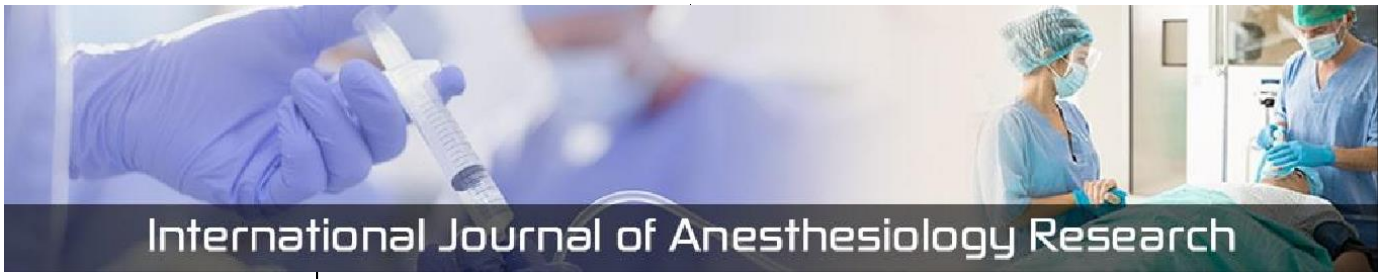

E-ISSN: 2664-8857
P-ISSN: 2664-8849
www.anesthesiologyjournal.in
IJAR 2024; 5(1): 17-21
Received: 22-11-2023
Accepted: 29-12-2023

Md. Mashfiqur Rahman Khan
Specialist, (Anaesthesia, ICU and Pain Medicine), Sheikh Fazilatunnessa Mujib Memorial KPJ Specialized Hospital and Nursing College, Dhaka, Bangladesh

Md. Saiful Islam
Assistant Professor (Anesthesiology), Green life Medical College, Dhaka, Bangladesh

Ashfaque Bar Chowdhury
Specialist (Anesthesiology), Square Hospitals Ltd., Dhaka, Bangladesh

Kazi Rafsan
Senior Specialist, (Anesthesiology), Evercare Hospital, Dhaka, Bangladesh

Saifuddin Mohammad Mamun
Associate Specialist, (Anaesthesia), Ministry of Health, Maldives

Corresponding Author:
Md. Mashfiqur Rahman Khan
Specialist (Anaesthesia, ICU and Pain Medicine), Sheikh Fazilatunnessa Mujib Memorial KPJ Specialized Hospital and Nursing College, Dhaka, Bangladesh

Evaluation of Effect of Intraperitoneal Dexmedetomidine Versus Remifentanil as Adjuvant of Ropivacaine Infiltration for Pain Relief After Laparoscopic Appendectomy

Md. Mashfiqur Rahman Khan, Md. Saiful Islam, Ashfaque Bar Chowdhury, Kazi Rafsan and Saifuddin Mohammad Mamun

DOI: https://doi.org/10.33545/26648849.2024.v6.i1a.38

Abstract
Introduction: Postoperative pain management **is** an important factor for good surgical outcomes.Pain after laparoscopic appendectomy is a combined effect of tissue injury, abdominal distension, local trauma secondary to appendix removal, chemical irritation of the peritoneum and effect of pneumoperitoneum. Dexmedetomidine (alpha-2 adrenergic agonists) has become one of the frequently used adjuvants with local anesthetics as it has been reported to provide postoperative analgesia, anxiolysis, and an anesthetic-sparing action with minimal respiratory depression with its sedative effect that mimics natural sleep. Intraperitoneal instillation of dexmedetomidine with ropivacaine reduces the pain after elective laparoscopic appendectomy in adults in comparison to that with remifentanil and ropivacaine. Morever, the postoperative requirement for rescue analgesia is reduced.
Objective: To assess the evaluation of effect of intraperitoneal dexmedetomidine versus remifentanil as adjuvant of ropivacaine infiltration for pain relief after laparoscopic appendectomy.
Methods: After the Institutional Ethics Committee approval, written informed consent was obtained from all patients, who were included in the study. Totally 50 patients, with the American Society of Anesthesiologists (ASA) physical status I and II, of both sexes, aged between 18 and 60 years, of both genders, with a suspected acute appendicitis scheduled for laparoscopic appendectomy, were included in this study. Group A: Dexmedetomidine 0.5 mcg/kg diluted to 1 ml. + 0.2% ropivacaine with 1 ml of normal saline. Group B: Remifentanil 1µg/kg IV+ 0.2% ropivacaine with 1 ml of normal saline. Repeated measure ANOVA was performed to check the effect of haemodynamic parameters over a time period and to compare between three groups. A p-value <0.05 was considered statistically significant. Statistical analysis was done by using SPSS software version 23 (IBM Corp., Armonk, NY).
Results: There was no statistically significant difference in respect to age, sex, weight, BMI, ASA physical status of the patients and the duration of surgery. VAS at different time intervals were statistically significantly lower at all times in A group compared to B group. None of the patients from both groups complained of shoulder pain. Furthermore, overall VAS in 24 h was also significantly lower in the A group (1.68 ± 0.46) compared to B group (4.47 ± 0.94). The time required for the first dose of rescue analgesia was longer in the A group (122.7±24.5 min) than in B group (89.3±13.2 min), indicating better and longer pain relief in the A group compared to that of B group. The difference was also statistically significant among the two groups. Total analgesic consumption was high in B group than in the A group. Total diclofenac consumption was also low in A group (95.3 ± 15.6 mg) than in B group (135.7 ± 75.1 mg). Incidence of nausea and vomiting was significantly lower in A group than in B group. There was no significant difference between both groups regarding other adverse effects.
Conclusion: Ropivacaine combined with Dexmedetomidine in comparison to Ropivacaine combined with Remifentanil significantly prolonged the duration of postoperative analgesia and reduced consumption of infiltration for pain relief after laparoscopic appendectomy.

Keywords: Intraperitoneal Dexmedetomidine, Remifentanil, Ropivacaine, Laparoscopic Appendectomy

Introduction
Dexmedetomidine (alpha-2 adrenergic agonists) has become one of the frequently used drugs in anesthesia as it has been reported to provide analgesia, anxiolysis, and an anesthetic-sparing action with minimal respiratory depression as well as sedative effect that mimics natural sleep [1]. Intraperitoneal instillation of dexmedetomidine with bupivacaine reduces the pain after elective laparoscopic

cholecystectomy in adults as compared to that with bupivacaine alone or with tramadol. In addition, the postoperative requirement for rescue analgesia is reduced [2]. Appendectomy is now widely performed by the less-painful laparoscopic approach. A Cochrane review concluded that pain was reduced by laparoscopic procedure comparing to open appendectomy in both children and adults [3]. Remifentanil is an opioid widely used for ambulatory anesthesia. Since it has a rapid onsetand short duration of action, it facilitates the control of the depth of anesthesia [4]. However, nausea, vomiting, and respiratory depression in the postoperative period may limit its use. Remifentanil (REMI) is a novel, synthetic short- acting mu-receptor opioid derivative with a unique modification of its chemical structure to include a methyl ester ring [5] REMI undergoes widespread extrahepatic metabolism by blood and tissue nonspecific esterases [6]. Dexmedetomidine, an α-2 agonist, is a new drug used for sedation, amnesia, and analgesia either in perioperative settings or in the intensive care units [7]. It is easy to titrate its effect and both drugs are used by continuous infusion [8]. Although dexmedetomidine may be an anesthetic in its own right, there have been no studies on the use of dexmedetomidine as a sole substitute for remifentanil in ambulatory anesthesia based on desflurane [9, 10]. The magnitude of the analgesic effect of dexmedetomidine is smaller than that observed with remifentanil, which is consistent with the clinical notion that the analgesic property of an α-2 agonists is not as effective as that of opioids. Ropivacaine, one of the most common long-acting local anesthetics, is widely used to treat postoperative pain. The use of ropivacaine for regional anesthesia promotes patient recovery after surgery by facilitating earlier ambulation [11], improving sleep quality [12], reducing opioid consumption [13], and decreasing gastrointestinal adverse reactions [14]. However, ropivacaine alone has a short duration when used for nerve block, usually lasting 2-4hours, and its role in postoperative analgesia is limited. Local anesthetic nerve block with ropivacaine is concentration-dependent, and ropivacaine has an improved sensory versus motor block profile at lower concentrations. Several clinical studies suggest that dexmedetomidine is effective when used as an adjuvant to regional anesthesia to prolong peripheral nerve block [15, 16]; however, concerns for side effects and potential toxicity persist. Analgesic effects with two synergistically interacting anesthetics should occurat lower doses. The safety and efficacy of dexmedetomidine as an adjuvant to ropivacaine have been investigated in randomized controlled trials (RCTs). Intraperitoneal instillation of dexmedetomidine with bupivacaine reduces the pain after elective laparoscopic cholecystectomy in adults as compared to that with bupivacaine alone or with tramadol. In addition, the postoperative requirement for rescue analgesia is reduced [17].

Methods & Materials

After the Institutional Ethics Committee approval, written informed consent was obtained from all patients, who were included in the study. Totally 50 patients, with the American Society of Anesthesiologists (ASA) physical status I and II, of both sexes, aged between 18 and 60 years, of both genders, with a suspected acute appendicitis scheduled for laparoscopic appendectomy, were included in this study.Inclusion criteria were patients of ASA physical status I-II aged between 18 to 60 years of either sex. Exclusion criteriawere patients with physical status of ASA III or greater, uncooperative patients, previous spinal surgeries, spine deformities, local site infection and coagulation abnormalities, allergy to local anesthetics (amide group), neuromuscular diseases, patients with poorly controlled hypertension, patients with hematological disease, neurologic, psychiatric disease, severe renal or hepatic derrangement and patients with history of drug abuse.

One of the anesthetists participating into the study randomized patients to one of 2 study groups, using a computer-generated random number table. Study drugs (dexmedetomidine and remifentanil) were prepared by a nurse without any mark on the syringe. The same nurse whoknew the study protocol adjusted the infusion dose, and the infusion syringe and screen were covered to enable double blindness throughout the operation, and no change of the dose was allowed. The anesthetist blinded to the drug continued with the anesthesia process and recorded the study parameters. On arrival to the operating theater, ECG, noninvasive blood pressure, and pulse oximeter monitoring were applied, and the hemodynamic parameters were evaluated throughout the operation. A S/5 M-BIS module (Datex-Ohmeda, Madison, WI) was used to measure bispectral index value (BIS). Patients were not premedicated. In the operating room, a 20-gauge venous cannula was inserted, and 0.9% saline solution was administered.

Study groups: Group A: Dexmedetomidine 0.5 mcg/kgdiluted to 1 ml. + 0.2% ropivacaine with 1 ml of normal saline.

Group B: Remifentanil 1μg/kg IV+ 0.2% ropivacaine with1 ml of normal saline.

Outcome measures: The primary outcome of the study was to assess the total duration of analgesia in hours (the time duration from the completion of surgery to the time patient requested the first analgesic medication) and the total rescue analgesic dose requirements (in mg) in the first 24 hours postoperatively. The secondary outcomes included the following: (1) comparing the intensity of pain using VAS score postoperatively every 30 minutes for two hours and then after six, 12, and 24 hours; (2) to compare the haemodynamic parameters (mean arterial pressure in mm ofHg and heart rate in beats per minute) intraoperatively at 0 minutes, 15 minutes, 30 minutes, 60 minutes, and 90 minutes and postoperatively every 30 minutes for the first two hours and then after six hours, 12 hours, and 24 hours;
(3) to study the incidence of postoperative nausea and vomiting using the Likert scale and shoulder tip pain after laparoscopic surgery using the VAS score. The outcomes were recorded by an observer who was blinded to the group allocation.

Statistical analysis: The continuous variables were expressed by mean ± standard deviation and the categorical variables were expressed by frequency and percentage. The data have undergone a normality test by the Shapiro-Wilk test. Student's t-test was done for comparison of two groups. The chi-square test was done to check the association between two categorical variables. Repeated measure ANOVA was performed to check the effect of haemodynamic parameters over a time period and to compare between three groups. A p-value <0.05 was considered statistically significant. Statistical analysis was done by using SPSS software version 23 (IBM Corp., Armonk, NY).

Results

There was no statistically significant difference with respect to age, sex, weight, BMI, ASA physical status of the patients and the duration of surgery. VAS at different time intervals were statistically significantly lower at all times in A group compared to B group (Table-1, 2).

Table 1: Demographic data (N=50)

Parameter	Group A (n=25)	Group B (n=25)	p value
Age (years)	37.3±9.2	36.1±9.4	0.88
Sex (female/male)	7/18	6/19	0.69
Weight (kg)	61.6±6.8	59.8±7.1	0.81
BMI (kg/m^2)	21.2±1.4	20.3±1.7	0.62
ASA grade (I/II)	20/5	18/7	0.74
Duration of surgery (min)	64.7±9.2	67.3±12.5	0.55

Data are represented as mean±SD. ASA=American Society of Anesthesiologists, BMI=Body mass index, SD=Standard deviation

Table 2: Visual analog scale pain score (N=50)

Time (h)	Group A (n=25)	Group B (n=25)	p value
At 0.5	3.27±1.40	2.08±0.72	0.001
At 1	4.81±0.10	2.24±0.36	0.001
At 4	4.28±1.02	2.03±0.70	0.001
At 8	3.64±1.40	1.64±0.42	0.001
At 12	3.22±0.80	2.07±0.25	0.001
At 16	4.10±0.90	1.71±0.70	0.001
At 24 h	2.04±0.82	1.02±0.61	0.001

Table 3: Pattern of pain (N=50)

Types of pain	Group A (n=25), n (%)	Group B (n=25), n (%)	p value
Incisional	10 (25)	4 (16)	0.007
Generalized abdominal	13 (32.5)	8 (36	0.001
Perineal	1 (2.5)	1 (2.5)	1
Shoulder	0	0	1
Total	15 (60)	9 (36)	0.002

Values are expressed as number of patients

Table 4: Postoperative overall vas score and analgesic requirements (N=50)

Variable	Group A (n=25)	Group B (n=25)	p value
Over all VAS over 24 h postoperatively	4.47±0.94	1.68±0.46	0.01
Time to first request of analgesia in postoperative period (min)	89.3±13.2	122.7±24.5	0.01
Total dose of diclofenac (mg) in 24 h	135.7±75.1	95.3±15.6	0.01
VAS=Visual analog scale	--	--	--

VAS=Visual analog scale

Table 5: Postoperative adverse/side effects (%) (N=50)

Adverse effect	Group A (n=25), n (%)	Group B (n=25), n (%)	p value
Nausea	5 (20)	2 (8)	0.03
Vomiting	3 (12)	1 (4)	0.02
Pruritus	1 (4)	0	0.29
Sedation	2 (8)	0	0.47

Values are expressed as number of patients

Regarding the pattern of pain, it was predominantly of the generalized abdominal type of pain occurring patients from both the groups (Table 3), followed by incisional pain. One patient from B group and one from A group complained of perineal pain. None of the patients from both groups complained of shoulder pain. Furthermore, overall VAS in 24 h was also significantly lower in the A group (1.68 ± 0.46) compared to B group (4.47 ± 0.94) (Table 4). The time required for the first dose of rescue analgesia was longer in the A group (122.7 ± 24.5 min) than in B group (89.3 ± 13.2min), indicating better and longer pain relief in the A group compared to that of B group. The difference was also statistically significant among the two groups (Table 4). Total analgesic consumption was high in B group than in the A group [Table 4]. Total diclofenac consumption was also low in B group (95.3 ± 15.6 mg) than in A group (135.7 ± 75.1 mg) (Table 4). Incidence of nausea and vomiting was significantly lower in A group than in B group. There was no significant difference between both groups regarding other adverse effects (Table 5).

Discussion

Laparoscopic procedures are gaining popularity in recent years for having advantage of minimal incisions, brief hospital stays, and early ambulation. The main reason for prolonged hospital stay after surgery is pain. Perception of pain is different for different individuals and causes haemodynamic alterations in patients [18]. This acute pain being complex in nature suggests that postoperative analgesia should be multimodal. Various multimodal analgesia techniques were studied for providing pain relief like performing surgery under the subarachnoid block, epidural infusion, parenteral opioids and non-steroidal anti-inflammatory drugs, and intraperitoneal instillation of local anaesthetics. Intraperitoneal instillation of local anaesthetics is a simple and effective method as a part of multimodal analgesia. There was no statistically significant difference with respect to age, sex, weight, BMI, ASA physical status of the patients and the duration of surgery. VAS at different time intervals were statistically significantly lower at all times in RD group compared to RF group. Dexmedetomidine offered also a shorter postoperative length of hospital stay with no significant side effects. Bisgaard *et al*., and Ure *et al*., suggested that parietal pain is the predominant cause of pain [19, 20]. In the present study, we used fixed dose and concentration of ropivacaine i.e. 15 ml of 0.75% ropivacaine in both the groups as the volume of the study drug because the influence of height and weight on the spread of epidural block is very little, and usually not clinically relevant unless considering the extremes of the spectrum [21]. Regarding the pattern of pain, it was predominantly of the generalized abdominal type of pain occurring patients from both the groups [Table 3], followed by incisional pain. One patient from B group and one from A group complained of perineal pain. None of the patients from both groups complained of shoulder pain. Furthermore, overall VAS in 24 h was also significantly lower in the A group (1.68 ± 0.46) compared to B group (4.47 ± 0.94) [Table 4]. The time required for the first dose of rescue analgesia was longer in the A group (122.7 ± 24.5 min) than in B group (89.3 ± 13.2 min), indicating better and longer pain relief in the A group compared to that of B group. The difference was also statistically significant among the two groups. Total analgesic consumption was high in B group than in the A group [Table 4]. Total diclofenac consumption was also low in A group (95.3 ± 15.6 mg) than in B group (135.7 ± 75.1 mg). Incidence of nausea and vomiting was significantly lower in A group than in B group. There was no significant difference between both groups regarding other adverse effects. The timing of the instillation of local anaesthetic intraperitoneally and the appropriate method of instillation are of utmost importance. Unlike bupivacaine used in previous studies, we preferred ropivacaine because of its better safety profile with minimal side effects. The vaso- constricting property of ropivacaine prevents the systemic absorption of the drug and hence avoids cardiac and neurological complications. However, surgically dissected wounds after laparoscopic surgery may increase the absorption of ropivacaine. A study was conducted where the total amount of intraperitoneal Dexmedetomidine consumed was lower in patients receiving ropivacaine as compared with the Remifentanil group. This correlated well with our current study where the rescue analgesic requirement was less after intraperitoneal instillation of ropivacaine [22]. Adding an adjuvant with a lower concentration of local anaesthetics will produce analgesia that is comparable to that produced by the higher concentration of anaesthetics alone. We used dexmedetomidine and ketamine as adjuvants to ropivacaine to compare the analgesic efficacy. This means their findings should be concluded cautiously, but the intent to reduce the need for opioids and pain following surgery is crucial. Lastly, one study presented that conventional versus single port (LA) have different pain levels following surgery, which indicates that it may be important to consider the type of LA performed. While publications focused on operative treatment, retrospective studies did not include the type of LA performed. Nonetheless, this review creates a ground for further research to be performed to reduce the use of opioids, either due to improving pain management or simply educating surgeons that there's already a reduced need for opioid use. Dexmedetomidine does not decrease gut motility, hence it prevents intraoperative and postoperative nausea and vomiting [23]. As far as α-2 agonists are concerned, the

respiratory depression is not a known feature of this group of drugs. Lack of respiratory depression in the patients who were administered dexmedetomidine was one of the most remarkable findings and the evidence was similar to the earlier studies where researchers have found complete absence of clinically detectable respiratory depression in theprevious multiple human studies [24-26]. Limitation of thepresent study is the post-operative pain, which is asubjective experience and can be difficult to quantify objectively and compare when comparing various treatment options. As there are very few studies in the past on addition of dexmedetomidine and Remifentanil to intraperitoneal ropivacaine, further studies with different doses of dexmedetomidine and Remifentanil, timing, concentrations of local anesthetics and routes of administration are needed to provide maximal benefit in terms of post-operative pain relief with minimal adverse effects after laparoscopic surgeries.

Conclusion

Ropivacaine combined with Dexmedetomidine in comparison to Ropivacaine combined with Remifentanil significantly prolonged the duration of postoperative analgesia and reduced consumption of infiltration for pain relief after laparoscopic appendectomy.

Conflict of Interest

None declared

Financial Support

Self funding

References

1. Chocron Y, Aljerian A, Thibaudeau S. Upper- Extremity Nerve Decompression Under Local Anesthesia: A Systematic Review of Methods for Reduction of Postoperative Pain and Opioid Consumption. Hand (N Y). 2020;15(4):447-55. doi: 10.1177/1558944719843635. PubMed Central PMCID: PMC7370381.
2. Zhu G, Kang Z, Chen Y, Zeng J, Su C, Li S. Ultrasound-guided stellate ganglion block alleviates stress responses and promotes recovery of gastrointestinal function in patients. Dig Liver Dis. 2021;53(5):581-6.
3. Kaye AD, Chernobylsky DJ, Thakur P, Siddaiah H,Kaye RJ, Eng LK, *et al*. Dexmedetomidine in EnhancedRecovery After Surgery (ERAS) Protocols for Postoperative Pain. Curr Pain Headache Rep. 2020;24(5):21.
4. Yao F, Xu S, Zhang W, Xiong H, Han J, Zhu A. Impacts of different administration modes of dexmedetomidine with 0.5% ropivacaine on intercostal nerve block. Ann Palliat Med. 2020;9(2):447-50.
5. Kamata M, Tobias JD. Remifentanil: Applications in neonates. J Anesth. 2016;30:449-60.
6. Egan TD. Remifentanil pharmacokinetics and pharmacodynamics. A preliminary appraisal. Clin Pharmacokinet. 1995;29:80-94.
7. Renaud-Roy E, Stöckle PA, Maximos S, Brulotte V, Sideris L, Dubé P, *et al*. Correlation between incremental remifentanil doses and the nociception level (NOL) index response after intraoperative noxious stimuli. Can J Anaesth. 2019;66:1049-61.
8. Kawano H, Manabe S, Matsumoto T, Hamaguchi E, Kinoshita M, Tada F, *et al*. Comparison of intraoperative blood loss during spinal surgery using either remifentanil or fentanyl as an adjuvant to general anesthesia. BMC Anesthesiol. 2013;13:46.
9. Yeom JH, Kim KH, Chon MS, Byun J, Cho SY. Remifentanil used as adjuvant in general anesthesia for spinal fusion does not exhibit acute opioid tolerance. Korean J Anesthesiol. 2012;63:103-7.
10. Colin PJ, Hannivoort LN, Eleveld DJ, Reyntjens KMEM, Absalom AR, Vereecke HEM, *et al*. Dexmedetomidine pharmacokinetic-pharmacodynamic modelling in healthy volunteers: 1. Influence of arousal on bispectral index and sedation. Br J Anaesth. 2017;119:200-10.
11. Djaiani G, Silverton N, Fedorko L, Carroll J, Styra R, Rao V, *et al*. Dexmedetomidine versus propofol sedation reduces delirium after cardiac surgery: A randomized controlled trial. Anesthesiology. 2016;124:362-8.
12. Tarıkçı Kılıç E, Aydın G. Effects of dexmedetomidine infusion during spinal anesthesia on hemodynamics and sedation. Libyan J Med. 2018;13:1436845.
13. Marquis K, Hohlfelder B, Szumita PM. Stability of dexmedetomidine in 0.9% sodium chloride in two types of intravenous infusion bags. Int J Pharm Compd. 2017;21:436-9.
14. Hasanin A, Taha K, Abdelhamid B, Abougabal A, Elsayad M, Refaie A, *et al*. Evaluation of the effects of dexmedetomidine infusion on oxygenation and lung mechanics in morbidly obese patients with restrictive lung disease. BMC Anesthesiol. 2018;18:104.
15. Adams JP, Murphy PG. Obesity in anaesthesia and intensive care. Br J Anaesth. 2000;85:91-108.
16. Wang T, Ge S, Xiong W, Zhou P, Cang J, Xue Z. Effects of different loading doses of dexmedetomidine on bispectral index under stepwise propofol target- controlled infusion. Pharmacology. 2013;91:1-6.
17. Schaub I, Lysakowski C, Elia N, Tramèr MR. Low- dose droperidol (≤1 mg or ≤15 μg kg-1) for the prevention of postoperative nausea and vomiting in adults: Quantitative systematic review of randomised controlled trials. Eur J Anaesthesiol. 2012;29:286-94.
18. Zhao J, Liao C, Wu Q, Wang L, Deng F, Zhang W. Evaluation of ropivacaine combined with dexmedetomidine versus ropivacaine alone for epidural anesthesia: A meta-analysis. Medicine (Baltimore). 2021;100(14):e25272.
19. Mahmoudi K, Rashidi M, Soltani F, Savaie M, Hedayati E, Rashidi P. Comparison of Intercostal Nerve Block with Ropivacaine and Ropivacaine- Dexmedetomidine for Postoperative Pain Control in Patients Undergoing Thoracotomy: A Randomized Clinical Trial. Anesth Pain Med. 2021;11(6):e118667.
20. Hamed MA, Ghaber S, Reda A. Dexmedetomidine and Fentanyl as an Adjunct to Bupivacaine 0.5% in Supraclavicular Nerve Block: A Randomized Controlled Study. Anesth Essays Res. 2018;12(2):475- 9.
21. Rao J, Gao Z, Qiu G, Gao P, Wang Q, Zhong W, *et al*. Nalbuphine and dexmedetomidine as adjuvants toropivacaine in ultrasound-guided erector spinae plane block for video-assisted thoracoscopic lobectomy surgery: A randomized, double-blind, placebo- controlled trial. Medicine (Baltimore). 2021;100(32):e26962.
22. Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, *et al*. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015;350:g7647.
23. Cumpston M, Li T, Page MJ, Chandler J, Welch VA, Higgins JP, *et al*. Updated guidance for trusted systematic reviews: a new edition of the Cochrane Handbook for Systematic Reviews of Interventions. Cochrane Database Syst Rev. 2019;10:ED000142.
24. Higgins JP, Altman DG, Gotzsche PC, Juni P, Moher D, Oxman AD, *et al*. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011;343:d5928.
25. Madan R, Bhatia A, Chakithandy S, Subramaniam R, Rammohan G, Deshpande S, *et al*. Prophylactic dexamethasone for postoperative nausea and vomiting in pediatric strabismus surgery: A dose ranging and safety

evaluation study. Anesth Analg. 2005;100:1622-6.
26. Williamson A, Hoggart B. Pain: A review of three commonly used pain rating scales. J Clin Nurs. 2005;14:798-804.
27. 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;24(5):21.
28. Yao F, Xu S, Zhang W, Xiong H, Han J, Zhu A. Impacts of different administration modes of dexmedetomidine with 0.5% ropivacaine on intercostal nerve block. Ann Palliat Med. 2020;9(2):447-50.
29. Kamata M, Tobias JD. Remifentanil: Applications in neonates. J Anesth. 2016;30:449-60.
30. Egan TD. Remifentanil pharmacokinetics and pharmacodynamics. A preliminary appraisal. Clin Pharmacokinet. 1995;29:80-94.
31. Renaud-Roy E, Stöckle PA, Maximos S, Brulotte V, Sideris L, Dubé P, *et al*. Correlation between incremental remifentanil doses and the nociception level (NOL) index response after intraoperative noxious stimuli. Can J Anaesth. 2019;66:1049-61.
32. Kawano H, Manabe S, Matsumoto T, Hamaguchi E, Kinoshita M, Tada F, *et al*. Comparison of intraoperative blood loss during spinal surgery using either remifentanil or fentanyl as an adjuvant to general anesthesia. BMC Anesthesiol. 2013;13:46.
33. Yeom JH, Kim KH, Chon MS, Byun J, Cho SY. Remifentanil used as adjuvant in general anesthesia for spinal fusion does not exhibit acute opioid tolerance. Korean J Anesthesiol. 2012;63:103-7.
34. Colin PJ, Hannivoort LN, Eleveld DJ, Reyntjens KMEM, Absalom AR, Vereecke HEM, *et al*. Dexmedetomidine pharmacokinetic-pharmacodynamic modelling in healthy volunteers: 1. Influence of arousal on bispectral index and sedation. Br J Anaesth. 2017;119:200-10.
35. Djaiani G, Silverton N, Fedorko L, Carroll J, Styra R, Rao V, *et al*. Dexmedetomidine versus propofol sedation reduces delirium after cardiac surgery: A randomized controlled trial. Anesthesiology. 2016;124:362-8.
36. Tarıkçı Kılıç E, Aydın G. Effects of dexmedetomidine infusion during spinal anesthesia on hemodynamics and sedation. Libyan J Med. 2018;13:1436845.
37. Marquis K, Hohlfelder B, Szumita PM. Stability of dexmedetomidine in 0.9% sodium chloride in two types of intravenous infusion bags. Int J Pharm Compd. 2017;21:436-9.
38. Hasanin A, Taha K, Abdelhamid B, Abougabal A, Elsayad M, Refaie A, *et al*. Evaluation of the effects of dexmedetomidine infusion on oxygenation and lung mechanics in morbidly obese patients with restrictive lung disease. BMC Anesthesiol. 2018;18:104.
39. Adams JP, Murphy PG. Obesity in anaesthesia and intensive care. Br J Anaesth. 2000;85:91-108.
40. Wang T, Ge S, Xiong W, Zhou P, Cang J, Xue Z. Effects of different loading doses of dexmedetomidine on bispectral index under stepwise propofol target- controlled infusion. Pharmacology. 2013;91:1-6.
41. Schaub I, Lysakowski C, Elia N, Tramèr MR. Low- dose droperidol (≤1 mg or ≤15 μg kg-1) for the prevention of postoperative nausea and vomiting in adults: Quantitative systematic review of randomised controlled trials. Eur J Anaesthesiol. 2012;29:286-94.
42. Zhao J, Liao C, Wu Q, Wang L, Deng F, Zhang W. Evaluation of ropivacaine combined with dexmedetomidine versus ropivacaine alone for epidural anesthesia: A meta-analysis. Medicine (Baltimore). 2021;100(14):e25272.
43. Mahmoudi K, Rashidi M, Soltani F, Savaie M, Hedayati E, Rashidi P. Comparison of Intercostal Nerve Block with Ropivacaine and Ropivacaine- Dexmedetomidine for Postoperative Pain Control in Patients Undergoing Thoracotomy: A Randomized Clinical Trial. Anesth Pain Med. 2021;11(6):e118667.
44. Hamed MA, Ghaber S, Reda A. Dexmedetomidine and Fentanyl as an Adjunct to Bupivacaine 0.5% in Supraclavicular Nerve Block: A Randomized Controlled Study. Anesth Essays Res. 2018;12(2):475- 479.
45. Rao J, Gao Z, Qiu G, Gao P, Wang Q, Zhong W, *et al*. Nalbuphine and dexmedetomidine as adjuvants to ropivacaine in ultrasound-guided erector spinae plane block for video-assisted thoracoscopic lobectomy surgery: A randomized, double-blind, placebo- controlled trial. Medicine (Baltimore). 2021;100(32):e26962.
46. Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, *et al*. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015;350:g7647.
47. Cumpston M, Li T, Page MJ, Chandler J, Welch VA, Higgins JP, *et al*. Updated guidance for trusted systematic reviews: a new edition of the Cochrane Handbook for Systematic Reviews of Interventions. Cochrane Database Syst Rev. 2019;10: ED000142.
48. Higgins JP, Altman DG, Gotzsche PC, Juni P, Moher D, Oxman AD, *et al*. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011;343:d5928.
49. Madan R, Bhatia A, Chakithandy S, Subramaniam R, Rammohan G, Deshpande S, *et al*. Prophylactic dexamethasone for postoperative nausea and vomiting in pediatric strabismus surgery: A dose ranging and safety evaluation study. Anesth Analg. 2005;100:1622-6.
50. Williamson A, Hoggart B. Pain: A review of three commonly used pain rating scales. J Clin Nurs. 2005;14:798-804.

How to Cite This Article
Khan MR, Islam S, Chowdhury AB, Rafsan K, Mamun SM. Evaluation of effect of intraperitoneal dexmedetomidine versus remifentanil as adjuvant of Ropivacaine infiltration for pain relief after laparoscopic appendectomy. International Journal of Anesthesiology Research. 2024;5(1):17-21.