Original Article

The Therapeutic Antiemetic and Hemodynamic Effects of Dexmedetomidine, Ephedrine, and Dexamethasone in Combination with Midazolam on Laparoscopic Cholecystectomy Patients: A Randomised Clinical Trial

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Abstract

Objective: The objective was to compare the hemodynamic and antiemetic effects of the combination of midazolam with ephedrine, dexamethasone, and dexmedetomidine in laparoscopic cholecystectomy surgical patients. **Materials and Methods:** This randomised, parallel-group, double-blind clinical trial was conducted by enrollment of 96 patients who were referred for laparoscopic cholecystectomy. Patients assigned into three equal-sized intervention arms having received anaesthesia induction with midazolam-ephedrine, midazolam-dexamethasone, and midazolam-dexmedetomidine using a block randomisation method. Frequency and severity of nausea and vomiting were observed from recovery to 24 h later, adverse events, and sedation on Ramsay sedation scale at recovery, 1, 2, and 4 h postoperatively. Data were recorded and analysed at a significance level lower than 0.05 in SPSS software. **Results:** The clinical parameters including mean blood pressure at all times and heart rate in 60–90 min were lower in the dexmedetomidine group when compared with other groups. The lowest severity of postsurgery nausea occurrence was observed in the midazolam-dexamethasone group and those receiving midazolam-dexmedetomidine from 4 to 24 h. In addition, vomiting scores were lower throughout recovery up to postoperative 4 h in the dexamethasone and dexmedetomidine groups (all $P < 0.05$). The highest sedation score was observed in the dexmedetomidine group during recovery up to 2 h ($P = 0.001$), reflecting a more clinically superior effect than dexamethasone ($P = 0.01$). **Conclusions:** A positive implication of dexmedetomidine was observed in attenuating postoperative nausea and vomiting and potentiating sedation. Nevertheless, it is providing a drop in the blood pressure and heart rate. Lending support to the potent adjuvant efficacy of dexamethasone following dexmedetomidine, consequently, a hypothesis can be put forward, stating that the dexmedetomidine and dexamethasone as adjuvants to midazolam are expected to bring the advantages of avoiding the adverse events and improving postoperative sedation.

Keywords: *Cholecystectomy, dexamethasone, dexmedetomidine, ephedrine, laparoscopic, midazolam, nausea, vomiting*

Introduction

No requirement exists to establish that roughly all of the follow-up documentation is consistently describing the occurrence of nausea and vomiting as surgical patient complaints on arrival to postanaesthesia care unit, frequently being linked with postoperatively developed pain.[1] It is occurring up to postoperative 24 h in 20%–30% of the patient population and is causing adverse events inherent but not limited to aspiration pneumonia and surgical wound opening.[2]

The up-to-date findings focused on the available pharmacy-driven initiatives for attenuating postoperative nausea and vomiting are currently being expanded, including those relevant to medication and complementary therapies as a standalone option or in combination with other standard treatments.[3] There have been further developments in our knowledge of the widespread benefits and risks associated with some medications such as metoclopramide,[4] ondansetron and dexamethasone, midazolam, ephedrine, dexmedetomidine,[4] and butyrophenones, alone or in combination of two or more.[3,5]

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The use of antihistamines and butyrophenones is critically limited by undesirable adverse effect profiles of excessive sedation, hypotension, dry mouth, extrapyramidal symptoms, and tachycardia.[3]

Currently, growing research efforts are hence being made to introduce novel ones with the least adverse events and the most efficacies. Benzodiazepines are proven to remain the basis of anxiety relief treatment, including midazolam, which is a water-soluble agent and the most commonly used sedative premedication, with the potential for public health benefits such as a rapid onset of action, effective relief, anterograde amnesia, tempering anxiety, and controlling postoperative vomiting.[6] The therapeutic efficacy of midazolam in affording appropriate postoperative nausea and vomiting prophylaxis is well established by bolus administration before or after anaesthesia induction or postoperative continuous infusion.[7] Several have published reports on the postoperative antiemetic effect of midazolam in treatment-resistant cases.[5,6] The possible mechanisms of the action of midazolam in attenuating postoperative nausea and vomiting include the gamma-aminobutyric acid (GABA) receptor antagonism, inhibition of dopamine release, and anxiolytic effects.[2,8]

Dexmedetomidine is used widely because of its anxiolytic, sedative, analgesic, and sympatholytic properties.[9] The drug's profile has been reported to be a potentially clinically viable option for alleviating postoperative pain without causing hemodynamic adverse effects, while preventing postoperative nausea and vomiting.[9] Though plentiful studies support the antiemetic effect of low dose rate of dexmedetomidine in affording the relief of postoperative nausea and vomiting.[9,10] The mechanism remains to be elucidated but may be due to the cost-saving of anaesthesia and opioids, which may contribute to postoperative nausea and vomiting, and there exist also some suggestions that the lessened sympathetic tone may contribute to the reduction.[11-13] Dexamethasone belongs to a class of cheap and available drugs known as corticosteroids to control postoperative nausea and vomiting,[9,13,14] although this remains controversial with other studies refuting such benefits.

Medical knowledge researchers spent two decades documenting the effects of dexamethasone in patients undergoing chemotherapy, exploring the anaesthesiologists' attention to the beneficial role of dexamethasone in attenuating the incidence and severity of postoperative nausea and vomiting.[15,16] The mechanism of the action of dexamethasone in the attenuation is through its effect on the centre of nausea and vomiting and peripheral impact.[4,16,17]

Considering that the lack of such previously reported comparative trial needed to firmly establish the efficacy of our medications, nausea and vomiting remains a serious and common postoperative complication. However, the present trial was designed and compared the hemodynamic and antiemetic effects of the combination of midazolam with ephedrine and dexamethasone and dexmedetomidine in laparoscopic cholecystectomy-treated patients to find the best drug to prevent postoperative nausea and vomiting in patients, with minimal hemodynamic adverse effects.

Materials and Methods

Study setting

This double-blind clinical trial recruited 96 laparoscopic cholecystectomy patients referred to the Valiasr Hospital (Arak, Iran) who were identified as meeting inclusion and exclusion criteria after the approval of the ethical committee and obtaining written informed personal consent.

Inclusion and exclusion criteria

Inclusion criteria included patients being considered for laparoscopic cholecystectomy after obtaining informed consent, American Society of Anesthesiologists (ASA) class II, no history of mental illness and psychosis, patients receiving general anaesthesia, aged 18–60 years, a duration of surgery of 60–150 min, a lack of sensitivity to medications. Besides, exclusion criteria included patients with hypertension, vascular problems, Parkinson's disease, and motion sickness, a history of chemotherapy, patients without informed consent, those expressing unwillingness to continue the study, and death in hospital.

Intervention

All subjects were hospitalised at least 1 day before surgery, and 8 h was defined as adequate adherence to preoperative fasting guidelines. After collecting the baseline demographic data, on arrival in the operation theatre, two intravenous lines were inserted, one for infusing the study drugs and the other for administering intravenous fluids or other drugs. Hemodynamic parameters including heart rate, mean arterial blood pressure, and arterial oxygen saturation were measured prior to the induction. Once the induction commenced, all were preloaded with 10 mL/kg of crystalloid solution (Ringer), preoxygenated with 100% oxygen via face mask, and received two μg/kg of intravenous fentanyl for anaesthetic premedication. After receiving general anaesthesia with 5 mg/kg thiopental sodium, 0.5 mg/kg atracurium, and endotracheal intubation by spiral cuffed endotracheal tube with an appropriate size, they were mechanically ventilated to maintain an ETCO2 of about 30–35 mmHg and an arterial oxygen saturation of 98%. Anaesthesia was maintained with oxygen and nitrous oxide (50:50) and isoflurane 1%–1.5%, when fentanyl and atracurium were administered intravenously at a dose of 10 mg every 20–30 min and 1 μg/kg every 1 h, respectively. Immediately after the anaesthesia induction, subjects were stratified into three equal-sized interventional arms based on a randomised block design with six blocks, and the patient allocation continued until each study arm had 32 patients.

A single intravenous dose of 0.075 mg/kg midazolam (Caspian Tamin Pharmaceutical Company, Rasht, Iran) was administered equally to all three arms receiving: 0.5 mg/kg ephedrine (BIOTIKA BOHEMIA spol. s r.o., Prague, Czech), 0.05 mg/kg dexamethasone (Caspian Tamin Pharmaceutical Company, Rasht, Iran), or 1 µg/kg dexmedetomidine (Iran Eksir, Tehran, Iran).[18] The dose of intervention drugs, i.e., midazolam with each adjuvant, was calculated and poured into 100 mL normal saline solution, and then all participants were given a slow intravenous infusion over 15 min, immediately after the induction of anaesthesia and endotracheal intubation.

Once the surgery was completed, the time to extubation was determined dependent on the proper respiratory minute volume and airway reflexes return, after the discontinuation of inhalation anaesthesia and reversal of the muscle relaxant effect. In recovery up to 24 h later, data were recorded as frequency of nausea and vomiting. The severity of nausea and vomiting score was measured by visual analog scale (VAS) as 0, no any compliant; 1, mild degree of nausea; 2, moderate degree nausea and vomit; 3, frequent vomit; and 4, continuous vomit. Patients were asked to mark their level of nausea and vomiting, which is rated by the distance from ruler's zero point to the point that they mark. Ten mg of metoclopramide (0.1 mg/kg) was injected intravenously and slowly to control symptoms of nausea and vomiting (VAS ≥ 3) in all subjects, while the first 24 h total dose was recorded at the patients' visits.

Furthermore, patients' vomiting scores were measured based on the criteria from zero to four, as described in the table below. Hemodynamic data were recorded every 15 min until the end of surgery and in recovery, 1, 2, and 4 h postoperatively at which times appropriate counter measurements have been performed and recorded to address the decrease in mean arterial blood pressure, heart rate, or arterial oxygen saturation. In addition to other adverse events such as confusion, dizziness, and hallucinations, Ramsay scores were recorded to evaluate procedural sedation in all patients in recovery, 1, 2, and 4 postoperative hours. It is remarkable to note that the anaesthesiologist prepared and administered medicines, while all participants and the data collection intern were not aware of the arm allocation to ensure a double-blind study design. All the data were entered into SPSS v. 20. Finally, data were analysed by chi-square for qualitative data, t-test, and analysis of variance (ANOVA) with repeated observations in SPSS Software (IBM Corp, USA).

Results

The median age of patients was 40.66 ± 1.62 years, and the minimum and maximum was 31 and 54 years, respectively. From all, 36 patients (37.5%) were male, and 60 patients (62.5%) were female.

The study revealed no statistically significant between-arm difference ($P > 0.05$) in terms of oxygen saturation, surgery duration, adverse events, and metoclopramide consumption in terms of which only three cases (9.37%) in the midazolam-ephedrine arm needed to receive the antiemetic agent. Data on patient gender, age, and body mass index were identical for all subjects.

Statistically significant [Table 1] between-arm differences were observed in terms of blood pressure, and the repeated measure confirmed the result (both $P < 0.05$), showing a significantly lower blood pressure in the midazolam-dexmedetomidine group [Chart 1].

As repeated measure confirmed ($P < 0.05$), heart rate differences ($P < 0.05$) were statistically significant among all subjects throughout intervals from 60 to 90 min after the start of surgery during which it was found lower in the midazolam-dexmedetomidine arm [Table 2].

Differences for nausea frequency [Table 3] were statistically significant among the subjects during recovery, 2, and 4 h after surgery and repeated measure confirmed the result ($P < 0.05$) when the incidence was lower in the midazolam-dexmedetomidine and midazolam-dexamethasone groups than in the first study arm.

Statistically significant differences [Table 4] were seen in the mean score of nausea severity among all participants from 4 to 24 h postoperatively ($P < 0.05$). Based on the repeated measure [Chart 2], the differences were also statistically significant

Table 1: Between-arm comparison of mean and SD of mean blood pressure

Group, mean blood pressure	Midazolam-ephedrine, mean ± SD	Midazolam-dexamethasone, mean ± SD	Midazolam-dexmedetomidine, mean ± SD	*P* value
Baseline	94.50 ± 4.90	94.46 ± 4.64	94.43 ± 3.65	0.998
15 min after baseline	95.57 ± 4.47	94.65 ± 4.48	93.03 ± 3.56	0.04
30 min after baseline	96.75 ± 3.81	95.12 ± 3.97	92.03 ± 3.44	0.001
45 min after baseline	97.00 ± 3.62	95.34 ± 3.72	91.43 ± 3.05	0.001
60 min after baseline	97.46 ± 3.32	95.96 ± 3.22	90.56 ± 2.89	0.001
75 min after baseline	96.68 ± 2.99	95.68 ± 2.96	91.28 ± 2.50	0.001
90 min after baseline	96.12 ± 2.81	95.81 ± 2.74	92.00 ± 2.18	0.001
105 min after baseline	95.50 ± 2.65	95.81 ± 2.49	92.71 ± 1.92	0.001
Recovery	95.25 ± 2.62	96.00 ± 2.38	93.18 ± 1.51	0.001
1 h postop	94.75 ± 2.57	96.18 ± 2.30	93.75 ± 1.60	0.001

SD: standard deviation

Table 2: Between-arm comparison of mean and SD of heart rate

Group, heart rate	Midazolam-ephedrine, mean ± SD	Midazolam-dexamethasone, mean ± SD	Midazolam-dexmedetomidine, mean ± SD	*P* value
Baseline	93.43 ± 6.30	93.50 ± 6.16	93.46 ± 6.05	0.999
15 min after baseline	94.09 ± 6.13	93.71 ± 93.71	92.62 ± 5.83	0.600
30 min after baseline	94.65 ± 5.82	94.03 ± 5.84	92.09 ± 5.49	0.181
45 min after baseline	95.03 ± 5.36	94.25 ± 5.76	91.78 ± 5.32	0.055
60 min after baseline	95.25 ± 5.24	94.43 ± 5.65	91.28 ± 5.04	0.009
75 min after baseline	95.37 ± 5.21	94.59 ± 5.63	92.12 ± 4.98	0.004
90 min after baseline	94.78 ± 4.90	94.09 ± 5.17	92.12 ± 4.52	0.083
105 min after baseline	94.00 ± 4.66	93.46 ± 4.69	93.12 ± 3.92	0.730
Recovery	94.90 ± 4.37	94.37 ± 4.52	94.40 ± 3.04	0.840
1 h postop	93.87 ± 3.85	93.59 ± 4.54	93.46 ± 2.92	0.910
2 h postop	93.50 ± 3.94	92.71 ± 3.83	92.25 ± 2.55	0.357
4 h postop	93.62 ± 3.92	93.03 ± 3.86	93.06 ± 2.24	0.739

SD: standard deviation

Table 3: Between-arm comparison of mean and SD of nausea frequency

Group, nausea incidence	Midazolam-ephedrine, mean ± SD	Midazolam-dexamethasone, mean ± SD	Midazolam-dexmedetomidine, mean ± SD	*P* value
Recovery	0.093 ± 0.296	00.00 ± 00.00	00.00 ± 00.00	0.04
2 h postop	0.093 ± 0.296	00.00 ± 00.00	00.00 ± 00.00	0.04
4 h postop	0.093 ± 0.296	00.00 ± 00.00	00.00 ± 00.00	0.04
6 h postop	0.000 ± 0.000	00.00 ± 00.00	00.00 ± 00.00	0.999
12 h postop	00.00 ± 00.00	00.00 ± 00.00	00.00 ± 00.00	0.999
24 h postop	00.00 ± 00.00	00.00 ± 00.00	00.00 ± 00.00	0.999

SD: standard deviation

Table 4: Between-arm comparison of mean score of nausea severity

Group, nausea severity	Midazolam-ephedrine, mean ± SD	Midazolam-dexamethasone, mean ± SD	Midazolam-dexmedetomidine, mean ± SD	*P* value
Recovery	0.687 ± 0.644	0.468 ± 0.507	0.437 ± 0.504	0.152
2 h postop	0.718 ± 0.634	0.468 ± 0.507	0.437 ± 0.504	0.088
4 h postop	1.00 ± 0.983	0.468 ± 0.507	0.437 ± 0.504	0.002
6 h postop	0.781 ± 0.608	0.468 ± 0.507	0.437 ± 0.504	0.023
12 h postop	0.812 ± 0.396	0.468 ± 0.507	0.437 ± 0.504	0.003
24 h postop	0.875 ± 0.336	0.437 ± 0.504	0.375 ± 0.491	0.001

SD: standard deviation

($P < 0.05$), with the lowest severity in the third study arm and no significant difference between the first two arms ($P > 0.05$).

Vomiting scores were statistically significant within recovery up to 4 h after surgery, while being lower in the last two arms. Repeated measure confirmed the result (all $P < 0.05$). No statistically significant difference was observed in vomiting scores [Table 5] between the midazolam-dexamethasone and midazolam-dexmedetomidine arms ($P > 0.05$).

Similarly, the repeated measure confirmed ($P < 0.05$) that the statistically significant between-arm difference was found in terms of sedation scores [Chart 3] in recovery up to 2 h after surgery ($P = 0.001$), whereas it was greater in the dexmedetomidine group. The score was higher in subjects in the midazolam-dexmedetomidine than in the midazolam-dexamethasone group ($P = 0.01$).

Discussion

The eligible patients were scheduled for laparoscopic cholecystectomy and randomly assigned into three interventional arms that receiving midazolam-ephedrine, midazolam-dexamethasone, or midazolam-dexmedetomidine. Our results show lower mean blood pressure in the third study arm and their lower heart rate during the interval of 60–90 min after the start of surgery. The nausea incidence was lower in the dexmedetomidine and dexamethasone group, and the lowest severity of nausea was related to the first from 4 to 24 h postoperatively, whereas these two arms showed no significant difference in the nausea severity.

Vomiting scores were lower in the midazolam-dexamethasone and the midazolam-dexmedetomidine arms during recovery up to postoperative 4 h, who demonstrated

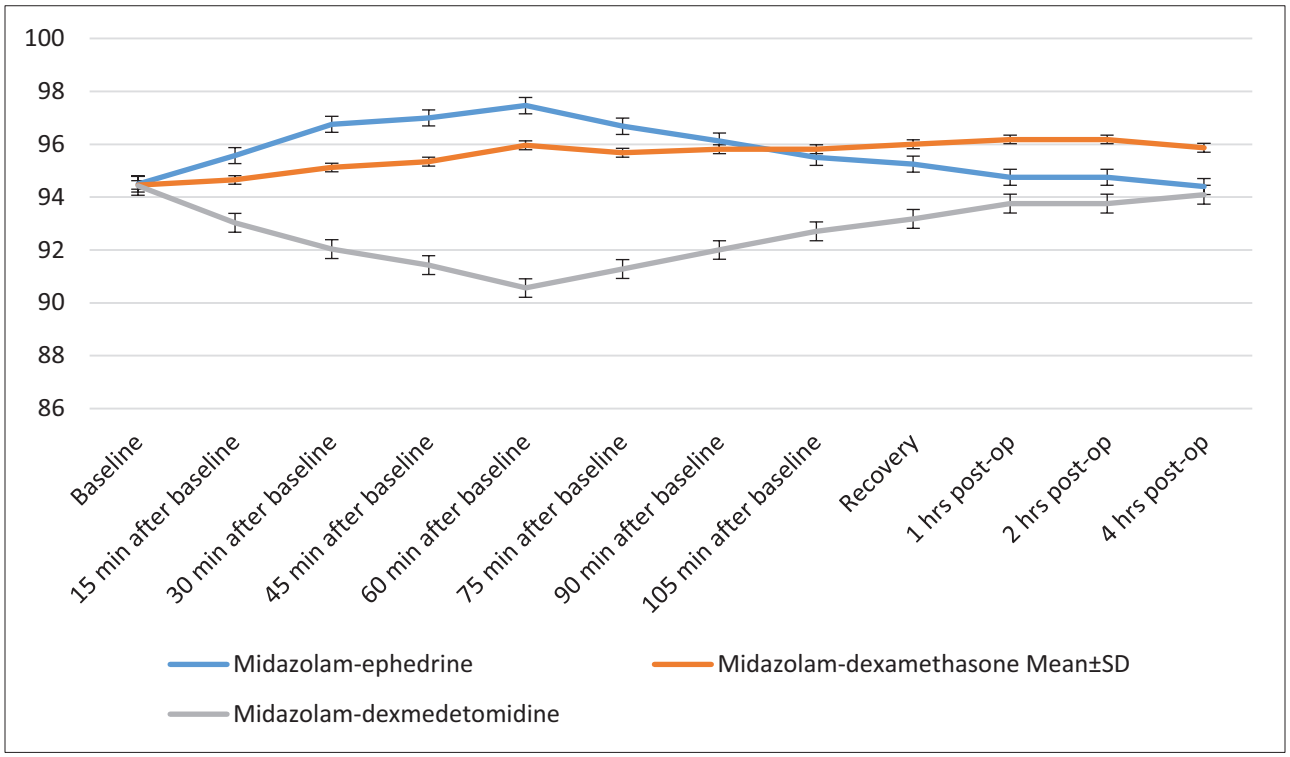

Chart 1: Between-arm comparison of mean blood pressure

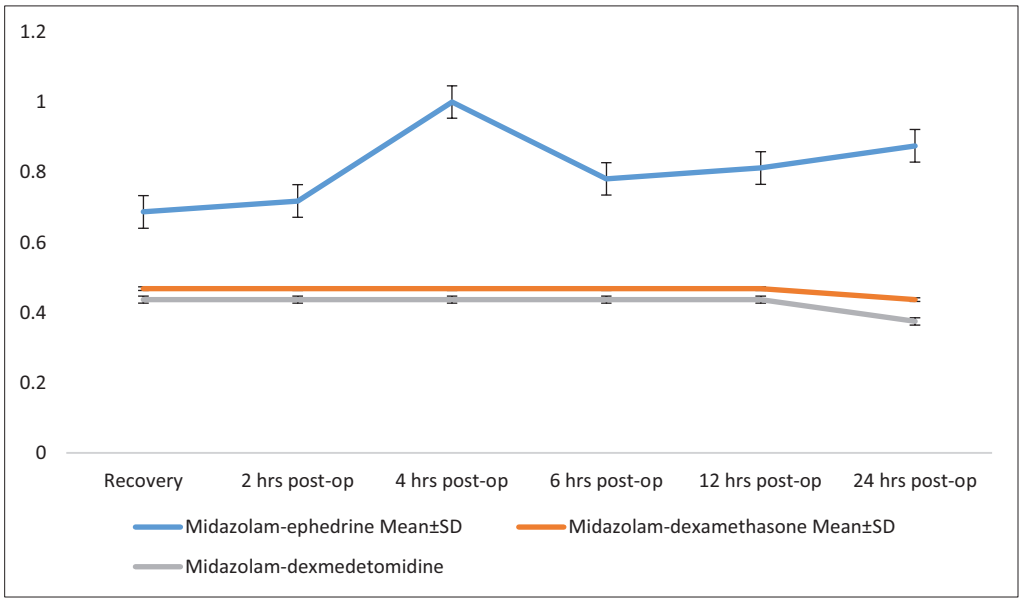

Chart 2: Between-arm comparison of mean nausea severity

no statistically significant difference, whereas sedation score was higher in the dexmedetomidine group during recovery up to 2 h after surgery. A higher score was observed in the study arm than those receiving dexamethasone. Overall, lower nausea and vomiting and higher sedation were observed in the dexmedetomidine group, whereas they were hemodynamically unstable, with lower blood pressure and lower heart rate within 60–90 min after the start of surgery.

Indeed, dexmedetomidine is a potent α2-adrenoceptor that has been widely used because of its anxiolytic, sedative, analgesic, sympatholytic, and hemodynamic regulatory properties.[9] Though a plenty of studies support the antiemetic effect of low doses of dexmedetomidine in attenuating postoperative nausea and vomiting,[10,16] the mechanism is still not fully understood; however, it may be due to the cost-saving of anaesthesia and opioids contributing to postoperative nausea and vomiting, and decreased sympathetic tone may also contribute to the reduction.[11,12,19]

As established by a study (Modir *et al.*, 2019) in line with our study, dexmedetomidine provided a more effective efficacy

Table 5: Between-arm comparison of mean and SD of vomiting score

Group, vomiting score	Midazolam-ephedrine, mean ± SD	Midazolam-dexamethasone, mean ± SD	Midazolam-dexmedetomidine, mean ± SD	*P* value
Recovery	0.093 ± 0.296	00.00 ± 00.00	00.00 ± 00.00	0.04
2 h postop	0.093 ± 0.296	00.00 ± 00.00	00.00 ± 00.00	0.04
4 h postop	0.187 ± 0.592	00.00 ± 00.00	00.00 ± 00.00	0.04
6 h postop	0.000 ± 0.000	00.00 ± 00.00	00.00 ± 00.00	0.999
12 h postop	00.00 ± 00.00	00.00 ± 00.00	00.00 ± 00.00	0.999
24 h postop	00.00 ± 00.00	00.00 ± 00.00	00.00 ± 00.00	0.999

SD: standard deviation

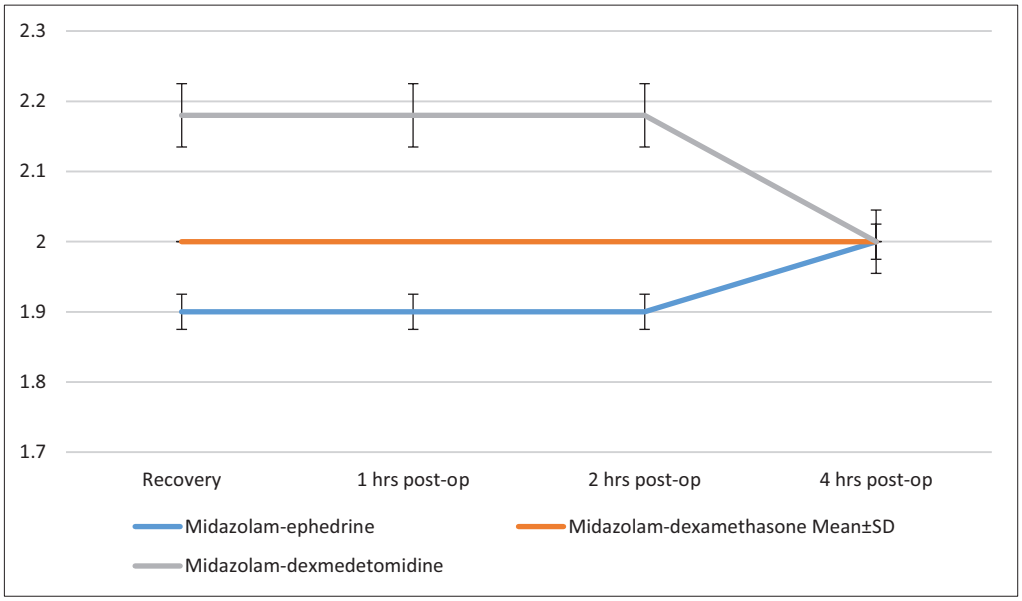

Chart 3: Between-arm comparison of mean sedation score

because of the higher Ramsey score than those of the other three arms; it should be used with caution because the adjuvant reduced the patient's blood pressure and heart rate and caused unexpected side effects.[20] Another comparative clinical trial on the efficacy of dexmedetomidine, dexamethasone, and metoclopramide on postoperative nausea and vomiting after tympanomastoidectomy (Modir *et al.*, 2019) demonstrated that the incidence of nausea and vomiting was equal to zero in the dexmedetomidine group. Moreover, they showed that the nausea score was the lowest in the group and that patients receiving dexmedetomidine and dexamethasone might have a better final nausea score, though nausea and vomiting decreased in all three groups.[21] Our results were consistent with those of Modir *et al.*'s study.

Likewise, as indicated by one review study on assessing dexmedetomidine in preventing nausea and vomiting during general anaesthesia (Jin *et al.*, 2017), they found that dexmedetomidine is associated with side effects such as bradycardia and hypotension; however, if can be reduced, it may be used to attenuate nausea and vomiting.[22] Our results were consistent with theirs. As Kleif *et al.*'s clinical study pointed out (2017), preoperative dexamethasone did not reduce nausea and vomiting,[23] whereas we found that the effects were more pronounced in patients treated with dexmedetomidine and midazolam and that dexamethasone also attenuated nausea and vomiting. Similarly, consistent with our results for reduced nausea but not vomiting, Geng *et al.* (2016) explored the effect of dexmedetomidine on 65 adult patients undergoing laparoscopic surgery by administering 0.5 μg/kg dexmedetomidine before anaesthesia until the end of the surgery and concluded that the medication can attenuate postoperative nausea but not vomiting within the 24 h postoperatively.[24]

As reported by Yoon *et al.*'s study, to evaluating dexmedetomidine combined with midazolam versus dexmedetomidine alone for sedation, nausea, and vomiting during spinal anaesthesia, the authors showed that though sedation depth, Ramsay score, and nausea and vomiting were not different in the two groups, they showed that the mean blood pressure and heart rate were lower in the dexmedetomidine alone group over 10 min after infusion and that midazolam and dexmedetomidine continuous infusion could be a promising sedation technique,[25] whose results on the impact of sedation were consistent with those we present herein. In line with our study, Bakri *et al.*'s study (2015)

conducted in Sudan[11] has compared dexmedetomidine and dexamethasone in nausea and vomiting prevention after laparoscopic cholecystectomy; they showed that lower blood pressure and heart rate were observed in the group receiving dexmedetomidine, without any adverse events. They concluded that like dexamethasone, it could attenuate the severity and incidence of postoperative nausea and vomiting and those dexmedetomidine-sedated patients had less pain during the first 24 h after surgery. In a 2015 meta-analysis of the efficacy of dexmedetomidine on postoperative nausea and vomiting involving 6480 subjects, Liang *et al.* observed that dexmedetomidine was more effective in controlling postoperative nausea and vomiting than placebo but could not prevent all postoperative complications.[26] The results from the review study were consistent with ours.

The combination of dexamethasone-midazolam is thus concluded to be useful in the sedation and inhibition of nausea and vomiting in our study, but the dexmedetomidine treatment was most effective. Our clinical trial showed that the combination of midazolam-ephedrine was not effective, whereas the strong beneficial effect was observed in the dexmedetomidine-sedated arm.

Hagemann *et al.* (2000) when exploring the efficacy of ephedrine on reducing nausea and vomiting after abdominal hysterectomy reported reduced nausea and vomiting within postoperative 24 h.[27] In contrast, the superior efficacy of dexmedetomidine-midazolam in controlling nausea and vomiting and potentiating sedation was supported by our study.

Conclusion

According to the results, dexmedetomidine showed the best effect in attenuating nausea and vomiting and potentiating postoperative sedation. Dexmedetomidine can reduce blood pressure and heart rate. Moreover, dexamethasone following dexmedetomidine, as adjuvants to midazolam, can afford beneficial effects in the attenuation of nausea and vomiting and potentiating postoperative sedation. Accordingly, dexmedetomidine and dexamethasone as adjuvants to midazolam can be recommended to attenuate nausea and vomiting and potentiate postoperative sedation for hemodynamically stable and unstable patients, respectively, undergoing laparoscopic surgery.

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Conflicts of interest

There are no conflicts of interest.

References

1. Shaikh SI, Nagarekha D, Hegade G, Marutheesh M. Postoperative nausea and vomiting: A simple yet complex problem. Anesth Essays Res 2016;10:388-96.
2. Gan TJ, Belani KG, Bergese S, Chung F, Diemunsch P, Habib AS, *et al*. Fourth consensus guidelines for the management of postoperative nausea and vomiting. Anesth Analg 2020;131:411-48.
3. Fujii Y, Nakayama M. Reduction of postoperative nausea and vomiting and analgesic requirement with dexamethasone in women undergoing general anesthesia for mastectomy. Breast J 2007;13:564-7.
4. Ko-Iam W, Sandhu T, Paiboonworachat S, Pongchairerks P, Junrungsee S, Chotirosniramit A, *et al*. Metoclopramide, versus its combination with dexamethasone in the prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy: A double-blind randomized controlled trial. J Med Assoc Thailand 2015;98:265-72.
5. Choi EK, Park SJ, Park C, Lim JA. Comparison of palonosetron with combined palonosetron and midazolam for preventing postoperative nausea and vomiting after laparoscopic cholecystectomy. Medicine 2021;100:e26997.
6. Sun Y, Lu Y, Huang Y, Jiang H. Is dexmedetomidine superior to midazolam as a premedication in children? A meta-analysis of randomized controlled trials. Paediatr Anaesth 2014;24:863-74.
7. Bauer KP, Dom PM, Ramirez AM, O'Flaherty JE. Preoperative intravenous midazolam: Benefits beyond anxiolysis. J Clin Anesth 2004;16:177-83.
8. Chatterjee S, Rudra A, Sengupta S. Current concepts in the management of postoperative nausea and vomiting. Anesthesiol Res Pract 2011;2011:748031.
9. Gupta N, Rath GP, Prabhakar H, Dash HH. Effect of intraoperative dexmedetomidine on postoperative recovery profile of children undergoing surgery for spinal dysraphism. J Neurosurg Anesthesiol 2013;25:271-8.
10. Massad IM, Mohsen WA, Basha AS, Al-Zaben KR, Al-Mustafa MM, Alghanem SM. A balanced anesthesia with dexmedetomidine decreases postoperative nausea and vomiting after laparoscopic surgery. Saudi Med J 2009;30:1537-41.
11. Bakri MH, Ismail EA, Ibrahim A. Comparison of dexmedetomidine and dexamethasone for prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy. Korean J Anesthesiol 2015;68:254-60.
12. Bakan M, Umutoglu T, Topuz U, Uysal H, Bayram M, Kadioglu H, *et al*. Opioid-free total intravenous anesthesia with propofol, dexmedetomidine and lidocaine infusions for laparoscopic cholecystectomy: A prospective, randomized, double-blinded study. Braz J Anesthesiol 2015;65:191-9.
13. Abdalla MW, Sahar M, El Sombaty AI, Abdalla NM, Zeedan RB. Propofol dexmedetomidine versus propofol ketamine for anesthesia

of endoscopic retrograde cholangiopancreatography (ERCP) (a randomized comparative study). Egypt J Anaesth 2015;31:97-105.
14. Habib AS, White WD, Eubanks S, Pappas TN, Gan TJ. A randomized comparison of a multimodal management strategy versus combination antiemetics for the prevention of postoperative nausea and vomiting. Anesth Analg 2004;99:77-81.
15. Wakamiya R, Seki H, Ideno S, Ihara N, Minoshima R, Watanabe K, *et al*. Effects of prophylactic dexamethasone on postoperative nausea and vomiting in scoliosis correction surgery: A double-blind, randomized, placebo-controlled clinical trial. Sci Rep 2019;9:2119.
16. Mohd Daut F, Seevaunnamtum S, Nik Mohamad N, Che Omar S, Wan Hassan W. Granisetron vs. granisetron and dexamethasone on the reduction of postoperative nausea and vomiting (PONV) after caesarean section with intrathecal morphine: A randomised controlled trial. Egypt J Anaesth 2021;37:196-201.
17. Grunberg SM. Antiemetic activity of corticosteroids in patients receiving cancer chemotherapy: Dosing, efficacy, and tolerability analysis. Ann Oncol 2007;18:233-40.
18. Kose EA, Honca M, Yılmaz E, Batislam E, Apan A. Comparison of effects of dexmedetomidine-ketamine and dexmedetomidine-midazolam combinations in transurethral procedures. Urology 2012;79:1214-9.
19. Turgut HC, Arslan M. An overview of treatment options for postoperative nausea and vomiting after laparoscopic surgical procedures. Anaesth Pain Intensive Care 2016:193-200.
20. Modir H, Moshiri E, Kamali A, Shokrpour M, Shams N. Prophylatic efficacy of dexamethasone, ketamine and dexmedetomidine against intra- and postoperative nausea and vomiting under spinal anesthesia. Formos J Surg 2019;52:17.
21. Modir H, Moshiri E, Kamali A, Khalifeh A, Mohammadbeigi A. Comparing the efficacy of dexmedetomidine, dexamethasone, and metoclopramide in postoperative nausea and vomiting of tympanomastoidectomy surgery: A double-blind randomized clinical trial. J Pharm Negat Results 2019;10:57-62.
22. Jin S, Liang DD, Chen C, Zhang M, Wang J. Dexmedetomidine prevent postoperative nausea and vomiting on patients during general anesthesia: A PRISMA-compliant meta analysis of randomized controlled trials. Medicine (Baltimore) 2017;96:e5770.
23. Kleif J, Kirkegaard A, Vilandt J, Gögenur I. Randomized clinical trial of preoperative dexamethasone on postoperative nausea and vomiting after laparoscopy for suspected appendicitis. Br J Surg 2017;104:384-92.
24. Geng Z-Y, Liu Y-F, Wang S-S, Wang D-X. Intra-operative dexmedetomidine reduces early postoperative nausea but not vomiting in adult patients after gynaecological laparoscopic surgery: A randomised controlled trial. Eur J Anaesthesiol 2016;33:761-6.
25. Yoon DK, Ban JS, Lee SG, Lee JH, Kim E, An J. Dexmedetomidine combined with midazolam vs. dexmedetomidine alone for sedation during spinal anesthesia. Korean J Anesthesiol 2016;69:446-52.
26. Liang X, Zhou M, Feng JJ, Wu L, Fang SP, Ge XY, *et al*. Efficacy of dexmedetomidine on postoperative nausea and vomiting: A meta-analysis of randomized controlled trials. Int J Clin Exp Med 2015;8:8450-71.
27. Hagemann E, Halvorsen A, Holgersen O, Tveit T, Raeder JC. Intramuscular ephedrine reduces emesis during the first three hours after abdominal hysterectomy. Acta Anaesthesiologica Scandinavica 2000;44:107-11.