Drug Design, Development and Therapy

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Effects of Glycopyrronium Bromide as an Adjuvant Treatment in the Prevention of Nausea and Vomiting After Abdominal, Thyroid, and Breast Surgery: A Multicenter Randomized Controlled Trial

Jie Chen[1,*], Guangxi Piao[1,*], Guohui Luan[2], Yunming Yu[3], Wei Zheng[4], Yue Li[5], Chao Zhang[6], Yunzhen Duan[7], Min Zhao[8], Yong Zhang[9], Wei Xiang[10], Lu Cheng[11], Chengcheng Ji[12], Guangyou Duan[1], He Huang[1]

[1]Department of Anesthesiology, The Second Affiliated Hospital, Chongqing Medical University, Chongqing, People's Republic of China; [2]Department of Anesthesiology, Qijiang District People's Hospital, Chongqing, People's Republic of China; [3]Department of Anesthesiology, Three Gorges Hospital of Chongqing University, Chongqing, People's Republic of China; [4]Department of Anesthesiology, People's Hospital of Yunyang County, Chongqing, People's Republic of China; [5]Department of Anesthesiology, Qianjiang Central Hospital of Chongqing, Chongqing, People's Republic of China; [6]Department of Anesthesiology, People's Hospital of Shapingba District, Chongqing, People's Republic of China; [7]Department of Anesthesiology, People's Hospital of Chongqing Hechuan, Chongqing, People's Republic of China; [8]Department of Anesthesiology, People's Hospital of Wulong District, Chongqing, People's Republic of China; [9]Department of Anesthesiology, People's Hospital of Jiulongpo District, Chongqing, People's Republic of China; [10]Department of Anesthesiology, People's Hospital of High-Tech Zone District, Chongqing, People's Republic of China; [11]Department of Anesthesiology, People's Hospital of Xiushan County, Chongqing, People's Republic of China; [12]Department of Anesthesiology, Chongqing Jiangbei Hospital of Traditional Chinese Medicine, Chongqing, People's Republic of China

*These authors contributed equally to this work

Correspondence: Guangyou Duan; He Huang, The Second Affiliated Hospital, Chongqing Medical University, No. 74, Linjiang Road, Yuzhong District, Chongqing, People's Republic of China, Tel +86-18323376014; +86-13708385559, Email duangy@hospital.cqmu.edu.cn; huanghe@cqmu.edu.cn

Background: Effective methods for the prevention of postoperative nausea and vomiting remain to be found. Building upon previous evidence, we examined whether glycopyrrolate bromide had a preventive effect on nausea and vomiting when used as an adjuvant treatment.

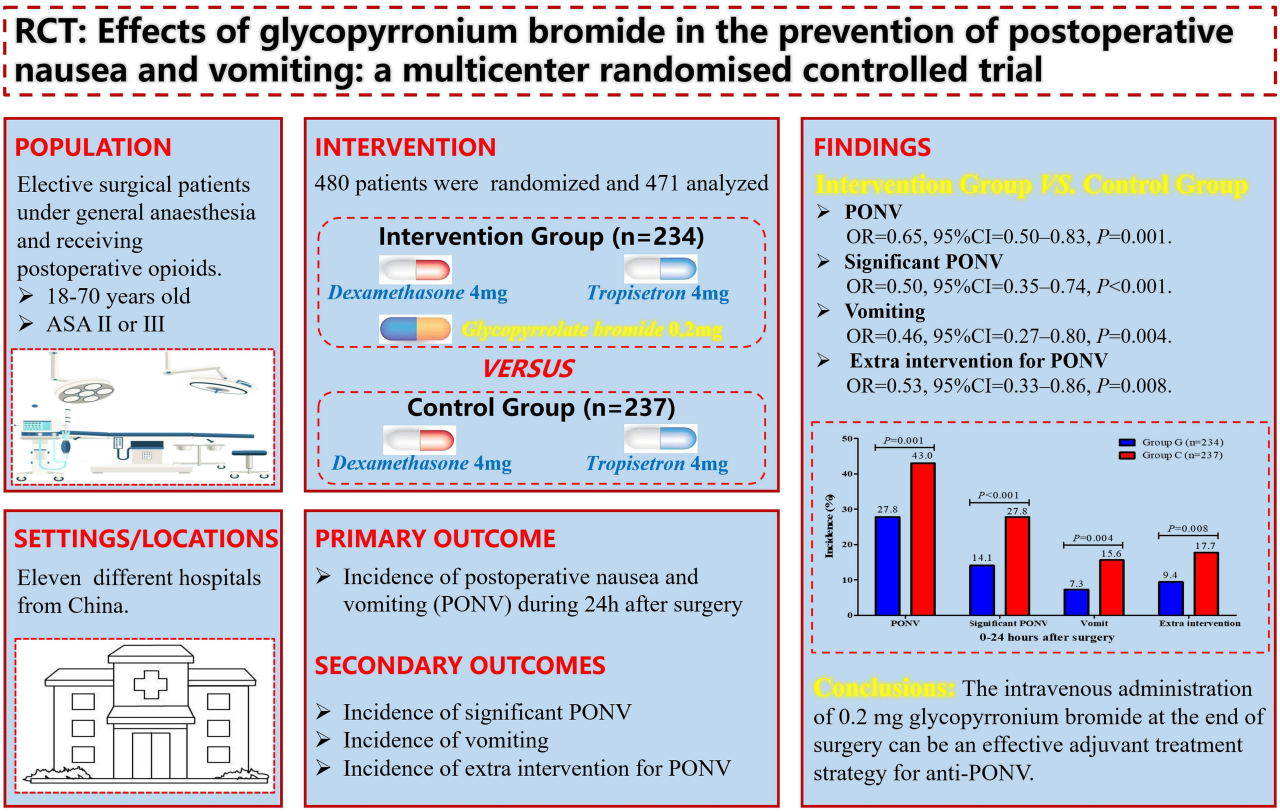
Methods: In 11 participating hospitals, patients who were scheduled to receive gynecological (n=123), gastrointestinal (n=201), thyroid (n=93), and breast surgery (n=51) under general anesthesia and received postoperative opioids were randomly allocated to receive 4 mg dexamethasone and 4 mg tropisetron (Group C) or 4 mg dexamethasone and 4 mg tropisetron combined with 0.2 mg glycopyrrolate bromide (Group G). The primary outcome of postoperative nausea and vomiting was assessed. The secondary outcomes included the incidences of significant nausea and vomiting (defined based on a rating scale of intensity ≥ 4), vomiting, and extra intervention.

Results: In total, 471 patients (234 in Group G and 237 in Group C) were included in the final analysis. The incidence of postoperative nausea and vomiting in Group G was lower than that in Group C (27.8% vs 43.0%, odds rate=0.65, 95% confidence interval =0.50–0.83, P=0.001). Furthermore, the incidences of significant nausea and vomiting (14.1% vs 27.8%, odds rate=0.50, 95% confidence interval=0.35–0.74, P<0.001), vomiting (7.3% vs 15.6%, OR=0.46, 95% confidence interval=0.27–0.80, P=0.004) and extra intervention (9.4% vs 17.7%, odds rate=0.53, 95% confidence interval=0.33–0.86, P=0.008) in Group G were all significantly lower than those in Group C. The two groups showed no significant difference in adverse events.

Conclusion: The intravenous administration of 0.2 mg glycopyrronium bromide at the end of surgery can be an effective adjuvant treatment strategy for prevention of nausea and vomiting in patients undergoing surgery under general anesthesia and receiving postoperative opioids.

Received: 4 January 2025
Accepted: 12 August 2025
Published: 19 August 2025

Graphical Abstract



Trial Registration: The Hospital Ethics Committee of the Second Affiliated Hospital, Chongqing Medical University (Approval ID: 2022–14-1) approved this study. This trial was registered with Identifier NCT05331651 on ClinicalTrials.gov.
Keywords: glycopyrronium bromide, nausea, vomit, general anesthesia. postoperative opioids

Introduction

Globally, an estimated 260–360 million surgical procedures are performed annually[1] in China, with over 70 million surgeries performed in 2021.[2] Postoperative nausea and vomiting (PONV) are one of the most common adverse effects in patients undergoing surgery, with an average incidence of 30% and approximately 80% in high-risk patients.[3–5] Furthermore, many common anesthetic risk factors, such as general anesthesia and postoperative opioids, could increase the risk of PONV.[6,7] To date, decreasing the incidence and intensity of PONV remains a challenge. As recommended in recent guidelines and reported in studies on PONV, several drugs, including 5-HT3 receptor antagonists (tropisetron), D2 receptor antagonists (metoclopramide), NK1 receptor antagonists (casopitant), histamine-1 receptor antagonists (meclizine), and corticosteroids (dexamethasone), are commonly used to treat PONV based on different mechanisms.[7–10] Nonetheless, the incidence of PONV remains high, as reported in several recent studies.[11–13] Therefore, it is necessary to explore novel drugs that can assist in treating PONV to provide better options in clinical practice.

Glycopyrronium bromide is a long-acting quaternary ammonium anticholinergic drug that can selectively antagonize the M receptor, with a three- to five-fold higher selectivity for M1 and M3 receptors than for M2 receptors. It mainly exhibits peripheral anticholinergic effects, including inhibitory effects on gastric acid secretion and gastrointestinal spasmolysis, with an action time of three to four times that of atropine.[14] Based on these peripheral effects,

glycopyrronium bromide may prevent nausea and vomiting. In addition, several studies have stated that intravenous injection of glycopyrronium bromide before a subarachnoid block can effectively prevent nausea and vomiting intra- and postoperatively, as reported in previous studies.[15,16] Therefore, we hypothesized that glycopyrronium bromide can prevent PONV in patients receiving general anesthesia and postoperative opioid analgesia. Therefore, this multicenter study aimed to verify whether using glycopyrronium bromide as an adjuvant medication reduced the incidence and severity of PONV.

Methods

Study Design

This study was designed as a multicenter randomized controlled trial to explore the effects of glycopyrronium bromide in preventing PONV, according to the Consolidated Standards of Reporting Trials 2010 statement guidelines.[17] Seventeen hospitals were invited to participate in this study, of which 11 agreed. This study was conducted following the Declaration of Helsinki of the World Medical Association, and the study protocol was approved by the Hospital Ethics Committee of the Second Affiliated Hospital, Chongqing Medical University (Approval ID: 2022–14-1). The study protocol was registered and initially released at clinicaltrials.gov (ID: NCT05331651) on Apr 11, 2022. The study protocol was also approved by the Hospital Ethics Committee of all included study centers, and all the patients provided written informed consent before the study. The full protocol and unidentified data can be acquired upon reasonable request from the corresponding author.

Patients

Patients aged 18–70 years undergoing non-cardiac surgery in the included hospitals were enrolled between April 21, 2022 and June 30, 2023. The inclusion criteria were the following: (1) undergoing elective non-cardiac surgery, (2) receiving general anesthesia, (3) American Society of Anesthesiologists classification I–III, and (4) voluntarily receiving postoperative intravenous controlled analgesia. Exclusion criteria included the following: (1) allergy or existing contra-indications to glycopyrronium, tropisetron, and other study drugs, (2) participation in other clinical drug trials within 3 months, (3) puerpera or lactating, and (4) the inability to follow the study procedure for any reason.

Randomization, Masking, and Allocation Concealment

Patients were randomly assigned to two groups following the PONV prevention procedure based on whether they received (Group G) or not (Group C) glycopyrronium bromide (Jiabo Pharmaceutical Co., Ltd. Guangdong, China). Central randomization based on computer-generated random numbers was performed. In every center, the non-blinded researcher performed the treatment according to the random numbers through an electronic randomization system (O-Trial+, Quanrong Company, Shanghai, China). Competitive enrollment was performed, and at least 20 subjects were asked to be recruited in each center. After the patients were included, an independent investigator randomly assigned them to the different groups. In this study, all the patients, the doctors involved in the procedure including the anesthesiologists, and the researchers responsible for follow-up were blinded to the group allocation. The anesthesiologists responsible for drug administration were not involved in the data collection, input, and analysis.

Anesthetic and Analgesic Procedures

Routine preoperative checkups were performed in all patients the day before surgery. Patients completed informed consent forms after receiving information about the study protocols and were advised on the use of patient-controlled intravenous analgesia (PCIA). Patients were informed of how to record the presentation of nausea and vomiting and how to evaluate the nausea intensity using the Numeric Rating Scale (NRS).[18]

Standard monitoring techniques, including electrocardiography, pulse oximetry, and heart rate and blood pressure monitoring, were applied as soon as the patient entered the operating room. The Bispectral Index (BIS) was used to continually monitor the level of anesthesia. Notably, both groups received the same anesthetic regimen. Rapid sequence induction was performed on all patients using midazolam 0.04 mg/kg, sufentanil 0.3–0.5 μg/kg, propofol 2–2.5 mg/kg,

and rocuronium bromide 0.6 mg/kg. Anesthesia was maintained using remifentanil infusion at 0.1–0.2 μg/kg/min, 1% sevoflurane inhalation anesthesia, and an intravenous infusion of propofol at 1–4 mg/kg/h, which was used to keep the anesthesia depth within the desired BIS range of 40–60, and rocuronium bromide was given as a loading dosage dependent on the surgical needs. Other anticholinergic drugs, such as atropine, were avoided in this study.

At the end of the surgical procedure, sufentanil 0.10 μg/kg and flurbiprofen ester 50 mg were administered, and a PCIA pump with opioids was attached for 24 h postoperatively. The patients were then sent to the post-anesthesia care unit until recovery, and nerve block or fascial block were given based on surgery type. Blockade reversal agents were used only if delayed recovery occurred, through sugammadex sodium based on the judgement of anesthesiologists. The 100-mL PCIA solution included sufentanil 0.2–0.3 μg/kg, flurbiprofen axetil 100 mg, and 0.9% normal saline. The PCIA pump loading dose was 2 mL, the background infusion rate was 2 mL/h, the patient-controlled dose was 2 mL, and the lockout duration was 15 min. Additional analgesics, such as flurbiprofen ester, tramadol, dezocine, or oxycodone, were provided when needed, based on the surgeon's judgement.

Regarding the intervention for PONV, dexamethasone, glycopyrronium bromide, tropisetron, and metoclopramide were used in this study. All patients were given a 4-mg dexamethasone injection after the induction of anesthesia. Glycopyrronium bromide (0.2 mg) and tropisetron (4 mg) were intravenously administered postoperatively to patients in Group G, while patients in group C only received tropisetron (4 mg). When rescue therapy for PONV was required by patients after surgery, metoclopramide 10 mg was given.

Outcome Measurement

The incidence of PONV was considered the primary outcome. Nausea and vomiting were recorded during the follow-up visits at 6±1 h and 24±1 h postoperatively. Regardless of the occurrence of nausea, the nausea intensity (NRS 0–10, with 0 representing no uncomfortable feeling and 10 representing tolerability), occurrence of vomiting, and intervention requirement for nausea and vomiting during 0–6 h and 6–24 h postoperatively were observed and recorded. Patients experiencing an NRS score of >3 for nausea or vomiting were defined as having significant PONV. The incidences of significant PONV, vomiting, and extra intervention were considered secondary outcomes.

Pain intensity was assessed using the NRS (0–10, with 0 representing no pain and 10 representing intolerable pain) from the end of surgery to 24 h postoperatively, and NRS >3 was recorded as moderate-to-severe pain. The total opioid consumption over 24 h postoperatively, calculated as morphine-equivalent doses, was recorded according to previous studies.[19] The degree of satisfaction was assessed in patients using the NRS (0–10, with 0 representing no satisfaction and 10 representing complete satisfaction), and NRS <3 was recorded as a bad experience.

In addition, adverse reactions potentially associated with glycopyrronium were recorded during the 24-h post-operative follow-up visits. Potential adverse events postoperatively included desaturation (pulse oxygen saturation <90%), hypotension (≥30% decrease from baseline blood pressure or systolic blood pressure ≤90 mmHg), hypertension (≥30% increase from baseline blood pressure or systolic blood pressure ≥180 mmHg), bradycardia (heart rate ≤40 beats per min) and tachycardia (heart rate ≥100 beats per min). Parched months, dizziness, urinary retention, blurred vision, photophobia, constipation, and bloating were also recorded.

Statistical Analysis

Based on our own preliminary experiment in the main hospital center, the incidence of PONV under conventional conditions was 35.7% (25/70), while the incidence was 16.7% (5/30) after the additional use of glycopyrronium bromide. The study was designed based on a 1:1 parallel controlled difference test, and the statistical test parameters were set at α=0.05 and 1-β=0.99. Each group's minimum required sample size was calculated as 192 cases using the PASS sample-size calculation software 11.0 (NCSS, LLC. Kaysville, Utah, USA). Considering a 20% dropout rate, 240 patients were required for each group. Therefore, this study included 480 patients to ensure a sufficient sample size.

Statistical analysis was performed using the SPSS software (version 26.0; SPSS, Chicago, IL, USA). Continuous values were presented using means ± standard deviations or medians (interquartile range) where appropriate, and qualitative values were presented using numbers (percentages). The incidences of PONV and other outcomes between groups G and C were compared using Chi-square or Fisher's exact tests, and the relative risk with a 95% confidence

interval (CI) was calculated. Continuous data between the two groups were compared using the independent sample-size *t*-test or Mann–Whitney test, and the mean difference with a 95% CI was calculated. In addition, univariate and multivariate logistic regression analysis were sequentially performed to explore the role of the grouping factors (groups G and C) in the occurrence of PONV, significant PONV, vomiting, and extra interventions. Confounding factors including multicenter factor, age (<60 years and ≥60 years), sex (male and female), body max index classification (<28 and ≥28), American anesthesiologist classification (ASA) classification (II and III), smoking status (yes and no), history of PONV or motion sickness (yes and no), surgery classification (gynecological, thyroid, breast, and gastro-intestinal surgeries), tumor surgery (yes and no), surgery type (open and endoscopic surgeries), and the classification of surgery time (<2 h and ≥2 h) were considered. Factors with P value <0.05 were included in the multivariate logistic regression model. Subgroup analyses based on whether the patient had a history of PONV and motion sickness and different types of surgery were also performed. Statistical significance was set at $P<0.05$.

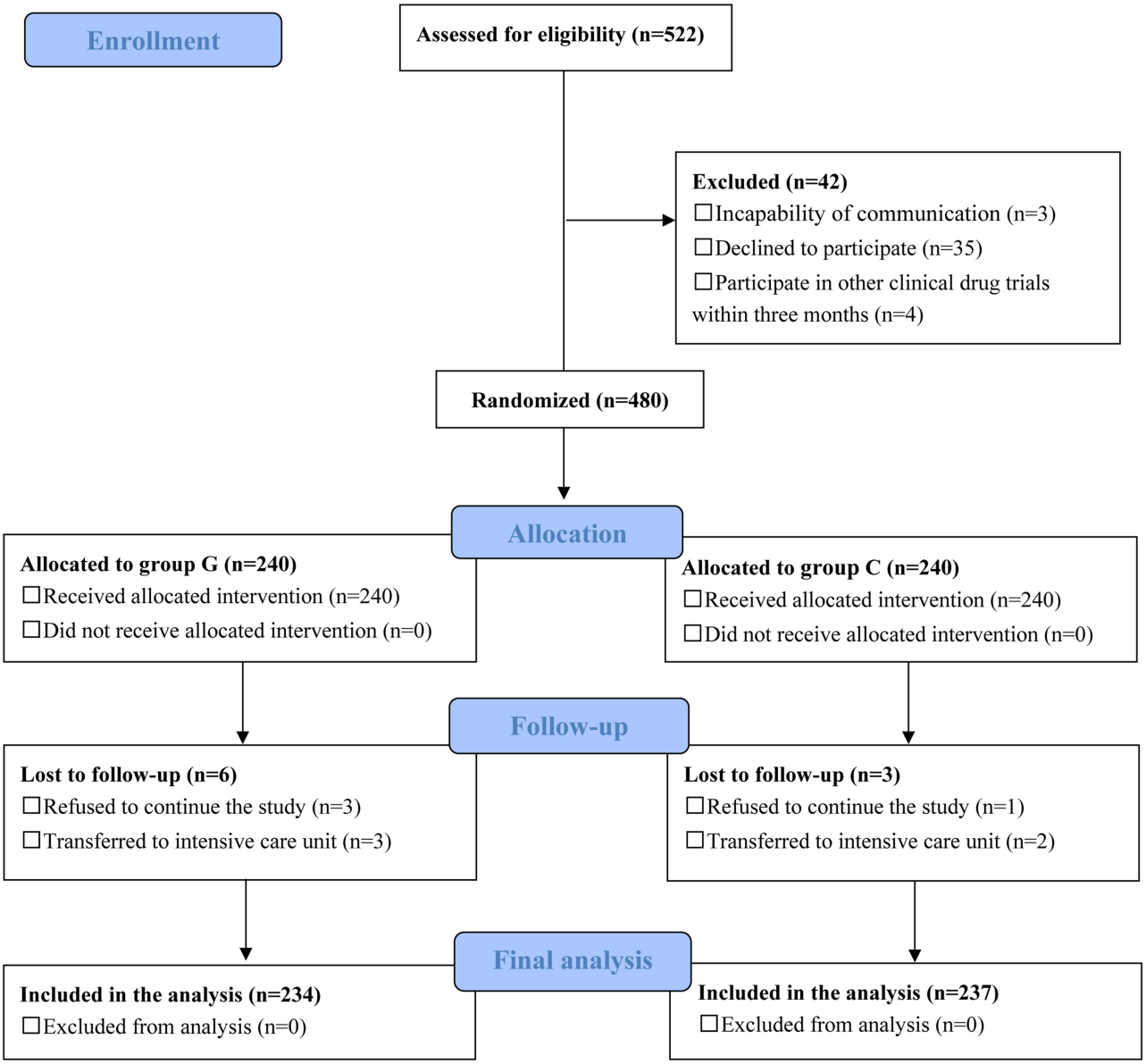


Figure 1 The study's flowchart.

https://doi.org/10.2147/DDDT.S515670

Table 1 The Baseline and Intraoperative Data of the Patients in the Two Groups

Variable	Group G (n=234)	Group C (n=237)	*P* Values
Age, year	46.5±12.5	47.2±12.0	0.537
Age group			0.840
≥60	34(14.5%)	36(15.2%)	
<60	200(85.5%)	201(84.8%)	
Sex			0.762
Male	39(16.7%)	42(17.7%)	
Female	195(83.3%)	195(82.3%)	
Height, cm	159.0±7.4	159.5±6.8	0.451
Weight, kg	59.4±10.2	59.7±10.1	0.800
BMI, kg/m^2	25.4±2.5	25.3±2.1	0.369
BMI classification			0.729
≥28	26(11.1%)	24(10.1%)	
<28	208(88.9%)	213(89.9%)	
ASA classification			0.277
II	226(96.6%)	224(94.5%)	
III	8(3.4%)	13(5.5%)	
Smoking status			0.617
Yes	206(88.0%)	205(86.5%)	
No	28(12.0%)	32(13.5%)	
History of PONV or motion sickness			0.142
Yes	70(29.9%)	86(36.3%)	
No	164(70.1%)	151(63.7%)	
Alphe score	3.2±0.5	3.3±0.5	0.449
Surgery type			0.479
Gynecological surgery	60(25.6%)	63(26.6%)	
Thyroid surgery	43(18.4%)	50(21.1%)	
Breast surgery	32(13.7%)	22(9.3%)	
Gastrointestinal surgery	99(42.3%)	102(43.0%)	
Surgery method			0.387
Endoscopic surgery	135(57.7%)	146(61.6%)	
Open surgery	99(42.3%)	91(38.4%)	
Tumor resection			0.372
Yes	76(32.5%)	68(28.7%)	
No	158(67.5%)	169(71.3%)	
Surgery duration, min	133(95–180)	135(90–183)	0.990
Major surgery			0.952
Yes (surgery duration≥2h)	129(55.1%)	130(54.9%)	
No (surgery duration<2h)	105(44.9%)	107(45.1%)	
Sugammadex using			0.814
Yes	14(6.0%)	12(5.1%)	
No	220(94.0%)	225(94.9%)	
Intraoperative blood loss, mL	50(11–75)	30(20–50)	0.585

Notes: Data are presented as mean ± standard deviation, number (percentage), or median (interquartile range).
Abbreviations: BMI, Body mass index; ASA, American Society of Anesthesiologists.

Results

In total, 522 patients were assessed for eligibility and 480 were included in the randomization (Figure 1). Six patients in Group G and three in Group C were lost to follow-up; 471 patients were included in the final analysis (234 in Group G and 237 in Group C). The demographic and baseline parameters of the patients in the different groups are listed in

Table 2 Postoperative Parameters Associated with Nausea and Vomiting in the Two Groups

Variable	Control G (n=234)	Group C (n=237)	Odds Rate (95% CI)	*P* Values
PONV (yes, %)	65(27.8%)	102(43.0%)	0.65(0.50 to 0.83)	0.001
Significant PONV (yes, %)	33(14.1%)	66(27.8%)	0.50(0.35 to 0.74)	<0.001
Vomiting (yes, %)	17(7.3%)	37(15.6%)	0.46(0.27 to 0.80)	0.004
Extra intervention for PONV (yes, %)	22(9.4%)	42(17.7%)	0.53(0.33 to 0.86)	0.008

Notes: Data were presented as number (percentage).
Abbreviations: PONV, postoperative nausea and vomiting; CI, confidence interval.

Table 1, and no significant differences were found between the two groups. Detailed characteristics of the patients in each center are presentedin Supplementary Table 1.

As shown in Table 2, the primary outcome of the study, the incidence of PONV, was significantly lower in Group G than in Group C (27.8% vs43.0%, odds ratio (OR)=0.65, 95% CI=0.50–0.83, *P*=0.001). Furthermore, the incidences of significant PONV (14.1% vs 27.8%, OR=0.50, 95% CI=0.35–0.74, *P*<0.001), vomiting (7.3% vs 15.6%, OR=0.46, 95% CI=0.27–0.80, *P*=0.004) and extra intervention for PONV (9.4% vs 17.7%, OR=0.53, 95% CI=0.33–0.86, *P*=0.008) were significantly lower in Group G than in Group C. Comparisons between Groups G and C for these outcomes at different time durations (0–6 h and 6–24 h postoperatively) are shown in Figure 2.

Logistic analysis including the multicenter factor showed no significant effect on the incidence of PONV. As shown in Table 3, univariate logistic regression showed that the risk of PONV in the glycopyrronium bromide group was

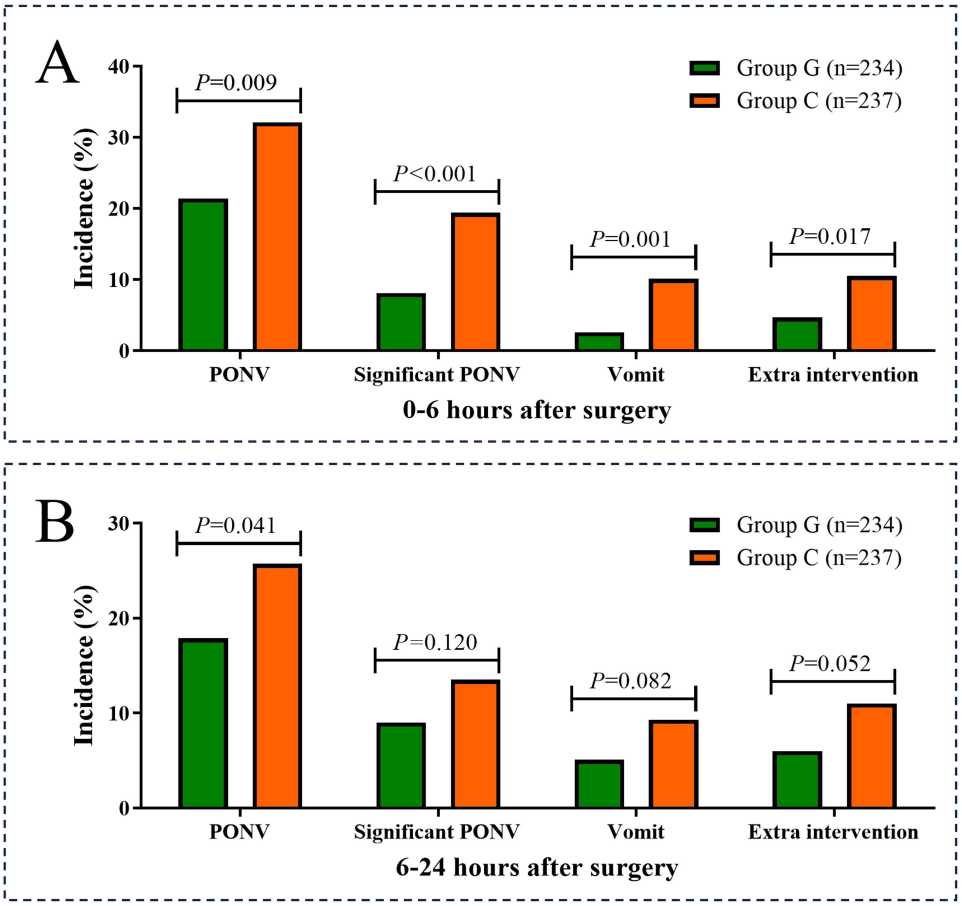


Figure 2 Comparisons between groups G and C in outcomes associated with PONV. (**A**) Incidences of PONV, significant PONV, Vomit and extra intervention for PONV at 0–6h after surgery between two groups. (**B**) Incidences of these outcomes at 6–24h after surgery between two groups.
Abbreviation: PONV, postoperative nausea and vomiting.

https://doi.org/10.2147/DDDT.S515670

Table 3 Univariable and Multivariable Logistic Regression Analysis for Postoperative Nausea and Vomiting

Variables	Univariate OR (95% CI)	P Value	Multivariate OR (95% CI)	P Value
Center		0.053		
Center A	Reference			
Center B	1.41(0.48,4.16)	0.538		
Center C	2.2(0.5,9.67)	0.296		
Center D	0.44(0.09,2.11)	0.304		
Center E	2.37(0.52,10.81)	0.266		
Center F	0.44(0.09,2.15)	0.312		
Center G	0.36(0.07,1.85)	0.221		
Center H	0.32(0.06,1.68)	0.18		
Center I	1.26(0.3,5.22)	0.751		
Center J	0.73(0.17,3.18)	0.678		
Center K	2.21(0.59,8.22)	0.238		
Glycopyrronium bromide group	0.49(0.33,0.75)	0.001	0.51(0.35,0.76)	0.001
Male	0.49(0.22,1.07)	0.072		
Age≥60, years	2.08(1.14,3.78)	0.017	1.83(1.06,3.16)	0.029
BMI≥28, kg/m^2	0.88(0.44,1.74)	0.71		
ASA II grade	0.7(0.26,1.85)	0.47		
Non-smoking	0.86(0.39,1.87)	0.702		
History of PONV or motion sickness	0.66(0.42,1.04)	0.074		
Surgery type		0.033		0.009
Gynecological surgery	Reference		Reference	
Thyroid surgery	1.75(0.94,3.25)	0.079	2.00(1.24,3.25)	0.005
Breast surgery	0.59(0.29,1.22)	0.154	1.10(0.64,1.89)	0.722
Gastrointestinal surgery	0.53(0.22,1.25)	0.147	0.71(0.35,1.43)	0.338
Tumor resection	1.56(0.93,2.61)	0.089		
Endoscopic surgery	1.15(0.62,2.12)	0.661		
Surgery duration≥2h	0.83(0.51,1.35)	0.455		

Abbreviations: OR, odds rate; CI, confidence interval; BMI, body max index; PONV, Postoperative nausea and vomiting.

significantly reduced (OR=0.49, 95% CI=0.33–0.75, *P*=0.001). The risk of PONV was also significantly associated with patients aged ≥60 years (≥60 years vs <60 years, OR=2.08, 95% CI=1.14–3.78, *P*=0.017), and surgery type was significantly associated with PONV (*P*=0.033). Variables with a P-value less than 0.05 from the univariate analysis were included in the multivariate logistic regression analysis. The results of the multivariate logistic regression analysis indicated that the glycopyrronium bromide group (OR=0.51, 95% CI=0.35–0.76, *P*=0.001), age ≥60 years (OR=1.83, 95% CI=1.06–3.16, *P*=0.029), and surgery type (thyroid surgery vs gynecological surgery, OR=2.00, 95% CI=1.24–3.25, *P*=0.005) were independent risk factors for PONV. In the other three models for predicting significant PONV, vomiting, extra intervention for PONV using glycopyrronium bromide, and a history of PONV and motion sickness were identified as independent factors as shown in Supplementary Tables 2-4.

Considering that a history of PONV and motion sickness was a risk factor, the differences in outcomes associated with PONV between Groups G and C were compared (Table 4). In patients with a history of PONV and motion sickness, the incidences of significant PONV (18.6% vs 39.5%, OR=0.47, 95% CI=0.27–0.82, *P*=0.005), vomiting (12.9% vs 26.7%, OR=0.48, 95% CI=0.24–0.97, *P*=0.033), and extra intervention (14.3% vs 27.9%, OR=0.51, 95% CI=0.26–0.99, *P*=0.040) were significantly lower in Group G than in Group C, unlike the general incidence of PONV (38.6% vs 51.2%, OR=0.75, 95% CI=0.53–1.08, *P*=0.116). The results of subgroup analyses of PONV incidences based on different types of surgeries are shown in Supplementary Table 5.

A comparison of the adverse events between the different groups is summarized in Table 5. Significant differences in the incidence of hypotension were observed; hypotension in Group G was significantly lower than in Group G (0.0% vs 3.0%, *P*=0.033). The two groups exhibited no other differences.

Table 4 Subgroup Analysis of Postoperative Parameters Associated with Nausea and Vomiting in the Two Groups

Variable	PONV (yes, %)	Significant PONV (yes, %)	Vomiting (yes, %)	Extra Intervention for PONV (yes, %)
Patients with history of PONV or motion sickness				
Control G (n=70)	27(38.6%)	13(18.6%)	9(12.9%)	10(14.3%)
Group C (n=86)	44(51.2%)	34(39.5%)	23(26.7%)	24(27.9%)
Odds rate (95% CI)	0.75(0.53 to 1.08)	0.47(0.27 to 0.82)	0.48(0.24 to 0.97)	0.51(0.26 to 0.99)
P values	0.116	0.005	0.033	0.040
Patients without history of PONV or motion sickness				
Control G (n=164)	38(23.2%)	20(12.2%)	8(4.9%)	12(7.3%)
Group C (n=151)	58(38.4%)	32(21.2%)	14(9.3%)	18(11.9%)
Odds rate (95% CI)	0.60(0.43 to 0.85)	0.58(0.34 to 0.96)	0.53(0.23 to 1.22)	0.61(0.31 to 1.23)
P values	0.003	0.032	0.126	0.164

Notes: Data were presented as number (percentage).
Abbreviations: PONV, postoperative nausea and vomiting; CI, confidence interval.

Table 5 Other Postoperative Parameters in the Two Groups

Variable	Group G (n=234)	Group C (n=237)	Mean Difference or Odds Rate (95% CI)	*P* Values
Total postoperative analgesia consumption, mg*	58.8±23.2	61.1±26.0	2.3(−6.7 to 2.5)	0.320
Desaturation (yes, %)	7(3.0%)	5(2.1%)	1.42(0.46 to 4.40)	0.544
Hypotension (yes, %)	8(3.4%)	16(6.8%)	0.51(0.22 to 1.16)	0.100
Hypertension (yes, %)	14(6.0%)	12(5.1%)	1.18(0.56 to 2.50)	0.100
Tachycardia (yes, %)	11(4.7%)	9(3.8%)	1.24(0.52 to 2.93)	0.627
Bradycardia (yes, %)	2(0.9%)	7(3.0%)	0.29(0.06 to 1.38)	0.096
Parched mouth (yes, %)	20(8.5%)	17(7.2%)	1.19(0.64 to 2.22)	0.579
Urinary retention (yes, %)	5(2.1%)	9(3.8%)	0.56(0.19 to 1.65)	0.289
Dizziness (yes, %)	12(5.1%)	9(3.8%)	1.35(0.58 to 3.14)	0.484
Blurred vision or photophobia (yes, %)	0(0.0%)	0(0.0%)	NA	1.000
Abdominal distension (yes, %)	6(2.6%)	7(3.0%)	0.87(0.29 to 2.54)	0.289
Moderate to severe pain (yes, %)	30(12.8%)	38(16.0%)	0.80(0.51 to 1.25)	0.321
Bad experience (yes, %)	5(2.1%)	4(1.7%)	0.99(0.97 to 1.02)	0.984
Hospital stay (day)	7.0(6.0–11.0)	7.0(6.0–10.5)	0.4(−0.5 to 1.3)	0.820

Notes: Data were presented as mean ± standard deviation, number (percentage) or median (interquartile range). *, Calculated as equivalent dose of morphine.
Abbreviations: NA, not applicable; CI, confidence interval.

Discussion

In this multicenter randomized controlled study, all patients were exposed to general anesthesia and postoperative opioids intraoperatively, and a combination of dexamethasone and tropisetron was used as a PONV prevention strategy in the control group. The incidence of PONV in these patients was 43.0%. However, we found that, compared with traditional interventions, the intravenous administration of glycopyrronium bromide at the end of surgery significantly decreased the incidence of PONV. Furthermore, glycopyrronium bromide showed preventive effects against significant PONV, postoperative vomiting, and additional postoperative intervention.

The mechanism of nausea and vomiting is mediated by peripheral stimulus signals causing the local release of neurotransmitters associated with nausea and vomiting, with the subsequent activation of the corresponding receptors in the vagus nerve, which acts on the nausea/vomiting centers to produce the nausea or the vomiting.[20] Notably, previous

studies have explored the PONV prevention effects of anticholinergic agents, including scopolamine and penehyclidine.[21,22] Combining with these results and considering that the effective time for scopolamine is approximately 1 h, we speculated that scopolamine may be more suitable for short-term interventions in outpatient settings. However, these anticholinergic agents have strong effects on the central nervous system, but relatively weak effects on gastric acid secretion and gastrointestinal spasmolysis. Unlike these three anticholinergic agents, glycopyrronium bromide is a long-acting quaternary ammonium anticholinergic drug that selectively inhibits gastric acid secretion and gastrointestinal spasmolysis.[14] In the current multicenter clinical study, the incidence of PONV was significantly lower when glycopyrronium bromide was used. Furthermore, the incidence of significant PONV, vomiting, and extra intervention, representing more severe symptoms in clinical practice, was also significantly reduced. Furthermore, in this study, no significant adverse events were observed postoperatively. These results indicate that glycopyrronium bromide can be a novel and effective supplementary treatment for preventing PONV.

In this study, logistic regression analysis was further performed to validate the role of glycopyrronium bromide in preventing PONV. The results showed that for all four outcomes, including PONV, significant PONV, vomiting, and extra intervention for PONV, glycopyrronium bromide use was an independent protective factor. In addition, we found that a history of PONV, or motion sickness, was a risk factor in many previous studies.[4,23,24] was consistently a risk factor for several outcomes in the current population. Furthermore, a subgroup comparison was performed based on the presence or absence of a history of PONV, or motion sickness. Notably, in patients with a history of PONV or motion sickness, glycopyrronium bromide showed statistically significant reductive effects on more severe symptoms, including significant PONV, vomiting, and additional intervention for PONV, but not on the incidence of PONV. This indicates that, even in high-risk populations, glycopyrronium bromide can improve severe symptoms associated with PONV.

PONV occurs more often within 24 h postoperatively, especially in the early 6 h.[8,25] In this study, we compared the PONV prevention effects of glycopyrronium bromide at 0–6 and 6–24 h postoperatively. The results showed that, at 0–6 h postoperatively, patients in Group G had a lower incidence of PONV, significant PONV, vomiting, and additional intervention for PONV, but not at 6–24 h. As reported in a previous study, the effective time of glycopyrronium bromide was approximately 6–8 h.[26] Based on these results, we speculated that another dose of glycopyrronium bromide 6 h postoperatively might be required to lengthen and improve its PONV prevention effects.

This study has a few limitations. First, based on previous studies, only fixed doses were selected, and no other dose gradients were used. In the future, it will be necessary to explore the clinical effects of different doses or determine the dosage based on patient weight. Second, this study only used a single dose and did not continue administration at other time points. It will be necessary to explore the PONV prevention effects of a broader range of administration methods in the future. Third, the wide range of surgical procedures in the analysis could introduce confounding factors that may influence the results; therefore, the effectiveness of glycopyrronium bromide in other different surgical types or methods still needs to be studied. Moreover, intravenous-inhalation combined anesthesia was performed in this study, which differs from total intravenous or inhalation anesthesia. Therefore, the effects of glycopyrronium bromide on PONV in these two methods require further validation. Finally, in this study, the postoperative 24 h with a high incidence of PONV was selected as the observation period. Therefore, the effect of glycopyrronium bromide on longer postoperative time still needs to be clarified.

Conclusion

This study demonstrated that the intravenous administration of 0.2 mg of glycopyrronium bromide at the end of surgery can be used as an adjuvant treatment strategy for patients undergoing surgery under general anesthesia and receiving postoperative opioids for prevention of nausea and vomiting after gynecological, gastrointestinal, thyroid and breast surgery.

Data Sharing Statement

All the data that support the current findings of this study are available from the corresponding author upon reasonable request.

Acknowledgments

We would like to thank Qiangting Deng from the editorial office of the Journal of Third Military Medical University (Chongqing 400038, China) for his help and valuable advice during our statistical analysis. We also thank the participants for their selfless contributions to this work.

Author Contributions

All authors made a significant contribution to the work reported, whether in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; agreed on the journal to which the article has been submitted; and agreed to be accountable for all aspects of the work.

Funding

This work was supported by the Young and Middle-aged Outstanding Medical Team of Chongqing.

Disclosure

The authors declare that there is no potential conflict of interest.

References

1. Holmer H, Bekele A, Hagander L, et al. Evaluating the collection, comparability and findings of six global surgery indicators. *Br J Surg*. 2019;106(2):e138–e50. doi:10.1002/bjs.11061
2. Liu Y, Xiao S, Yang H, et al. Postoperative pain-related outcomes and perioperative pain management in China: a population-based study. *Lancet Regional Health Western Pacific*. 2023;39:100822. doi:10.1016/j.lanwpc.2023.100822
3. Weibel S, Schaefer MS, Raj D, et al. Drugs for preventing postoperative nausea and vomiting in adults after general anaesthesia: an abridged Cochrane network meta-analysis. *Anaesthesia*. 2021;76(7):962–973. doi:10.1111/anae.15295
4. Ding S, Wang Z, Li C, et al. Effects of Fospropofol Disodium and Propofol on the Postoperative Recovery of Elderly Patients Who Underwent Total Hip Arthroplasty: a Retrospective Study. *Drug Des Devel Ther*. 2025;19:2767–2777. doi:10.2147/dddt.S501222
5. Cai Y, Nong L, Li H, Luo Q, Zhu Y, Shu H. Effect of bilateral superficial cervical plexus block on postoperative pain, nausea, and vomiting in thyroid surgery: a systematic review and meta-analysis. *Anesthesiol Perioperative Sci*. 2023;1(2):13. doi:10.1007/s44254-023-00012-8
6. Hoshijima H, Miyazaki T, Mitsui Y, Omachi S, Yamauchi M, Mizuta K. Machine learning-based identification of the risk factors for postoperative nausea and vomiting in adults. *PLoS One*. 2024;19(8):e0308755. doi:10.1371/journal.pone.0308755
7. Weibel S, Rücker G, Eberhart LH, et al. Drugs for preventing postoperative nausea and vomiting in adults after general anaesthesia: a network meta-analysis. *Cochrane Database Syst Rev*. 2020;10(10):Cd012859. doi:10.1002/14651858.CD012859.pub2
8. Gan TJ, Belani KG, Bergese S, et al. Fourth Consensus Guidelines for the Management of Postoperative Nausea and Vomiting. *Anesth Analg*. 2020;131(2):411–448. doi:10.1213/ane.0000000000004833
9. Benhamou D. Postoperative nausea and vomiting: is the big little problem becoming a smaller little problem? *Br J Anaesth*. 2023;131(1):22–25. doi:10.1016/j.bja.2023.04.004
10. Zhang Y, Luo X, Fan Q, et al. Efficacy of fosaprepitant for the prevention of postoperative nausea and vomiting in patients undergoing gynecologic surgery: a multicenter, randomized, double-blind study. *Anesthesiol Perioperative Sci*. 2024;2(4):40. doi:10.1007/s44254-024-00075-1
11. Lee DC, Vetter TR, Dobyns JB, et al. Sociodemographic Disparities in Postoperative Nausea and Vomiting. *Anesth Analg*. 2023;137(3):665–675. doi:10.1213/ane.0000000000006509
12. Klenke S, de Vries GJ, Schiefer L, et al. CHRM3 rs2165870 polymorphism is independently associated with postoperative nausea and vomiting, but combined prophylaxis is effective. *Br J Anaesth*. 2018;121(1):58–65. doi:10.1016/j.bja.2018.02.025
13. Klenke S, de Vries GJ, Schiefer L, et al. Genetic contribution to PONV risk. *Anaesth Crit Care Pain Med*. 2020;39(1):45–51. doi:10.1016/j.accpm.2019.04.012
14. Howard J, Wigley J, Rosen G, D'Mello J. Glycopyrrolate: it's time to review. *J Clin Anesth*. 2017;36:51–53. doi:10.1016/j.jclinane.2016.09.013
15. Ngan Kee WD, Lee SW, Khaw KS, Ng FF. Haemodynamic effects of glycopyrrolate pre-treatment before phenylephrine infusion during spinal anaesthesia for caesarean delivery. *Int J Obstet Anesth*. 2013;22(3):179–187. doi:10.1016/j.ijoa.2013.03.008
16. Hwang J, Min S, Kim C, Gil N, Kim E, Huh J. Prophylactic glycopyrrolate reduces hypotensive responses in elderly patients during spinal anesthesia: a randomized controlled trial. *Can J Anaesth*. 2014;61(1):32–38. doi:10.1007/s12630-013-0064-y
17. Moher D, Hopewell S, Schulz KF, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. *Int J Surg*. 2012;10(1):28–55. doi:10.1016/j.ijsu.2011.10.001
18. Koo CH, Ji SY, Han JH, et al. Effect of patient-controlled analgesia on development of postoperative nausea and vomiting in patients undergoing microvascular decompression: a prospective randomized controlled trial. *J Neurosurg*. 2024;141(1):260–267. doi:10.3171/2023.12.Jns231817
19. You S, Xu F, Wu Y, et al. Effect of noise isolation using noise-cancelling headphones during laparoscopic surgery for postoperative pain reduction: a randomized clinical trial. *J Clin Anesth*. 2024;92:111286. doi:10.1016/j.jclinane.2023.111286
20. Zhong W, Shahbaz O, Teskey G, et al. Mechanisms of Nausea and Vomiting: current Knowledge and Recent Advances in Intracellular Emetic Signaling Systems. *Int J Mol Sci*. 2021;22(11):5797. doi:10.3390/ijms22115797

21. Sun J, Cao X, Lu T, Li N, Min X, Ding Z. Penehyclidine mitigates postoperative nausea and vomiting and intraoperative oculocardiac reflex in patients undergoing strabismus surgery: a prospective, randomized, double-blind comparison. *BMC Anesthesiol*. 2021;21(1):49. doi:10.1186/s12871-021-01266-0
22. Lee HH, Kim HM, Lee JE, et al. The Effect of a Transdermal Scopolamine Patch on Postoperative Nausea and Vomiting after Retromastoid Craniectomy with Microvascular Decompression: a Preliminary Single Center, Double-Blind, Randomized Controlled Trial. *J Clin Med*. 2020;9(1):56. doi:10.3390/jcm9010156
23. Yu L, Dong Y, Shi S, Liu X, Wang M, Jiang G. Analysis of postoperative nausea and vomiting in patients with lung cancer undergoing thoracoscopic surgery under general anesthesia and its influencing factors: a observational study. *BMC Surg*. 2024;24(1):316. doi:10.1186/s12893-024-02614-w
24. von Peltz CA, Baber C, Nou SL. Australian perspective on Fourth Consensus Guidelines for the management of postoperative nausea and vomiting. *Anaesth Intensive Care*. 2021;49(4):253–256. doi:10.1177/0310057x211030518
25. Gecaj-Gashi A, Hashimi M, Sada F, et al. Propofol vs isoflurane anesthesia-incidence of PONV in patients at maxillofacial surgery. *Adv Med Sci*. 2010;55(2):308–312. doi:10.2478/v10039-010-0033-4
26. Haddad EB, Patel H, Keeling JE, Yacoub MH, Barnes PJ, Belvisi MG. Pharmacological characterization of the muscarinic receptor antagonist, glycopyrrolate, in human and Guinea-pig airways. *Br J Pharmacol*. 1999;127(2):413–420. doi:10.1038/sj.bjp.0702573