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ORIGINAL ARTICLE

Intra-operative dexmedetomidine reduces early postoperative nausea but not vomiting in adult patients after gynaecological laparoscopic surgery

A randomised controlled trial

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BACKGROUND Few studies have investigated the use of dexmedetomidine in patients with a high risk of postoperative nausea and vomiting (PONV) following gynaecological laparoscopic surgery.

OBJECTIVE To investigate if the intra-operative use of dexmedetomidine could reduce the incidence of PONV in this patient population.

DESIGN A randomised, double-blind, placebo-controlled trial.

SETTING A tertiary hospital in Beijing, China.

PATIENTS 130 adult patients scheduled for gynaecological laparoscopic surgery.

INTERVENTIONS Patients in the dexmedetomidine group (Dex group, $n = 65$) received a loading dose of dexmedetomidine (0.5 $\mu g\,kg^{-1}$ over 10 min) before induction of anaesthesia, followed by a continuous infusion (0.1 $\mu g\,kg^{-1}\,h^{-1}$) until the end of surgery. Patients in the control group (Ctrl group, $n = 65$) received volume-matched normal saline. Propofol and remifentanil were used for induction and maintenance of anaesthesia. Intravenous patient-controlled analgesia with morphine was provided after surgery.

MAIN OUTCOME MEASURES The incidence of 24-h PONV.

RESULTS The incidence of nausea within the first 2 postoperative hours was lower in the Dex group than in the Ctrl group [0% (0/65) vs. 9% (6/65), $P = 0.037$]. The overall incidence of PONV within the first 2 postoperative hours was slightly lower in the Dex group than in the Ctrl group, but the difference was not statistically significant [5% (3/65) vs. 14% (9/65), $P = 0.069$]. There was no significant difference between the two groups regarding the incidence of 24-h PONV.

CONCLUSION For adult patients undergoing gynaecological laparoscopic surgery, supplemental use of dexmedetomidine during general anaesthesia reduced the incidence of early postoperative nausea but not vomiting within the 24 h after surgery.

TRIAL REGISTRATION Chinese Clinical Trial Registry ChiCTR-IPR-15006914.

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Introduction

Postoperative nausea and vomiting (PONV) is one of the most common, unpleasant and distressing adverse effects of general anaesthesia. Patients after gynaecological laparoscopic surgery are at particularly high risk, and the incidence of PONV may be as high as 80%.[1–3] The occurrence of PONV may lead to a prolonged stay in the recovery room, increased nursing workload and more discomfort and dissatisfaction for patients. Despite multiple prophylactic methods, the effectiveness of PONV prophylaxis are far from optimal in high-risk patients.[4,5]

Dexmedetomidine is a highly selective α2-adrenoreceptor agonist with sedative, analgesic, sympatholytic and

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anxiolytic properties. It has been increasingly used as an adjuvant during anaesthesia because of benefits such as reducing perioperative catecholamine release, maintaining haemodynamic stability, sparing intra-operative requirements for anaesthetics and opioids, and improving the quality of recovery.[6,7] Two recent meta-analyses showed that intra-operative dexmedetomidine significantly lowered postoperative pain scores and opioid consumption,[8,9] and this opioid-sparing effect may lead to a reduction of opioid-related adverse events including PONV. In a small randomised controlled trial of patients undergoing modified radical mastectomy, a single dose of 0.5 $\mu g\,kg^{-1}$ dexmedetomidine, administered 5 min before the end of surgery, reduced both the requirement for analgesics and the incidence of nausea and vomiting in the early postoperative period.[10]

We hypothesised that supplemental use of dexmedetomidine during general anaesthesia would reduce the incidence of PONV in this patient population. The purpose of this study was to compare the effect of intra-operative dexmedetomidine vs. placebo on the incidence of nausea and vomiting after gynaecological laparoscopic surgery.

Methods

This was a randomised, double-blind and placebo-controlled trial. The study protocol was approved by the Ethics Committee of Peking University First Hospital (2014–03, Chairperson: Dr Chaoshu Tang) on 9 April 2014 and was registered at Chinese Clinical Trial Registry (ChiCTR-IPR-15006914). The study was performed in Peking University First Hospital. Written informed consent was obtained from all patients enrolled in the study.

Patients

Potential participants were screened the day before surgery. The inclusion criteria were adult female patients (age between 18 and 65 years old) who were scheduled to undergo elective gynaecological laparoscopic surgery. Patients were excluded if they met any of the following criteria: preoperative American Society of Anaesthesiologists physical status at least III, a history of brain injury, a history of uncontrolled hypertension, atrioventricular block at least 2°, obesity (BMI > 30 $kg\,m^{-2}$), pregnancy or breastfeeding, known hypersensitivity to drugs used in the study protocol, comorbidities that were known to increase the risk of PONV (e.g. impaired gastric motility and vestibular disease), liver or renal dysfunction (liver enzyme or creatinine 1.5 times higher than normal), alcoholism or drug abuse, or use of antiemetics and psychotropic drugs or glucocorticoids within 24 h before surgery.

Randomisation and study drug administration

Random numbers were generated by a biostatistician using computer software. Patients were randomly allocated into two groups in a 1 : 1 ratio. According to the random numbers, study drugs were prepared by a study coordinator (G.Y-G), either dexmedetomidine (100 $\mu g\,ml^{-1}$, diluted with normal saline to a final concentration of 4 $\mu g\,ml^{-1}$) or normal saline. The randomisation numbers were then sealed in envelopes.

For patients in the dexmedetomidine (Dex) group, a loading dose of dexmedetomidine (0.5 $\mu g\,kg^{-1}$) was administered over 10 min by intravenous (i.v.) infusion before the induction of anaesthesia, followed by a continuous infusion at a rate of 0.1 $\mu g\,kg^{-1}\,h^{-1}$. The infusion was discontinued 30 min before the expected end of surgery. For patients in the control (Ctrl) group, normal saline was administered at the same rate and volume as in the Dex group.

The investigators assessing outcomes, healthcare team members and patients were blinded to group assignment and blinding was maintained throughout the study period.

Anaesthesia and perioperative care

No pre-medication was administered. Intra-operative monitoring included ECG, non-invasive blood pressure, pulse oxygen saturation, Bispectral index and end-tidal carbon dioxide partial pressure.

All patients received a loading infusion of lactated Ringer's solution (10 $ml\,kg^{-1}$) before anaesthesia induction. General anaesthesia was induced intravenously with midazolam (0.03 $mg\,kg^{-1}$), remifentanil (target controlled infusion with an effect-site concentration of 3 $ng\,ml^{-1}$) and propofol (1 to 2 $mg\,kg^{-1}$). Rocuronium (0.6 $mg\,kg^{-1}$) was administered to facilitate endotracheal intubation. Anaesthesia was maintained with an i.v. infusions of propofol and remifentanil, with their rates adjusted to maintain the Bispectral index level between 40 and 60. Rocuronium was administered intermittently to maintain muscle relaxation. Mechanical ventilation was with a mixture of oxygen and air (FiO_2 0.5) adjusted to maintain an end-tidal carbon dioxide partial pressure between 4.6 and 7.3 kilopascals. Lactated Ringer's solution was infused at a rate of 6 $ml\,kg^{-1}\,h^{-1}$ throughout surgery.

Mean arterial blood pressure and heart rate were maintained within ±20% of baseline. Bradycardia (heart rate <40 beats min^{-1}) was treated with i.v. atropine (0.2 mg increments). Tachycardia (heart rate >110 beats min^{-1}) was treated with i.v. esmolol (20 mg increments). Hypotension (mean arterial blood pressure <60 mmHg) was treated with i.v. ephedrine (6 mg increments). Hypertension (mean arterial blood pressure >110 mmHg) was treated with i.v. nicardipine (0.2 mg increments). All patients received tropisetron 4 mg and parecoxib sodium 40 mg before the end of the surgery. At the end of surgery, muscle relaxation was antagonised with neostigmine 0.04 $mg\,kg^{-1}$ and atropine 0.02 $mg\,kg^{-1}$.

Upon completion of surgery, the patient's trachea was extubated and the patient was transferred to the post-anaesthesia care unit (PACU). Postoperative pain was treated with morphine via a patient-controlled analgesia pump, programmed to deliver a background infuse at a rate of 0.5 mg h^{-1}, and a 1-mg bolus on demand with a lockout interval of 8 min. This patient-controlled analgesia regimen was continued until 24 h after surgery. Patients were monitored in the PACU for 2 hours, and were then transferred to the general ward.

Data collection

Data were collected by research personnel who were blinded to the randomisation and not involved in the clinical care of the patients. Baseline characteristics of patients' including factors that might potentially influence the occurrence of PONV (such as previous history of PONV, chronic smoking, co-existing systemic diseases and concurrent medications), were carefully recorded. Intra-operative parameters including duration of anaesthesia and surgery, doses of anaesthetics and analgesics, and total fluid balance were collected. Postoperative data, including sedation scores and occurrence of adverse events in the PACU, as well as the cumulative doses of morphine and the numerical rating scale (NRS) pain scores at various time points after surgery, were documented.

The primary outcome was the incidence of 24-h PONV. Patients who experienced at least one episode of nausea, vomiting or retching or any combination of these during the first 24 h after surgery were considered to have PONV. Patients were asked to rate their degree of nausea using a four-point scale (none, mild, moderate or severe).[11] Postoperative vomiting was defined as at least one episode of vomiting or retching. Droperidol 1 mg or ondansetron 4 mg was used as the rescue antiemetic. Rescue antiemetics were administered on the following conditions: two or more episodes of vomiting or retching, any nausea lasting for more than 30 min, a 'severe' degree of nausea or whenever treatment was requested by the patient.

The secondary outcomes included the occurrence of nausea and/or vomiting at 2, 6 and 24 h after surgery, the consumption of morphine at 2 and 24 h after surgery, the level of sedation during PACU stay as well as the occurrence of adverse events and complications. In the PACU and the ward, pain intensity was assessed using an 11-point NRS on which 0 indicated no pain and 10 indicated the worst pain imaginable. For severe pain (NRS > 5), supplemental morphine of up to 5 mg was administered i.v. In the PACU, sedation levels were assessed using the Ramsay sedation scale (1 = agitated and uncomfortable, 2 = co-operative and orientated, 3 = can follow simple directions, 4 = asleep but strong response to stimulation, 5 = asleep and slow response to stimulation and 6 = asleep and no response to stimulation). Over sedation was defined as a sedation score of 4 or greater.[12]

Sample size calculation

According to our previous studies,[3,13] we estimated an incidence of PONV of 50% in the control group for this patient population. A sample size of 58 patients per group was needed to demonstrate a 50% reduction in the incidence of PONV (from 50 to 25%) with a power of 80% and a significance level of 0.05. To allow for an anticipated 10% dropout rate, we aimed to enrol 64 patients in each group.

Statistical analysis

Categorical data are presented as number (percentage) and were analysed using the χ^2 test or the Fisher's exact test as appropriate. Continuous data are presented as mean ± SD or medians (interquartile range) and were analysed with the unpaired Student's *t*-test or Mann–Whitney *U* test as appropriate. A two-sided *P* value less than 0.05 was considered statistically significant. The analyses were performed using the SPSS 14.0 software (SPSS, Inc., Chicago, Illinois, USA).

Results

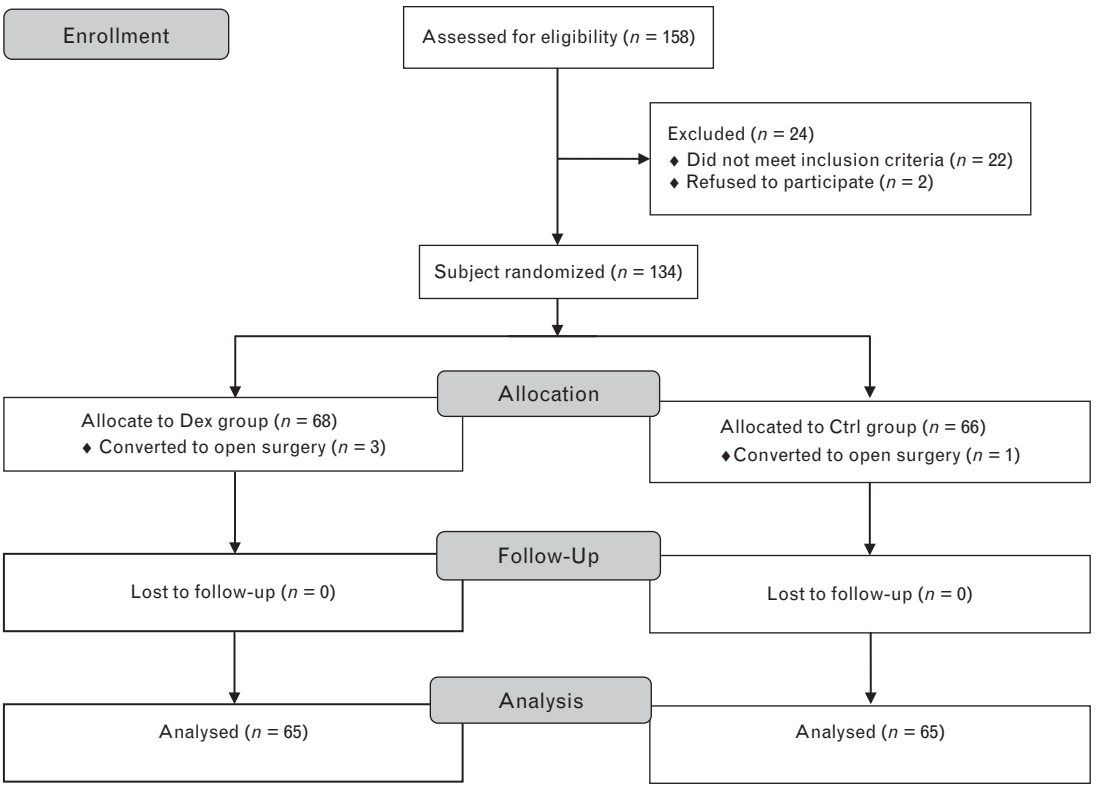
Between October 2014 and February 2015, a total of 134 patients were enrolled and 130 completed the study (Fig. 1). There were no significant differences with regard to baseline characteristics, risk score of PONV, or type of surgery between the two groups (Table 1).

The durations of anaesthesia and surgery were similar in the two groups. The infusion rate of propofol during anaesthesia was lower in the Dex group than in the Ctrl group ($P < 0.001$). The percentage of patients who received atropine for the treatment of bradycardia was significantly higher in the Dex group than in the Ctrl group ($P = 0.017$). There were no significant differences with regard to other intra-operative variables between the two groups (Table 2).

The percentage of patients who shivered during the PACU stay was significantly lower in the Dex group than in the Ctrl group ($P = 0.008$). The cumulative consumption of morphine during the stay in PACU, and for the first 24 h after surgery were slightly less in the Dex group than in the Ctrl group, but the differences were not statistically significant ($P = 0.050$ and 0.054, respectively) (Table 3).

The incidence of nausea during the first 2 h after surgery was significantly lower in Dex group than in the Ctrl group ($P = 0.037$). The incidence of PONV during the first 2 h after surgery was slightly lower in the Dex group than in the Ctrl group, but this difference was not statistically significant ($P = 0.069$). There were no significant differences between the two groups with regard to the incidences of vomiting and PONV at any time points,

Fig. 1



Consort flow diagram. Ctrl, control; Dex, dexmedetomidine.

the requirement of rescue antiemetics, or the time to first PONV. The incidence of 24-h PONV was 38.5% (25/65) in the Dex group and 43.1% (28/65) in the Ctrl group ($P = 0.592$) (Table 3).

Discussion

Our study demonstrated that, for adult patients undergoing gynaecological laparoscopic surgery, combined use of dexmedetomidine during general anaesthesia decreased the incidence of nausea during the first 2 h after surgery. However, it did not reduce the later occurrence of PONV, thus no difference was found regarding the incidence of 24-h PONV between groups.

Previous studies suggested that intra-operative use of dexmedetomidine reduces the incidence of PONV in

Table 1 Demographic characteristics and baseline data

	Dex group ($n = 65$)	Ctrl group ($n = 65$)	*P* value
Age, years	39.6 (8.3)	41.7 (10.6)	0.212
BMI, kg m^{-2}	22.9 (3.0)	23.5 (3.2)	0.331
Smoking	3 (5)	2 (3)	1.000
History of motion sickness	26 (40)	20 (31)	0.271
History of PONV	3 (5)	2 (3)	1.000
Type of surgery			0.421
Ovarian cystectomy/tumour resection	19 (29)	21 (32)	
Myomectomy	20 (31)	21 (32)	
Laparoscopy-assisted vaginal hysterectomy	21 (32)	22 (34)	
Laparoscopy for others	5 (8)	1 (2)	
Risk score for PONV			0.283
3	36 (55)	42 (65)	
4	29 (45)	23 (35)	
Risk score for PONV, score	3.4 (0.5)	3.4 (0.5)	0.373

Results are presented as mean (SD) or number (%). Ctrl, control; Dex, dexmedetomidine; PONV, postoperative nausea and vomiting.

Table 2 Comparison of intra-operative variables

	Dex group ($n = 65$)	Ctrl group ($n = 65$)	P value
Duration of anaesthesia, min	127 (63)	117 (50)	0.324
Dose of anaesthetics during anaesthesia			
Propofol, mg kg^{-1} h^{-1}	4.1 (0.7)	4.8 (1.2)	< 0.001
Remifentanil, μg kg^{-1} h^{-1}	7.8 (1.4)	8.0 (1.7)	0.516
Dexmedetomidine, μg kg^{-1}	0.6 (0.1)	NA	NA
Use of atropine during anaesthesia	19 (29)	8 (12)	0.017
Duration of surgery, min	114 (59)	106 (53)	0.442
Intra-operative fluids infusion, ml	1488 (376)	1392 (404)	0.162

Results are presented as mean (SD) or number (%). Ctrl, control; Dex, dexmedetomidine. NA, not applicable.

some types of surgeries. For example, Kim *et al.*[10] found that 0.5 μg kg^{-1} dexmedetomidine administered 5 min before the end of surgery reduced analgesic requirements and the incidence of PONV in patients after modified radical mastectomy. The incidences of PONV during PACU stay (21 vs. 43%, $P = 0.026$) and between 6 and 24 h after surgery (10 vs. 41%, $P = 0.012$) were significantly lowered in the dexmedetomidine group. Guven *et al.*[14] reported that administration of dexmedetomidine (1 μg kg^{-1} loading dose followed by an infusion of 0.2 μg kg^{-1} h^{-1} infusion) significantly decreased the occurrence of PONV in patients undergoing functional endoscopic sinus surgery. Gupta *et al.*[15] observed paediatric patients undergoing surgery for spinal dysraphism and found that intra-operative dexmedetomidine (1 μg kg^{-1} followed by 0.5 μg kg^{-1} h^{-1} infusion) decreased the consumption of fentanyl and the incidence of PONV (11.1 vs. 50%, $P = 0.03$). Turgut *et al.*[16] also reported that dexmedetomidine (0.6 μg kg^{-1} followed by 0.2 μg kg^{-1} h^{-1} infusion) produced more stable haemodynamics and less frequent PONV (nausea 32.0 vs. 72.0%, $P = 0.005$; vomiting 12.0 vs. 48.0%, $P = 0.005$) in patients undergoing spinal laminectomy.

Table 3 Comparison of overall postoperative nausea and vomiting outcomes

	Dex group ($n = 65$)	Ctrl group ($n = 65$)	P
Adverse events in the PACU			
Shivering	3 (5)	13 (20)	0.008
Agitation	4 (6)	7 (11)	0.344
Over sedation	9 (14)	7 (11)	0.593
Cumulative morphine consumption			
0 to 2 h, mg	2 (0 to 2)	2 (1 to 3)	0.050
0 to 24 h, mg	14.8 (3.2)	16.0 (3.5)	0.054
Nausea			
0 to 2 h	0 (0)	6 (9)	0.037
2 to 6 h	1 (2)	3 (5)	0.611
6 to 24 h	11 (17)	10 (15)	0.812
Vomiting			
0 to 2 h	3 (5)	3 (5)	0.676
2 to 6 h	4 (6)	1 (2)	0.362
6 to 24 h	13 (20)	13 (20)	1.000
PONV			
0 to 2 h	3 (5)	9 (14)	0.069
2 to 6 h	5 (8)	4 (6)	1.000
6 to 24 h	24 (37)	21 (32)	0.580
24-h PONV	25 (38.5)	28 (43.1)	0.592
Time to first PONV, h	17 [6, 18]	10 [1, 18]	0.182
Use of rescue antiemetics	6 (9)	8 (12)	0.571

Results are presented as number (%), mean (SD) or median [lower quartile, upper quartile]. Ctrl, control; Dex, dexmedetomidine; PACU, post-anaesthesia care unit; PONV, postoperative nausea and vomiting.

The mechanism by which dexmedetomidine decreases the incidence of PONV may include the following: it spares intra-operative consumption of anaesthetics and opioids, which in turn decreases the risk of PONV; it decreases sympathetic tone, which in turn decreases the incidence of PONV, as PONV may be triggered by high catecholamine concentrations; it may produce a direct antiemetic effect by activating the α2-adrenoceptor.[8,9,17] However, in the previous studies, PONV was reported as a secondary endpoint. In the present study, we observed the incidence of PONV as the primary outcome, and patients in both groups had a comparable preoperative risk of developing PONV.

Apfel *et al.*[18] created a simplified risk score chart and identified four primary risk factors for PONV in patients receiving balanced inhaled anaesthesia: female sex, non-smoking status, history of PONV and/or motion sickness and use of postoperative opioids. The expected incidences of PONV in the presence of 0, 1, 2, 3 and 4 risk factors are approximately 10, 20, 40, 60 and 80%, respectively. In the present study, the baseline risk score of patients was high (3 to 4 risk score) and, therefore, a multimodal prophylactic approach (including total i.v. anaesthesia with propofol, avoidance of nitrous oxide and prophylactic antiemetics) was used.[19] Our results showed that dexmedetomidine administration in addition to a multimodal PONV prophylaxis strategy significantly lowered the 2-h incidence of nausea after surgery and slightly lowered the incidence of overall 2-h PONV, although the later difference did not reach statistical significance. However, dexmedetomidine administration did not further decrease the incidence of 24-h PONV. These results were consistent with the terminal half-life of dexmedetomidine of about 2 h.

Several reasons might explain our neutral results. First, the method of anaesthesia maintenance was different. In previous studies, sevoflurane and nitrous oxide were used for anaesthesia maintenance, whereas in our study, propofol i.v. anaesthesia was used.[10,14–16] This might have

decreased the baseline incidence of PONV. Le Guen *et al.*[20] also used i.v. propofol for anaesthesia maintenance, and their results showed that dexmedetomidine administration significantly reduced the consumption of propofol (but not remifentanil) during maintenance of anaesthesia and had no effect on the incidence of PONV during the first 6-h period after surgery. Second, the dose of dexmedetomidine was relatively small. In previous studies, a relatively large dose of dexmedetomidine ($1\,\mu g\,kg^{-1}$ loading dose followed by an infusion of 0.2 to $0.8\,\mu g\,kg^{-1}\,h^{-1}$) was used, but a delayed recovery was reported during the first few hours after extubation.[21,22] The hypnotic and sedative effects of dexmedetomidine were dose-dependent. To guarantee a prompt postoperative recovery, we adopted a lower dose ($0.5\,\mu g\,kg^{-1}$ loading dose followed by an infusion of $0.1\,\mu g\,kg^{-1}\,h^{-1}$) in the present study. This perhaps reduced the antiemetic effect of dexmedetomidine dosing regimen. Despite the decreased dose and the slow infusion rate of dexmedetomidine in our study, the percentage of patients who received atropine to treat intra-operative bradycardia was higher in the Dex group than in the Ctrl group. Thus the dexmedetomidine dosing regimen used in our study still increased the incidence of intraoperative bradycardia, a phenomenon that is consistent with previous results.[8,9,16]

There are several limitations of this study. First, the sample size was relatively small, and both the incidence of PONV and the antiemetic effect of dexmedetomidine were lower than we expected. These factors decreased the ability of our study to detect a significant difference between the two groups. Second, only one dose regimen was adopted in the present study and that dose might have been be too small to produce significant effects in patients undergoing gynaecological surgery. Third, multimodal antiemetic prophylaxis was administered to both groups and this might have masked the antiemetic effect of dexmedetomidine.

Conclusion

Our study showed that for adult patients undergoing gynaecological laparoscopic surgery, supplemental use of dexmedetomidine during general anaesthesia reduced the incidence of early postoperative nausea but not vomiting within the first 24 h after surgery.

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References

1 Gan TJ, Diemunsch P, Habib AS, *et al.*, Society for Ambulatory Anesthesia. Consensus guidelines for the management of postoperative nausea and vomiting. *Anesth Analg* 2014; **118**:85–113.
2 Wu O, Belo SE, Koutsoukos G. Additive antiemetic efficacy of prophylactic ondansetron with droperidol in out-patient gynecological laparoscopy. *Can J Anaesth* 2000; **47**:529–536.
3 Geng ZY, Hu X. Clinical observation of postoperative nausea and vomiting in patient undergone gynecological laparoscopy under total intravenous anesthesia. *Chin J Min Inv Surg* 2009; **9**:892–895.
4 Tang J, Wang B, White PF, *et al.* The effect of timing of ondansetron administration on its efficacy, cost-effectiveness, and cost-benefit as a prophylactic antiemetic in the ambulatory setting. *Anesth Analg* 1998; **86**:274–282.
5 Mraovic B1, Simurina T, Sonicki Z, *et al.* The dose-response of nitrous oxide in postoperative nausea in patients undergoing gynecologic laparoscopic surgery: a preliminary study. *Anesth Analg* 2008; **107**:818–823.
6 Shin HW, Yoo HN, Kim DH, *et al.* Preanesthetic dexmedetomidine 1 μg/kg single infusion is a simple, easy, and economic adjuvant for general anesthesia. *Korean J Anesthesiol* 2013; **65**:114–120.
7 Bekker A, Haile M, Kline R, *et al.* The effect of intraoperative infusion of dexmedetomidine on the quality of recovery after major spinal surgery. *J Neurosurg Anesthesiol* 2013; **25**:16–24.
8 Schnabel A1, Meyer-Frießem CH, Reichl SU, *et al.* Is intraoperative dexmedetomidine a new option for postoperative pain treatment? A meta-analysis of randomized controlled trials. *Pain* 2013; **154**:1140–1149.
9 Blaudszun G, Lysakowski C, Elia N, *et al.* Effect of perioperative systemic α2 agonists on postoperative morphine consumption and pain intensity: systematic review and meta-analysis of randomized controlled trials. *Anesthesiology* 2012; **116**:1312–1322.
10 Kim SH, Oh YJ, Park BW, *et al.* Effects of single-dose dexmedetomidine on the quality of recovery after modified radical mastectomy: a randomised controlled trial. *Minerva Anestesiol* 2013; **79**:1248–1258.
11 McKeen DM, Arellano R, O'Connell C. Supplemental oxygen does not prevent postoperative nausea and vomiting after gynecological laparoscopy. *Can J Anaesth* 2009; **56**:651–657.
12 Gurbet A, Basagan-Mogol E, Turker G, *et al.* Intraoperative infusion of dexmedetomidine reduces perioperative analgesic requirements. *Can J Anaesth* 2006; **53**:646–652.
13 Geng ZY, Wang DX, Liu YH. Prevention of nausea and vomiting in patients undergoing gynecological laparoscopy: a comparison of tropisetron and ondansetron. *Chi J New Drugs* 2009; **18**:2316–2319.
14 Guven DG, Demiraran Y, Sezen G, *et al.* Evaluation of outcomes in patients given dexmedetomidine in functional endoscopic sinus surgery. *Ann Otol Rhinol Laryngol* 2011; **12**:586–592.
15 Gupta N, Rath GP, Prabhakar H, *et al.* Effect of intraoperative dexmedetomidine on postoperative recovery profile of children undergoing surgery for spinal dysraphism. *J Neurosurg Anesthesiol* 2013; **25**:271–278.
16 Turgut N, Turkmen A, Gökkaya S, *et al.* Dexmedetomidine-based versus fentanyl-based total intravenous anesthesia for lumbar laminectomy. *Minerva Anestesiol* 2008; **74**:469–474.
17 Afonso J, Reis F. Dexmedetomidine: current role in anesthesia and intensive care. *Rev Bras Anestesiol* 2012; **62**:118–133.
18 Apfel CC, Läärä E, Koivuranta M, *et al.* A simplified risk scores for predicting postoperative nausea and vomiting. *Anesthesiology* 1999; **91**:693–700.
19 Apfel CC, Korttila K, Abdalla M, *et al.*, IMPACT Investigators. A factorial trial of six interventions for the prevention of postoperative nausea and vomiting. *N Engl J Med* 2004; **350**:2441–2451.
20 Le Guen M, Liu N, Tounou FA, *et al.* Dexmedetomidine reduces propofol and remifentanil requirements during bispectral index-guided closed-loop anesthesia: a double-blind, placebo-controlled trial. *Anesth Analg* 2014; **118**:946–955.
21 Lee J, Kim Y, Park C, *et al.* Comparison between dexmedetomidine and remifentanil for controlled hypotension and recovery in endoscopic sinus surgery. *Ann Otol Rhinol Laryngol* 2013; **122**:421–426.
22 Patel CR, Engineer SR, Shah BJ, *et al.* Effect of intravenous infusion of dexmedetomidine on perioperative haemodynamic changes and postoperative recovery: a study with entropy analysis. *Indian J Anaesth* 2012; **56**:542–546.