A Randomised Controlled Trial for Comparison between Supplemental Oxygen and Standard Practice in Reduction of Post-Operative Nausea and Vomiting

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ABSTRACT

Background. Post-operative nausea and vomiting (PONV) is a common occurrence after surgery. With an increasing number of day surgeries and the emphasis on shorter length of hospital stay, there is an imperative need to improve the management of PONV. Post-operatively, patients are usually offered antiemetic only at the onset of nausea and vomiting. However, numerous studies have shown that the use of supplemental oxygen has considerable influence in reducing the incidence of PONV in the first 24 hours after surgery. Hence, in a bid to provide new evidence within the local setting, this study was undertaken to determine whether supplemental oxygen reduces PONV.

Methods. A total of 120 patients from a surgical ward were randomised to one of two groups. The control group received Metoclopromide only at the onset of nausea and vomiting. The study group received both supplemental oxygen immediately post-surgery and Metoclopromide at the onset of nausea and vomiting. The patients were monitored for 24 hours post-operatively for evidence of PONV using a 100mm visual analogue scale. Approval for the study was sought from the SGH Ethics Committee and the Head of Department.

Results. The occurrence of PONV in patients who had supplemental oxygen post-operatively and those who did not was 57 (57%) and 43 (43%), respectively, which was not significantly different (p=0.10). The onset of PONV in both groups was also not significantly related to supplemental oxygen (p=0.099). However, a logistic regression showed that body weight was a significant predictor, in that heavier patients were 1.1 times more likely to have nausea (p=0.037, OR = 1.07, 95% CI 1.00 to 1.15). Moreover, the results indicated a downward time trend of PONV over the first 24 hours, with peak PONV occurring during the first 30 minutes post-operatively.

Conclusion. The study showed that the use of supplemental oxygen post-operatively did not have any effect on PONV. However, the findings demonstrated that there is a potential to improve the management of PONV by initiating oxygen therapy in the Recovery Room, especially for patients at higher risk for PONV.

Keywords: nausea, post-operative, vomiting

INTRODUCTION

Post-operative nausea and vomiting (PONV) seems to be accepted as an unavoidable risk associated with surgery. Apparently, this negative attitude has remained unchanged for over 100 years, as described by Jolley.[1] Nausea and vomiting are considered to be the worst possible effects after an operation. Patients find PONV distressing, undignified, embarrassing and many consider it worse than pain.[2,3] It also prevents patients from the resumption of eating and drinking and generally delays recovery.[1]

The majority of nurses believe that PONV should be prevented to ensure a more pleasant and shorter length of hospital stay. The vast majority of patients are not aware that they can take medication to reduce the likelihood of post-operative sickness from occurring.[1] Despite increasing knowledge and research on the management of PONV, physicians still question the

necessity of treating PONV as most episodes of PONV resolve within 24 hours of surgery.

Studies have documented that more attention needs to be given to the management of PONV, as it has a major impact on patients, especially those undergoing day surgery. The currently accepted practice appears to be the administration of antiemetic only at the onset of vomiting for the majority of patients after surgery. In the Singapore General Hospital (SGH), patients are offered an antiemetic only when they are experiencing nausea and vomiting post-operatively. Supplemental oxygen has not being considered as a preventive strategy for reducing PONV.

In this era of evidence-based practice, it is important to substantiate this standard practice with current scientific evidence. Hence, this study was undertaken to determine whether the use of supplemental oxygen could reduce the incidence of PONV in SGH.

METHODS

This study aimed to answer the following questions:

1. Does supplemental oxygen effectively reduce post-operative nausea and vomiting in the first 24 hours post-surgery?
2. Does supplemental oxygen delay the onset of post-operative nausea and vomiting?

It was hypothesised that supplemental oxygen significantly reduces the incidence of post-operative nausea and vomiting when used post-operatively during the first 24 hours following surgery.

A randomised controlled trial was conducted from November 2002 to February 2003.

The target population was all adult surgical patients admitted to a general surgical ward. Patients who were scheduled for procedures in which the skin was not incised, major abdominal surgeries requiring nasogastric tube and operations done under local and epidural anaesthesia were excluded from the study. Those who had a previous history of medical problems requiring oxygen therapy before and after surgery, chronic obstructive pulmonary disease and metroclopromide allergy were also excluded.

Clinical observation suggested that the incidence of nausea and vomiting post-operatively were approximately 60% in the control group. It was anticipated that using supplemental oxygen would reduce the incidence of PONV to 30 to 40%. Based on this assumption, it was determined that a sample size of 120 patients was needed to yield a power of 80%. Each group thus comprised 60 patients.

The patients were randomised into 1 of 2 groups, using a random numbers list that was generated by the statistician. The ward clerk, who was blinded to the purpose of the study, was responsible for allocating the patients into the groups based on the list. The ward clerk then gave the group allocation number to the nurse who was transporting the patient from the Recovery Room.

In the control group, patients were given 10mg of metoclopromide after onset of nausea of 30 minutes, 2 episodes of vomiting or upon request of the patient or attending physician. No routine antiemetic was given to this group of patients.

In the study group, patients were given supplemental oxygen of 4L/min via nasal prongs within half an hour on transfer to the bed after arrival from the operating theatre, for a duration of 24 hours. In addition, metoclopromide was given after onset of nausea of 30 minutes, 2 episodes of vomiting or upon request of the patient or attending physician. In this group, no routine antiemetic was given.

The antiemetics and oxygen therapy were prescribed in the Inpatient Medication Record (IMR) and Treatment and Nurses Notes, respectively.

For each nausea rating, the number of vomiting episodes was determined from the nursing records and charts. Vomiting was scored as none, mild if there was 1 episode, moderate if there were 2 or 3 episodes, and severe if there were more than 3 episodes. Patients were asked to rate their nausea using a 100mm Visual Analogue Scale (VAS). The rating of nausea and vomiting was done by the nurses on the patients' arrival at the ward, on the second, fifth, eighth and twenty-fourth hour after surgery. Prior to the study, the staff nurses and enrolled nurses were trained on the use of the VAS, and were tested for reliability and consistency of their evaluation of nausea and vomiting by the investigators.

Using a standard questionnaire, data on patient demographics, type and duration of surgery, presence of risk factors for PONV, use of opioids for post-operative pain during the first 24 hours, and frequency and occurrence of PONV were collected:

All data were entered into SPSS version 11. Frequencies, cross-tabulation, chi-square tests and t-tests were used to analyse the data. Regressions were performed to determine the presence of PONV

Table 1. Demographics of patients in the control and study groups.

Characteristics	Control Group (n=56)		Study Group (n=60)		p-value
	Freq	%	Freq	%	
Gender					
Male	21	44.7	26	55.3	0.52
Female	35	48.3	34	51.7	
Age					
Mean (Years)	51.0		54.7		0.17
Range	22.0–82.0		20.0–80.0		
SD	13.4		15.3		

Table 2. Type of surgery.

Characteristics	Control Group (n=56)		Study Group (n=60)		Total		p-value
	Freq	%	Freq	%	Freq	%	
Type of Surgery							
Hernia Repair	11	41	16	59	27	23	
Thyroidectomy	4	50	4	50	8	7	
Cholecystectomy	12	39	19	61	31	27	
Breast	17	74	6	26	23	20	
Rectal	2	50	2	50	4	3	0.15
Excision Biopsy	6	46	7	54	13	11	
Appendicectomy	1	25	3	75	4	3	
Vascular	2	40	3	60	5	4	
Saucerisation	1	100	0	0	1	1	

between the 2 groups, adjusted for co-variates. Statistical significance was established if p=0.05.

Approval was sought from the SGH Ethics Committee and the Head of Department before commencement of the study. The patients were informed of the purpose of the study and a written consent was obtained. Patients' data were coded to ensure their anonymity. All information obtained was kept confidential and only the investigator had access to the information.

RESULTS

A total of 120 patients was randomised. However, 4 patients were withdrawn from the study because they required nasogastric tube aspiration post-surgery, leaving a final sample of 116 patients. There were 56 and 60 patients in the control and study group, respectively.

Demographic Profile

Table 1 presents the patients' gender and age. There were no significant differences in these variables between the control and study groups.

Type of Surgery

Table 2 presents the various types of surgery the patients had undergone. The main surgeries were cholecystectomy (27%), hernia repair (23%), and breast surgery (20%). No significant differences were noted between the 2 groups.

Pre-operative Risk Factors

The patients' pre-operative risk factors for PONV are presented in Table 3. There were no significant differences between the 2 groups.

Table 3. Pre-operative risk factors of patients by group.

Characteristics	Control Group (n=56)		Study Group (n=60)		p-value
	Freq	%	Freq	%	
History of PONV	7	54	6	46	0.67
History of Motion Sickness	2	50	2	50	1.0
Smoking status	6	46	7	54	0.87
Body Weight					
Mean (Kg)	60.9		58.7		
Range	38.0–90.0		35.0–89.0		0.44
SD	12.3		12.2		
LMP to Date of Surgery					
Mean (Days)	13.3		18.1		
Range	2.0–26.0		1.0–34.0		0.23
SD	7.0		11.3		

Table 4. Intra-operative risk factors of patients by group.

Characteristics	Control Group (n=56)		Study Group (n=60)		p-value
	Freq	%	Freq	%	
Opioid Anaesthesia					
Use of Fentanyl	10	48	11	52	
Use of Morphine	15	50	15	50	0.98
Use of Fentanyl and Morphine	31	48	34	52	
Anaesthetic Agent					
Use of Propofol	51	50	50	50	0.22
Use of Nitrous Oxide	47	48	51	52	0.87
Duration of Surgery					
Mean (Hours)	1.10		1.16		
Range	0.05–02.05		0.20–02.55		0.30
SD	0.31		0.33		

Table 5. Post-operative risk factors by group.

Characteristics	Control Group (n=56)		Study Group (n=60)		p-value
	Freq	%	Freq	%	
Presence of hypotension	7	54	6	46	0.67
Time of ambulation					
Mean (Hours)	15:41		15:14		
Range	1:30–22:00		4:30–23:00		0.48
SD	4:57		4:38		
Time of first oral intake					
Mean (Hours)	16.56		15.40		
Range	0.45–24.00		6.00–21.30		0.06
SD	3.57		3.43		

Table 6. Use of antiemetic post-operatively.

Characteristics	Control Group (n=56)		Study Group (n=60)		p- value
	Freq	%	Freq	%	
Antiemetic given	20	50	20	50	0.79
Antiemetic & Analgesia given	12	41	17	59	0.39
Frequency of antiemetic given					
Mean	0.5		0.6		
Range	0.0–2.0		0.0–4.0		0.95
SD	0.7		1.0		

Table 7. Use of post-operative opioid analgesia.

Characteristics	Control Group (n=56)		Study Group (n=60)		p- value
	Freq	%	Freq	%	
Presence of pain	40	49	42	51	0.89
Use of opioid analgesia	20	44	25	56	0.51
Frequency of opioid analgesia use					
Mean	0.6		0.6		
Range	0.0–4.0		0.0–4.0		0.81
SD	1.0		1.0		

Table 8. Occurrence of PONV during the first 24 hours.

Characteristics	Control Group (n=56)		Study Group (n=60)		p-value
	Freq.	%	Freq.	%	
Nausea during first 24 hrs	34	43	45	57	0.10
Vomiting during first 24 hrs	7	50	7	50	0.90

Intra-operative Risk Factors

Data on intra-operative risk factors for PONV are presented in Table 4. There were no significant differences between the 2 groups.

Post-operative Risk Factors

The post-operative risk factors for PONV are presented in Table 5. No significant differences were noted in the 2 groups.

Use of Antiemetic Post-operatively

Table 6 presents the frequency of antiemetic used post-operatively and whether it was given in combination with analgesia. Antiemetic was given equally in the 2 groups but more than 50% were given in combination with analgesia.

Use of Post-operative Opioid Analgesia

Table 7 shows the distribution of post-operative opioid analgesia used by the study and control groups. About half of these patients required opioid analgesia. The most common opioid analgesia used were pethidine (22%), followed by codeine phosphate (8%).

Occurrence of PONV during First 24 hours

Table 8 presents the occurrence of PONV in the 2 groups during the first 24 hours post-operatively. No significant differences were noted.

Use of Antiemetic in the Recovery

Table 9 shows the distribution of antiemetic given in the recovery in the control and study groups. About three-quarters of patients in the control group were

Table 9. Use of antiemetic in the recovery.

Characteristics	Control Group (n=56)		Study Group (n=60)		p-value
	Freq.	%	Freq.	%	
Use of Antiemetic	9	75	3	25	0.05

Table 10. Visual Analogue Scale for nausea by group.

Hours	Control Group (n=56)					Study Group (n=60)					p-value
	0.50	2.00	5.00	8.00	24.00	0.50	2.00	5.00	8.00	24.00	
VAS Nausea											
Mean	1.4	1	0.7	0.3	0.2	1.6	1.5	1.0	0.5	0.2	
Range	0–8	0–6	0–4	0–4	0–3	0–7	0–8	0–7	0–7	0–3	0.63
SD	1.9	1.5	1.2	0.7	0.6	1.8	2	1.7	1.4	0.6	

given antiemetic. A significant difference was noted between the 2 groups.

Visual Analogue Scale for Nausea by Group

The VAS scores for PONV during the first 24 hours in the 2 groups are presented in Table 10. There was no differences between the groups (p=0.142).

The VAS scores for the 2 groups were also plotted in Figure 1. It can be noted that there was no significant difference between the treatment (p=0.142) but a significant downward time trend effect (p<0.001). However, there is no treatment-time interaction (p=0.628).

Predicators for PONV

A multiple linear regression was performed for the maximum nausea VAS score, and was adjusted for the risk factors (gender, age, body weight, history of PONV, history of motion sickness, smoking status) and treatment groups. The finding showed that body weight was a significant predictor, that is, heavier patients were 1.1 times more likely to have nausea (p=0.037, OR=1.07, 95% CI 1.00 to 1.15) compared to lighter patients.

DISCUSSION

Studies have shown that the occurrence of PONV averages about 20 to 30%.[4] The peak incidence of nausea and vomiting is said to be about 6 hours after surgery.[5]

Nausea and vomiting can pose potential serious complications, such as aspiration pneumonia, wound dehiscence, raised intracranial pressure, dehydration and electrolyte imbalance.[5] Nausea and vomiting can also have psychological effects on patient, such as discomfort and distress; shame and embarrassment; exhaustion; dissatisfaction with the outcome of the operation and fear of further surgery.[2] In addition, PONV leads to increased economic cost from increased time spent in the recovery area, and in nursing and medical time. Additional drugs and supplies, increased time to retention of normal diet and prolonged hospital stay also increase the cost of care. There will also be time lost from work by patients and those looking after them.[5]

In her study, Thompson studied the various risk factors that trigger PONV.[4] These include stimuli before, during and after the operative procedure. The pre-operative stimuli that may trigger PONV include patient-related factors such as age, gender, hormonal balance, weight, gastric contents, prior experience, and history of motion sickness and anxiety. Adults over the age of 55 are less likely to experience PONV than their younger counterparts.[6] Until the onset of puberty, the incidence of PONV is essentially the same in males and females. After puberty, women are 3 times more likely to experience PONV and vomiting tends to be more severe as shown in the study by Hawthorn quoted by Jolley.[1]

Recent literature has shown that the closer a woman is to menstruation, the more likely the woman is to

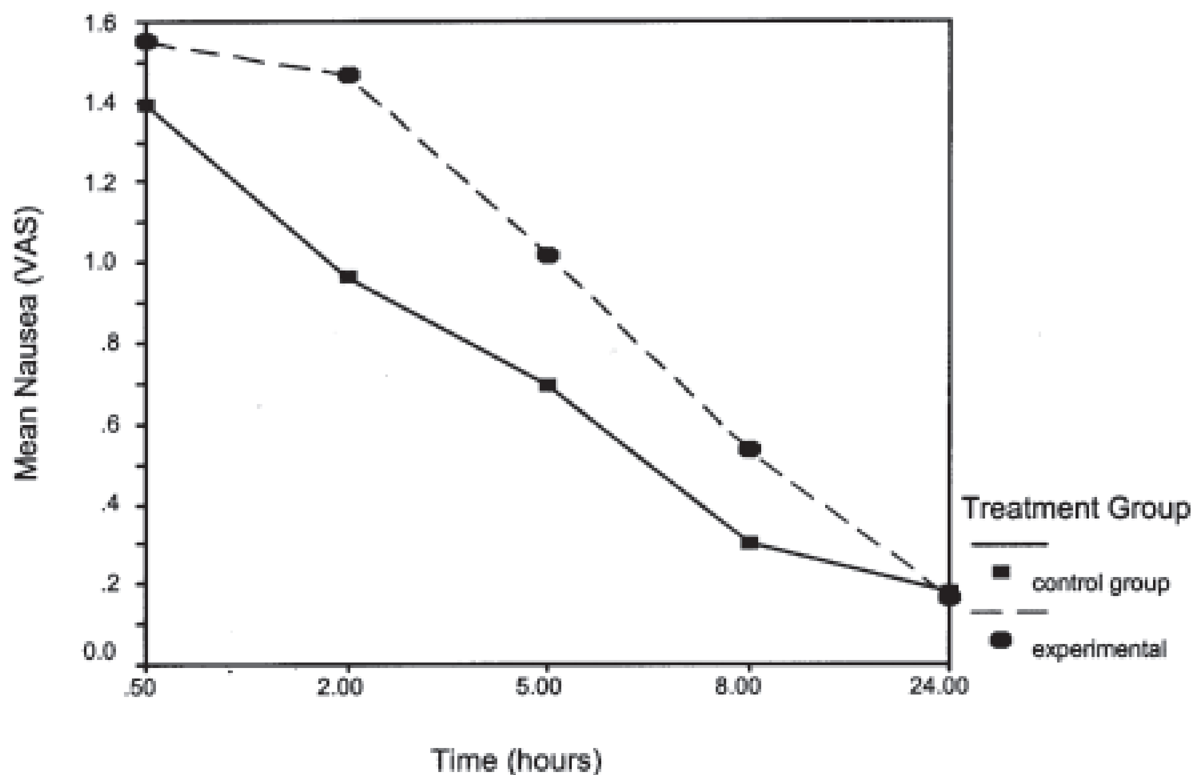

Fig. 1. VAS Scores for the control and study groups.

experience PONV.[6] A retrospective study by Beattie *et al* showed that menstruation at the time of surgery increased the likelihood of vomiting to four times greater than normal.[7] An obese patient is more likely to experience PONV due to the longer time required to clear anaesthetics from the body because of the affinity of adipose tissue for agents used in anaesthesia. A full stomach is associated with increased incidence of vomiting both during induction and recovery from anaesthesia.[1] Eating and digestion trigger the release of gut hormones that may sensitise the area postrema in the brain stem and facilitate emesis.[8,9] A patient with previous history of PONV or motion sickness is known to experience increased anxiety and subsequently has a higher likelihood of PONV.[10]

Intra-operatively, various factors, such as the type of operation performed, duration of the operation and type of anaesthetic drug used, have also been shown to have an influence on PONV. Gynaecological and abdominal surgical procedures have an increased risk due to disturbance of the gut during the procedure.[11] Patients undergoing laparoscopic surgeries are at risk of PONV due to abdominal distension secondary to the use of carbon dioxide for visualisation during the surgery.[4] The risk of developing PONV is increased with longer anaesthesia time due to increased time to clear anaesthesia from the system and increased time of intestinal ileus.[6] General anaesthesia is associated with a higher rate of PONV than face-mask anaesthesia or regional blocks.[12] Inhalation agents including nitrous oxide and volatile anaesthetic are associated with PONV.[13]

The post-operative factors influencing the development of PONV include pain, hypotension, use of opioid analgesia, movement and oral intake. The sensation of pain is known to be a factor in the development of nausea due to a reduction in the oxygen supply available to tissues.[14] Although narcotics given for sedation and analgesia increase frequency of PONV, Andersen and Krohg found less PONV when patients received adequate narcotic analgesia in the Recovery Room.[15] Use of opioid for analgesia has an emetic influence. Use of morphine slows the gastrointestinal tract motility and stimulation of the vestibular nerve, and thus may induce PONV. Postural hypotension as a result of restriction of fluids pre-operatively, intra-operative blood loss or use of anaesthetics and analgesics may also induce nausea.

Movement of the patient has also been associated with increased incidence of PONV. Patients who rate high on motion sickness susceptibility surveys were found

to have increased incidence of movement-induced PONV and a decreased incidence when movement of the conscious patient was avoided.[16] The restriction of oral intake until return of bowel function has also been shown to delay and possibly decrease the incidence of PONV.[6] Early ingestion of fluid in the post-operative period also contributes to emesis.[17]

PONV should not be considered as unavoidable by the patient, as many strategies for successful prevention and management are available. Metoclopramide has been used for almost 40 years to prevent PONV and is a standard drug used in SGH. Metoclopramide has both peripheral and central antiemetic actions by blocking the dopaminergic receptor in the Chemoreceptor Trigger Zone and increasing gastric motility and sphincter tone.[18]

Prophylactic administration of effective antiemetic drugs is said to reduce the incidence of gastrointestinal complications, thereby lowering the risk of PONV, although antiemetic therapy is costly and has a 3% incidence of complications.[19] However, a study by Henzi *et al* showed no evidence of dose responsiveness or significant anti-nausea effect after the use of Metoclopramide post-surgery.[20] Nonetheless, it was recommended that for the prevention of PONV, anti-emetic drugs may be given prior to induction of anaesthesia or shortly after surgery. The question of whether to provide prophylactic treatment for PONV will depend upon an assessment of the risk factors associated with the individual patient and type of surgical procedure being undertaken. Repeated dosing for patients who continue to experience nausea and/or vomiting post-operatively has not been studied.

Greif *et al* speculated that oxygen therapy may be useful to reduce PONV due to its potential in preventing surgically induced intestinal ischaemia.[14] During abdominal surgery, the intestines do not get the usual amount of oxygen, due to surgical cutting or temporary displacement of organs to facilitate surgery. Tissues are known to react to an inadequate oxygen supply by releasing neurotransmitters and other potent chemical messengers that in turn cause nausea and vomiting. The extra oxygen may help the tissue avoid this reaction. In their study, routine 30% oxygen and supplemental 80% oxygen were administered and maintained during and for 2 hours after colon resection via a rebreathing mask to 2 groups of patients. The results showed that supplemental oxygen reduced the incidence of PONV from 30% in those patients given 30% oxygen to 17% in those given 80% oxygen (P=0.027). The incidence was nearly reduced by half by giving supplemental oxygen.

In another study, Goll *et al* compared the effectiveness of ondansetron (an antiemetic) and supplemental oxygen in the prevention of PONV.[21] The study concluded that supplemental oxygen effectively prevented PONV after gynaecological laparoscopic surgery. Furthermore, ondansetron was noted to be no more effective than supplemental oxygen. Other studies have also shown that oxygen may also be effective in the management of PONV. Kober *et al* noted that oxygen administration during ambulance transport reduced nausea and vomiting by 50% in patients with minor trauma.[22]

Since supplemental oxygen is inexpensive and essentially risk-free, it appears preferable to pharmacologic anti-emetics in the prevention of PONV. One reason why physicians have been cautions about increasing oxygen administration during surgery is concern about an increased risk of atelectasis. However, Greif *et al* showed that atelectasis was not a problem.[14] A study by Rothen *et al* showed that the composition of inspired gas was important in atelectasis formation during general anaesthesia.[23] The study suggested that the use of a lower oxygen concentration might prevent the early formation of atelectasis.

In view of the low cost of oxygen administration and the few risks associated with it, supplemental oxygen therapy is a reasonable and cost-effective way to achieve better post-surgical outcomes such as the unpleasantness of nausea and vomiting. Supplemental oxygen at low flow of 4l/min (36%) via nasal prongs would be ideal therapy for 24 hours after surgery.

In this study, the use of supplemental oxygen did not significantly reduce the occurrence of nausea and vomiting in post-surgery patients. However, in absolute numbers, there is a trend suggesting lower occurrence of PONV in the study group. This non-significant finding is in contrast with that of a previous study done by Greif *et al* in 1999.[18] Three main factors may have contributed to the similarity in PONV occurrence between the control and study groups.

Between 4 to 10% of patients were given antiemetic either intra-operatively or in the Recovery Room. It was interesting to note that 50% more of the patients in the control group received antiemetic in the Recovery Room than the study group. As a consequence, it would be expected that patients in the control group would experience a decrease in PONV on arrival to the ward when compared to the experimental group. This may have contributed to the non-significant finding.

A second factor may be related to the administration of analgesia. When patients experience pain, it is a standard practice in the general surgical ward that opioids and antiemetic are given concurrently as a prophylaxis. As a result, patients in this study received antiemetic together with their analgesia regardless of whether they were experiencing nausea or vomiting. As this factor potentially confounds the result, it could not be conclusively drawn that supplemental oxygen was not effective for preventing PONV.

Third, the study group, on the average, had their first oral intake an hour earlier than the control group. This might explain the non-significant difference between the two groups considering that oral intake is a potential risk factor for PONV. This finding adds support to the evidence that timing of first oral ingestion can have an important effect on the onset of PONV.

An interesting finding from this study was that there was a downward trend of VAS rating on nausea in conjunction with the duration of post-operative time in the ward. The peak incidence of nausea and vomiting has been reported to be about 6 hours after surgery.[7] However, this study showed that the highest rating of nausea was in the first 30 minutes on arrival to the ward for both groups. This suggests that supplemental oxygen therapy should commence as early as in the Recovery Room to reduce the early effect of PONV, rather than on arrival to the ward as was the case in this study.

Another notable finding was that body weight was a significant predictor for PONV, with heavier patients more likely to experience it. The other risk factors were not found to be significant predictors, as opposed to the findings of Greif *et al.*[18]

LIMITATIONS OF THE STUDY

This study did not take into consideration the standard practice of giving opioids concurrently with antiemetic as a prophylaxis. A difference in PONV between the 2 groups may have been apparent if this confounding factor had been controlled for in the study. In addition, although the study stipulated that supplemental oxygen was to be given for a duration of 24 hours post-operatively, it was not possible to do so due to early discharge of patients.

CONCLUSION

This study showed that the administration of supplemental oxygen post-operatively did not have a significant effect on PONV. However, the findings highlighted a downward trend of nausea, despite the mode of intervention. More importantly, the finding of peak PONV within the first 30 minutes post-surgery suggested that there was a potential to improve the management of PONV by initiating oxygen therapy in the Recovery Room, especially for those patients with known risk factors for PONV.

Despite the non-significant finding, it may still be worthwhile to explore the possibility of using oxygen therapy instead of giving antiemetics concurrently with opioids as a prophylaxis, especially since supplemental oxygen is inexpensive and essentially risk-free.

Arising from this study's findings and evidence from literature, it is suggested that prophylactic supplemental oxygen should be initiated at the Recovery Room for patients at risk of developing PONV; an appropriate assessment tool should be formulated to assist in identifying a patient's risk factors and providing pre-operative teaching on prevention of PONV, and a more precise assessment for PONV using the VAS should be designed so that early intervention and treatment can be given to the patient.

ACKNOWLEDGEMENTS

The research team gratefully acknowledges the following persons for their kind assistance and contributions: Dr Chan Yiong Huak, Ms Wong Hwee Bee, staff of Medical Record Office, Mdm Png Hong Hock, Ms Tracy Carol Ayre, Ms See Keow Ann, staff of Ward 57and Ms Carol Ong.

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