiting, and pain were actively evaluated at least every 15 minutes in the operating room and in the PACU by trained observers until the patient was sent back to the ward. Patients were transferred back to the ward when they could move their toes and independently lift their lower limbs against gravity. In the ward, observations were conducted every 4 hours for the first 24 hours after surgery. Patients self-rated their severity of nausea using a four-point verbal rating scale (0 = none, 1 = mild, 2 = moderate, 3 = severe). Retching and vomiting were recorded separately according to the presence or absence of vomitus, but retching was counted as vomiting during subsequent analysis. An antiemetic (prochlorperazine, 5 mg) was given when patients felt severe nausea and asked for an antiemetic or vomited more than twice. Pain intensity was rated using a visual analog pain scale (VAPS) scored from 0 (no pain) to 10 (highest level). Premedication with opioids (fentanyl, 50 μg) was given when a patient could not tolerate the positioning because of pain. During the intraoperative period, meperidine (25 mg) was applied to patients experiencing shivering; fentanyl (50 μg) was given to patients feeling soreness or pain in the operative field. Although patients were in the PACU or the ward, meperidine (50 mg) or patient control analgesic (PCA) with morphine or fentanyl was given for pain in the area of the operation. Premedication with opioids or use of intraoperative or postoperative opioids were all recorded as use of opioids. Anesthesia-related factors were preoperative anxiety, premedication with midazolam, delayed supine position, peak sensory block level, intraoperative sedation, intraoperative hypotension, use of opioids, use of supplemental oxygen, preinduction hydration, preoperative anxiety, dosage of atropine given, pain scores in the recovery room and on postoperative Day 1 (at 24 hours), dosage of ephedrine given, and total amount of intravenous fluid required. Surgery-related factors were type of surgery, supine surgical position, amount of total blood loss, and length of surgery. In the subsequent analysis, nausea and vomiting (including retching) after the induction of spinal anesthesia (including intraoperative and postoperative periods) were considered the two outcomes of interest.

Patients were analyzed separately as elderly ($>$ 65 years) and younger than 65 years (nonelderly). Chi-square tests and Student's *t*-tests were performed to investigate between-group differences (demographic variables and anesthesia- or surgery-related putative risk factors). The associations between the variables and the status of nausea or vomiting were tested by chi-square tests and Student's *t*-tests, but the results were not present in our tables. Variables significantly associated with the status of nausea or vomiting were incorporated as predictors into multiple logistic regression models using a forward stepwise procedure. The power of discrimination was determined based on the area under the receiver operating curve (AUC). Significance was set at $p = 0.05$. All statistical analyses were performed using SPSS version 12.0 (SPSS Inc., Chicago, IL, USA).

3. Results

The mean age of participants was 75.0 years for the 421 elderly patients and 45.9 years for the 482 nonelderly participants

(Table 1); both groups were predominantly men (67.9% vs. 65.1%, $p = 0.376$). The elderly patients had higher ASA physical status than the nonelderly. They were less likely to have a history of motion sickness and more likely to be first-time anesthesia users. They were also less likely to have migraine, to smoke, or have a history of PONV. Of all the 903 patients, 245 (27.1%) experienced nausea and 179 (19.8%) vomited during the intraoperative and postoperative 24 hours observation period. The incidence of nausea did not significantly differ between the elderly and nonelderly patients (25.9% vs. 28.2%), but the older patients were more likely to vomit (24.7% vs. 15.6%, $p = 0.001$).

Preoperative anxiety and intraoperative sedation were less common in elderly patients (Table 2). Delayed supine position and intraoperative hypotension were more frequent in elderly patients. Elderly patients received higher dosages of preinduction hydration and total intravenous fluid. They also had more total blood loss. Although the pain scores in recovery room were not significantly different between the two groups, elderly patients reported lower pain scores at 24 hours after operation (pain scores on postoperative Day 1).

The following factors met the criteria for association with experiencing nausea: male sex (adjusted odds ratio [OR]: 0.60), history of PONV (adjusted OR: 4.35), use of opioids (adjusted OR: 2.35), lower ASA score, greater fluid intake (adjusted OR: 1.11), a higher dose of ephedrine (adjusted OR: 1.04), and higher VAPS scores in the PACU (adjusted OR: 1.11) (Table 3).

After adjustment, vomiting was positively associated with a history of PONV, using opioids, female sex, more fluids and ephedrine, and age ≥ 65 years. AUC values for these models were 0.74 (95% CI: 0.71-0.77) for nausea and 0.78 (95% CI: 0.75-0.82) for vomiting.

Table 1
Patient-related factors of patients undergoing spinal anesthesia.

	Age ≧ 65 (yr)		Age < 65 (yr)		*p* value for chi-square or t-test
	n = 421 (mean)	% (SD)	*n* = 482 (mean)	% (SD)	
Sex					0.376
Men	286	67.9	314	65.1	
Women	135	32.1	168	34.9	
ASA physical status					0.000
I	13	3.1	193	40.0	
II	366	86.9	278	57.7	
III or IV	42	10.0	11	2.3	
History of motion sickness					0.003
Yes	53	12.6	96	19.9	
No	368	87.4	386	80.1	
Migraine					0.000
Yes	50	11.9	104	21.6	
No	371	88.1	378	78.4	
Smoking					0.000
Yes	73	17.3	135	28.0	
No	348	82.7	374	72.0	
First-time anesthesia					0.029
Yes	292	69.4	301	62.4	
No	129	30.6	181	37.6	
PONV history					0.031
Yes	24	5.7	46	9.5	
No	397	94.3	436	90.5	
Nausea					0.433
Yes	109	25.9	136	28.2	
No	312	74.1	346	71.8	
Vomiting					0.001
Yes	104	24.7	75	15.6	
No	317	75.3	407	84.4	
Age (yr)	75.02 ± 5.61		45.89 ± 13.77		0.000
Body mass index	25.16 ± 4.12		25.01 ± 4.37		0.599

ASA = American Society of Anesthesiologists; PONV = postoperative nausea and vomiting; SD = standard deviation.

Table 2
Anesthesia-, and surgery-related factors of patients in the patient groups.

	Age ≧ 65 yr		Age < 65 yr		*p* value for chi-square or t-test
	n = 421 (Mean)	% (SD)	*n* = 482 (Mean)	% (SD)	
Preoperative anxiety					0.001
Yes	281	66.7	370	76.8	
No	140	33.3	112	23.2	
Premedication with midazolam					0.616
Yes	18	4.3	24	5.0	
No	403	95.7	458	95.0	
Delayed supine position					0.038
Yes	64	15.2	51	10.6	
No	357	84.8	431	89.4	
Peak sensory block level ≥ T6					0.872
Yes	102	24.2	119	24.7	
No	319	75.8	363	75.3	
Intraoperative sedation					0.000
Yes	68	16.2	124	25.7	
No	353	83.8	358	74.3	
Intraoperative hypotension (systolic blood pressure 20% below baseline)					0.000
Yes	301	71.5	259	53.7	
No	120	28.5	223	46.3	
Use of opioids					0.978
Yes	294	69.8	337	69.9	
No	127	30.2	145	30.1	
Preinduction hydration (100 ml)	1.18 ± 1.04		1.03 ± 1.11		0.048
Atropine (mg)	0.03 ± 0.15		0.03 ± 0.13		0.750
Pain scores in recovery room (VAPS)	1.04 ± 2.03		1.14 ± 2.06		0.471
Pain scores on postoperative Day 1 (VAPS)	3.04 ± 2.72		3.54 ± 2.65		0.005
Ephedrine (mg)	4.87 ± 8.28		3.97 ± 7.70		0.092
Total intravenous fluid (100 ml)	9.33 ± 5.10		7.49 ± 4.60		0.000
Type of surgery					0.203
Plastic	49	11.6	76	15.8	
Urologic	126	29.9	125	25.9	
Orthopedic	195	46.3	215	44.6	
General surgery	45	10.7	53	11.0	
Colon, rectal, or other (vascular or gynecologic)	6	1.4	13	2.7	
Total blood loss (100 ml)	0.87 ± 1.55		0.63 ± 1.64		0.025
Duration of surgery (h)	1.42 ± 0.72		1.38 ± 0.83		0.517

VAPS = visual analog pain scale.

4. Discussion

Disparities between studies in reported nausea, vomiting incidences, or both after spinal anesthesia have been attributed mainly to differences in study design.[16] In this study, the incidences of intraoperative nausea (9.5%) and vomiting (5.4%) were close to the 18% for nausea and 7% for vomiting reported by Carpenter and colleagues.[9] Furthermore, 16.8% of patients experienced PON and 10.1% had POV, consistent with previous reports of 18%–52% for PON and 7%–25% for POV.[5,9,17,18] In a study of regional anesthesia, Koivuranta and coworkers[5] reported PONV rates of 48% for women and 26% for men. In a similar group, Quinn and others[19] reported a PON rate of 28% in women and 14% in men and a POV rate of 17% in women and 7% in men. No sex differences were found in the preadolescent group or in patients older than 80 years.[19,20] In this study, female sex was an independent risk factor for both nausea and vomiting. This suggests that variations in sex hormones may contribute to the higher incidence of emesis in women. In addition, we found that sex differences in PON and POV rates differed significantly between elderly and nonelderly patients. However,

Table 3
Regression models for prediction of nausea and vomiting.

	Nausea		Vomiting	
	Adjusted OR	95% CI	Adjusted OR	95% CI
Patient-related factors				
Sex: man = 1, woman = 0	0.60	0.43–0.84**	0.31	0.22–0.45***
Age ≧ 65 yr (yes/no)			1.84	1.26–2.68**
ASA physical status	—	—		
II/I	0.66	0.45–0.97*		
III or IV/I	0.40	0.18–0.88*		
PONV history (yes/no)	4.35	2.49–7.60***	3.20	1.81–5.68***
Anesthesia-related factors				
Ephedrine (mg)	1.04	1.02–1.06***	1.02	1.00–1.05*
Use of opioids (yes/no)	2.35	1.54–3.60***	4.30	2.42–7.67***
Pain scores in recovery room (VAPS)	1.11	1.03–1.19**		
Total intravenous fluid (100 ml)	1.11	1.03–1.20***	1.06	1.02–1.10**

*$p < 0.05$.
**$p < 0.01$.
***$p < 0.001$.
ASA = American Society of Anesthesiologists; CI = confidence interval; OR = odds ratio; PONV = postoperative nausea and vomiting; VAPS = visual analog pain scale.

when we defined elderly patients as those ≥ 80 years, the sex difference was no longer significant for nausea ($p = 0.522$) or vomiting ($p = 0.013$), consistent with previous studies.[19,20]

In a prospective trial plus a systematic review of adult patients who underwent general anesthesia, Kranke and colleagues[21] concluded that increased body mass index (BMI) was not a risk factor for PONV. Recently, increasing BMI has been reported to be related to chronic gastrointestinal symptoms[22] and abnormal upper endoscopic findings in the general population.[23] In a study of spinal anesthesia, however, obese women experienced significantly more vomiting than females with normal BMI.[10] When we accounted for other variables in our study, higher BMI was not an independent predictor for either nausea or vomiting. This result implies that a higher BMI may not contribute to a lower threshold for nausea or vomiting.

The relationship between age and PONV is controversial.[3,5] Standl and others[24] found a nonlinear relationship between age and PONV in patients undergoing orthopedic surgery, with the lowest PONV incidence in patients aged 40–60 years. Kalso[25] reported an increased incidence of PONV in 50 older patients (60–80 years) receiving spinal anesthesia for orthopedic surgery. In this study, patients younger than 30 years complained most often of nausea (38.6%), less so for those aged 30–65 years (26.1%) and those older than 65 years (25.9%). This result implies that younger patients are more sensitive to spinal anesthesia or operation and more likely to complain of nausea.

Vomiting is a more objective event than nausea. The incidence of vomiting was 15.6% and 24.6%, respectively, among the two age groups (≤ 65, and ≥ 65 years). Patients 65 years and older had a significant higher incidence of vomiting, making being in this age group an independent risk factor for vomiting.

In Taiwan, 50% of the elderly patients have three chronic diseases and they showed higher ASA physical status than non-elderly patients in our study. The relationship of ASA status and nausea or vomiting is not concluded. Koivuranta and others[5] surveyed 1107 patients, and found that higher ASA status were negatively associated with vomiting. Marsha and others[26] found that higher ASA status was negatively associated with nausea and vomiting. Besides, in the two studies above, only 26% and 15.6% of the participants respectively received regional anesthesia. Among patients received spinal anesthesia, we found higher ASA status was negative associated with nausea but vomiting after adjustment.

Opioid usage is a known risk factor for PONV in combination with inhalation general anesthesia[12] and regional anesthesia[27]. Furthermore, Roberts and colleagues[28] found a strong logarithmic dose-response relationship between postoperative opioid consumption and PON and POV. Conscious patients are more likely to respond to certain medications (e.g., opioids) with nausea and vomiting.[16] In this study, 711 (78.7%) participants were awake and we found that the use of opioids was an independent predictor for nausea and vomiting.

Our study differed from previous ones in several important points. The observation periods of previous studies[9,10] in spinal anesthesia did not cover 24 hours as Apfel[7] suggested and led to a different conclusion from ours. Various studies have found gut hypoperfusion a factor for PONV in cardiac surgery.[29,30] It is routine to have patient fast overnight before surgery and this practice combined with the surgical losses of fluid is posited to result in state of transient and relative gut ischemia through mesenteric hypoperfusion. However, we observed dosage of total intravenous fluid to be positively associated with nausea and vomiting. The result suggests that the total intravenous fluid may influence nausea and vomiting by some mechanism other than hypoperfusion.

No study has definitively linked postoperative pain and PONV, although opioid administration clearly can provoke nausea. Opioid analgesia reduced PONV in 80% of patients who experienced both pain and PONV.[31] Studies differ on the relationship between pain, the use of opioids, and PONV in patients receiving regional anesthesia.[16] In this study, we found that pain scores in the recovery room were independently associated with nausea in spinal anesthesia patients.

Delayed supine position after induction is a unique factor for nausea and vomiting in patients receiving spinal anesthesia. However, we did not find delayed supine position after induction a significant predictor for nausea or vomiting.

Previous surveys do not allow us to ascertain the influence of type of surgery on PONV due to great variation across study populations. After adjusting for other risk factors, we did not find surgery type independently associated with nausea or vomiting.

A mixed general and regional anesthesia study reported that some risk factors were predictive for both nausea and vomiting (female sex, nonsmoking status, and general anesthesia), whereas history of migraine and type of surgery were predictive of nausea but not vomiting.[17] In this study, female sex was also a predictor of both outcomes, but type of surgery was not a predictor of either nausea or vomiting.

The protective effect of smoking on PONV has been well demonstrated, and smoking appears to be an important negative predictor of PONV in patients receiving general anesthesia with or without regional anesthesia.[32] Local anesthetics are directly injected intrathecally with a single shot, whereas general anesthesia is inhaled into the patient's lungs or infused into the circulation system. Many possible mechanisms have been proposed for the protective effect of smoking.[33] In this study, smoking was not an independent protective factor for these outcomes. This may be due to the different metabolic pathway rather than the antiemetic effect of smoking.

In conclusion, although elderly patients did not show higher incidence of nausea than younger ones, they had higher incidence of vomiting after spinal anesthesia. It is important to prevent vomiting by means such as prescribing antiemetics for elderly patients.

There are some limitations in the study. To treat patients with nausea or vomiting, our staff usually administered oxygen, increased the infusion rate of intravenous fluid and used boluses of ephedrine. Therefore, ephedrine and total intravenous fluid are significantly associated with both nausea and vomiting. In future

studies, baseline levels of these data should be recorded before the first episode of nausea or vomiting. In addition, these patients did not receive standardized preoperative sedation. In addition, rather than using length of surgery, we should find a better way to define anesthesia duration and record the use of opioids as a continuous rather than a binary variable.

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