Journal of Iranian Medical Council, Volume 7, Issue no. 2
http://dx.doi.org/10.18502/jimc.v7i2.15038

Original Article

Impact of Dexmedetomidine on Postoperative Nausea and Vomiting in Opiate-Addicted Patients Undergoing Elective Laparoscopic Cholecystectomy: A Randomized, Placebo-Controlled Clinical Trial

Hamidreza Azizi Farsani[1], Gholamreza Mohseni[2], Mohammad Hossein Rezaee[2], Shayesteh Khorasanizadeh[1], Faranak Behnaz[3], Padideh Ansar[1] and Houman Teymourian[4*]

1. Anesthesiology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
2. Department of Anesthesiology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
3. Anesthesiology Department, Shohada Tajrish Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
4. Clinical Research Development Unit, Shohada-e-Tajrish Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Abstract

Background: Postoperative Nausea and Vomiting (PONV) is one of the most common complications of general anesthesia, moreover opioid addiction increases the risk of PONV. Hence, this study evaluates the effect of administering dexmedetomidine infusion as an intraoperative analgesic on PONV in opium-addicted patients who underwent elective laparoscopic cholecystectomy.

Methods: In a randomized clinical trial, 100 opium-addicted patients who were candidates for elective laparoscopic cholecystectomy surgery under general anesthesia were studied in two groups of 50 participants. The intervention group received dexmedetomidine infusion 10 *min* after induction of anesthesia until the end of surgery. The placebo group received normal saline at the same time. The rate of PONV was compared between the two groups.

Results: Both groups had no significant difference in terms of hemodynamic parameters during surgery, including pulse rate, systolic and diastolic blood pressure, and duration of anesthesia. In the dexmedetomidine group, patients had less PONV than the control group, and this difference was significant (p=0.0164).

Conclusion: Dexmedetomidine administration during laparoscopic surgery can reduce PONV, especially in patients addicted to opium.

Keywords: Dexmedetomidine, Laparoscopic cholecystectomy, Opioid-related disorders, Postoperative nausea and vomiting

*** Corresponding author**

Houman Teymourian, MD
Clinical Research Development Unit, Shohada-e-Tajrish Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
Tel: +98 21 2271 8001
Email: houman72625@yahoo.com

Received: 6 Feb 2023
Accepted: 28 Oct 2023

Citation to this article
Azizi Farsani H, Mohseni G, Rezaee MH, Khorasanizadeh S, Behnaz F, Ansar P, *et al*. Impact of Dexmedetomidine on Postoperative Nausea and Vomiting in Opiate-Ad-dicted Patients Undergoing Elective Laparoscopic Cholecystectomy: A Ran-domized, Placebo-Controlled Clinical Trial. *J Iran Med Counc*. 2024;7(2):263-9.

Introduction

General anesthesia is used in many surgeries and sometimes it is accompanied by many side effects such as nausea, vomiting, chills and hemodynamic instability (1). Postoperative Nausea and Vomiting (PONV) and chills are common complications of general anesthesia (2). PONV can cause more serious complications such as aspiration and suture loosening (3). It causes electrolyte disorders, increased bleeding, prolonged recovery and hospitalization in patients (4). The probability of a patient suffering from PONV depends on several risk factors and increases with the increase in the number of those risk factors. Apfel *et al* identified female gender, being non-smoker, history of PONV/motion sickness and the need for postoperative narcotics as independent risk factors (5). Although prophylactic actions are more effective than rescue actions to reduce PONV, a proportion of patients require treatment in the Postanesthesia Care Unit (PACU) even after appropriate prophylactic treatment (6,7). Some studies have shown several drugs to be effective in reducing PONV, but there is still no proven drug (8).

In 2010, 15.5 million people worldwide were dependent on opium. Age standardized prevalence was higher in males than females and peaked at 25-29 years of age. According to this estimate, opium addiction in 2010 was associated with a 73% increase in DALYs compared to 1990. Opium addiction is an important factor in the global disease burden. Its contribution to premature mortality (relative to prevalence) varies geographically (9).

Dexmedetomidine, a selective α2 agonist, has analgesic effects and has a different mechanism of action compared to narcotics. Intraoperative use of dexmedetomidine has clearly improved postoperative outcomes when used as part of ERAS protocols (10). This drug has sedative, analgesic, sympatholytic and amnestic properties (11). Dexmedetomidine can reduce the perioperative consumption of narcotics and in PACU as well as the intensity of postoperative pain (12). The effectiveness of dexmedetomidine administration during or before surgery on reducing PONV has been evaluated in some studies (13-15).

Therefore, the present trial was conducted to study the effects of dexmedetomidine administered intraoperatively on PONV in opium addicted patients who underwent elective laparoscopic cholecystectomy.

Materials and Methods

This study was a randomized and placebo-controlled clinical trial that included 178 opium-addicted patients (between 20-60 years old) candidates for elective laparoscopic cholecystectomy surgery, referring to "Shohadaye Tajrish Hospital" (affiliated to Shahid Beheshti University of Medical Sciences). The study included all patients who used at least 1 gram of opium per day (natural or semi-synthetic alkaloids) orally or by inhalation for more than previous six months. All the enrolled patients met the inclusion criteria such as American Society of Anesthesiologists (ASA) class 1 and 2, systolic blood pressure between 140 and 90 *mmHg* during 24 *hr* before the operation. Any history of cardiovascular disease, history of gastrointestinal disease, preoperative nausea-vomiting, preoperative opiate withdrawal symptoms, use of antiemetic drugs, and a history of motion sickness or PONV caused the participants to be removed from the study and replaced with another 70 suitable participants. During the operation, severe bleeding, conversion to laparotomy and operation duration of more than four hours led to removal from the study and replacement with a suitable participant.

Calculation of sample size

According to similar studies (13-15) in this field, and while considering the assumptions: (power) 80%, (error) 5%, (effect size) 40% and risk ratio of about 3% in two groups and considering the ratio of one to one in two group. Considering a 5% drop in the total number resulting from calculations, a total of at least 50 patients were required in each group.

Random allocation

Using a computer program based on a random number generation protocol, we randomly assigned the participating patients to the control or intervention group with an aspect ratio of 1:1. The patients were divided into two groups of 50 people.

The participants were classified by an online calculator at www.calculator.net and based on the output of the calculator, each patient was randomly assigned a number. The control group included numbers 1 to

50 and the intervention group consisted of numbers 51 to 100. In addition, both groups were the same in terms of age and gender frequency distribution. The diagram of the sampling process of the study is presented in figure 1.

Intervention

Dexmedetomidine drug and placebo were prepared with the same shape, color, size and packaging and were coded as A&B by a person other than the researcher before the infusion. Both groups received midazolam 0.03 *mg/kg*, fentanyl 2-4 *μg/kg*, propofol 1.5-2 *mg/kg*, and cisatracurium 0.23 *mg/kg* for induction of anesthesia, and during the operation, propofol was infused in 100-300 *μg/kg/min* as maintenance. The exact dose criterion for propofol infusion was maintaining BIS (Vista, Covedian, USA) between 40-60. The intervention group was given Dexmedetomidine 1 *μg/kg/min* 10 *min* after induction until the end of the procedure. The placebo group was also given normal saline infusion in the same time interval. If the patients needed analgesia, Apotel was used instead of narcotics. Ten minutes before the end of the procedure, 4 *mg* of ondansetron was prescribed intravenously for the prevention of nausea and vomiting. Relevant information (systolic and diastolic blood pressure, heart rate, and operation 111 duration.) were extracted and recorded during the operation by an anesthesiologist or a trained nurse. At the end of the operation, the patient was extubated

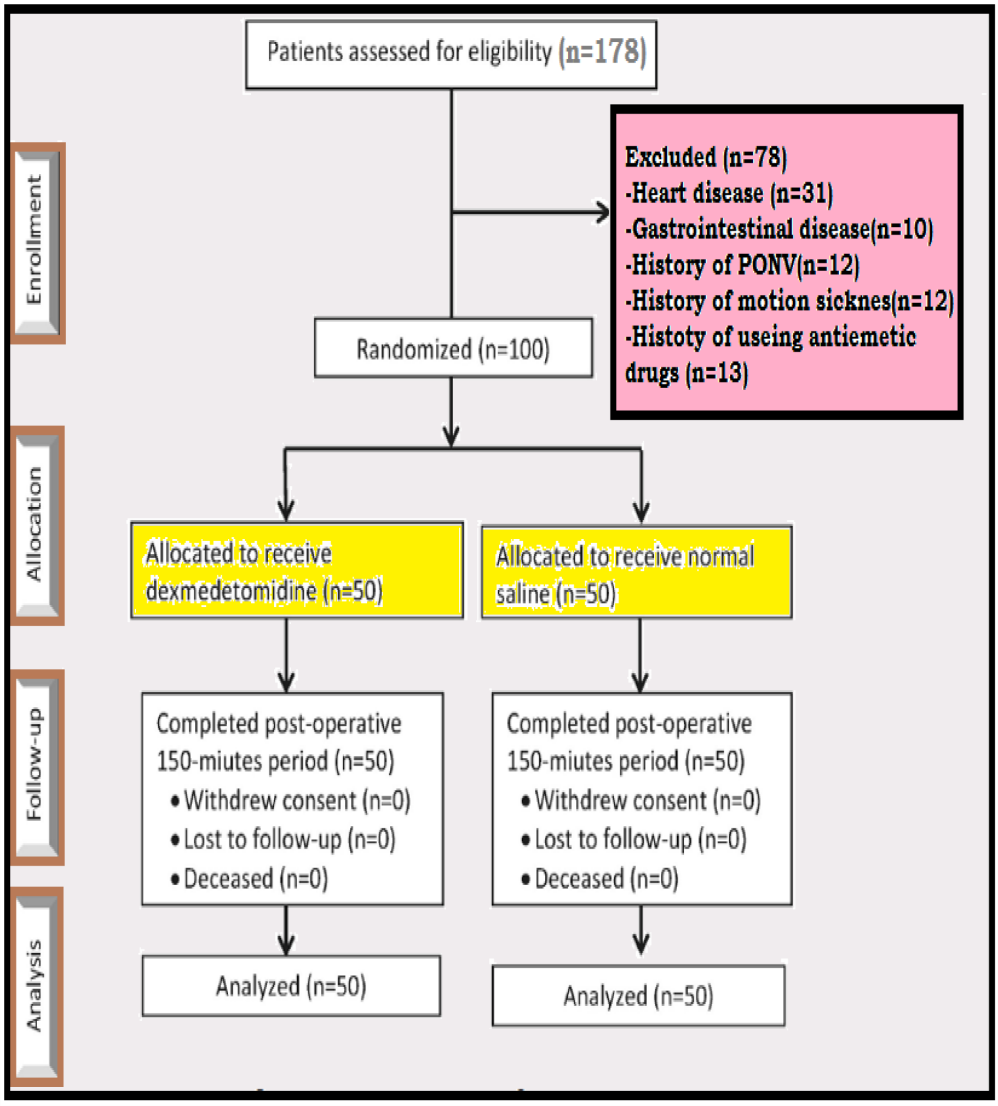

Figure 1. Consort flow diagram of this trial.

after obtaining the necessary criteria and reverse of neuromuscular block and was transferred to the PACU with hemodynamic and ventilation monitoring.

Primary outcomes

During the recovery period, the observation and recording method was used by an anesthesiologist and a trained nurse to evaluate and record the degrees of PONV (nausea, retching, regurgitation and vomiting). The information was recorded from the time of arrival until 120 *min* later. After collecting all the patients' information, the information was aggregated and used statistically. During the patients' stay in PACU, in case of nausea, vomiting or any other complications, appropriate treatments were performed.

Ethical considerations

The present study was evaluated by Vice President of Research and Technology of Shahid Beheshti University of Medical Sciences and was approved by the ethical committee (IR. SBMU. MSP. REC.1399.704). Also, the written informed consent was obtained from all the study participants.

Statistical analysis

The resulting data were analyzed by SPSS statistical software for social sciences (version 21, IBM. Corporation, Armonk, NY, USA). Descriptive statistics including mean, Standard Deviation (SD) for quantitative variables and number and percentage for qualitative variables were used. Independent sample t-test was used to compare the average parameters in each of the two groups. At the same time, Chi-square test was utilized to compare the quality variables of the two groups. In addition, analysis of variance (ANOVA) with interaction effect was used to analyze the statistical data. p-values less than 0.05 were considered statistically significant.

Results

Table 1 shows the demographic characteristics of the two groups including age, weight and gender. The average age of the participants in the intervention group was 46.87±10.3 and in the control group was 44.01±13.3 years (p-value=0.073). The average weight of the participants in the intervention group was 70.12 ± 10.8 *kg* and in the control group was 74.23±10.1 *kg* (p-value=0.670). It was not possible to include an equal number of patients of both sexes, which caused the number of male patients to dominate over female patients in both groups (p-value=0.631). However, there was no significant difference between the two groups in the comparison of these basic data.

Clinical efficacy endpoints

According to table 2, both groups did not differ in terms of intraoperative hemodynamic parameters including pulse rate, systolic and diastolic blood pressure. According to the same table, there was no significant difference between the two groups regarding the duration of the operation (p-value=0.741). The two groups were significantly different in terms of the number of patients suffering from PONV (p-value=0.002). In addition, it was a significant difference between two group in terms of postoperative nausea (one of the degrees of PONV), (p-value=0.030). No significant difference was found between the two groups in terms of retching, regurgitation and vomiting in PACU (Table 3). From

Table 1. General information of the two examined samples

Variables		Saline group (n=50)	Dexmedetomidine group (n=50)	p-value
Age (year), mean±SD, SD=Standard Deviation		46.87±10.3	44.01±13.3	0.073
Weight (*kg*), mean±SD		70.12±10.8	74.23±10.1	0.670
Gender, number	Male	33	31	0.631
	Female	17	19	

Table 2. Comparison of hemodynamic parameters between two groups

Parameters	Saline group (n=50)	Dexmedetomidine group (n=50)	p-value
Heart rate	79	73	0.741
SBP (*mmHg*), mean±SD	113.9±3.5	124.6±9	0.230
DBP (*mmHg*), mean±SD	74.1±7.5	82.3±5.5	0.321
Duration of anesthesia (*min*), means±SD	141.3±15.5	159.2±36.1	0.090

Table 3. Retching, regurgitation and vomiting in PACU

PONV variables	Control group	Dexmedetomidine group	p-value
Nausea	24	10	0.015
Retching	2	1	0.030
Regurgitation	1	0	0.055
Vomiting	1	0	0.049
PONV	24	10	0.002

the beginning of recovery after anesthesia until the 50th *min* (p-value=0.055), there were remarkably fewer patients with PONV in the dexmedetomidine group, compared to the saline group (p-value=0.049). From the 60th minute, both groups were the same in this regard (Figure 2).

Discussion

As the present study showed, intraoperative infusion of dexmedetomidine reduces postoperative nausea and PONV in opium addicted patients. It can be stated that the administration of dexmedetomidine during surgery reduces the frequency of postoperative nausea and PONV and the duration of these annoying postoperative complications in patients who undergo laparoscopic surgeries.

PONV is a common complaint among patients after general anesthesia (16). Several risk factors, including anesthetic agent, anesthetic technique, surgical technique and patient characteristics, can cause post-anesthetic PONV (17,18). Therefore, anesthesiologists and surgeons strive to identify patients at risk of developing PONV in order to implement the necessary preventive actions (19). Recently, multimodal approaches have been employed in order to reduce the occurrence of PONV, among which the administration of combined antiemetics, preoperative antianxiety, adequate hydration, and local analgesic techniques are notable (20). The effectiveness of dexmedetomidine administration during or before surgery on reducing PONV has

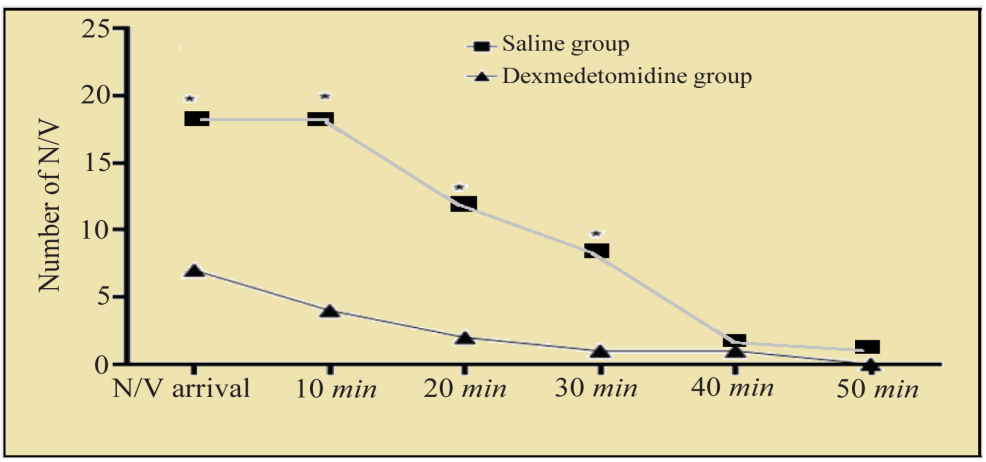

Figure 2. Number of PONV occurrence over time in two groups.* p<0.05 *vs.* saline group.

been discussed in some studies (21,22). In 2017, Jin *et al* reported that dexmedetomidine prevents PONV in patients under GA and prescribing continuous infusion of dexmedetomidine has the advantage of preventing PONV and also reducing side effects such as bradycardia and hypotension (13). Rajabi *et al* demonstrated in 2021 that the administration of dexmedetomidine before major surgery can reduce the occurrence of (PONV) and 192 post-operative shivering, especially in patients addicted to opium (15).

The present study shows that intraoperative infusion of dexmedetomidine can reduce postoperative nausea and PONV in opium-addicted patients. Of course, we faced some limitations. For example, it was not possible to include the same number of patients of both sexes, which led to a preponderance of male patients. Thus, apparently, we cannot generalize our results to both sexes. Another limitation was that no laboratory testing of the patients' blood opioid level or opiate level was included in the screening results. Regarding the commitment to respect the rights of the patients and avoiding the request for drug abuse tests, which is always with the reluctance and resentment of the patients, we had to rely on the history provided by the patients themselves about addiction.

Conclusion

Finally, we concluded that the administration of dexmedetomidine during laparoscopic surgeries can reduce postoperative nausea and PONV, especially in patients addicted to opium. This effect is probably more obvious in the first hour after surgery. In addition, it can be used as a safe drug to reduce the recovery time after general anesthesia and the duration of postoperative complications such as nausea and vomiting. Reduction in PONV mechanism seems to decrease in intraoperative fentanyl consumption and the antiemetic effect of Dexmedetomidine induced by direct effect on α_2 receptor through inhibition of catecholamine by parasympathetic tone (23).

Acknowledgements

We would like to thank all the patients who participated and all the individuals who collaborated in the implementation of this study. The authors received no financial support for the research, writing and/or publication of this study.

Conflict of Interest

The authors declare no conflict of interest in this study.

References

1. Giesbrecht GG, Sessler DI, Mekjavic IB, Schroeder M, Bristow GK. Treatment of 219 mild immersion hypothermia by direct body-to-body contact. J Appl Physiol 1994;76(6):2373-9.

2. Stadler M, Bardiau F, Seidel L, Albert A, Boogaerts JG. Difference in risk factors for postoperative nausea and vomiting. Anesthesiology 2003;98(1):46-52.

3. Cao X, White PF, Ma H. An update on the management of postoperative nausea and vomiting. J Anesth 2017;31(4):617-26.

4. Lin CJ, Williams BA. Postoperative nausea and vomiting in ambulatory regional anesthesia. Int Anesthesiol Clin 2011;49(4):134-43.

5. Apfel CC, Philip BK, Cakmakkaya OS, Shilling A, Shi YY, Leslie JB, et al. Who is at risk for postdischarge nausea and vomiting after ambulatory surgery? Anesthesiology 2012; 117:475–86.

6. Apfel CC, Korttila K, Abdalla M, Kerger H, Turan A, Vedder I, et al. A factorial trial of six interventions for the prevention of postoperative nausea and vomiting. N Engl J Med 2004;350(24):2441–51.

7. Gan TJ, et al. Consensus guidelines for the management of postoperative nausea and vomiting. Anesth Analg 2014; 118:85–113.

8. Domino KB, Anderson EA, Polissar NL, Posner KL. Comparative efficacy and safety of ondansetron,

droperidol, and metoclopramide for preventing postoperative nausea and vomiting: a meta-analysis. Anesth Analg 1999;88(6):1370-9.

9. Degenhardt L, Charlson F, Mathers B, Hall WD, Flaxman AD, Johns N, et al. The global epidemiology and burden of opioid dependence: results from the global burden of disease 2010 study. Addiction 2014 Aug;109(8):1320-33.

10. Kaye AD, Chernobylsky DJ, Thakur P, Siddaiah H, Kaye RJ, Eng LK, et al. Dexmedetomidine in enhanced recovery after surgery (ERAS) protocols for postoperative pain. Curr Pain Headache Rep 2020 Apr 2;24(5):21.

11. 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(3):191-9.

12. Liu Y, Liang F, Liu X, Shao X, Jiang N, Gan X. Dexmedetomidine reduces perioperative opioid consumption and postoperative pain intensity in neurosurgery: a meta-analysis. J Neurosurg Anesthesiol 2018 Apr;30(2):146-55.

13. Jin S, Liang DD, ChenC, Zhang M, Wang J. Dexmedetomidine prevent postoperative nausea and vomitingon patients during general anesthesia: a PRISMA-compliant meta-analysis ofrandomized controlled trials. Medicine (Baltimore) 2017;96(1):1-7.

14. 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(12):1537-41.

15. Rajabi M, Ommi D, Zali A, Arefian NM. Effects of dexmedetomidine on the postoperative shivering, nausea, and vomiting among opium user patients undergoing elective supratentorial brain tumor surgery: a randomized, placebo, controlled clinical trials. Galen Med J 2021;10:1-8.

16. Gan TJ, Meyer T, Apfel CC, Chung F, Davis PJ, Eubanks S et al. Consensus guidelines for managing postoperative nausea and vomiting. Anesth Analg 2003;97(1):62-71.

17. Watcha MF, White PF. Postoperative nausea and vomiting. Its etiology, treatment, and prevention. Anesthesiology 1992;77(1):162-84.

18. Bryson EO, Silverstein JH. Addiction and substance abuse in anesthesiology. Anesthesiology 2008 NOV;109(5):905-17.

19. Lee SJ, Lee SM, Kim SI, Ok SY, Kim SH, Park SY et al. The effect of aprepitant for the prevention of postoperative nausea and vomiting in patients undergoing gynecologic surgery with intravenous patient controlled analgesia using fentanyl: aprepitant plus ramosetron vs ramosetron alone. Korean J Anesthesiol 2012;63(3):221-6.

20. Riley TJ, McKenzie R, Trantisira BR, Hamilton DL. Droperidol-ondansetroncombination versus droperidol alone for postoperative control of emesis after total 276 abdominal hysterectomies. J Clin Anesth 1998;10(1):6-12.

21. 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(1):1-7.

22. 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(12):1537-41.

23. 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 2017 Jan;96(1):e5770.