DO THE CHOICES OF AIRWAY AFFECT THE POST-ANESTHETIC OCCURRENCE OF NAUSEA AFTER KNEE ARTHROPLASTY? A COMPARISON BETWEEN ENDOTRACHEAL TUBES AND LARYNGEAL MASK AIRWAYS

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Abstract

Objectives: The primary goal of this study was to assess the impact of airway devices on the incidence of nausea after knee arthroplasty and their interaction with the use of nitrous oxide.

Methods: Charts were reviewed for 499 patients after knee arthroplasty under general anesthesia. Demographic data, type of airway device, nitrous oxide, sevoflurane, desflurane, isoflurane, fentanyl, metoclopramide, ondansetron, dexamethasone, rocuronium and neostigmine were analyzed. Fisher's exact test was used to compare the categorical factors and t-test was used for continuous variables. Sinclair scores were used for post-operative nausea and vomiting (PONV) risk stratification. Multivariate logistic regression model was constructed to identify the factors contributing to the frequency of PONV.

Results: PONV was documented in 10.3% of patients. Nitrous oxide was associated with a higher frequency of PONV than those received air mixture (12.5% vs. 8.7%, $P < 0.01$). Prior to risk stratification, the frequency of PONV was 17% in the endotracheal tube (ETT) vs. 6.7% in the laryngeal mask airway (LMA) group ($P < 0.01$). Sinclair score was 0.51 ± 0.17 for the ETT group and 0.74 ± 0.12 for the LMA group ($P < 0.001$). After risk stratification and matching, the incidence of PONV was 15.8% with the use of ETT compared with 7.9% for LMA ($P < 0.05$).

Conclusion: The frequency of PONV was almost twice with ETT as with LMA. Longer duration of anesthesia, neuromuscular blockade and non-standardized antiemetic regimen may have contributed to the increase PONV in ETT group. Prospective randomized studies are necessary to further explore whether and to which extend airway devices influence the incidence of PONV.

Key words: postoperative nausea, vomiting, anesthesia, nitrous oxide, adult males

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Introduction

Post-operative nausea and vomiting (PONV) is a common occurrence that can lead to additional escalated care and increased costs, as well as discomfort to the patient. There are known risk factors for PONV[1,2], but the role of airway devices on PONV is less clear[1]. Previously published conflicting results in regards to the influence of airway device on PONV are outlined in Table 1. PONV can increase length of stay in the post-anesthesia care unit (PACU) [1,2].

Nader et al. reported that barometric changes in the middle ear pressure upon discontinuation of nitrous oxide anesthesia could predict PONV[3]. The authors specifically demonstrated that the gradient in the middle ear pressure was greater with the use of nitrous oxide, and therefore a larger gradient was associated with PONV. Increased PONV with the use of nitrous oxide is possibly dose-dependent. This occurrence was also found in another study that looked at gynecological surgeries[4], and in a study that measured specifically severe PONV[5].

In a single-blinded, randomized, controlled study, Swann et al. found a higher incidence of PONV in patients with laryngeal mask airways (LMA) than those with endotracheal tubes (ETT) following inhalational anesthesia with nitrous oxide[6]. Nader et al. noticed a trend in use of a LMA increasing the pressure gradient in the middle ear compared with the use of an ETT[3]. The possible mechanisms may have been related to the obstruction of Eustachian canal or stimulation of different parts of the airway. However, this difference did not reach statistical significance in regards to the incidence of PONV. Another study contradicted this finding, concluding that middle ear pressure did not change with the choice of airway device[7]. Yet, this study did not specifically address the issue of PONV in relationship to the various airway devices or gaseous agents used. The same author reported that LMA reduced the absolute risk of PONV by 40% in comparison to ETT in females undergoing general anesthesia without nitrous oxide[8].

Other investigators have demonstrated that in otologic surgeries the use of ETT versus LMA created no statistically significant difference in terms of PACU recovery time and PONV. Therefore, the multiplicity of factors involved in PONV and the contradicting results in the literature left the possibility that selection of airway device may change the incidence of PONV [Table 1][9,10].

We undertook this retrospective review to assess the differences in the incidence of PONV between the LMA and ETT groups in patients undergoing knee arthroplasty. Secondary aim was to assess influence of the airway choices on PONV in a subgroup of patients receiving nitrous oxide as well as to explore predictors for PONV in the study population. We hypothesized that the use of LMA was associated with a higher frequency of PONV after general anesthesia.

Table 1

Post-operative nausea and vomiting with LMA vs. ETT

Author		Surgery	N	Anesthesia & Duration	ASA Class	Airway Device	Outcome
Holhrieder[8]		Breast & GYN	200	N_2O 88-95 min	I & II	LMA vs. ETT	Less PONV in LMA group
Holhrieder[7]		Orthopedic	80	N_2O/Air 70 min	I & II	LMA vs. ETT	No significant change in MEP
Nader[3]		Orthopedic	27	N_2O/Air <120 min	I & II	LMA vs. ETT	N2O →PONV, Similar PONV in LMA and ETT
Swan[6]		GYN	60	N_2O	I & II	LMA vs. ETT	LMA 13.0% VS ETT 9.4% PONV
Klockgethe[9]		PED-Eye	100	N_2O	I & II	LMA vs. ETT	ETT group more PONV followed up for 24 hours

LMA = Laryngeal Mask Airway, ETT = Endotracheal Tube, PED = Pediatric, N_2O = Nitrous Oxide, GYN = Gynecology, MEP = Middle Ear Pressure

PONV = Post-operative nausea and vomiting, PACU = Post anesthesia care unit, LOS = length of stay

Methods

Patients and Data Collection:

The study was reviewed and approved by the Institutional Review Board at the Veteran's Administration Western New York Health Care System. Due to its retrospective nature, the study was exempted from obtaining informed consents. Electronic charts were reviewed retrospectively from 499 ASA physical status I through III patients with age ranging 18-80 years old who had undergone knee arthroplasty surgery under general anesthesia, from September 30, 2004 to October 1, 2009. Patients were excluded from the review if they received regional anesthesia or had preexisting nausea, vertigo, and otitis media. Patients, who required neostigmine in excess of 2.5 mg for reversal of muscle relaxants, were also excluded. Patients, who received general anesthesia by the use of an airway device other than ETT or LMA, were also excluded from the study as well as patients in lateral and prone positions. Furthermore, patients whose duration of surgery was longer than 240 minutes were excluded.

Demographic data analyzed patient's age, history of motion sickness, smoking history, PONV, race, gender, ASA physical status, and body mass index (BMI). The intra-operative use of nitrous oxide was limited to 50% in all patients. The use of volatile anesthetics (sevoflurane, isoflurane or desflurane), total intraoperative dose of fentanyl, neuromuscular blocking drugs (rocuronium), neuromuscular reversal agents (neostigmine), prophylactic antiemetic drugs (metoclopramide, ondansetron or dexamethasone), and the duration of surgery were recorded. Perioperative fluid strategy in our hospital is restrictive and all patients received Plasmalyte 4-6 mL/Kg/hour.

Upon transfer to the PACU, the patients were monitored and supplemental oxygen was provided in supine position with mild (20°) head of the bed elevation. Nausea was defined as the feeling of sickness with an inclination to vomit. Vomiting, or emesis, was defined as the expelling of gastric content through the mouth. The incidence of PONV was assessed and recorded electronically by a certified post-anesthesia nurse (CPAN) in the PACU and a registered nurse on the surgical floor for a period of 24 hours. The use of prophylactic antiemetic drugs included dexamethasone 4 mg, metoclopramide 10 mg and ondansetron 4 mg with fixed dose and not calculated based on body weight. Ondansetron 4 mg was administered for the first episode of PONV and repeated if symptoms persisted. If the patient did not respond to second dose of ondansetron, metoclopramide was administered in the PACU. PACU length of stay (PACU LOS) was calculated from the time of arrival until the patients were deemed to meet the criteria to leave the PACU as document in the Nurses' note.

Furthermore, we recorded the incidence of a composite adverse events including: hypoxia defined as arterial oxygen saturation less than 90%, hypoventilation defined as respiratory rate of less than 8 per minute, reintubation, acute congestive heart failure requiring inotropic drug and positive pressure ventilation, hypotension with the systolic pressures <20% of the baseline and intractable pain documented by an 11 point numeric pain score (0-10). Patients were medicated with pain scores of more than 4 and if unresponsive to low dose opioid treatment (hydromorphone <2 mg) with an intravenous administration of 30 mg ketorolac, provided adequate renal function.

Statistical Analysis

NCSS 2007 (Salt Lake, UT) was used for statistical analysis. All identifiable information was removed before exporting the data into the statistical software. The primary endpoint was the occurrence of PONV until discharge criteria's were met. The secondary outcome variable included PACU LOS. Fisher's exact test with chi-squared cross tabulation was used to identify the difference in the incidence of PONV. Continuous variables such as age, duration of surgery, and length of stay in the PACU were examined by Student's t-test and the data were expressed mean values with standard deviation were reported if the given variable passed the normality test, otherwise median values were reported with interquartile range. Since neuromuscular blockade was only used in patients whose airway was established by endotracheal intubation, the use of these drugs and related reversal

agents were only analyzed for ETT subgroup of patients. Sinclair score was calculated for every patient using the following formula and was used for risk stratification:

logit (P) = -5.97 + -0.14 *Age + -1.03 *Sex + -0.42*Smoking + 1.14 *PONV History + 0.46 *Duration + 2.36 *GA + 1.48 *ENT + 1.9 *Plastic + 1.2 *Gyn.

Sinclair scoring uses age, sex, smoking status, previous PONV, type of anesthesia, duration of anesthesia, and type of surgery to identify independent predictors of PONV. This model predicted PONV accurately and yielded an area under the receiver operating characteristic curve of 0.79 ± 0.01 using an independent validation set[11]. Calculated predictive risk score was used as the propensity scoring in order to match the data based on the airway choice. Therefore, equal numbers of ETT and LMA patients were compared. Multivariate logistical regression was used with PONV as the primary outcome variable. The following variables were listed in constructing the multivariate model: the use prophylactic antiemetic, rocuronium, neostigmine, nitrous oxide, volatile anesthetics (sevoflurane, isoflurane vs. desflurane), gender, race, ASA status and the airway device (ETT vs. LMA). *P* values of less than 0.05 were considered significant.

Table 2

Basic Preoperative characteristics of the patients with and without postoperative nausea and vomiting

		No PONV (N =446)	PONV (N =51)	P Value
Gender				
	Female	35 (7.8%)	8 (15.6%)	0.06
Race				
	White	382 (85%)	44 (86%)	
	Black	57 (12%)	7 (14%)	0.66
	Others	7 (1%)	0 (0%)	
Age		51.3 ±16.1	51.6 ±16.1	0.90
BMI	(Kg/m^2)	28.5 ±5.8	28.3 ±6.2	0.83
ASA Class				
	PS-1	45 (11%)	2 (4%)	
	PS-2	254 (56%)	32 (62%)	0.34
	PS-3	147 (33%)	17 (33%)	
Smoking Status				
	Smokers	112 (26%)	7 (14%)	
	Ex-smokers	263 (58%)	28 (55%)	0.011*
	Non-smokers	71 (16%)	16 (31%)	
Airway Device	ETT/LMA	141/305	29/22	<0.001*

P <0.05 is statistically significant

BMI: body mass index; ASA: American Society of Anesthesiologists; PS: physical status; ETT: endotracheal tube; LMA: laryngeal mask airway; *signifies significant difference

Ex-smokers were defined, *as* people who were formerly daily smokers but currently do not smoke at all.

Table 3

Intra-operative and anesthetic characteristics of the patients with and without PONV

		No PONV (N = 446)	PONV (N = 51)	P Value
Anesthetics				
	N2O	280 (62%)	40 (78%)	0.03*
	Sevofluorane	396 (88%)	43 (84%)	0.47
	Desfluorane	39 (9%)	6 (11%)	0.57
	Isoflurane	10 (2.2%)	2 (3.9%)	0.80
VAS pain		3[2-3]IQR	3[1-4]IQR	0.44
Fentanyl citrate (mcg/kg)		2.25 ± 2.13	2.77 ± 3.8	0.13
Duration of Surgery (min)		61.8 ± 41.0	72.3 ± 46.5	0.03*
Length of PACU Stay (min)		96.4 ± 63.0	130.7 ± 78.8	<0.001*
Prophylactic				
Antiemetic	Metoclopramide	189 (42%)	19 (37%)	0.55
	Ondansetron	146 (32%)	17 (33%)	0.93
	Dexamethasone	18 (4%)	2 (3%)	0.97
	Any	255 (50%)	28 (54%)	0.87
Rocuronium	Yes	136 (30%)	28 (54%)	<0.001*
	No	310 (70%)	23 (46%)	
Neostigmine	Yes	37 (8%)	11 (21%)	<0.01*
	No	409 (91%)	40 (78%)	

N_2O: nitrous oxide; PACU: Post-anesthesia Care Unit; NMBD: neuromuscular blocking drug
VAS: Visual analog scale, IQR: Interquartile range
* Signifies statistical difference

Table 4

Demographic characteristics and Perioperative Data

	LMA (N = 327)	ETT N = 170)	P Value	LMA (N = 157)	ETT (N = 157)	
	Before Match			After Match		P Value
Sinclair Score	0.74 ± 0.12	0.51 ± 0.17	0.001	0.56 ± 0.16	0.58 ± 0.15	0.87
N2O	216 (66%)	102 (60%)	NS	118 (75%)	99 (63%)	NS
Female	37 (11%)	6(4%)	0.003*	8 (5.0%)	6 (3.8%)	NS
Race White	279	147	0.32	121	123	NS
Black	45	19		32	31	
Others	3	4		4	3	
Age (years)	46 ± 15	62 ± 13	<0.001*	54 ± 13	62 ± 12	<0.001*
BMI (Kg/m2)	28.4 ± 5.1	28.7 ± 5.9	NS	28.3 ± 11.8	28.5 ± 12.1	NS
ASA PS-1	47	0	<0.001*	13	0	<0.01*
PS-2	203	83		95	72	
PS-3	77	87		46	83	
Fentanyl (mcg/kg)	2.4 ± 2.9	2.2 ± 2.0	0.38	2.3 ± 2.4	2.5 ± 2.2	NS
Duration (min)	94 ± 45	47 ± 28	<0.001*	53 ± 34	97 ± 46	<0.001*
Prophylactic Antiemetic	194 (59%)	89 (52%)	0.13	74 (47%)	51 (32%)	0.01*

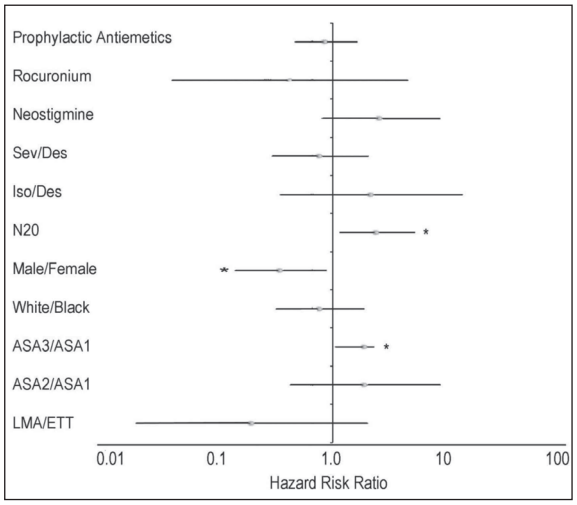
BMI: body mass index; ASA: American Society of Anesthesiologists; PS: physical status; ETT: endotracheal tube; LMA: laryngeal mask airway;

● Asterisks signify significant difference between ETT and LMA groups

Data matching was done using Sinclair PONV risk score as the propensity score:

Logit (P) = -5.97 + -0.14 *Age + -1.03 *Sex + -0.42*Smoking + 1.14 *PONV History + 0.46 *Duration + 2.36 *GA + 1.48 *ENT + 1.9 *Plastic + 1.2 *Gyn.

Fig. 1



Hazard risk ratio for nitrous oxide was 2.5 [1.1-5.4]. Gender hazard risk ratio for male was 0.34 [0.13-0.87]. The greater risk of PONV in patients with ETT when compared to those with LMA was shown in univariate analyses. It did not turn to be an independent predictor of PONV in multivariate analysis [Fig. 1]. LMA vs. ETT was not significant with hazard ratio 0.19 [0.02-2.06].

Results

The charts from 499 patients were reviewed. Two patients were excluded because their airways were controlled by means other than ETT or LMA. There were a total of 43 female patients in the review. The average age was 51.4 ± 16.1 years for all patients. PONV occurred in 51/497 (10.3%) patients. The incidence of PONV was 29/170(17%) with the use of ETT and 22/327 (6.7%) with LMA (P <0.001) [Table 2]. Average PACU length of stay for all patients was 107 ± 61 minutes. The average PACU length of stay for patients without and with PONV was 96 ± 63 minutes and 130 ± 79 minutes, respectively (P <0.001). When nitrous oxide was used as a part of anesthetic mixture, the incidence of PONV was 18 out of 102 (17.5%) in the ETT group vs. 22/216 (10.1%) in the LMA group. Additionally, an ETT was used in 55 out of 177 patients and a LMA for the remaining 122 patients without nitrous oxide. The incidence of PONV among patients not receiving nitrous oxide was 11 out of 177 (8.7%). However, there was no statistical difference among the patients with ETT and LMA in the subgroup analysis without nitrous oxide. All intraoperative parameters for patients with or without PONV are shown in Table 3. Neostigmine was used in 11/51 patients who had PONV while it was used in 37/446 (8.2%) patients without PONV [Table 3].

Preoperative risk of PONV was calculated for every patient using the Sinclair formula. Sinclair score for the ETT group was 0.51 ± 0.17 while the risk for the LMA group was 0.74 ± 0.12 (P <0.001). The LMA group was identified as higher risk group for PONV based Sinclair scoring system. In order to evenly distribute the patients into airway groups, Sinclair risk was used as propensity score to match the patients for equal risk of PONV. All the values were reanalyzed before and after match demonstrated in Table 4. The incidence of PONV was 25/157 (15.8%) with the use of ETT compared with 12/157 (7.9%) for the LMA group (P <0.05) after matching [Table 4].

We also analyzed the data examining the use of prophylactic antiemetic drugs. Notably, prophylactic antiemetic medications were administered to 52.4 % of patients with ETT and 59.3%, of the patients with LMA (P = 0.13). When specifically looking at the use of ondansetron, 32.7% of patients in ETT group received this medication prophylactically versus 37% of patients in the LMA group (P = 0.4). The average length of surgery for patients with ETT was 94 ± 45 minutes and for patient with LMA was 47 ± 28 minutes (P <0.001).

Multivariate logistic regression model was constructed for all preoperative risk factors as listed in the Methods section. This analysis showed that gender, age, duration of surgery and nitrous oxide use to be independent risk factors for PONV [Fig. 1]. The odds ratio for the length of surgery was 1.008 [1.000-1.920]. Therefore for each added minute of surgery, the risk of PONV increased by 0.8%. Age had the opposite effect on PONV with an odds ratio of 0.993 [0.962-0.998]. Therefore each added year of age protected an individual from PONV by 0.7%.

Discussion

We have shown that the incidence of PONV is significantly higher in patients who had an ETT

compared to those with a LMA in univariate analysis. This association seemed to be related to some other confounding variables since multivariate analyses indicated that an airway device was not an independent predictor of PONV. There has been very little data on the influence of airway device and post-operative incidence of nausea and vomiting. Several publications report contradictory results[6,8,9]. More information and research is needed to establish the role of airway devices on PONV. Previous study by our group had suggested that changes in middle ear pressure might have contributed to the PONV[3]. But since the etiology of PONV is multifactorial in origin, it would be difficult to draw any solid conclusion on the cause and effect relationship.

The use of nitrous oxide is a known risk factor for PONV[12] and our study confirms that nitrous oxide is an independent factor for PONV and the relative risk of nitrous oxide is greater among those with ETT than those with LMA. A meta-analysis from 1996 states that nitrous oxide was associated with increased emesis in 24 of 27 studies analyzed, but did not record the type of airway device used for anesthesia[13]. More recent studies have also identified nitrous oxide as a risk factor for PONV, but the influence of choice of airway device on PONV was not reported. Apfel *et al.* limited the study to surgeries of less than one hour[14]. Many of the surgeries (65.7%) recorded in our study were of a shorter time frame usually less than 60 minutes. Selection of an airway device was influenced by the duration of surgery and experience of the anesthesiologist[15]. In view of these findings, we suggest that several risk assessment tools that are used in clinical setting to predict the incidence of PONV should modify to include nitrous oxide as part of their formula.

The LMA has been in use since 1984, so presumably some of the above studies may have included patients using this airway device[16]. Other investigators have reported the type of airway device used, but only matched this variable across study populations instead of examining its effect on PONV[17]. One meta-analysis found that eliminating the use of nitrous oxide did not reduce the incidence of nausea, but it did reduce the incidence of early and late vomiting[2]. Perhaps, the findings in our study also represent a subset of patients in which nitrous oxide is not the predictor for PONV, namely in patients in which LMA was used as the airway device. Future studies will help us to delineate this finding.

Increased duration of surgery is a well-accepted risk factor for PONV and has been repeatedly supported by the literature in the pediatric population[11,17-19]. Of note, our study did not include any pediatric patient. One study found that the incidence of PONV increased by 59% for every 30 minute increase in duration of surgery[11]. Our findings followed the same trend (24% increases for every additional 30 minutes). Additionally, we found that when variables were matched, the incidence of PONV was significantly different between the ETT and LMA groups. If the groups were separated, patients with ETT had a significantly longer length of surgery compared with LMA. This finding could have accounted for the fact that ETT was associated with significantly more PONV than LMA.

It has been noted in previous publication that children and young adults are at risk for increased PONV[20]. Publications have found many variations on this trend over time. One author found that age over 50 showed a linear decrease in incidence of PONV[11]. Another researcher found that age under 50 increased the risk of PONV as compared to age over 70 years old[21]. Our study did not have any pediatric subjects and the average age of our subjects was 51 years with a range from 20 to 80 years. Similarly, our findings demonstrated that increasing age was protective against PONV. For every one year increase in age, the risk decreased by 0.7%.

We were unable to establish any correlation between the ASA physical status and the incidence of PONV. Lower ASA class has been suggested by two studies as a risk factor for PONV[21,22], and they were adopted by the Consensus Practice Guidelines published in 2003[23]. However, these studies were survey-based and therefore might have missed patients with higher ASA class. Since in our study we have excluded ASA 4 and ASA 5 patients, we cannot comment on the true effect of ASA class on PONV. Furthermore, it is likely that ETT would have been the main airway device in this high-risk population (ASA-4 and ASA-5 patients).

We also established that PONV increased PACU length of stay. Intuitively this makes sense and has been supported by studies in the past. One study found that each episode of vomiting increased time in the recovery room by about 20 minutes[23]. Our study does not address data encompassing the number of episodes of vomiting.

One factor that could not be controlled for between patients using ETT and those with LMA was neuromuscular blockade. ETT patients were all paralyzed while LMA patients were not. Neostigmine was the only reversal agent used to reverse neuromuscular blockade at the end of surgery. Neostigmine has been associated with PONV at doses greater than or equal to 2.5 mg[2]. We excluded patients receiving doses of greater than 2.5 mg.

One limitation of this study is its retrospective nature. PONV could only be determined by chart review of electronic medical records entered by PACU nurses during post-anesthesia recovery. Patients who experienced the subjective sensation of nausea but did not report these symptoms or did not want medications may have been missed.

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