e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2023; 15(8); 288-294

Original Research Article

Efficacy of Dexmedetomidine and Ketamine as Adjuvant to Epidural Bupivacaine in Gynaecological Pelvic Surgeries: An Observational Study

Biswajit Sutradhar[1], Subhash Ranjan Das[2], Anand Jadhao[3], Swapan Debbarma[4]

[1]Associate Professor, Department of Anaesthesiology, Agartala Government Medical College, Agartala, Tripura, India

[2]Professor and Head, Department of Anaesthesiology, Agartala Government Medical College, Agartala, Tripura, India

[3]Associate Professor, Department of Physiology, SRMSIMS, Bareilly, India

[4]Postgraduate Resident (JR III), Department of Anaesthesiology, Agartala Government Medical College, Agartala, Tripura, India

Received: 20-05-2023 / Revised: 21-06-2023 / Accepted: 25-07-2023

Corresponding author: Dr. Swapan Debbarma

Conflict of interest: Nil

Abstract:

Background: Epidural anesthesia is commonly used for surgical anesthesia and postoperative analgesia. It provides superior pain relief compared to spinal anesthesia and offers segmental blockade for better hemodynamic stability. However, large volumes of local anesthetic can lead to hemodynamic fluctuations. To address this, adjuvants like dexmedetomidine and preservative-free ketamine are used in epidural anesthesia. This study aims to assess the effects of bupivacaine with dexmedetomidine and bupivacaine with preservative-free ketamine in gynecological surgeries under epidural anesthesia, focusing on stable hemodynamics and prolonged analgesia.

Methods: This single-blinded cross-sectional observational study was conducted for one and a half years at Agartala Government Medical College and G.B.P. Hospital. The study included patients undergoing gynecological pelvic surgeries, with ASA physical status I & II, aged 20 to 60 years, and height 145 to 165 centimeters. Exclusion criteria were applied. Ethical approval and written informed consent were obtained. Patients were randomized into two groups: Group BK (Bupivacaine + Ketamine) and Group BD (Bupivacaine + Dexmedetomidine). The technique involved pre-anesthetic check-up, drug administration, hemodynamic monitoring, and assessment of outcomes. Statistical analysis used SPSS software version 19.0.

Results: In this study, a total of 60 gynecological cases undergoing pelvic surgeries were included, divided into two groups of 30 each. The mean age of participants was 51.10 ± 6.90 years, with no significant difference between the groups. Baseline characteristics such as religion, ASA grade, and diagnosis were comparable between the groups. The onset of sensory and motor block was faster in the BD group, with significantly longer duration of motor block and analgesia compared to the BK group. Side effects and hemodynamic parameters did not differ significantly between the groups, except for blood pressure, which showed variations at different time intervals. Sedation scores were consistently higher in the BD group.

Conclusion: Our study findings support that the addition of epidural dexmedetomidine to bupivacaine as an adjuvant yielded several advantages compared to ketamine. Specifically, dexmedetomidine led to a quicker onset of sensory and motor blockade, as well as a longer duration of both types of blockades.

Keywords: Gynecological surgeries, Epidural anesthesia, Dexmedetomidine, Ketamine, Sensory and motor blockade

Introduction

The word pain is derived from the Greek word poine (penalty)[1]. The International Association for the Study of Pain defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage". Other than psychological trauma, pain is shown to affect the physiology of almost all the systems including respiratory, cardiovascular and metabolic profiles thereby increasing morbidity [2]. Epidural anaesthesia is the most popular technique for providing not only surgical anaesthesia but also postoperative analgesia[3].

The practice of neuraxial anaesthesia dates back to the nineteenth century. Experiments by scientists such as Corning, Bier, and Pages, as well as progressive research, have led to its application in a

variety of clinical situations[1,2]. because it offers superior and extensive postoperative pain relief, epidural anaesthesia has recently replaced spinal anaesthesia as the preferred anaesthetic technique for most abdominal and lower limb surgeries. This versatility makes it more adaptable than spinal anaesthesia[1]. Contrary to spinal anaesthesia, it results in segmental blockade, which leads to less sympathetic blockade and better hemodynamic stability [3].

Epidural anaesthesia is a popular regional anaesthesia technique today. As opposed to subarachnoid block/anaesthesia, it produces segmental anaesthesia, which provides prolonged post-operative analgesia and reduces the incidence ofhemodynamic changes caused by sympathetic blockade beside effective surgical anaesthesia for prolonged surgeries. As the dura is not pierced, there is no risk of PDPH (post-dural puncture headache). By blocking nociceptive impulses from the operative site, epidural anaesthesia reduces surgical stress, reduces blood loss, improves respiratory and bowel function, and reduces the incidence of deep vein thrombosis [1]. However, because large amounts(volume) of local anaesthetic drugs are used to achieve the desired effect, epidural anaesthesia may be associated with haemodynamic fluctuations, which can have negative consequences if local anaesthetic is used as a sole agent [2].

To address these issues, researchers are working to develop adjuvant in neuraxial anaesthesia. The main desirable qualities of an adjuvant in neuraxial block are stable haemodynamics, and the ability to provide smooth and prolonged postoperative analgesia[3]. Various additives have been used to prolong the effect of local anaesthetic agents by extending the duration of central neuraxial block. Opioids, Ketamine, Midazolam, Neostigmine, and alpha_2 adrenergic agonists are examples of such medications[4]. When used as an adjuvant in regional anaesthesia, alpha2 adrenergic agonists have both analgesic and sedative properties.

Dexmedetomidine is a highly selective α2 adrenergic agonist with anxiolytic and perioperative sympatholytic anti-hypertensive properties. It also enhances post operative analgesia.4 N-methyl-D-Aspartate (NMDA) receptor was found to play a significant role in injury induced spinal hypersensitivity. Also, sensitisation of the central nervous system may account for significant post operative pain. Blockade of NMDA receptors before and during injury may prevent or reduce development of central sensitisation. NMDA receptor antagonists like Ketamine can potentiate the effects of other analgesics like morphine, local anaesthetics and non-steroidal anti-inflammatory agents[5]. Preservative-free ketamine Hcl is used to achieve the above effect as preservative may cause neurotoxicity. As an NMDA receptor antagonist, Ketamine may produce additive or synergistic effect with intra operative and post operative pain relief. Hence, in our study, we aimed to assess the effects of Bupivacaine with Dexmedetomidine and Bupivacaine with preservative-free Ketamine during epidural anaesthesia in gynecological surgeries.

Materials and Methods

This was a single blinded cross-sectional observational study conducted for one and half year under department Anaesthesiology & Critical Care at Agartala Government Medical College and G.B.P. Hospital among patients who underwent gynaecological pelvic surgeries [ASA (American Society of Anaesthesiologists) physical status I & II only, with age between 20 to 60 years, and height between 145 to 165 centimetres). Patients with bleeding diatheses, psychiatric illness, neurological and musculoskeletal disease, history of hypersensitivity to anaesthetic agents, and Infection at the injection site were excluded from the study. The study was done after approval of the ethical and screening committee of AGMC and G.B.P. Hospital. Written and inform consent was obtained from each patient prior to the procedure. The study population were randomly divided using computer generated randomization into 2 groups. Group BK (Bupivacaine + Ketamine): Group BK received epidural bupivacaine 0.5% (15ml)+0.5mg/kg of ketamine (diluted to1ml); and Group BD (Bupivacaine+Dexmedetomidine): Group BD received bupivacaine 0.5%(15ml)+ 0.5 µg/kg of dexmedetomidine(diluted to1ml).

Technique

Pre-anesthetic check-up was done one day prior to the surgery. Patients were evaluated for any systemic diseases and laboratory investigations were recorded. Patients were be prepared by overnight fasting. Each patient received Tablet Alprazolam 0.5 mg and Tablet Ranitidine 150 mg orally at bedtime on the night before surgery. In the operation theatre, patient's Pulse rate and Blood Pressure was recorded. Multipara monitor was connected and – Heart rate, NIBP, ECG and Spo2 was recorded. With the patients in sitting position, under all available aseptic precautions, the epidural space was identified by the loss of resistance technique using 18 G Tuohy needle via midline approach at either L_{2-3} or L_{3-4} interspinous space. An epidural catheter was threaded and fixed at 3cm inside epidural space. A test dose of 3ml of 2% Lignocaine with 1:200000 Adrenaline was injected through the epidural catheter after negative aspiration of blood and CSF. After confirmation of epidural placement of the catheter tip the drug under study was injected in increments of 5ml. The patient were then turned to supine position.

Haemodynamic status was assessed intra operatively at 0,2,4,6,8,10,15,20,25,30,45,60 min and then half hourly (30 mins) up 3 hrs, one hourly up to 6 hours and then 2 hourly up to 12 hours. After the surgery, patients were referred to the recovery room where they remained till the complete recovery from sensory and motor blockade. Intra or post operative adverse effects such as hypotension (systolic below 90mmhg), Bradycardia (pulse rate below 60 beats per minute), respiratory depression (respiratory rate below 10 per minute or oxygen saturation less than 90%), nausea, vomiting, shivering. Complications were treated symptomatically, like for hypotension with crystalloids and Inj. Mephentermine 6mg bolus IV, for bradycardia Inj. Atropine 0.6 mg. IV, for respiratory depression oxygen if required, for nausea or vomiting Inj. Ondansetron 4mg IV, for shivering Inj. Tramadol hydrochloride 50mg IV.

Outcome variables

Sensory And Motor Blockade was assessed 15 minutes interval in intra and post operative period. Sensory block was assessed by pinprick method in the midclavicular line using 22G needle, every minute until the block reaches T10 dermatome level. Grades of sensory blockade were as Grade 0 - Sharp pain felt, Grade 1 - Analgesia, dull sensation felt, and Grade 2 - Anesthesia, no sensation felt. Onset of sensory blockade was defined as the time interval between the end of anesthetic injection to loss of sensation to pinprick (Grade 2) at T10 level. Duration Of sensory block was determined by sensory regression up to T10 (thoracic 10th) dermatome level. The onset of motor block was measured by time interval from epidural injection to achievement of motor block of Bromage 1 score. Duration of motor block was measured from the onset of motor block to regression time by Bromage score up to 0. Modified Bromage scale for motor blockade were as 0 = No block, 1=inability to raise extended leg, 2=inability to flex knee, and 3=inability to flex ankle and foot, able to move toes 4=inability to flex ankle and foot, not able to move toes[6].Sedation score was recorded just before initiation of surgery and every 10 minutes till 1 hour and then every 30 minutes throughout the surgical procedure. Grading of sedation was evaluated by Five-point scale were as 1=Alert and wide awake, 2=Arousable to verbal command, 3=Arousable with gentle tactile stimulation. 4=arousable with vigorous shaking, and 5=unarousable[7].

Statistical Analysis

The comparison of normally distributed variables between the groups was performed through t-test. Nominal categorical data between the study groups was compared using chi square or fisher's exact test as appropriate. Statistical analysis was done using Statistical Package for Social Science Evaluation (SPSS) software version 19.0.

Results

Total 60 gynecological cases that underwent pelvic surgeries were included in the study. Total 60 patients were divided in 2 groups of 30 each in the study. The mean age of the participants was 51.10 ± 6.90 years. The mean age of Group BK (n=30) is 53.23+6.45 years, while in Group BD (n=30), it is 50.97+7.21 years. The difference in mean age between the two groups is not statistically significant (p = 0.206). Regarding religion, there are no statistically significant differences observed in the distribution of participants among Hindu, Muslim, and Christian groups in both BK and BD groups(p value <0.05). Similarly, there are no significant differences in the distribution of participants among different ASA grades and diagnoses(p value <0.05)(Table 1).

Table 1: Comparison of baseline characteristics of patients among two groups.

Variables	Group BK (n=30)	Group BD (n=30)	P value
Mean age (in years)	53.23+6.45	50.97+7.21	0.206
Religion			
Hindu (n=44)	23 (52.3)	21 (47.7)	0.773
Muslim (n=13)	6 (46.2)	7 (53.8)	
Christian (n=3)	1 (33.3)	2 (66.7)	
ASA grade			
Grade 1 (n=49)	24 (49.0)	25 (51.0)	0.793
Grade 2 (n=11)	6 (54.5)	4 (45.5)	
Diagnosis			
DUB (n=18)	8 (44.4)	10 (55.6)	0.891
Fibroid (n=30)	15 (50.0)	15 (50.0)	
Ovarian tumour (n=10)	6 (60.0)	4 (40.0)	
Uterine prolapse (n=2)	1 (50.0)	1 (50.0)	

Onset of sensory and motor block was faster in BD group as compared to BK group and the difference is statistically significant (p value <0.05). Duration of motor block was higher in BD group as compared to BK

group and the difference is statistically significant (p value <0.05). Duration of analgesia was longer in BD group as compared to BK group and the difference is statistically significant (p value <0.05) (Table 2).

Table 2: Comparison of sensory and motor block among patients in two groups

Duration (in minutes)	Group BK (n=30)	Group BD (n=30)	P value
Onset of Sensory block T10	17.27+0.90	12.77+1.10	0.001
Onset of Motor block Bromage 1	27.87+1.19	25.17+0.95	0.004
Duration of motor block	171.90+5.17	189.33+6.10	0.000
Duration of analgesia	179.60+9.16	207.50+8.88	0.000

Based on the occurrence of side effects, there are no statistically significant differences between Group BK and Group BD in both intraoperative and postoperative periods (p value >0.05). The proportions of participants experiencing side effects are generally similar between the two groups, indicating that the treatment or intervention applied to both groups does not significantly differ in terms of side effect occurrence (Table 3).

Table 3: Comparison of side effects among patients in the two groups

Side effects	Group BK (n=30)	Group BD (n=30)	P value
Intraoperative			
Nausea (n=3)	1 (33.3)	2 (66.7)	0.551
Shivering (n=5)	2 (40.0)	3 (60.0)	0.643
Hypotension (n=4)	2 (50.0)	2 (50.0)	1.000
Bradycardia (n=3)	1 (33.3)	2 (66.7)	0.551
Postoperative			
Nausea (n=3)	2 (66.7)	1 (33.3)	0.551
Shivering (n=2)	1 (50.0)	1 (50.0)	1.000
Hypotension (n=2)	1 (50.0)	1 (50.0)	1.000
Bradycardia (n=1)	0 (50.0)	1 (100.0)	0.333

Based on the sedation scores at different time intervals, the BK group generally exhibits lower sedation levels compared to the BD group, with statistically significant differences observed at various time points. (p value <0.05) (Figure 1).

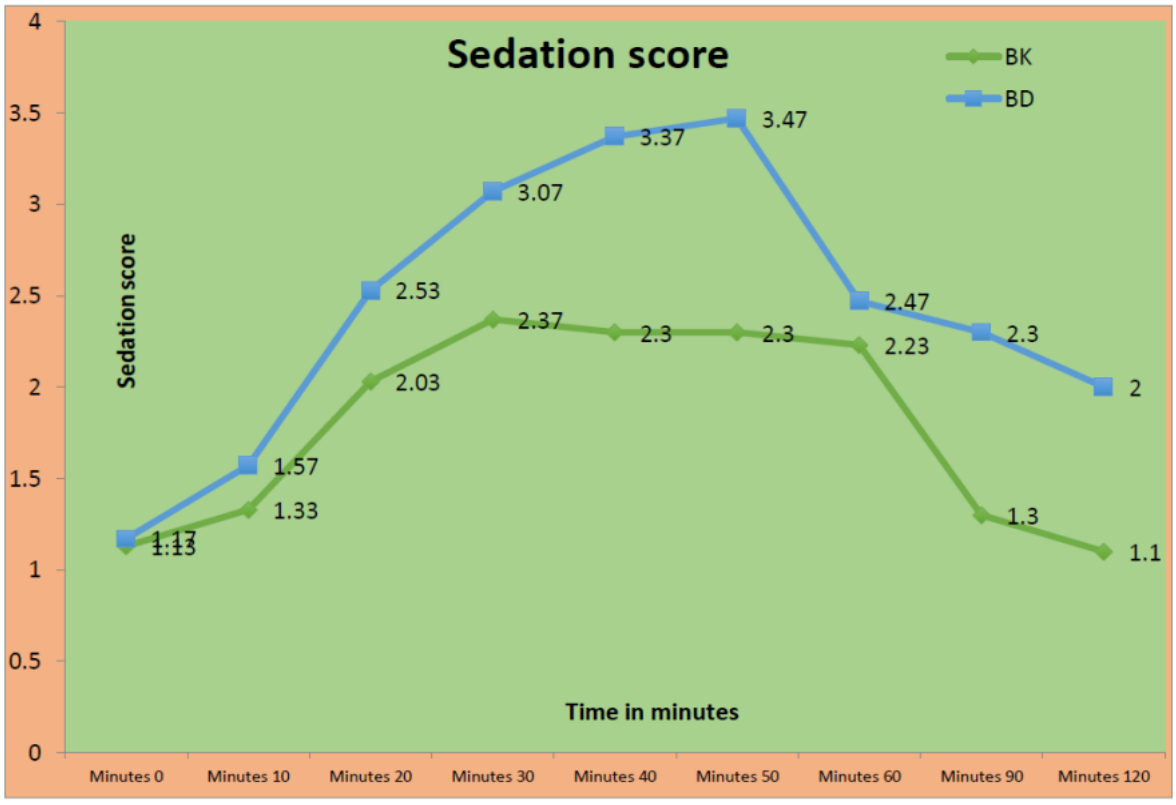

Figure 1: Comparison of sedation score among patients in the two groups.

In our study, although, Intra-operative RR, PR, SPO2 of patients of both the groups were comparable and was not statistically significant (p value >0.05), but based on the median blood pressure values at different time

intervals, there are statistically significant differences between Group BK and Group BD at several time points(p value <0.05). The blood pressure values in Group BK tend to be consistently lower than those in Group BD, indicating a potential difference in the effect of the treatment or intervention on blood pressure regulation between the two groups(Table 4).

Table 4: Comparison of intraoperative blood pressure among patients in the two groups

Time interval (in minutes)	Blood pressure [Median (mm/Hg)]		P value
	Group BK (n=30)	Group BD (n=30)	
Pre-anaesthesia	120/80	128/86	0.231
0	110/70	130/74	0.001
5	110/70	120/86	0.043
10	110/70	120/80	0.043
15	110/70	120/80	0.046
20	110/70	130/76	0.001
25	110/70	140/78	0.000
30	112/72	120/80	0.563
35	110/70	130/76	0.002
40	110/70	130/76	0.013
45	110/70	120/80	0.062
50	112/72	130/80	0.004
55	110/70	120/80	0.084
60	116/76	120/80	0.054
75	120/80	130/86	0.025
90	116/76	120/80	0.785
105	112/72	120/86	0.773
120	110/70	118/88	0.452
135	130/86	140/78	0.018
150	116/72	120/80	0.069
165	118/88	128/82	0.019

Discussion

In our study, Group BD shows faster onset times for both sensory and motor blocks compared to Group BK. Mahapatra et al., found that the onset of sensory and motor block was earlier in group BD compared to group BK, and this difference was statistically significant [8]. Pandya et al., reported no significant difference between the two groups (p>0.05) in terms of the highest sensory level achieved and time for complete motor block [9]. Soliman et al., and Fatima et al., concluded that the mean time to achieve complete motor block in Group D (Dexmedetomidine) compared to Group K (Ketamine) was statistically insignificant (p > 0.05) [10,11]. Bajwa et al., compared dexmedetomidine with fentanyl for epidural analgesia in lower limb orthopedic surgeries and found that the time to reach complete motor block was shorter in patients receiving Dexmedetomidine (18.16 ± 4.52 minutes) compared to the Fentanyl group (22.98 ± 4.78 minutes) (p < 0.05) [12].

In our study, Group BD has longer durations of motor block and analgesia compared to Group BK. Mahapatra et al., also reported that block regression was significantly delayed with the addition of epidural dexmedetomidine (Group BD) compared to group BK [8]. Sonawane et al., observed that the receding time for sensory block (pain sensation to pin-prick perceived at L5) in Group D was 9.33 ± 4.34 hours, while in Group K it was 7.03 ± 3.79 hours. The mean duration of sensory block was compared between the groups, and the difference was statistically significant (P = 0.033). For motor block (Modified Bromage scale in the non-operated limb), the receding time in Group D was 7.10 ± 3.53 hours, whereas in Group K it was 3.80 ± 1.49 hours. The mean duration of motor block was compared between the groups, and the difference was statistically significant (P = 0.000) [13]. Pandya et al., reported that the time to regression of sensory level to L5 in Group D was 594 ± 63.04 minutes compared to 362.4 ± 45.76 minutes in Group K (p < 0.001). Similarly, the time to regression of motor block to Bromage scale 1 in Group D was 488.4 ± 42.88 minutes, while in Group K it was 303.6 ± 36.04 minutes (p < 0.001) [9].

In our study, the BK group generally exhibits lower sedation levels compared to the BD group, with statistically significant differences observed at various time points. Mahapatra et al., also found that the duration of analgesia was significantly prolonged in group BD compared to group BK [8]. Pandya et al., reported that the duration of analgesia was longer with dexmedetomidine, and none of the patients in either group K required rescue analgesics [9]. Sethi et al., showed that the mean morphine consumption in group I after the 1st and

2nd postoperative day was 8.38+2.85 mg and 7.64+1.95 mg, respectively, compared to 6.81+1.35 mg and 6.25+1.22 mg (P<0.05) in group II. Although group II consumed significantly less morphine, pain relief at rest and during movement after 6, 12, 24, and 48 hours postoperatively was significantly better in group II (P<0.05) than in group I. These findings suggest that adding a small dose of ketamine to a multimodal patient-controlled epidural analgesia (PCEA) regimen provides better postoperative analgesia and reduces morphine consumption [14]. Babu et al., compared epidural dexmedetomidine with clonidine and found that the Visual Analog Scale (VAS) score was higher in the clonidine group; however, the difference was statistically insignificant (p > 0.05) [15].

In our study, the blood pressure values in Group BK tend to be consistently lower than those in Group BD, indicating a potential difference in the effect of the treatment or intervention on blood pressure regulation between the two groups. Mahapatra et al., reported no significant difference in haemodynamic parameters between the two groups [8]. Sonawane et al., observed that the change in heart rate (HR), systolic blood pressure (SBP), and diastolic blood pressure (DBP) between groups was statistically insignificant [13]. Bajwa et al., and Fatima et al., concluded that epidural infusion of dexmedetomidine had no significant haemodynamic side effects [11,12]. Soliman et al., studied dexmedetomidine and fentanyl as epidural adjuvants for postoperative pain relief in patients undergoing total knee replacement and found that the decrease in heart rate and mean blood pressure was significantly higher in the dexmedetomidine group compared to the fentanyl group (p < 0.05) [10].

In our study, there are no statistically significant differences between Group BK and Group BD in both intraoperative and postoperative periods. Mahapatra et al., found no significant difference in the incidence of side effects between the two groups [8]. Pandya et al., reported that the patients in both groups were hemodynamically stable throughout the study [9]. Sonawane et al., stated that six out of thirty patients in Group D and eleven out of thirty patients in Group K required rescue analgesia, and the difference was statistically insignificant (P = 0.150). Two out of thirty patients in Group D experienced bradycardia (HR < 60/min), with one requiring treatment using intravenous glycopyrrolate 0.2 mg. One patient in Group D had significant prolongation of the motor blockade, which required discontinuation of the infusion pump. No adverse events were observed in Group K [13]. Pandya et al., reported that the incidence of sedation, nausea, vomiting, and other side effects was comparable between the groups [9]. Xue et al., in a study conducted in 2017, investigated the effects of epidural ketamine and observed that mean arterial pressure (MAP) in the control group was significantly lower compared to the ketamine group at various time intervals [16].

Limitations

The study's findings should be interpreted within the context of several limitations. Firstly, the inclusion of a small group of patients from a specific geographical location limits the generalizability of the results to larger populations or different regions. Additionally, the use of a single local anesthetic drug with a fixed concentration and dose restricts the applicability of the findings to other drugs or dosing regimens. The study's reliance on fixed doses of adjuvants per kilogram of body weight may not account for variations in patient characteristics. Moreover, the inclusion of only ASA grades 1 and 2 patients excludes individuals with higher ASA grades or complex medical conditions. Lastly, the exclusion of children, elderly individuals, those with co-morbidities, and pregnant patients further narrows the scope of the study's applicability. Therefore, caution should be exercised when generalizing the findings to broader patient populations or diverse clinical settings.

Conclusion

Our study findings support that the addition of epidural dexmedetomidine to bupivacaine as an adjuvant yielded several advantages compared to ketamine. Specifically, dexmedetomidine led to a quicker onset of sensory and motor blockade, as well as a longer duration of both types of blockades. Moreover, patients who received dexmedetomidine experienced improved postoperative analgesia, excellent hemodynamic stability, and higher sedation levels with minimal side effects. These results suggest that epidural dexmedetomidine can be a beneficial option in enhancing anesthesia and postoperative outcomes.

References

1. Rigg JR, Jamrozik K, Myles PS, et al., MASTER Anaesthesia Trial Study Group. Epidural anaesthesia and analgesia and outcome of major surgery: a randomised trial. The Lancet. 2002;359:1276-1282.
2. Schultz AM, Webra A, Ulbing S, et al., Peri-operative thoracic epidural analgesia for thoracotomy. Eur J Anaesthesiol. 1997;14:600-603.
3. Vadalouca AN. Adjucant drugs. In: Raj PP, editor. Textbook of Regional Anaesthesia. Pennsylvania: Churchill Livingstone; 2002. p. 215-223.
4. Khobragade SM, Kalbhor J, Saran R, et al., A comparative study of Dexmedetomidine and nalbuphine as an adjuvant to Bupivacaine in lower limb surgeries done under epidural

anaesthesia. MedPulse Int J Anaesthesiol. 2017;3:34-42.
5. Brull R, Macfarlane AJR, Chan VWS. Spinal, Epidural and Caudal Anaesthesia. In: Miller RD, Cohen NH, Eriksson LI, Fleisher LA, Wiener-Kronish JP, Young WL, editors. Miller's Anaesthesia. International ed. Canada: Saunders, Elsevier; 2015. p.1684-1716.
6. Horlocker T, Vandermeulen E, Kopp S, et al., Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy. American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (Fourth edition). Reg Anes Pain Med. 2018; 43:263–309.
7. Elhakim M, Abdelhamid D, Abdelfattach H, et al., Effect of epidural Dexmedetomidine on intraoperative awareness and post-operative pain after one-long ventilation. Acta Anaesthesiologica Scandinavica. 2010; 54(6): 703-709.
8. Mahapatra M, Sahu A. Comparison of prophylactic infusion of phenylephrine with ephedrine for prevention of hypotension in hysterectomies under spinal anaesthesia: a randomized clinical trial. JMSCR [Internet]. 2018;06(12):784-790.
9. Pandya M J, Shah A, Comparative evaluation of dexmedetomidine and ketamine for epidural analgesia in lower limb orthopedic surgeries. Indian J Clin Anaesth. 2020;7(1):166-171.
10. Soliman R, Eltaweel M. Comparative study of dexmedetomidine and fentanyl as an adjuvant to epidural bupivacaine for postoperative pain relief in adult patients undergoing total knee replacement: a randomized study. J Anesthesiol Clin Sci. 2016;5:1.
11. Fatima N, Singh NR, Singh LPK, et al., Comparative study of the effect of dexmedetomidine and butorphanol as epidural adjuvants in abdominal hysterectomy under intrathecal levobupivacaine anesthesia. J Med Soc. 2016;30(3):166–171.
12. Bajwa SJS, Arora V, Kaur J, et al., Comparative evaluation of dexmedetomidine and fentanyl for epidural analgesia in lower limb orthopedic surgeries. Saudi J Anesthesia. 2011;5(4):365–370.
13. Sonawane NB, Balavenkatasubramanian J, Gurumoorthi P, et al., Quality of post-operative analgesia after epidural dexmedetomidine and ketamine: A comparative pilot study. Indian J Anesthesia. 2016;60(10):766–768.
14. Sethi M, Sethi N, Jain P, et al. Role of epidural ketamine for postoperative analgesia after upper abdominal surgery. Indian J Anaesth. 2011;55:141-145.
15. Babu S, Kumar VA. A comparative study in the post-operative spine surgeries: epidural ropivacaine with dexmedetomidine and ropivacaine with clonidine for post-operative analgesia. Indian J Anaesth. 2013;57(4):371–376.
16. Xue X, Lv Y, Zhao Y, et al., Efficacy of prophylactic epidural ketamine for reducing shivering in patients undergoing caesarean section with combined spinal-epidural anesthesia. Biomedical Reports. 2018;8(5): 485–490.