Study to Compare the Efficacy of Thoracic Epidural 0.125% Bupivacaine and 0.125% Bupivacaine with Buprenorphine for Postoperative Analgesia in Upper Abdominal Surgeries

Kasturi Nirmala Devi[1], Desavanth Srinivas Naik[2], Kailashnath Reddy[3]

[1]Associate Professor, Department of Anaesthesiology, BLDE University, Vijayapur, Andhra Pradesh, India.
[2]Associate Professor, Department of Anaesthesiology, Gandhi Medical College, Secunderabad, India.
[3]Professor and HOD, Department of Anaesthesiology, Kurnool Medical College, Kurnool, Andhra Pradesh, India.

ABSTRACT

BACKGROUND

Pain is a complex subjective experience which has proved difficult to measure in reproducible way and indwelling catheter facilitates further administration of analgesic doses for postoperative analgesia as and when required. We wanted to evaluate the quality and duration of analgesia produced by fixed dose of epidural bupivacaine 0.125% and fixed dose of epidural bupivacaine 0.125% with buprenorphine for post-operative analgesia in upper abdominal surgeries.

METHODS

Patients of ASA grade I and grade II, aged between 20 - 60 yrs., of both sexes, who underwent upper abdominal surgeries were included in the study. Patients were randomly divided into two groups, group A (n=25) and group B (n=25). Group A patients received 8 ml of epidural 0.125% bupivacaine in normal saline and Group B patients 8 ml of 0.125% bupivacaine with 2 µg/Kg of buprenorphine in normal saline for postoperative analgesia. Onset and duration of analgesia, haemodynamic and respiratory parameters, side effects like nausea, vomiting, respiratory depression, pruritus, and motor blockade were recorded.

RESULTS

Group B patients had early onset of analgesia compared to Group A. Duration of analgesia was significantly longer in Group B than Group A (10.04 ± 2.25 vs 4.85 ± 0.64). The incidence of side effects like nausea, vomiting, pruritus, was more in Group B than Group A. No patient developed respiratory depression or motor blockade in either group.

CONCLUSIONS

Addition of buprenorphine to epidural bupivacaine produced superior analgesia than bupivacaine alone with fewer side effects.

KEYWORDS

Post-Operative Pain, Epidural Analgesia, Bupivacaine and Buprenorphine

Corresponding Author:
Dr. Desavanth Srinivas Naik,
Associate Professor,
Department of Anaesthesiology,
Gandhi Medical College,
Secunderabad, India.
E-mail: srinivasanaik75@gmail.com

DOI: 10.18410/jebmh/2020/288

How to Cite This Article:
Nirmala Devi K, Srinivas Naik D, Reddy K. Study to compare the efficacy of thoracic epidural 0.125% bupivacaine and 0.125% bupivacaine with buprenorphine for postoperative analgesia in upper abdominal surgeries. J. Evid. Based Med. Healthc. 2020; 7(28), 1358-1362. DOI: 10.18410/jebmh/2020/288

Submission 01-05-2020,
Peer Review 08-05-2020,
Acceptance 04-06-2020,
Published 13-07-2020.

BACKGROUND

Pain is an unpleasant sensory and emotional experience, perceived only by the sufferer and the observer can only assess its magnitude from what the sufferer tells him. The pain apart from causing psychological trauma, it affects physiology of other systems including respiratory, cardiovascular and metabolic system and increases morbidity. Though pain may be protective, defensive or diagnostic, it causes or precipitates the adverse effects like nausea, vomiting, constipation, psychological depression, restlessness, sleeplessness, tachycardia and hypertension.[1]

Epidural analgesia has become one of the most useful and well-known procedure for the management of acute postoperative pain. It can be given at any level of spine, thus allowing more flexibility in clinical practice. It is more versatile in comparison to spinal anaesthesia, as it provides anaesthesia and analgesia by introducing catheter in epidural space. Epidural analgesia can be used to supplement the General anaesthesia, as it reduces the requirement of depth of anaesthesia, thereby maintaining hemodynamic stability during surgery and decreases the post-operative pulmonary complications and ileus.[2]

Bupivacaine is most commonly used drug in epidural anaesthesia, It is an amide group of local anaesthetic. Epidural local anaesthetics alone not gained popularity due to failure rate from the regression of sensory block and unwanted complication of motor blockade and hypotension.[3] A local anaesthetic–opioid combination produces superior analgesia during intraoperative and postoperative period. Epidural opioids produce superior analgesia compared to systemically administered opioids. The knowledge of specific opiate receptors in the substantia gelatinosa of posterior horn of spinal cord resulted in wide spread use of epidural opioids in the treatment of acute and chronic pain.[4] Though morphine has already established its role in epidural administration for pain relief, its side effects like respiratory depression, nausea, vomiting, urinary retention has made physician to search for a better drug. Buprenorphine is a semisynthetic, highly lipophilic opioid, thebaine derivative with μ receptor partial agonistic and antagonistic action. It is 33 times more potent than morphine. It has high affinity for opioid receptors, can be used epidurally safely with less side effects.[5]

In our study, we compared the thoracic epidural bupivacaine 0.125% and epidural bupivacaine 0.125% with buprenorphine 2 mcg/Kg for postoperative analgesia in upper abdominal surgeries. The main aim of our study was to compare the quality and duration of postoperative analgesia and also any side effects associated with them.

METHODS

It is a randomized prospective, double blind study was carried out in department of Anaesthesia. Total 50 patients of scheduled for elective upper abdominal surgeries were selected for study. After approval of the institutional ethical committee, after obtaining written informed consent from patients, single anaesthesiologist performed the anaesthesia procedures. Patients were randomized using sealed envelope technique into two groups of 25 patients in each. Inclusion criteria: ASA grade I and II of both sexes, aged between 20 to 60 years posted for elective upper abdominal surgeries. Patients who refused epidural, patients with spine deformity, coagulation disorders, local infection at the site of epidural injection were excluded from the study.

Postoperative pain relief was provided using epidural analgesia. Group A Patients were given 8 ml of inj. 0.125% Bupivacaine in normal saline and Group B patients were given inj. 0.125% Bupivacaine with inj. buprenorphine 2 mcg/Kg body weight mixture in 8 ml of normal saline. First dose was given when VAS score ≥4 or on patient demand for analgesic. If analgesia remained inadequate and patient complained of pain, planned to give rescue analgesic inj. Diclofenac sodium 75 mg I.M. and epidural catheter was tested with 5 ml of Lignocaine 1% to ensure correct placement.

Preanaesthetic evaluation was done to all the patients on the previous day of the surgery. Preoperative assessment included detailed history, general physical examination, systemic examination, airway assessment and routine investigations such as complete blood count, bleeding time, clotting time, platelet count, blood sugar, blood urea and serum creatinine. Electrocardiography and chest X-ray were done if required. All patients received Tab. Alprazolam 0.5 mg and tab. Ranitidine orally the night before surgery and preoperative fasting of 8 hrs. Was ensured.

On the day of surgery, patient was shifted to operating room. Arrangements for general anaesthesia, drugs and equipment required for procedure and resuscitation were kept ready. Monitors such as noninvasive blood pressure, pulse oximeter and ECG were attached. Basal parameters like blood pressure, pulse rate, respiratory rate and SpO_2 were recorded. All patients were secured 18-gauge IV cannula. Preloading of ringer's lactate solution 10 ml/Kg was given. Premedication inj. Glycopyrrolate 0.2 mg, inj. Midazolam 0.05 mg/Kg, inj. Ondansetron 4 mg, and inj. Ranitidine 50 mg iv was given. The patients were placed in either right or left lateral position. Under aseptic precautions, 2 ml of inj. 2% Lignocaine infiltrated to raise skin wheal at T8 –T10 interspace. Epidural space was identified by loss of resistance technique using 18-gauge Tuohy needle. An 18-gauge epidural catheter was passed into the epidural space, and fixed keeping 5 cm inside the space. Inj. 2% Lignocaine with adrenaline 1:2,00,000 was given as test dose. Pulse rate and blood pressure were observed for 5 min. After excluding intrathecal placement of catheter, patient positioned supine for general anaesthesia. Anaesthesia was induced with inj. Propofol 2 mg/Kg, inj. Fentanyl 2 mcg/Kg, and tracheal intubation was done using 2 mg/Kg of inj. Succinylcholine. Bilateral air entry confirmed, and controlled ventilation was done. $ETCO_2$ connected for monitoring. Intraoperative management included integrated epidural-

general anaesthesia. Anaesthesia was maintained with 30% O_2, 70% N_2O, Isoflurane and inj. Vecuronium 0.08 mg/Kg to facilitate muscle relaxation. Epidural dose of 10 ml of inj. 0.5% Bupivacaine in Normal saline was given and repeated based on hemodynamic parameters. Intraoperative pulse rate, blood pressure (systolic and diastolic) and oxygen saturation were monitored. Intraoperative values were taken at 10 min interval for the first 30 min, and every 30 min thereafter till the end of the surgery. Duration of surgery was noted, and assessment of blood loss was done and managed accordingly. At the end of the surgery neuromuscular blockade was reversed with inj. Neostigmine 0.05 mg/Kg and inj. glycopyrrolate 0.01 mg/Kg IV. After extubation patient was shifted to PACU.

Noninvasive arterial blood pressure, heart rate, oxygen saturation and occurrence of untoward events like nausea, vomiting, hypotension, bradycardia, pruritus, respiratory depression, sedation score and motor blockade were noted at 1,2,4,8,12,18 and 24 hrs. After the end of the surgery. Patients could not be monitored for urinary retention in both the groups due to catheterization.

Motor block was assessed using the Modified Bromage Scale.

Modified Bromage Scale:

0- No motor blockade
1- Inability to raise extended leg.
2- Inability to flex the knee
3- Inability to flex ankle joint.
4- No movement possible in legs.

VAS Pain Score

0-10 (Visual Analogue Scale)
0- Absolutely no pain
1-3 Mild pain
4-6 Moderate pain
7-9 Severe pain
10- Maximum intolerable pain.

Ramsay 4 Point Sedation Scale

Alert 1
Mildly drowsy 2
Moderately drowsy 3
Asleep 4

Statistical Analysis

From the result of previous studies, for the duration of analgesia an alpha error 0.01 and beta error of 0.01, the study group was estimated to be 23 in each group, to compensate failures we have included 25 patients in each group, and total 50 patients in the study. Continuous variables are expressed as mean ± standard deviation or median. Differences between groups were examined for statistical significance by using student's t- test. Chi-square test, and Mann-Whitney U test were used for statistical analysis. A p-value <0.05 was considered statistically significant.

RESULTS

Characteristics	Group-A (N=25)	Group-B (N=25)	P Value
Age in yrs. (Mean ± SD)	39.52 ± 5.35	41.64 ± 4.86	0.128
Weight in kgs (Mean ± SD)	54.92 ± 12.56	55.52 ± 10.73)	0.997
Height in cms (Mean ± SD)	153.24 ± 2.21	152.06 ± 3.43	0.154
Gender M/F	17/8	18/7	0.757
ASA Grade I	17	19	0.528
ASA Grade II	8	6	

Table 1. Demographic Data in the Present Study

Demographic variables such as age, gender, height, weight (kg) and ASA grading were comparable. There was no statistical significance among the both groups of patients.

	Group-A	Group-B	P-Value
Onset of analgesia (mins)	22.04 ± 2.64	16.52 ± 2.25	0.0001
Duration of analgesia (hrs.)	4.85 ± ± 0.69	10.04 ± 2.25	0.0001
No. of top up doses required in 24 hrs.	4.72 ± 0.79	2.38 ± 0.63	0.0001

Table 2. Comparison of Post-Operative Analgesia

The mean onset of analgesia in group A was 22.04 ± 2.64 min and in group was B 16.52 ± 2.25 min, which was statistically significant. Duration of analgesia (time at which patient complaint of pain or VAS score 4 or more.) in group-A was 4.85 ± 0.69 hrs and in group B it was 10.34 ± 2.25 hrs. Which was statistically significant ($p<0.05$).

VAS Score (0-10)	Group-A (n=25) Mean ± SD	Group-B (n=25) Mean ± SD	P-Value
0 hr	5.18 ± 0.64	5.57 ± 0.82	0.066
1 hr	1.67 ± 0.54	0.58 ± 0.45	0.0001
2 hr	2.24 ± 0.78	1.06 ± 0.64	0.0001
4 hrs.	4.53 ± 1.56	1.25 ± 1.42	0.0001
8 hrs.	3.04 ± 1.12	1.42 ± 1.26	0.0001
12 hrs.	2.56 ± 1.28	3.18 ± 1.26	0.090
18 hrs.	3.22 ± 1.14	2.08 ± 1.54	0.004
24 hrs.	2.64 ± 1.57	1.63 ± 1.28	0.016

Table 3. VAS Scores the Post-Operative Period

Top up dose was given when the VAS score 4 or more or patient requested for analgesia. Number of top up doses required in 24 hrs. Was noted in both the groups. VAS scores were recorded at 0, 1, 2, 4, 8, 12, 18 and 24 hrs. The pain scores in Group- A were high compared to Group-B and they were statistically significant except at 12 hrs.

5 patients in Group - A required rescue analgesia apart from epidural analgesia, and in Group-B no patient demanded for rescue analgesia.

Side Effects	Group-A	Group-B	P-Value
Nausea	2 (8%)	7 (28%)	0.065
Vomiting	1 (4%)	3 (12%)	0.297
Urinary retention	-	-	-
Pruritus	3 (12%)	8 (32%)	0.087

Table 4. Side Effects Studied

The adverse effects were comparable in both the Groups (Table-4). No patient developed hypotension (SBP<90 mm hg or decrease in systolic blood pressure >30% of baseline value) in both the groups. Bradycardia

(PR<50 beats/min) was not observed in any patient in both the Groups. Nausea and vomiting were observed in 2 patients in group A (8%), and in 7 patients in group B (28%) which was treated by inj. Ondansetron 4 mg I.V. Pruritus was observed in 3 patients in Group-A (12%) and 8 patients in Group-B (32%). The adverse effects between Group-A and Group-B were statistically not significant (P>0.05).

No patient was developed motor block in both the groups and respiratory depression (respiratory rate <8 or peripheral oxygen saturation <95%) was not observed in any patient in both the groups. Patients in bupivacaine and buprenorphine were alert and no patient was drowsy in our study.

DISCUSSION

Post-operative pain results in physiological, neuroendocrinal, respiratory and cardiovascular changes which ultimately increases the risk of postoperative morbidity and mortality. Epidural analgesia apart from attenuating acute surgical stress response, it also provides post-operative analgesia with reduced visual analogue pain scores at rest and on movement.[6] The discovery of opioid receptors in the spinal cord has opened new frontier in the pain management. Pert and Synder in their study on opiate receptor demonstration confirmed the existence of opioid receptors in the nervous tissue by specific binding assay and also by autoradiography.[7]

Addition of epidural opioids to local anaesthetics not only speeded up the onset, increased the duration of sensory block but also prolonged the postoperative analgesia without affecting the motor block. The opioid drugs are known to exert a direct antinociceptive influence on the spinal cord (Yaksh and Rudy).This may be an indication of the relative importance of the spinal cord compared with the brain as target area of analgesia.[8] Behar et al and Magora et al introduced epidural administration of morphine for the relief of acute and chronic pain and demonstrated the presence of morphine in the CSF after epidural injection.[9]

In the present study, we compared the thoracic epidural bupivacaine 0.125% and thoracic epidural bupivacaine 0.125% with buprenorphine 2 mcg/Kg for post-operative analgesia in upper abdominal surgeries. We have observed that onset of analgesia i.e., time from the administration of drug to loss of pin prick sensation, was less in Group B (16.52 ± 2.25 min) compared to Group A (22.04 ± 2.64 min). Duration of analgesia was taken from the time of drug administration to till patient complaints of pain or patient pain score was ≥4. In our study, the mean duration of analgesia in Group B (10.34 ± 2.25 hrs.) was significantly prolonged compared to Group A (4.35 ± 1.68 hrs.). Shinichi Sakura in their comparative study concluded that combination of bupivacaine and morphine significantly provided superior analgesia with less deleterious complications compared with either bupivacaine or morphine alone.[10] Similar results have found in previous studies by Hirabayashi Y et al,[11] Dona Elsa Jose et al[12] and Mathur S K.[13] Long duration of analgesia of buprenorphine can be explained by its high affinity for spinal opiate receptors, due to its high lipid solubility which favours its diffusion into the spinal cord. The diffusion from the spinal cord into blood stream is slow and does not approach the bulbar centers.

The incidence of side effects like nausea, vomiting and pruritus were more in Group-B but was statistically insignificant. Compared to Group A. Hypotension was not observed in our study. No patient in either group developed respiratory depression or motor block. Placing the epidural catheter at a thoracic level may help in minimizing the development of motor block in upper abdominal surgeries. Patients in Group-B were developed more nausea & vomiting may be due to the action of buprenorphine on chemoreceptor trigger zone in the medulla. These patients responded well to antiemetics.

A study by Agarwal et al found that addition of buprenorphine hastens onset of analgesia compared to bupivacaine alone. They also observed that duration of analgesia was 170 ± 31 min. In bupivacaine group and 690 ± 35 min. In bupivacaine and buprenorphine group with reduced VAS scores. Patients in buprenorphine group had more incidence of side effects like nausea, vomiting and pruritus than in bupivacaine group, and no patient developed respiratory depression, sedation or hypotension in their study which was similar to our study results.[14]

Opioid related pruritus is usually limited to face and torso. The mechanism by which opioids produce pruritus not known but it papers to be centrally mediated and is dose dependent, responds well to naloxone 200 mcg, and ondansetron 4-8 mg. But in our study patients were nor required any intervention. M. Dhakshinamurthy in their comparative study have shown that duration of analgesia in buprenorphine and bupivacaine group was 766.6 ± 169.67 min, and also found no significant haemodynamic changes.[15]

A study on epidural analgesia in lower abdominal surgeries using buprenorphine as an adjuvant to bupivacaine has found urinary retention in buprenorphine group, this is due to increased tone of detrusor muscle and vesical sphincter.[16] This was not seen in our study, placing epidural catheter at thoracic level spared this effect.

CONCLUSIONS

In our present study, bupivacaine 0.125% with buprenorphine was more effective and produced more prolonged duration of analgesia compared to bupivacaine 0.125% alone. Though addition of buprenorphine produced more incidence of side effects, it was statistically insignificant and responded to treatment.

REFERENCES

[1] Pal N, Malhotra K, Chitra, et al. Effect of morphine on postoperative respiratory functions: comparission

between systemic and epidural routes. Indian J Anaesth 2004;48(3):204-207.
[2] NYSORA. Epidural anaesthesia and analgesia. https://www.nysora.com/regional-anaesthesia-for-specific-surgical-procedures/abdomen/epidural-anaesthesia-analgesia/
[3] Wheatley RG, Schug SA, Watson D. Safety and efficacy of postoperative epidural analgesia. BJA: British Journal of Anaesth 2001;87(1):47-61.
[4] Bhattacharyya R, Dutta B. Postoperative analgesia with local anaesthetic and opioid combinations, using double space CSE technique. Indian J Anaesth 2007;51(5):409.
[5] Ravi Kanth SV, Ramarao V, Latha PS, et al. Epidural administration of low-dose Bupivacaine with Buprenorphine vs Bupivacaine with morphine for postoperative analgesia in the caesarean delivery. National Journal of Basic Medical Science 2012;3(2):141-144.
[6] Nimmo SM, Harrington LS. What is the role of epidural analgesia in abdominal surgery? Continuing Education in Anaesthesia Critical Care & Pain 2014;14(5):224-229.
[7] Ghelardini C, Di Cesare Mannelli L, Bianchi E. The pharmacological basis of opioids. Clin Cases Miner Bone Metab 2015;12(3):219-221.
[8] Yaksh TL. Multiple opioid receptor systems in brain spinal cord: Part I. Eur J Anaesthsiol 1984;1(2):171-199.
[9] Bujedo BM. A clinical approach to neuraxial morphine for the treatment of postoperative pain. Pain Res Treat 2012;2012:612145.
[10] Sakura S, Uchida H, Saito Y, et al. Continuous epidural infusion for postoperative pain relief: a comparison of three regimens. J Anaesth 1990;4(2):138-144.
[11] Hirabayashi Y, Saitoh K, Fukuda H, et al. Continuous epidural infusion of bupivacaine and buprenorphine for postoperative pain relief. Masui 1992;41(12):1875-1880.
[12] Josh DE, Ganapathi P, Anish Sharma NG, et al. Postoperative pain relief with epidural buprenorphine versus epidural butorphanol in laparoscopic hysterectomies: a comparative study. Anaesth Essays Res 2016;10(1):82-87.
[13] Mathur SK, Jain S, Agrawal D, et al. Comparison of interpleural and thoracic epidural bupivacaine with buprenorphine for post- thoracotomy analgesia. Indian J Anaesth 2008;52(4):432.
[14] Agarwal K, Agarwal N, Agarwal V, et al. Comparative analgesic efficacy of buprenorphine or clonidine with bupivacaine in the caesarean section. Indian J Anaesth 2020;54(5):453-457.
[15] Dhakshinamoorthy M, Srinivasan SK, Sittaramane S. Comparative study of the effect of buprenorphine and fentanyl as an adjuvant to bupivacaine in epidural analgesia for lower abdominal and lower limb surgeries. International Journal of Scientific Study 2017;5(1):22-26.
[16] Gupta AK, Osahan NK, Abraham V, et al. Comparative study of epidural fentanyl and buprenorphine for post-operative analgesia in lower abdominal and lower limb surgeries. IOSR Journal of Dental and Medical Science (IOSR-JDMS) 2015;14(6):17-24.