Central European Annals of Clinical Research

Original Paper

Evaluation of Three Concentrations of Epidural Bupivacaine for Postoperative Pain Relief: A Prospective Observational Study

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Submitted: 30 August 2020, accepted: 22 September 2020, published: 30 September 2020

Abstract: Background: Postoperative dynamic pain is often associated with increased morbidity and hospital stays. Thoracic epidural analgesia is the gold standard for postoperative pain control in patients with upper abdominal surgeries, providing significant improvements in dynamic pain scores and early mobilisation. The primary objective of this study is to evaluate postoperative static and dynamic pain control with three concentrations of thoracic epidural bupivacaine mixed with a fixed dose of fentanyl infusion in major abdominal surgeries. Method: The patients meeting the inclusion criteria were randomly allocated to three different groups. Thoracic epidural bupivacaine infusions, with concentrations of 0.0625%, 0.1% and 0.125%, mixed with fentanyl 1 μg/mL, were given through a Baxter elastomeric pump at the rate of 5 mL/hour, and labelled as Group A, Group B and Group C, respectively. The patients were followed up to the third postoperative day for the assessment of static pain score, dynamic pain score, respiratory depression, blood pressure, sedation, motor weakness, postoperative nausea and vomiting. Results: Group B and Group C, with bupivacaine concentrations of 0.1% and 0.125%, respectively, had significantly better static and dynamic pain control in comparison to Group A, with a bupivacaine concentration of 0.0625%. Hypotension was significantly higher in Group C than in other groups. The incidence of other side effects, including motor block, pruritus, postoperative nausea and vomiting, were found to be highest in Group C compared to the other groups, though the difference was not significant. Conclusion: We recommend a thoracic epidural infusion with a bupivacaine concentration of 0.1% with 1 μg/mL fentanyl for postoperative pain management in patients undergoing major abdominal surgery.

Keywords: major abdominal surgery; postoperative dynamic pain; thoracic epidural analgesia; bupivacaine concentration

How to cite: Mohammad, H.; Gautam, S.; Agarwal, A.; Kausar, S.; Kaushal, A.; Shamim, R. Evaluation of Three Concentrations of Epidural Bupivacaine for Postoperative Pain Relief: A Prospective Observational Study *Cent. Eur. Ann. Clin. Res.* **2020**, *2*(1), 6; doi:10.35995/ceacr2010006.

Introduction

Pain continues to be a significant problem for many patients after major surgery. In addition to improving patient satisfaction and decreasing pain scores, enhanced perioperative pain control can improve clinical outcomes. Despite improvements in perioperative care, major surgical operations are still followed by postoperative pain, leading to organ dysfunction and prolonged convalescence. Patients recovering from major abdominal surgeries can tolerate mild to moderate discomfort at rest, but are distressed and often incapacitated by severe pain during movement and positioning. This increase in pain intensity, termed as dynamic pain, results from abdominal wall tissue trauma during surgery and muscle spasms [1,2].

Postoperative pain management should attempt to relieve both rest and dynamic pain [3]. This is because optimal dynamic pain relief helps in ensuring that normal functions, including ventilation, coughing and mobility, are only minimally impaired [4]. The most common modalities for postoperative pain control are intravenous analgesics (non-steroidal anti-inflammatory drugs, intravenous opioids) peripheral nerve blocks and central neuraxial blockades (spinal analgesia, epidural analgesia). Among the postoperative pain control modalities, the epidural analgesia is an established method for patients undergoing major abdominal surgery and it is highly effective in providing dynamic pain relief after major surgical procedures [1]. Local anaesthetic and opioid combinations for epidural analgesia result in better dynamic pain relief compared to local anaesthetics or opioids used alone. Epidural bupivacaine in a dose of 4–12 mg/hour with fentanyl has been shown to provide effective dynamic pain relief [5]; however, the optimal concentration of epidural fentanyl seems to lie in the range of 1–5 μg/mL [6].

The use of the thoracic rather than the lumbar approach to the epidural space has been one of the major changes in anaesthetic practice over the last 20 years, and has been used in the majority of studies that have demonstrated improved dynamic pain relief [7,8]. This technique has a number of potential benefits when used for the administration of local anaesthetic–opioid mixtures. The thoracic approach facilitates the incision-congruent administration of lipophilic opioids in small doses, and minimises motor and sympathetic blockades of the lower limbs.

The present prospective observational study evaluates three concentrations of thoracic epidural bupivacaine with fentanyl for postoperative pain relief in patients who had undergone major abdominal surgery.

Materials and Methods

Study Design

The present study is a prospective observational study; the study protocol was approved by the institutional ethical committee (IEC code no: 2015-135-MD-88) and written informed consent was obtained from all the patients.

Inclusion Criteria

Adult patients (20–65 years) of either sex, American Society of Anesthesiologists (ASA) physical status I or II, who were scheduled for major abdominal surgery with a planned upper abdominal incision under general anaesthesia and thoracic epidural analgesia, were included in the study.

Exclusion Criteria

Patient refusal, coagulation disorders, signs of local or systemic infection, patients with acute or chronic renal disease, spinal deformities, patients in whom epidural analgesia could not be started, owing to intraoperative hypotension secondary to blood loss, and patients who could not be extubated at the end of surgery and required mechanical ventilation in the postoperative period.

Randomisation, Group Allocation and Study Intervention

Patients who met the inclusion criteria during the pre-anaesthetic check-up were randomly assigned into three equal groups of 30 each with the help of a computer-generated table of random numbers. Each group received intra-operative and postoperative epidural infusions with a solution containing either 0.0625%, 0.1% or 0.125% bupivacaine with 1 μg/mL fentanyl at a rate of 5 mL/hour, and were labelled as Group A, B, and C, respectively.

A random allocation sequence concealed in 90 consecutively numbered, sealed envelopes, determining group distribution, were computer-generated by a project nurse not otherwise involved in the trial. The envelopes were opened by a preoperative nurse (not involved in the study) on the morning of surgery; the nurse also prepared the drug for epidural infusion as per group allocation in an elastomeric pump (Baxter Healthcare Corporation, Hayward, CA, USA) and labelled the pump with the patient's name.

An 18G thoracic epidural catheter was placed at T8-9 or T9-10 intervertebral spaces in the operating theatre by an anaesthesiology resident not otherwise involved in the study. The elastomeric pump received by the patient was connected to the epidural catheter after the induction of anaesthesia and infusion started at a rate of 5 mL/hour. The standard anaesthesia technique was used in all patients. The patient's induction was done by fentanyl 2–3 μg/kg and propofol 1.5–2.5 mg/kg; orotracheal intubation was facilitated by vecuronium 0.1 mg/kg. Anaesthesia was maintained with propofol, sevoflurane, and oxygen air mixture. Hypotension was treated by an infusion of isotonic sodium chloride or mephentermine (5 mg) intravenously, in incremental doses, when systolic blood pressure was below 90 mm Hg. At the end of surgery, residual neuromuscular paralysis was antagonised with neostigmine 0.04 mg/kg and glycopyrrolate 0.01 mg/kg. Following satisfactory recovery, the patients were extubated and shifted to the post-anaesthesia care unit.

Outcome Measures and Patient Assessment

Primary outcome measures were postoperative pain during lying supine (rest pain), coughing and rising from supine to sitting position (i.e., dynamic pain); secondary outcome measures were postoperative nausea and vomiting (PONV), sedation and respiratory depression. All these measures were assessed by an acute pain nurse blinded to group allocation.

The assessment of pain was done by a visual analogue scale (VAS); 0 = no pain, 10 = worst imaginable pain. Pain scores were assessed on arrival to the post-anaesthesia care unit (PACU) (0 h), then at 8 p.m. on the day of surgery (POD 0), 8 a.m. and 8 p.m. on postoperative day 1 (POD 1), 8 a.m. and 8 p.m. on postoperative day 2 (POD 2), and 8 a.m. on postoperative day 3 (POD 3). All patients received acetaminophen 1 g intravenously (IV) every 6 h during that period. If any patient complained of a VAS score of more than 4, an injection of diclofenac (75 mg) was given IV over 30 min in 50 mL saline, up to a maximum dose of 150 mg per day. If the patient's VAS score did not come below 4 following diclofenac injection, then it was followed by a bolus injection of fentanyl at a dose of 25 μg IV. A maximum of 2 boluses of fentanyl were permitted every hour. If analgesia was inadequate even after these measures, the case was considered

as an efficacy failure and alternative analgesic measures were adopted. Motor block was measured by using the modified Bromage scale (0 = no motor block, 1 = inability to raise an extended leg, 2 = inability to flex the knee, 3 = inability to flex ankle). The severity of PONV was graded on a 4-point ordinal scale (0 = no nausea or vomiting, 1 = mild nausea, 2 = moderate nausea, and 3 = severe nausea with vomiting). Rescue antiemetic ondansetron (4 mg IV) was given to all patients with PONV of grade $\geq$2. The Ramsay sedation scale (awake levels are: 1—anxious, agitated or restless; 2—cooperative, oriented and tranquil; 3—responds to command; asleep levels depend on patient's response to a light glabellar tap or loud auditory stimulus; 4—brisk response; 5—a sluggish response; 6—no response) was used to assess the sedation; the patients with a sedation scale of $\geq$4 were considered as sedated. Respiratory depression was defined as a respiratory rate $\leq$8 breaths/min and oxygen saturation <90% without oxygen supplementation.

Statistical Analysis

Sample Size Estimation

The sample size calculation was based on primary outcome measures. Assuming that the therapeutic drug would reduce postoperative dynamic VAS scores by 30% compared to the placebo (assumed mean postoperative dynamic VAS score of 55 mm and standard deviation of 10 mm at all time points in the placebo group), a sample size of 25 patients was required in each group for the results to be significant (with α = 0.05 and power = 80%). To take care of any dropouts, we enrolled 30 patients in each group.

Statistical Methods

Descriptive and inferential statistical analysis was carried out in the present study. The results of continuous measurements are presented as the mean $\pm$ SD (min–max) and the results of categorical measurements are presented as numbers (%). Significance is assessed at a 5% level of significance.

An analysis of variance (ANOVA) was used to find the significance of study parameters between three or more groups of patients. Tukey's post-hoc test (two tailed, independent) was used to find the significance of study parameters on a continuous scale between two groups (intergroup analysis) for metric parameters.

A chi-square test/Fisher's exact test was used to find the significance of study parameters on a categorical scale between two or more groups in a non-parametric setting for qualitative data analysis.

Results

Patients who met the inclusion criteria during the pre-anaesthetic check-up were randomly assigned into three equal groups of 30 each with the help of a computer-generated table of random numbers, for a total of 90 patients assessed for eligibility between October 2015 and September 2016; each group received an intraoperative and postoperative epidural infusion of either 0.0625%, 0.1% or 0.125% bupivacaine with 1 μg/mL fentanyl. There was no difference amongst the groups with regard to age, sex or weight distribution (p > 0.05) (Table 1).

Table 1. Demographic data.

Groups Variables	Group A (N = 30)	Group B (N = 30)	Group C (N = 30)	*p* Value
Age (y)	42.23 ± 13.25	46.50 ± 13.29	47.97 ± 11.88	$p = 0.204$
Weight (kg)	53.27 ± 9.83	56.20 ± 12.61	59.23 ± 11.21	$p = 0.129$
Sex (M/F)	12/18	16/14	16/14	$p = 0.491$

Data are presented either as mean ± SD or numbers.

Bupivacaine 0.1% and 0.125% provided significantly better pain relief at rest (Table 2), deep breathing (Table 3), coughing (Table 4), and sitting (Table 5) than bupivacaine 0.0625%.

Table 2. Comparison of pain scores at rest.

Pain-Resting Pain	Results			Overall *p* Value	Pairwise Significance		
	Group A	Group B	Group C		A-B	A-C	B-C
POD 0, 0 hrs	3.23 ± 1.07	2.07 ± 0.69	2.03 ± 0.81	<0.001 **	<0.001 **	<0.001 **	0.988
POD 0, 8 p.m.	2.80 ± 0.89	1.73 ± 0.64	1.63 ± 0.56	<0.001 **	<0.001 **	<0.001 **	0.848
POD 1, 8 a.m.	2.07 ± 0.83	1.40 ± 0.56	1.13 ± 0.35	<0.001 **	<0.001 **	<0.001 **	0.215
POD 1, 8 p.m.	1.80 ± 0.76	1.13 ± 0.35	1.03 ± 0.19	<0.001 **	<0.001 **	<0.001 **	0.726
POD 2, 8 a.m.	1.27 ± 0.52	1.07 ± 0.25	1.03 ± 0.19	0.027 *	0.078+	0.035 *	0.935
POD 2, 8 p.m.	1.07 ± 0.25	1.00 ± 0.00	1.00 ± 0.00	0.137	0.192	0.197	1.000
POD 3, 8 a.m.	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00	-	-	-	-

ANOVA test; post-hoc test; Tukey's test. *: *moderately significant* (p value: $0.01 < p \leq 0.05$), **: *Significant* (p value < 0.05).

Table 3. Comparison of pain scores on deep breathing.

Pain-Deep Breathing	Results			Overall *p* Value	Pairwise Significance		
	Group A	Group B	Group C		A-B	A-C	B-C
POD 0, 0 hrs	3.60 ± 1.19	2.10 ± 0.71	2.07 ± 0.78	<0.001 **	<0.001 **	<0.001 **	0.989
POD 0, 8 p.m.	3.00 ± 0.91	1.80 ± 0.71	1.73 ± 0.58	<0.001 **	<0.001 **	<0.001 **	0.936
POD 1, 8 a.m.	2.43 ± 0.94	1.43 ± 0.57	1.27 ± 0.45	<0.001 **	<0.001 **	<0.001 **	0.613
POD 1, 8 p.m.	1.97 ± 0.72	1.17 ± 0.38	1.07 ± 0.26	<0.001 **	<0.001 **	<0.001 **	0.729
POD 2, 8 a.m.	1.33 ± 0.61	1.07 ± 0.25	1.07 ± 0.26	0.018 *	0.035 *	0.040 *	1.000
POD 2, 8 p.m.	1.10 ± 0.31	1.00 ± 0.00	1.00 ± 0.00	0.047 *	0.079+	0.083+	1.000
POD 3, 8 a.m.	1.03 ± 0.18	1.00 ± 0.00	1.00 ± 0.00	0.378	0.446	0.452	1.000

ANOVA test; post-hoc test; Tukey's test. *: *moderately significant* (p value: $0.01 < p \leq 0.05$), **: *Significant* (p value < 0.05).

Table 4. Comparison of pain scores on coughing.

Pain-Coughing	Results			Overall *p* Value	Pairwise Significance		
	Group A	Group B	Group C		A-B	A-C	B-C
POD 0, 0 hrs	4.63 ± 1.16	3.23 ± 1.14	3.20 ± 1.03	<0.001 **	<0.001 **	<0.001 **	0.993
POD 0, 8 p.m.	4.07 ± 0.98	2.77 ± 1.10	2.67 ± 0.66	<0.001 **	<0.001 **	<0.001 **	0.910
POD 1, 8 a.m.	3.57 ± 0.94	2.33 ± 0.99	2.07 ± 0.78	<0.001 **	<0.001 **	<0.001 **	0.495
POD 1, 8 p.m.	3.07 ± 0.87	2.13 ± 0.94	1.93 ± 0.70	<0.001 **	<0.001 **	<0.001 **	0.629
POD 2, 8 a.m.	2.4 ± 0.67	1.73 ± 0.78	1.59 ± 0.63	<0.001 **	0.001 **	<0.001 **	0.699
POD 2, 8 p.m.	2.07 ± 0.52	1.37 ± 0.56	1.21 ± 0.41	<0.001 **	<0.001 **	<0.001 **	0.442
POD 3, 8 a.m.	1.47 ± 0.57	1.10 ± 0.31	1.10 ± 0.31	0.001 **	0.003 **	0.003 **	0.999

ANOVA test; post-hoc test; Tukey's test. **: *Significant (p value < 0.05).*

Table 5. Comparison of pain scores on sitting.

Pain-Sitting	Results			Overall *p* Value	Pairwise Significance		
	Group A	Group B	Group C		A-B	A-C	B-C
POD 0, 0 hrs	4.93 ± 1.20	3.30 ± 1.21	3.27 ± 0.83	<0.001 **	<0.001 **	<0.001 **	0.992
POD 0, 8 p.m.	4.17 ± 0.99	2.73 ± 1.17	2.70 ± 0.60	<0.001 **	<0.001 **	<0.001 **	0.990
POD 1, 8 a.m.	3.50 ± 0.97	2.27 ± 0.94	2.23 ± 0.57	<0.001 **	<0.001 **	<0.001 **	0.987
POD 1, 8 p.m.	3.00 ± 0.79	1.87 ± 0.82	1.69 ± 0.71	<0.001 **	<0.001 **	<0.001 **	0.656
POD 2, 8 a.m.	2.30 ± 0.65	1.57 ± 0.68	1.31 ± 0.60	<0.001 **	<0.001 **	<0.001 **	0.285
POD 2, 8 p.m.	1.77 ± 0.73	1.20 ± 0.48	1.10 ± 0.31	<0.001 **	<0.001 **	<0.001 **	0.770
POD 3, 8 a.m.	1.20 ± 0.48	1.00 ± 0.00	1.00 ± 0.00	0.009 **	0.019 *	0.021 *	1.000

ANOVA test; post-hoc test; Tukey's test. *: *moderately significant* (p value: $0.01 < p \leq 0.05$), **: *Significant* (p value < 0.05).

The incidence of hypotension was significantly higher in the bupivacaine 0.125% group compared to the other groups (Figure 1; $p = 0.024$; Fisher'sexact test).

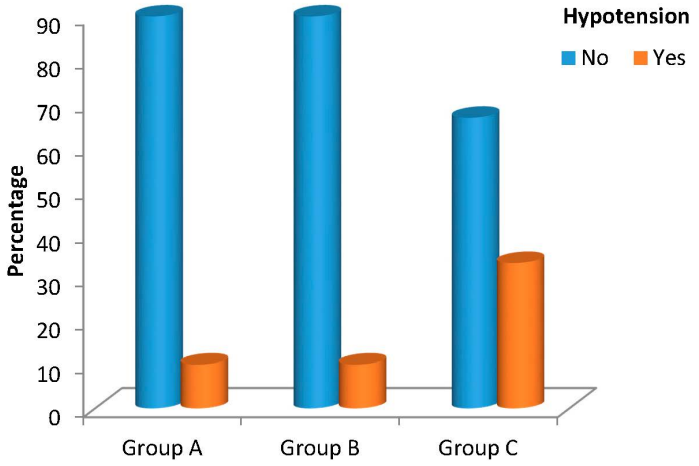

Figure 1. Incidence of hypotension in each group.

The incidence of other side effects like PONV, motor block, and pruritus was found to be highest in the bupivacaine 0.125% group compared to the other groups (Figures 2–4), though the difference was not significant.

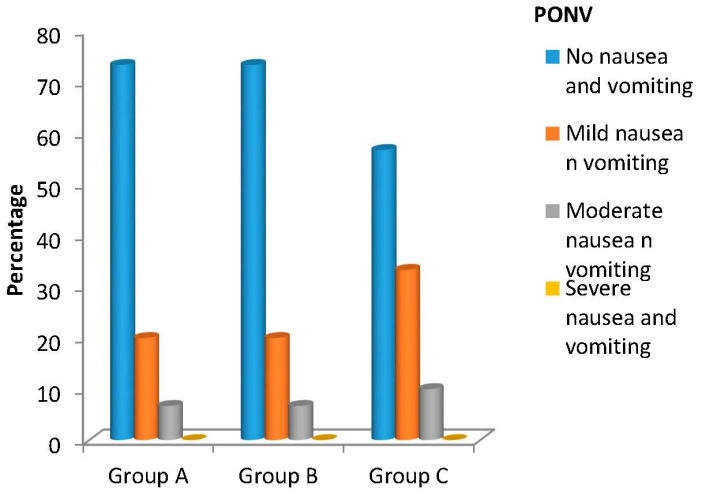

Figure 2. Incidence of postoperative nausea and vomiting in each group.

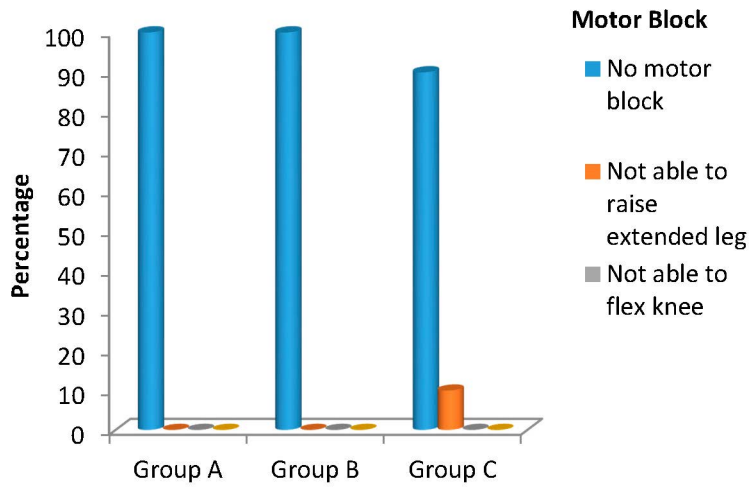

Figure 3. Incidence of motor block in each group.

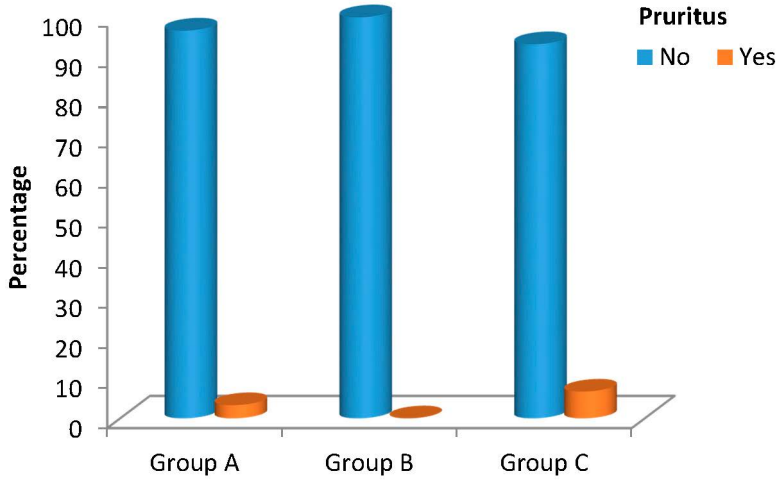

Figure 4. Incidence of pruritus in each group.

Discussion

The key pathogenic factor in postoperative morbidity is the surgical stress response to its potential for multi-organ damage. Thoracic epidural anaesthesia (TEA) significantly dampens the stress response and relieves postoperative pain. It offers a maximal sympathetic blockade of the heart and bowel, which promotes coronary perfusion and gastrointestinal motility, and provides freedom from lower extremity motor blockades and opioid-induced side effects. Moreover, in upper-abdominal surgery, there could be additional routes of transmission of noxious stimuli to the central nervous system (CNS) through the phrenic nerve and the vagus nerve, which almost always need a very high dose of opioids in cases where general anaesthesia is given without a neuraxial block. In our institute, we are routinely practicing thoracic epidural anaesthesia in patients undergoing upper abdominal surgery and will continue until there is any contraindication for it. In the present study, we studied the postoperative quality of analgesia and the side effects of three commonly used concentrations of bupivacaine in an epidural for postoperative pain relief and we found that there is better pain relief with 0.100% bupivacaine with 1 μg/mL and 0.125% bupivacaine with 1 μg/mL fentanyl groups, but there is a higher incidence of side effects in the latter group.

In our study, a total of 90 patients were selected during the period of October 2015 to September 2016; 30 patients in each group were randomly assigned to one of three groups:

Group A—0.0625% bupivacaine with 1 μg/mL fentanyl, Group B—0.100% bupivacaine with 1 μg/mL fentanyl, and Group C—0.125% bupivacaine with 1 μg/mL fentanyl.

We followed up with the patients until the morning of the third postoperative day and measured the static and dynamic pain (primary outcome measure), and the incidence of motor block, hypotension, postoperative nausea and vomiting, sedation and respiratory depression as secondary outcome measures. In the present study, we used bupivacaine as a local anaesthetic, as this is the protocol in our institute. There are many studies which report that there is no significant difference between bupivacaine, levobupivacaine and ropivacaine in the quality of analgesia at equipotent doses, and in adverse effects at low concentrations in thoracic epidurals.

Casati et al. [9] evaluated the quality of postoperative analgesia provided with a patient-controlled epidural infusion of 0.125% bupivacaine, 0.125% levobupivacaine or 0.2% ropivacaine, and showed similar pain relief and postoperative sensory/motor differentiation. Launo et al. [10] compared 0.125% levobupivacaine and 0.2% ropivacaine in combination with fentanyl (2 μg/mL) for thoracic epidural analgesia after aortic surgery, and reported no differences in the quality of analgesia and the degree of motor block. In our study, we used bupivacaine and, as per the above studies and many other studies, bupivacaine is equipotent to levobupivacaine and is 1.5–1.6 times more potent than ropivacaine. Therefore, a higher concentration of ropivacaine is required for the same epidural analgesic effect.

A study by Takako Hamada, Mariko Baba et al. [11] concluded that 0.06% levobupivacaine combined with 2 μg/mL of fentanyl does not provide sufficient epidural analgesia for labour. Our result coincides with the above study, as in our study there was significantly insufficient pain control with 0.0625% bupivacaine with 1 μg/mL fentanyl (Group A) compared to 0.100% bupivacaine with 1 μg/mL fentanyl (Group B) and 0.125% bupivacaine with 1 μg/mL fentanyl (Group C). Another study by Shen-Chih Wang et al. [12] compared three concentrations of ropivacaine, and concluded that 0.1% ropivacaine failed to offer adequate postoperative pain relief for ambulation or coughing in the first 12 h after surgery. From a clinical point of view, this is crucial, as ambulation and coughing play a particularly important role in the recovery of intestinal movement and respiratory function after abdominal surgery. In this study, the VAS pain scores during ambulation and coughing in group 1 (i.e., 0.1% ropivacaine with 1 μg/mL fentanyl) patients 12 h after surgery were much higher ($p < 0.05$) and they found no significant difference in the pain scores at 36 h and 60 h postoperatively. Group 1 (0.1% ropivacaine) patients obviously needed more additional loading doses than the other two groups. Therefore, we also concluded that a background infusion at a rate of 5 mL/hr could offer good analgesia during ambulation or coughing for either 0.15% or 0.2% ropivacaine, but not for 0.1%.

In our study, we found significantly better static and dynamic pain relief with 0.1% bupivacaine (Group B) and 0.125% bupivacaine (Group C). There was a significant difference in resting pain relief in Group B and Group C from Group A until the evening of the first postoperative day, and afterward there was no significant difference. In contrast to the study of Shen-Chih Wang et al., we found a significant difference in dynamic pain relief (pain during coughing/coughing effort and during sitting/sitting effort) between groups throughout the follow up period i.e., until the morning of the third postoperative day. In the above study, they found no significant difference in adverse effects in three groups, and found sensory blocks (they assessed it by loss of temperature sensation) in 4/11 of Group C (getting 0.2% ropivacaine), which were physically insignificant. In contrast in our study, we found differences in adverse effects, which were higher in patients getting 0.125% bupivacaine (Group C), and we also found 3/30 (10%) cases of grade 1 motor block in Group C, while 3/30 (10%) patients also complained of dizziness on standing in Group C.

A prospective analysis of 1014 patients getting an epidural infusion of 0.1% bupivacaine with 5 μg/mL fentanyl by David A. Scott et al. [6] found a 67/1014 (6.6%) incidence of hypotension. In our study, the total incidence of hypotension, 17/90 (17.8%), is much higher than the above prospective analysis. There was a 10% incidence of hypotension in the 0.0625% bupivacaine (Group A) and 0.100% bupivacaine (Group B) patients, which was not much higher in comparison to the above prospective analysis. However, the incidence was much higher in 10/30 of the 0.125% bupivacaine (Group C) patients (33.3%), which is also significantly higher than Group A and Group B. In the above prospective analysis, pruritus was noted in 10.3% of cases and was the most common side effect. Ready's [13] series had a 25% incidence and Stenseth's [14] series had 11%. In our study, there were total of 3/90 (3.3%) patient complaints of pruritus and there was no significant difference among the three studied groups. In our study, there is a low incidence of pruritus, which can be explained by the low concentration of opioids used.

In the prospective analysis by David A. Scott et al., nausea and vomiting were recorded in 31 cases (3.1%), and this was probably under-reported, but many factors contribute to postoperative nausea and vomiting. A study by H. A. Noble et al. [15] in which they studied different dilutions of epidural bupivacaine for labour analgesia found a 9/56 (16%) incidence of nausea and vomiting. In our study, 29/90 (32%) of patients complained of nausea and vomiting, out of which 22/90 (24.4%) complained of mild nausea and vomiting and 7/90 (7.8%) complained of moderate nausea and vomiting, and there was no significant difference among the three studied groups. As we studied upper abdominal surgery patients, gut handling is itself a predisposing factor for nausea and vomiting, so this is a probable explanation for the higher incidence of nausea and vomiting in our study.

The limitations of our study are that there could be a confounding factor for some of the observed adverse effects of epidural analgesia, like hypotension, and postoperative nausea and vomiting could also be because of gastrointestinal surgery. Another limitation is that we selected patients who were undergoing upper abdominal surgery as our sample, which includes various different kinds of surgeries and each kind has different associations that cannot be matched. Additionally, we noted some side effects in our study and did a comparison of those between the three study groups; however, the sample size is not adequate to enable us to comment on significance, and we therefore suggest further studies with larger sample sizes that could adequately address these issues.

Conclusions

We conclude that bupivacaine 0.1% and 0.125% provided significantly better pain relief (both static and dynamic components) than bupivacaine 0.0625%, but bupivacaine 0.125% was significantly associated with a higher incidence of side effects compared to the other two concentrations. Hence, we recommend a thoracic epidural infusion of bupivacaine 0.1% with 1 μg/mL fentanyl for postoperative pain management in patients undergoing major abdominal surgery.

Author Contributions: Conceptualization, H.M., A.A., S.G. and S.K.; methodology, H.M., S.G., A.A. and S.K.; software, H.M. and S.G.; validation, all authors; formal analysis, H.M., S.G., A.A. and A.K.; investigation, H.M., S.K., A.K. and R.S.; resources, H.M., S.G., A.A., A.K. and R.S.; data curation, H.M., S.G. and A.A.; writing—original draft preparation, H.M.; writing—review and editing, all authors; visualization, all authors.; supervision, all authors; project administration, S.G., A.A.

Funding: This research received no external funding.

Acknowledgments: The authors wish to acknowledge Mohd Qasim (B. Tech (IIT), MBA (IIM)) for his technical support and grammar editing.

Conflicts of Interest: The authors declare no conflicts of interest.

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