British Journal of Anaesthesia **112** (3): 460–8 (2014)
Advance Access publication 14 October 2013 · doi:10.1093/bja/aet335

BJA

CARDIOVASCULAR

Effect of palonosetron on the QTc interval in patients undergoing sevoflurane anaesthesia

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Editor's key points

- Many anti-emetics, including all first-generation 5-HT$_3$ receptor antagonists, increase the duration of the QT interval of the electrocardiogram.
- Recent preliminary data suggest that palonosetron, a longer-acting anti-emetic, may have lower risk of inducing QT prolongation.
- This study finds that sevoflurane anaesthesia was associated with a small increase in the mean duration of the QT interval, including a minority with a QT-corrected interval >500 ms.
- Palonosetron given before induction of anaesthesia had no effect on the QT interval after its administration and during surgery.

Background. Palonosetron is a recently introduced 5-HT$_3$ receptor antagonist for postoperative nausea and vomiting. Detailed standardized evaluation of corrected QT (QTc) interval change by palonosetron under sevoflurane anaesthesia is lacking. We evaluated QTc intervals in patients who are undergoing surgery with sevoflurane anaesthesia and receive palonosetron.

Methods. Our study included 100 patients who were undergoing elective surgery under sevoflurane anaesthesia. The patients were randomly assigned to two groups: those who received an i.v. injection of palonosetron 0.075 mg immediately before induction of anaesthesia (pre-surgery group, n=50) and those who received it after surgery in the recovery room (post-surgery group, n=50). QTc intervals were measured before operation, intraoperatively (baseline, immediately after tracheal intubation, and at 2, 10, 15, 30, 60, and 90 min after administration of palonosetron or placebo), and after operation (before and at 3, and 10 min after administration of palonosetron or placebo). QTc intervals were calculated using Fridericia's, Bazett's, or Hodges formulas.

Results. The perioperative QTc intervals were significantly increased from the baseline values, but were not affected by the pre- or post-surgical timing of palonosetron administration.

Conclusions. There was no significant difference in the QTc intervals during the perioperative period, whether 0.075 mg of palonosetron is administered before or after sevoflurane anaesthesia. Palonosetron may be safe in terms of QTc intervals during sevoflurane anaesthesia.

Clinical trial registration. ClinicalTrials.gov: NCT01650961.

Keywords: anti-emetics; electrocardiography; palonosetron; postoperative nausea and vomiting; serotonin 5-HT$_3$ receptor antagonists; sevoflurane

Accepted for publication: 26 July 2013

5-HT$_3$ receptor antagonists have been widely used for the prevention and treatment of postoperative nausea and vomiting (PONV) in patients receiving general anaesthesia.[1] However, the first-generation 5-HT$_3$ receptor antagonists such as ondansetron, dolasetron, and granisetron have been associated with cardiovascular adverse events such as ventricular arrhythmia, atrial fibrillation, myocardial ischaemia, and cardiac arrest.[2–7] One reason for cardiac complications seems to be a tendency to block cardiac potassium and sodium ion channels, resulting in increasing corrected QT (QTc) intervals.[8–10]

Palonosetron is the second-generation 5-HT$_3$ receptor antagonist which has recently been approved for PONV prophylaxis. It has the greatest potency and the longest duration of action of 24 h among 5-HT$_3$ receptor antagonists.[11 12] Several clinical studies have shown that palonosetron is effective for PONV prophylaxis.[13 14] However, by possessing similar pharmacological mechanisms as ondansetron, palonosetron may theoretically prolong the QTc interval and increase the risk of life-threatening arrhythmias. Therefore, some anaesthesiologists are reluctant to use palonosetron in patients who have an increased risk of QTc interval prolongation. Although the prescribing information deleted the warnings of QTc prolongation of palonosetron for the PONV dose recently,[15] the study will be helpful in investigating QTc prolongation by palonosetron in detailed and standardized methods.

Some randomized studies have shown that palonosetron does not increase the QTc interval when compared with control groups in patients undergoing surgery.[13 14] However, since the primary outcome of these studies was not QTc data, QTc intervals were measured only two times regardless of anaesthetic duration. The types of anaesthetic agents which influence the heart during anaesthesia have not yet been fully identified, although sevoflurane is known to induce QTc interval prolongation.[16 17] The mechanism of QTc interval prolongation of sevoflurane is the inhibition of cardiac potassium ion channels similar to that of the first-generation 5-HT_3 receptor antagonists. Therefore, if palonosetron and sevoflurane have combined effect on the cardiac ion channels, palonosetron may induce QTc interval prolongation under sevoflurane anaesthesia. However, to the best of our knowledge, there have been no randomized studies to investigate the effects of palonosetron on the QTc interval under sevoflurane anaesthesia.

We hypothesized that palonosetron would increase the QTc interval in patients who were undergoing sevoflurane anaesthesia. Therefore, this study was conducted to evaluate the effects of palonosetron on QTc intervals in patients undergoing surgery under sevoflurane anaesthesia.

Methods

This prospective, randomized, double-blind study was approved by the Institutional Review Board of Seoul National University Hospital (Ref: H-1203-050-401) and registered at ClinicalTrials.gov (NCT01650961). Written informed consent was obtained from each patient after complete description of the study protocol.

Patients

We enrolled 100 patients aged 20–75 who were undergoing elective abdominal or gynaecological surgery under general anaesthesia with an expected duration of more than 1.5 h between July 2012 and December 2012. Exclusion criteria were as follows: histories of previous PONV; ischaemic heart disease; valvular heart disease; diabetes mellitus; significant arrhythmias, including atrial fibrillation, bundle branch block, or atrioventricular block; QTc prolongation of more than 500 ms on preoperative ECG; hypokalaemia on preoperative laboratory tests; patients who received QT-prolonging medications, such as antiarrhythmics, antibiotics, calcium channel blockers, β-blockers, or antipsychotics;[18 19] patients who received antiemetics, opioids, steroids, cancer chemotherapy, or radiotherapy within 1 month before surgery.

Groups

Patients were randomly divided into two groups—the pre-surgery (n=50) and post-surgery (n=50) groups—using a computer-generated random number table. Medication was administered to the two groups as follows.

- The pre-surgery group received palonosetron (Aloxi®, Helsinn Healthcare, SA, Switzerland) 0.075 mg i.v. immediately before induction of general anaesthesia and 1.5 ml of normal saline, which is the same volume as 0.075 mg of palonosetron, i.v. immediately after the first postoperative QTc interval was recorded in the recovery room.
- The post-surgery group received 1.5 ml of normal saline, which is the same volume as 0.075 mg of palonosetron, i.v. immediately before induction of general anaesthesia and 0.075 mg palonosetron i.v. immediately after the first postoperative QTc interval was recorded in the recovery room.

Palonosetron or normal saline was prepared by a single nurse who was not involved in the collection of data and patient care. These two medications of the same colour and volume were indistinguishable to the anaesthesiologists who were in charge of anaesthesia.

Anaesthesia

Routine monitoring of arterial pressure, three-lead ECG, oxygen saturation, and bispectral index (BIS) were applied. General anaesthesia was induced with propofol in doses of 2–2.5 mg kg^{-1} and tracheal intubation was facilitated with rocuronium in a dose of 0.6 mg kg^{-1}. Anaesthesia was maintained using sevoflurane 1–3% with oxygen/air (fractional inspired oxygen 0.4) targeting BIS values between 40 and 60. To measure serum concentrations of potassium, calcium, and magnesium, 4 ml blood samples were obtained from all patients before the start of surgery. The anaesthesiologists who conducted general anaesthesia were blinded to the study groups. Medications were used for haemodynamic stabilization and analgesic supplementation during surgery at the discretion of the anaesthesiologists. Patient-controlled analgesia (PCA) was applied at the end of surgery in the operating theatre. The PCA regimen consisted of fentanyl 25 μg kg^{-1} diluted with 100 ml of normal saline in a bolus dose of 0.5 ml at lockout intervals of 15 min and with a background infusion of 1 ml h^{-1}. After tracheal extubation, patients were transferred to the recovery room and observed for at least 1 h. A cardiac defibrillator and a resuscitation cart containing emergency medications such as magnesium sulphate were available in the operating theatre and the recovery room for the immediate treatment in the case of developing a life-threatening arrhythmia.

QTc interval measurement

In all patients, preoperative QTc intervals were recorded routinely using a 12-lead ECG machine in the ward or outpatient clinic. Intraoperative QTc intervals were obtained at the following time points: before anaesthetic induction (baseline), immediately after tracheal intubation, and 2, 10, 15, 30, 60, and 90 min after administration of palonosetron or placebo in the operating theatre. Postoperative QTc intervals were assessed three times (before and at 3 and 10 min after administration of palonosetron or placebo) in the recovery room; these time points were expressed as R, R3, and R10, respectively.

ECG signals were recorded using the continuous monitoring ECG system (Solar® 8000 M, GE Medical System, Milwaukee, WI, USA) in the operating theatre and recovery room. ECG data in

lead II were extracted with the analogue-to-digital converter (DI-149, DATAQ instruments Inc., Akron, OH, USA), which was connected into the analogue output on the patient monitor and stored on a personal computer. The sampling rate was 1000 Hz.

ECG data were analysed using LabChart software (Version 6, AD Instruments, Colorado Springs, CO, USA).[20] At first, the QTc interval was measured automatically by LabChart software. At the time of each QTc interval measurement, the ECG curves of the four consecutive beats were averaged to acquire a more accurate representation of the ECG waveform. The start of the QRS wave and the end of the T wave were determined automatically and the QT interval was calculated.

All automatic measurements were checked manually by a single trained researcher (H.J.K.) and then confirmed by a single cardiologist (E.-K.C.). They were all blinded to the study groups during the process. If the automatic method did not correctly detect the onset of the QRS complex or the end of the T wave, the QT interval was measured manually after the markers on the ECG wave were dragged to more exact positions.

The QTc interval was calculated using three formulas to preclude interference by heart rate (HR) on the QT interval: Bazett's formula ($QTcB=QT/RR^{1/2}$), Fridericia's formula ($QTcF=QT/RR^{1/3}$), or Hodges formula [$QTcH=QT+105(1/RR-1)$].[21 22] The perioperative mean arterial pressure (MAP), HR, and the end-tidal concentration of sevoflurane (ETsevo) were also measured.

Postoperative nausea and vomiting

The trained nursing staff, who was blinded to the study groups, recorded the episodes of PONV in the recovery room. The other nurses, who were also blinded to the study groups, recorded the occurrences of PONV in the ward after the patients were transferred to the ward. The anaesthesiologist (Y.S.J.), who was blinded to the study groups, assessed PONV by visiting the patients in the ward and checking the data recorded by the nurse. The occurrences of PONV were evaluated at intervals of 0–2 and 2–24 h after surgery and the incidence was recorded. Nausea was defined as an unpleasant sensation accompanied by the urge to vomit. Vomiting was defined as spasmodic contraction of the respiratory muscles with or without forceful expulsion of stomach contents.[23] The severity of nausea was assessed based on a four-point categorical scale of none, mild, moderate, and severe nausea.[14] The use of additional anti-emetics was at the discretion of anaesthesiologists when the patient had severe nausea or requested the rescue anti-emetics. A complete response was defined as an absence of both emetic episodes and the use of rescue medications for PONV.[24] Side-effects, such as headache, dizziness, drowsiness, myalgia, and constipation, were also evaluated.

Statistical analysis

The primary outcome was the QTcF interval which was measured immediately after tracheal intubation.[21] Assuming that the standard deviation (SD) of the QTcF intervals was 23 ms based on a previous report[20] for a type 1 error of 0.05 and a power of 0.9, sample size was determined to detect a difference of 15 ms in the QTcF intervals between the pre-surgery and post-surgery groups. The assumed means of the QTcF intervals were 444 and 429 ms in the pre-surgery and post-surgery groups, respectively. Power analysis suggested that a minimum of 100 patients would be required. The Student

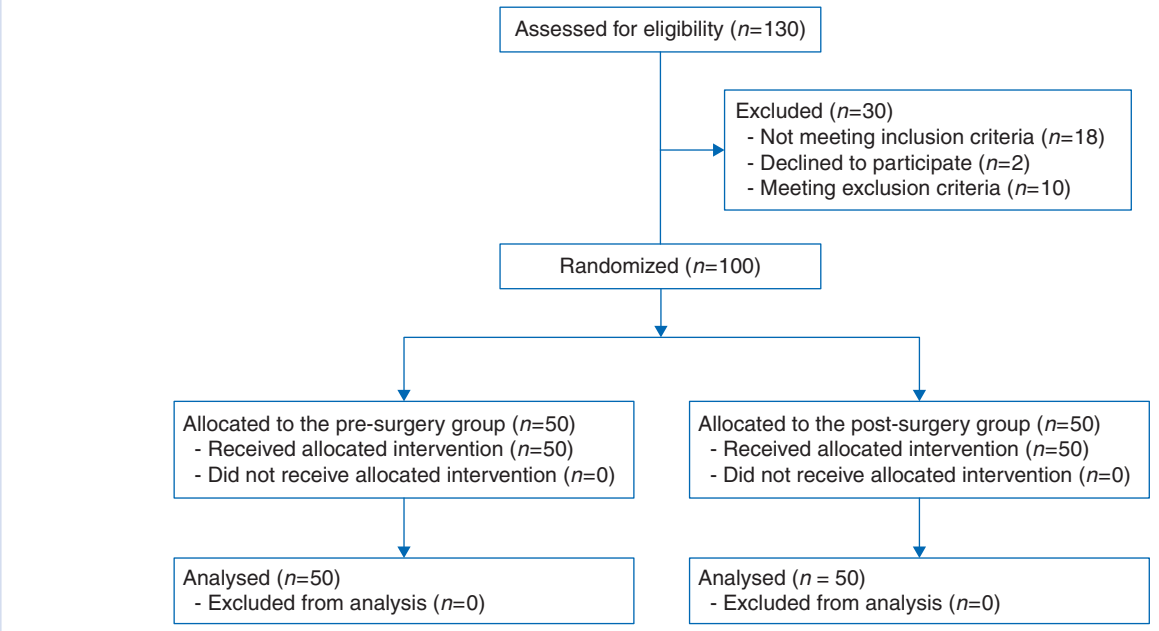

Fig 1 Flow diagram.

t-test or Mann–Whitney *U*-test was used to compare continuous variables between the pre-surgery and post-surgery groups. The χ^2 test or Fisher's exact test was used for categorical variables. The QTc intervals at different time points were compared using repeated-measures analysis of variance (RMANOVA) by using the Bonferroni method. The MAP and HR at different time points were also compared using RMANOVA. A QTc interval >500 ms is commonly considered to be clinically important as an alarming sign indicative of increased risk for life-threatening arrhythmia after drug administration.[19] Therefore, we identified and compared the number of patients with a QTc interval of >500 ms at measured time points between the pre-surgery and post-surgery groups using Fisher's exact test according to the US guidelines.[25] Data were presented as means (SD) or number of patients (%). SPSS for Windows version 18.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Results were considered statistically significant if the *P*-value was <0.05.

Results

Of the 130 patients who were screened for enrolment, 30 were excluded because they did not meet inclusion criteria or refused to participate in the study (Fig. 1). A total of 100 enrolled patients completed this study. Patient characteristics were not significantly different between the pre-surgery and post-surgery groups (Table 1). Nor were there any significant differences in preoperative QTc intervals on ECG between the groups (Table 1).

Serum electrolyte levels of calcium, potassium, and magnesium were not significantly different between the pre-surgery and post-surgery groups during anaesthesia before the start of surgery. The number of patients who were administered one of the drugs during anaesthesia, including ephedrine, phenylephrine, labetalol, nicardipine, esmolol, atropine, fentanyl, or calcium, were not significantly different between the two groups. The ETsevo were not significantly different between the two groups at 2, 10, 15, 30, 60, and 90 min after administration of palonosetron or placebo (Table 1). At the time point of immediately after the tracheal intubation, ETsevo was not significantly different between the pre-surgery and post-surgery groups [1.4 (0.4)% *vs* 1.5 (0.5)%, *P*=0.17]. There were no significant differences in perioperative HR or MAP changes between the two groups (*P*=0.25 and 0.65, respectively) (Fig. 2).

The perioperative QTc intervals are shown in Figure 3. There were no significant differences in perioperative QTc changes over time between the pre-surgery and post-surgery groups, regardless of the calculation methods, including Bazett's, Fridericia's, and Hodges formulas (*P*=0.87, 0.75, and 0.87, respectively) (Fig. 3). The perioperative QTcF or QTcH intervals were significantly increased at all measured time points compared with the baseline values (Fig. 3). The perioperative QTcB intervals were also significantly increased at 10 min after the anaesthetic induction compared with the baseline value, and this significant increase was observed until the last measured time point (Fig. 3). At the time point of immediately after tracheal intubation, QTcF, QTcB, and QTcH intervals were not significantly different between the pre-surgery and post-surgery groups [427.3 (24.6) *vs* 425 (21.2) ms, *P*=0.62; 462.9

Table 1 Patient characteristics and clinical data. Data are presented as the mean (range or SD) or the number of patients. ETsevo, end-tidal concentrations of sevoflurane; PCA, patient-controlled analgesia

	Pre-surgery group (*n*=50)	Post-surgery group (*n*=50)	*P*-value
Age (yr)	54 (31–75)	51 (25–75)	0.29
Weight (kg)	64.8 (10.2)	61.6 (10.8)	0.13
Height (cm)	164.3 (8.3)	163.5 (9.3)	0.66
Body mass index (kg cm^{-2})	23.9 (3.1)	22.9 (2.8)	0.08
Male/female	31/19	30/20	1.00
Smoking status			
Current smoker	8	11	0.61
Non-smoker	42	39	
Type of surgery			
Abdominal surgery	47	47	1.00
Gynaecological surgery	3	3	
Laparoscopic surgery	13	8	0.32
Open surgery	37	42	
Preoperative QTc interval	418.5 (18.8)	419.9 (20.9)	0.72
Duration of anaesthesia (min)	250.6 (80.9)	254.5 (81.3)	0.81
Serum electrolyte levels			
Calcium (mmol litre^{-1})	1.09 (0.08)	1.09 (0.07)	0.89
Potassium (mmol litre^{-1})	3.83 (0.37)	3.83 (0.35)	0.98
Magnesium (mg dl^{-1})	2.08 (0.51)	2.03 (0.36)	0.56
Use of drugs during anaesthesia			
Ephedrine	28	28	1.00
Phenylephrine	1	0	1.00
Labetalol	3	1	0.62
Nicardipine	9	7	0.79
Esmolol	3	3	1.00
Atropine	1	1	1.00
Fentanyl	20	22	0.84
Calcium	15	8	0.10
ETsevo (%) during anaesthesia			
2 min	1.4 (0.4)	1.3 (0.5)	0.9
10 min	1.3 (0.4)	1.4 (0.4)	0.2
15 min	1.4 (0.3)	1.4 (0.4)	0.3
30 min	1.6 (0.4)	1.6 (0.4)	0.9
60 min	1.7 (0.4)	1.7 (0.4)	0.4
90 min	1.7 (0.4)	1.7 (0.4)	0.3
Fentanyl in PCA regimen within 24 h after surgery (μg)	478.3 (191.5)	480.8 (188.7)	0.39

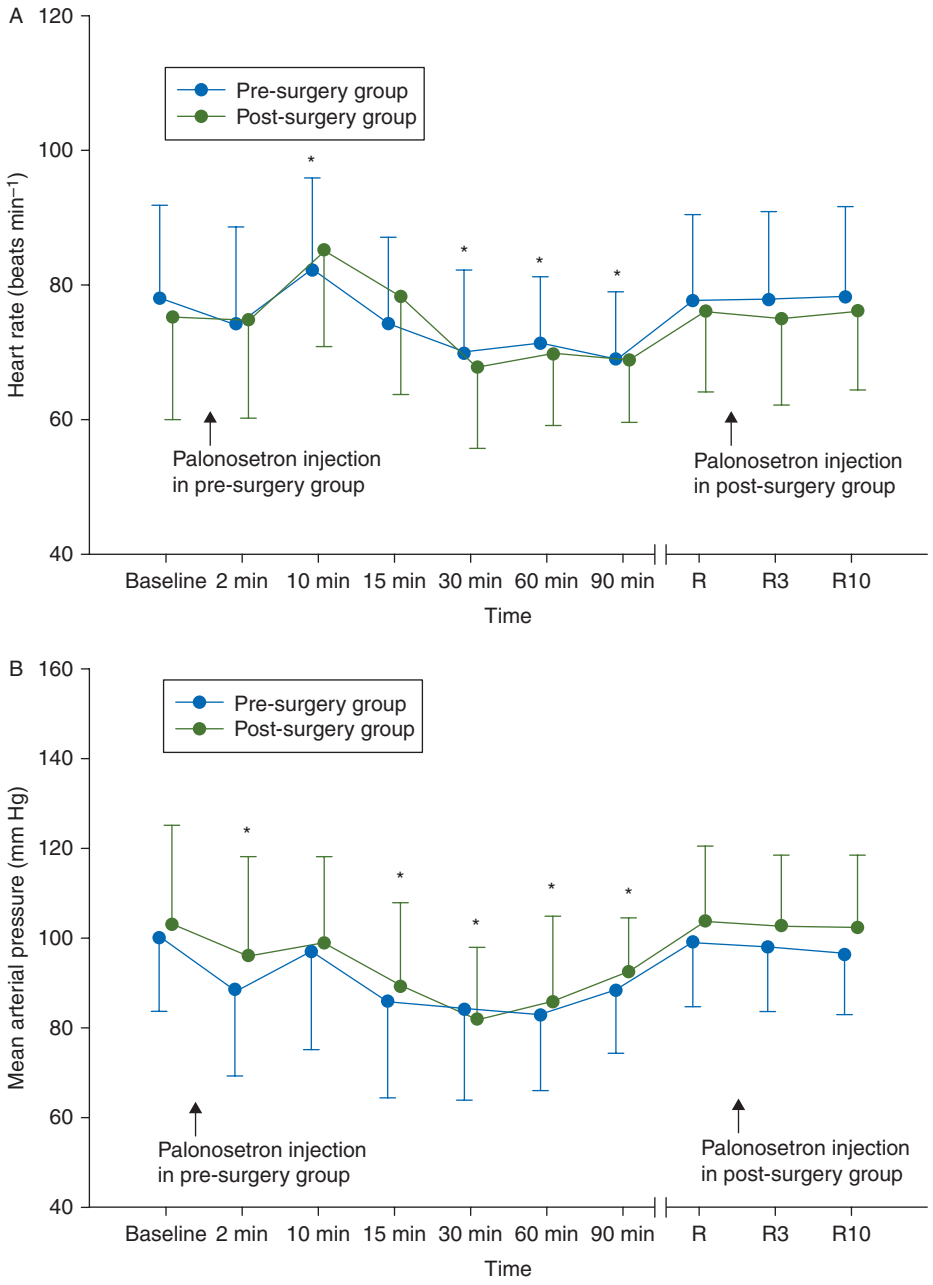

Fig 2 Changes in HR (A) and MAP (B) during the perioperative period. Baseline; 2, 10, 15, 30, 60, and 90 min after administration of palonosetron or placebo in the operating theatre; R, in the recovery room; R3 and R10, 3 and 10 min after administration of palonosetron or placebo in the recovery room. *$P<0.05$ *vs* the baseline value. Error bars indicate SD.

(28.5) *vs* 465.3 (24.9) ms, $P=0.66$; 431.4 (21.9) *vs* 432.7 (19.1) ms, $P=0.75$, respectively]. The number of patients, who showed QTc intervals >500 ms, is presented in Table 2. There was no significant difference in the occurrence of QTc intervals >500 ms between the pre-surgery and post-surgery groups during the perioperative period ($P>0.05$).

There were no significant differences in the incidence of PONV during 24 h after surgery, the use of additional antiemetics, and the incidence of side-effects, such as headache, dizziness, drowsiness, constipation, and myalgia between the two groups (Table 3). The number of patients who showed complete responses during 24 h after surgery were not significantly different between the pre-surgery and post-surgery groups [47 (94) *vs* 45 (90), $P=0.72$]. None of the patients experienced significant arrhythmias or cardiovascular events during the observation period.

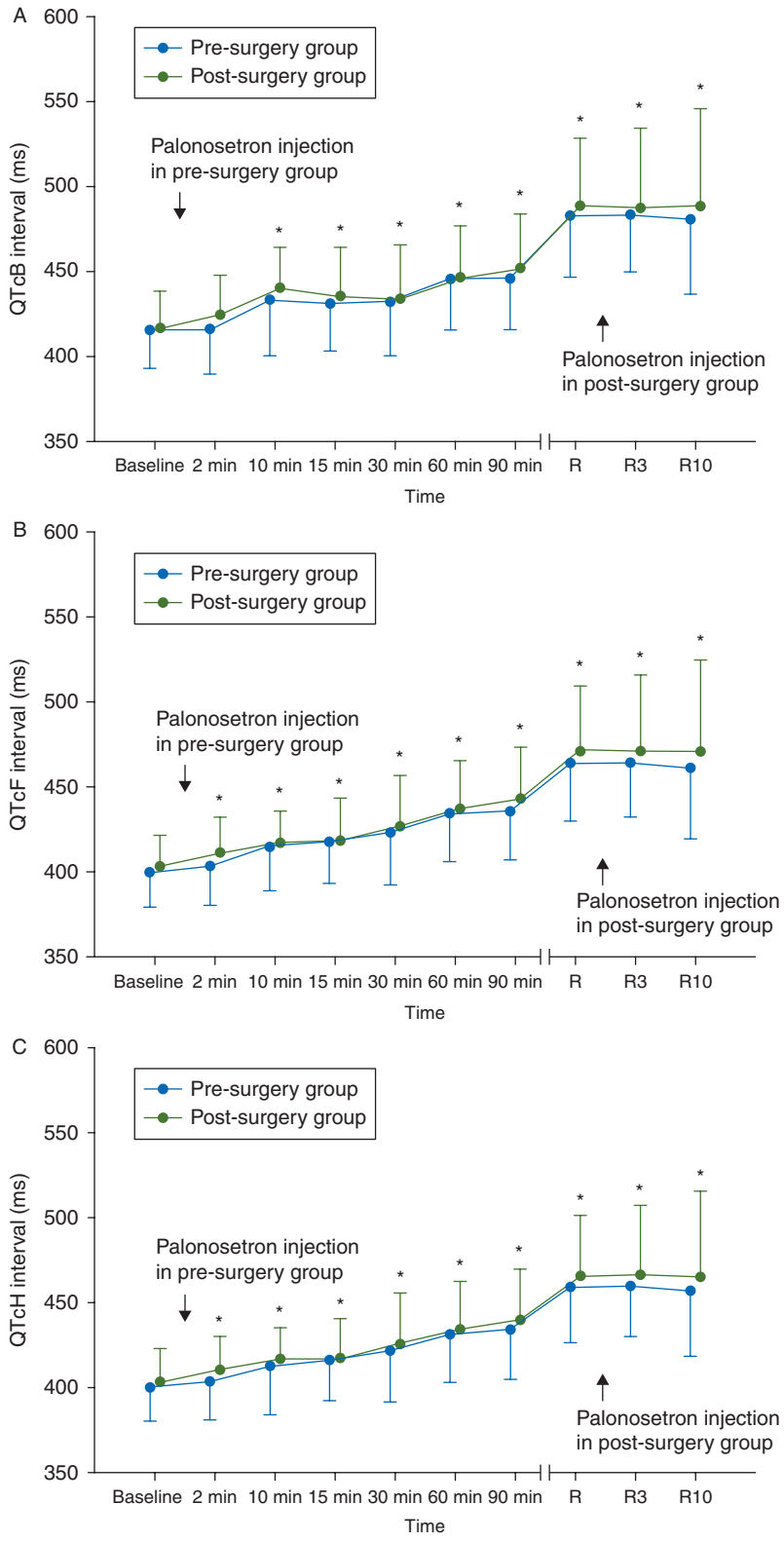

Fig 3 Changes in QTc intervals during the perioperative period. QTc intervals were calculated using Bazett's (QTcB), Fridericia's (QTcF), and Hodges formulas (QTcH). Baseline; 2, 10, 15, 30, 60, and 90 min after administration of palonosetron or placebo in the operating theatre; R, in the recovery room; R3 and R10, 3 and 10 min after administration of palonosetron or placebo in the recovery room. *$P<0.05$ compared with the baseline value. Error bars indicate SD.

Table 2 Number of patients with perioperative QTc interval >500 ms. Data are presented as the number of patients. QTc intervals were calculated using Bazett's (QTcB), Fridericia's (QTcF), and Hodges formulas (QTcH). Baseline; 2, 10, 15, 30, 60, and 90 min after administration of palonosetron or placebo in the operating theatre; R, in the recovery room; R3 and R10, 3 and 10 min after administration of palonosetron or placebo in the recovery room

	Baseline	2 min	10 min	15 min	30 min	60 min	90 min	R	R3	R10
QTcB interval										
Pre-surgery group (n=50)	0	0	0	0	0	1	1	11	15	15
Post-surgery group (n=50)	0	0	0	1	1	3	4	18	17	16
P-value	—	—	—	1.00	1.00	0.62	0.36	0.19	0.83	1.00
QTcF interval										
Pre-surgery group (n=50)	0	0	0	0	0	1	0	6	5	6
Post-surgery group (n=50)	0	0	0	0	0	1	3	7	7	7
P-value	—	—	—	—	—	1.00	0.24	1.00	0.76	1.00
QTcH interval										
Pre-surgery group (n=50)	0	0	0	0	0	0	0	3	4	3
Post-surgery group (n=50)	0	0	0	0	0	0	2	5	5	6
P-value	—	—	—	—	—	—	0.50	0.72	1.00	0.49

Table 3 PONV and side-effects. Data are presented as the number of patients (%). 0–2 h, during 2 h after surgery; 2–24 h, between 2 and 24 h after surgery; PONV, postoperative nausea and vomiting

	Pre-surgery group (n=50)	Post-surgery group (n=50)	P-value
Nausea			
0–2 h, none/mild/moderate/severe	14 (28), 36/10/2/2	12 (24), 38/8/3/1	0.86
2–24 h, none/mild/moderate/severe	14 (28), 37/9/2/2	10 (20), 40/7/1/2	0.88
Vomiting			
0–2 h	0	0	
2–24 h	2 (4)	1 (2)	1.00
Use of additional anti-emetics	3 (6)	4 (8)	1.00
Side-effects			
Headache	4 (8)	2 (4)	0.68
Dizziness	15 (30)	7 (14)	0.09
Drowsiness	16 (32)	18 (36)	0.83
Myalgia	2 (4)	5 (10)	0.44
Constipation	1 (2)	1 (2)	1.00

Discussion

In this study, the QTc interval increased over time for at least 90 min during sevoflurane anaesthesia. However, there was no significant difference in the QTc intervals across the perioperative period for those administered palonosetron 0.075 mg before or after sevoflurane anaesthesia.

To the best of our knowledge, this is the first study which investigated the effects of palonosetron on QTc intervals during sevoflurane anaesthesia. Time to reach the maximum plasma concentration after the i.v. administration of palonosetron is 2–9 min.[11] Therefore, the concentration of palonosetron will be at its highest during induction of general anaesthesia if palonosetron is administered immediately before anaesthetic induction according to its instructions for use.[11] Moreover, the concentration of sevoflurane is frequently elevated just before tracheal intubation during anaesthetic induction. Sevoflurane may be one of the most commonly used QT-prolonging drugs during the perioperative period and was proven to increase QTc intervals in a dose-dependent manner in several clinical studies.[26 27] Our study showed that QTc intervals increased over time for at least 90 min after sevoflurane anaesthesia. This result is consistent with those of previous studies which reported that 2–2.5% of sevoflurane lengthens QTc intervals by 22–24 ms at 10–20 min after anaesthetic induction.[17 26] Kweon and colleagues[28] demonstrated that the increase in the QTc interval was calculated to be 11 ms at 15 min after sevoflurane induction. If palonosetron is administered before anaesthetic induction as in our study, concomitant high concentrations of sevoflurane and palonosetron may occur during anaesthetic induction. Owczuk and colleagues[29] have shown that in patients undergoing breast surgery, isoflurane and anthracycline showed additive QT-prolonging effect.

Therefore, if sevoflurane and palonosetron have an additive QT-prolonging effect, we expect that the anaesthetic induction period may be the most dangerous in terms of QTc prolongation. However, in our study, palonosetron did not increase QTc intervals including the anaesthetic induction period, suggesting that palonosetron might be a safe anti-emetic during sevoflurane anaesthesia in terms of QTc prolongation.

Two recent clinical studies already demonstrated that changes in QTc intervals do not increase after administration of palonosetron in patients undergoing surgery, which is consistent with our results.[13 14] However, those studies did not report or standardize QT-prolonging risk factors, such as the use of QT-prolonging drugs, advanced heart disease, and hypokalaemia.[19 30] In addition, the method of anaesthesia including sevoflurane and opioids has not been reported.[13 14] The use of opioids, including remifentanil and fentanyl, prevent the QT-prolonging effects of sympathetic stimuli.[28 31] In our study, there was no difference between the two groups in the amount of fentanyl which was used during the intraoperative and postoperative periods. Moreover, sympathetic activation during anaesthesia, caused by tracheal intubation, surgical incision, or emergent events, is reported to increase QTc intervals.[16 32] Although it was difficult to standardize these factors, we measured the QTc interval at short intervals during these potentially vulnerable periods in order to detect QTc prolongation by sympathetic stimuli, unlike previous studies.[13 14]

We used Fridericia's and Hodges formulas to calculate the QTc interval, formulas that are less dependent on HR than Bazett's formula.[21 28] The HR is very changeable during anaesthesia; therefore, traditional Bazett corrections may be inappropriate for evaluating QT-prolonging effects in surgical patients.

In this study, 0.075 mg of palonosetron decreased the incidence of PONV, irrespective of whether it was administered before or after anaesthesia. Therefore, palonosetron seems to be effective in preventing PONV even when it is administered in the recovery room after surgery. However, PONV was not the primary outcome of this study and our inclusion criteria did not take into account risk factors of PONV, such as a history of PONV or non-smoking status as in previous studies.[13 14] This may be the reason why complete response rates were higher in our study than in previous studies (43–56%).

The primary limitation of this study is that we did not include a group that did not receive palonosetron. All patients received palonosetron during the observation period in this study. Therefore, the QTc intervals measured during the postoperative period could not be compared between patients who received palonosetron or not. Further studies are needed on this issue. Secondly, we excluded patients who had increased risk of QTc prolongation, such as hypokalaemia or preoperative prolonged QTc$>$500 ms. Therefore, our results may not be applicable to the patients who may actually be at increased risk of clinically important torsade de pointes. Thirdly, there exists controversy about the value of QTc intervals as a surrogate marker for the risk of arrhythmias. However, the QT interval may be the standard parameter for monitoring cardiac safety of 5-HT_3 receptor antagonists.[30]

In conclusion, 0.075 mg of palonosetron administered before anaesthetic induction did not affect the QTc interval during the intraoperative period in patients undergoing sevoflurane anaesthesia. In addition, there was no significant difference in the QTc intervals during the perioperative period, whether 0.075 mg palonosetron is administered before or after anaesthesia. Palonosetron can safely be used to prevent PONV in patients undergoing surgery under sevoflurane anaesthesia.

Authors' contributions

H.J.K.: study concept, study design, data analysis, and writing up of the first draft of the paper; H.-C.L.: patient recruitment and technical support; Y.S.J.: data collection; J.L.: data collection; J.J.M.: statistical analysis; D.-M.H.: statistical analysis; E.-K.C.: study design, data analysis, and interpretation; S.O.: study design and revising the manuscript for important intellectual content; Y.J.: study concept, design, and supervision.

Declaration of interest

None declared.

Funding

This work was supported by the Department of Anaesthesiology and Pain Medicine, Seoul National University Hospital.

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Handling editor: P. S. Myles