Ramdev *et al.*
Ain-Shams Journal of Anesthesiology (2023) 15:46
https://doi.org/10.1186/s42077-023-00343-5

Ain-Shams Journal of Anesthesiology

ORIGINAL ARTICLE

Open Access

Safety and efficacy of patient controlled epidural analgesia versus conventional epidural analgesia in lower limb orthopedic surgeries: a prospective randomized study

Babita Ramdev[1], TVenu Gopal[1] and Dinesh Kumar Sharma[2*]

Abstract

Background Orthopedic surgeries lead to moderate to severe postoperative pain, treating which is a challenge to the anesthesiologist. The present prospective, randomized study was carried out to compare the efficacy of postoperative pain relief between patient controlled epidural analgesia (PCEA) and conventional intermittent bolus epidural analgesia (IBEA) \with very low concentration of bupivacaine plus fentanyl in 60 ASA I and ASA II patients for orthopedic lower limb surgeries. Following variables like heart rate, mean arterial pressure, oxygen saturation, visual analogue scale (VAS) score, total analgesic consumption, patient satisfaction (Likert scale) and side effects were assessed for 24 h postoperatively.

Results The hemodynamic parameters were comparable in both the groups at various time intervals. There was a significant decrease in VAS score, less analgesic consumption, less rescue analgesia requirement and more patient satisfaction in PCEA group as compared to IBEA group.

Conclusions Patient controlled epidural analgesia (PCEA) with a combination of bupivacaine and fentanyl has more efficacy and safety than intermittent bolus epidural analgesia (IBEA) so it should be used more often.

Keywords Patient-controlled, Epidural, Analgesia, Intermittent

Background

Pain as a phenomenon involves both sensory-discriminative and motivational-affective components and causes release of inflammatory mediators. In orthopedic surgeries, uncontrolled postoperative pain leads to delayed recovery and increased postoperative morbidity. Also, the restriction of mobility increases the risk of thromboembolism and the increased catecholamine response leads to increased oxygen consumption. Various modalities for pain relief in orthopedic surgeries include systemic analgesics, central neuraxial analgesia, epidural analgesia, and peripheral blocks.

Epidural analgesia promotes early mobilization and reduces rehabilitation time especially after joint surgeries. It has evolved from conventional intermittent bolus epidural to continuous epidural infusion to patient-controlled epidural analgesia (Kang S et al. 2013). Local anesthetics plus opioid in an epidural infusion reduces the dose of individual drugs and provides good hemodynamic stability (Aitkenhead A et al. 1987; Wheatley RG et al. 2001). Bupivacaine and ropivacaine are used because they produce a selective clinically sensory block with a minimum restriction of motor function. Lipophilic opioids are preferred over hydrophilic opioids as they have rapid onset, clearance, and less respiratory

*Correspondence:
Dinesh Kumar Sharma
drdinesh11@gmail.com
[1] Anaesthesia Department, MMIMSR, Mullana, India
[2] ENT Department, GMC, Patiala, India

depression (Patil SS et al. 2018). In the intermittent bolus epidural analgesia (IBEA) local anesthetic is given epidurally at prefixed regular intervals and does not need sophisticated delivery devices. Whereas patient-controlled epidural analgesia (PCEA) enables the patients to adjust the bolus dose of analgesics themselves by using a programmable infusion pump according to their needs (El Sayed and Mokbel 2014). It thus allows individualization of postoperative analgesia requirement.

There are various studies which have compared PCEA and conventional intermittent top ups during labor (Duncan LA et al. 1998) and continuous and intermittent epidural analgesia in gynecological surgeries (Pennington P et al. 2009). Also PCEA and I/V analgesia have been compared (El Sayed MH and Mokbel E 2014). Outcome after labor analgesia with continuous epidural infusion has been compared with programmed intermittent epidural bolus with patient controlled epidural analgesia (A.Bullingham et al 2018). These studies have found PCEA to be better as quality of analgesia is better with less drug consumption.

So, in this present study, we compared the efficacy and safety of patient controlled epidural analgesia(PCEA) with conventional intermittent bolus epidural analgesia (IBEA) using bupivacaine with fentanyl in orthopedic surgeries with primary objective of measuring the VAS score and secondary objective of measuring total analgesic consumption, patient satisfaction, hemodynamic variables and post operative complications.

Methods

After approval of the Institute Ethical Committee, vide IEC Project No. 1205 we obtained a written informed consent from 60 patients, 18–65 years old, ASA status I and II who were posted for elective lower limb orthopedic surgeries in our hospital. The following patient were excluded: those with infection at the site, bleeding disorders, allergy, and sensitivity to local anesthetics, patients with significant cardiovascular, renal, hepatic, pulmonary diseases, and if the patient refused.

The study was registered in UMIN-CTR vide ID number UMIN000044487. The study was conducted and adherent to the CONSORT guidelines.

The study was prospective, randomized, double blind, and controlled. The patients were randomized into either PCEA ($n=30$) or conventional IBEA group ($n=30$) by using computer generated number tables. Allocation concealment was done using sequentially numbered, coded and sealed envelopes. Randomization was done by an anesthesia resident who was blinded to the procedure and was not involved in the study.

In the pre-operative room, an 18 G IV line was secured and preloading was done with 10 ml/kg of RL solution. In the operation theater standard ASA monitors were attached like heart rate, ECG, blood pressure and SpO_2 by Avance CS^2 GE, USA. Under all aseptic precaution epidural catheter (Smiths Medical) was introduced in sitting position using Tuohy's needle(18G) in the L3–L4 lumbar intervertebral space (IVS) using loss of resistance (LOR) technique. For confirmation of the epidural catheter placement a test dose of 3 ml lignocaine and adrenaline was given. Then subarachnoid block was given by 23 G or 25 G Quinke's needle at the lower IVS, with 3 ml 0.5% heavy bupivacaine. A sensory level of T_{10} dermatome was achieved. Three liters of oxygen by nasal prongs was given to maintain Sp02 between 97 and 99%. Intraoperatively hemodynamic parameters were observed and if they fell below 20% of baseline then injection atropine 0.5 mgI/V and injection mephenteramine 3 mg I/V bolus were given to maintain HR and BP within normal limits. After the surgery, epidural was activated in both the groups with a loading dose of 10 ml of 0.0625% bupivacaine and fentanyl 1.5 µg/ml.

Group 1 or group PCEA (patient-controlled epidural analgesia group) (($n=30$): PCA machine (Model6300 Ambulatory Infusion Pump, Smiths Medical) was attached to epidural catheter with a drug combination of bupivacaine 0.0625% and fentanyl 1.5 mcg /ml with setting of continuous rate of 4 ml/h. A bolus demand dose of 3 ml and a lockout period 20 min was set. The demand dose was given for maximum two times with maximum dose of 10 ml per hour.

Group 2 or group IBEA (intermittent bolus epidural analgesia)($n=30$) – 10 ml of 0.0625% bupivacaine and fentanyl 1.5 mcg/ml was given per hour for 24 h.

The patients were explained about the visual analogue score.

The VAS score was graded as the following:

0—no pain
1–3—mild pain
4–6—moderate pain

7–10—severe pain

The HR, MAP, SpO_2, and VAS score were recorded in both groups at baseline and at 1, 2,6, 10, 14, 18, 22, and the 24 h of catheter activation.

After 24 h postoperatively, the patient satisfaction about post-operative analgesia was documented using the Likert Scale (Pennington P et al. 2009) (Table 1).

Post-operatively nausea, vomiting, hypotension, bradycardia, pruritus, and urinary retention were observed and documented by an observer who was blinded to

Table 1 Patient satisfaction level

Satisfaction level	Score
Very much satisfied	5
Somewhat satisfied	4
Undecided	3
Not satisfied	2
Not at all satisfied	1

the intervention. Rescue analgesia was given with Inj. diclofenac 75 mg, if the VAS score was more than or equal to 4. After 24 h amount of drug delivered and the number of patients who needed rescue analgesia in both the groups was recorded. If the surgery was prolonged more than 3 h or if failure of spinal anesthesia occurred, cases were done under epidural anesthesia and were excluded from the study.

The epidural catheter was removed after 3 days and patients received analgesia as per Institute protocol with paracetamol (1 g) and diclofenac (75 mg) IV.

Statistical analysis

The data was systematically compiled and statistically analyzed using Statistical Package for Social Sciences (SPSS) version 21 (IBM, Chicago, USA) for windows. Data was expressed as mean ± SD and range for continuous measurement. If the data was normally distributed, Student's *t* test was used otherwise Mann–Whitney test was used. For categorical data, chi-square test was applied. *P* value < 0.05 was significant.

A post hoc power analysis was done by using the G*Power version 3.1.9.2 (Franz Faul, Kiel, Germany). The sample size was 30 patients in each group with power of 0.96 and an effect size of 0.55 with 10% chance of error $\alpha = 0.05$, $\beta = 0.20$ and a confidence interval 95%.

Results

Eighty-eight patients were assessed for eligibility in this study. Twenty-eight were not randomized out of which 14 did not meet inclusion criteria, 4 patients declined to participate and 10 patients were excluded due to duration more than 3 h, failed spinal and postponement of surgery, which left 60 patients (30 patients/group) for data analysis (Fig. 1).

The demographic variables and baseline hemodynamic parameters were comparable in group PCEA and group IBEA (Table 2).

The VAS score difference at 1st hour after the catheter activation in both PCEA and IBEA group was not significant (p value = 1.00). While at 2, 6, 10, 14, 18, 22, and 24 h after catheter activation there was decrease in VAS score in group PCEA as compared to group IBEA and the difference between them was significant ($p < 0.05$) (Fig. 2).

The mean amount of drug given in group PCEA (131 ml) as compared to group IBEA (250 ml) was less which was highly significant ($p = 0.00$) (Table 3).

Likert scale was more in group PCEA (4.50 + 0.51) as compared to group IBEA (3.33 ± 0.48) which was highly significant ($p = 0.00$) (Table 4).

Less patients required rescue analgesia in group PCEA (2) as compared to group IBEA (10) (p value = 0.021) (Table 5).

The mean HR and MAP measured at different times were comparable in both PCEA and IBEA groups (Figs. 3 and 4) respectively.

Postoperative nausea was seen in 4 patients in group PCEA and in 10 patients in group IBEA ($p = 0.125$). Postoperative vomiting was not seen in group PCEA but seen in 5 patients in group IBEA which was significant (p value = 0.052). Pruritus was not seen in group PCEA and seen in 3 patients in group IBEA (p value = 0.237). Respiratory depression and paraesthesia did not occur in both PCEA and IBEA group (Table 6).

Discussion

Acute pain postoperatively is a challenge to treat as 20% of lower limb orthopedic surgical patients experience it on the first day after surgery (Maca J et al. 2020). Appropriate pain management is required to tackle social, psychological, and biological aspects associated with pain (Small C and Laycock H 2020). Epidural analgesia provides pre-emptive analgesia and thus avoids polypharmacy, prevents central sensitization, allows early mobilization, and facilitates physiotherapy (Renck H and Edstrom H.1976). Epidural analgesia using local anesthetics with opioids helps to decrease the requirement of total dose of each drug with fewer side effects, provides better pain control, faster recovery of bowel function, improved pulmonary function, and decreased endocrine response to peri-operative stress (Rutberg H et al. 1984). In the field of orthopedic surgeries the procedure specific pain management (PROSPECT) recommendation prefers PCA over analgesia on patient request (Maca J et al. 2020).

The PCEA technique involves continuous background infusion of analgesic at same rate as the drug is removed from the epidural space. Therefore, it is better as the level of the block does not change acutely. In intermittent epidural bolus there are peaks and then troughs in analgesic level and tachyphylaxis occurred more rapidly which are avoided in PCEA (Cuschieri RJ et al. 1985), Toxicity does not occur in PCEA since no peak plasma concentration of local anesthetic occurs which is seen with IBEA. Rapid bolus injection

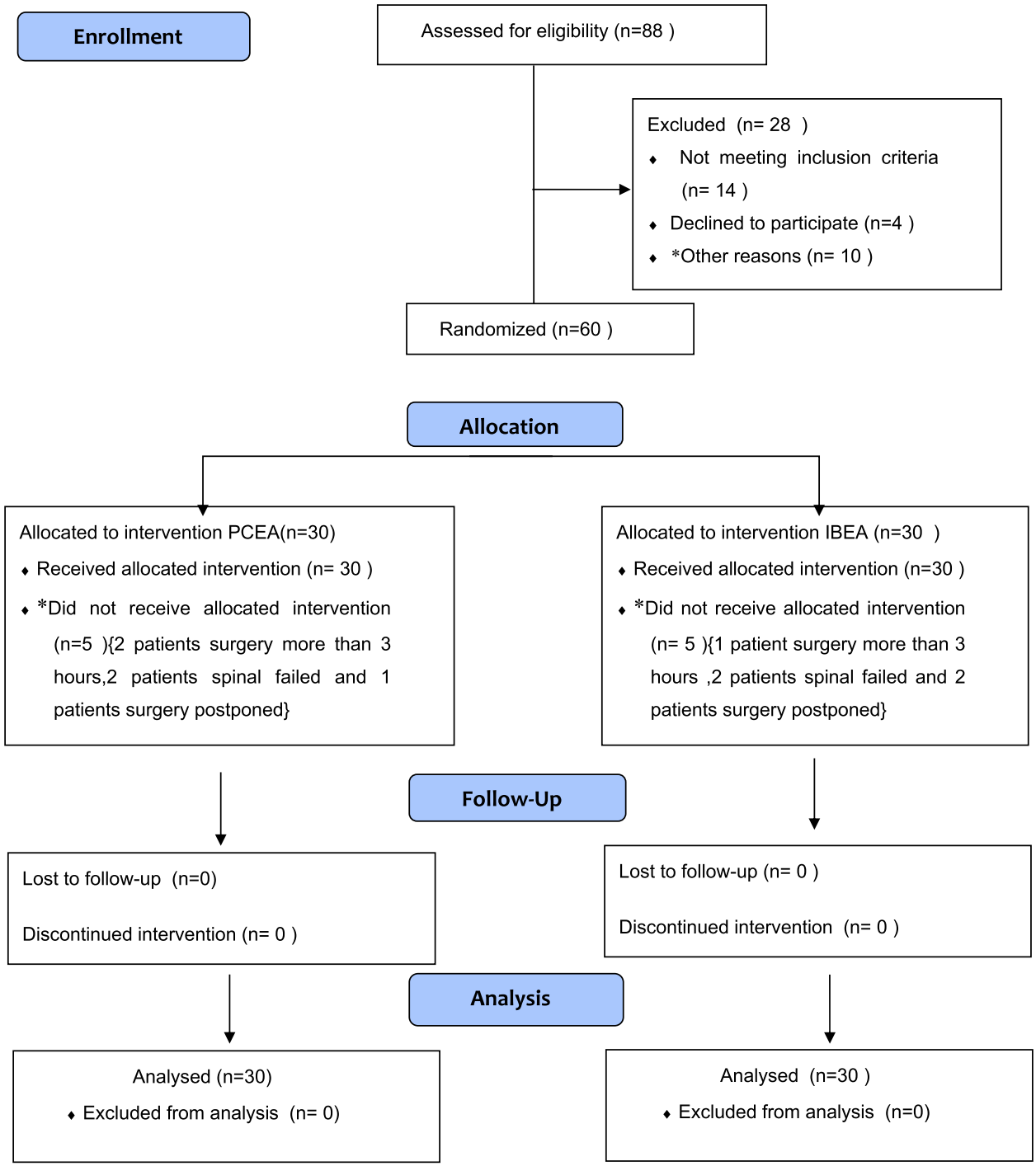

Fig. 1 Consort flow diagram

in intermittent epidural bolus has a potential risk of intrathecal or intravascular injection due to epidural catheter migration. Wheatley et al. on analysis of four studies reported that local anesthetic and lipophilic opioid combination as a continuous epidural infusion group had much better dynamic relief than group which received either of the drug alone (Wheatley RG et al. 2001). So, we added opioids as they reduce local anesthetic requirement, increase analgesia, and decrease the complications. Lipophilic opioid like

Table 2 Demographic data and baseline haemodynamic parameters of both the groups

	Group PCEA ($n=30$)	Group IBEA ($n=30$)	*T* value	*P* value
Age (years) Mean ± S.D	38.63 ± 12.58	39.43 ± 8.80	− 0.285	0.776
Weight (kg) Mean ± S.D	66.93 ± 9.74	68.13 ± 11.69	− 0.432	0.667
Sex(F:M)	6:24	13:17	3.774	0.095
ASAI:ASAII	18:12	20:12	0.287	0.592
Mean HR (baseline)	77.77 ± 8.81	77.93 ± 7.64	− 0.078	0.938
MAP (mmHg)(baseline)	94.47 ± 7.07	94.67 ± 7.18	− 0.10	0.914
SpO_2	99.53 ± 0.86	99.87 ± 0.35	− 1.969	0.054

ASA American Society of Anaesthesiologists, *HR* Heart rate, *MAP* Mean arterial pressure, $Sp0_2$ Saturation of oxygen

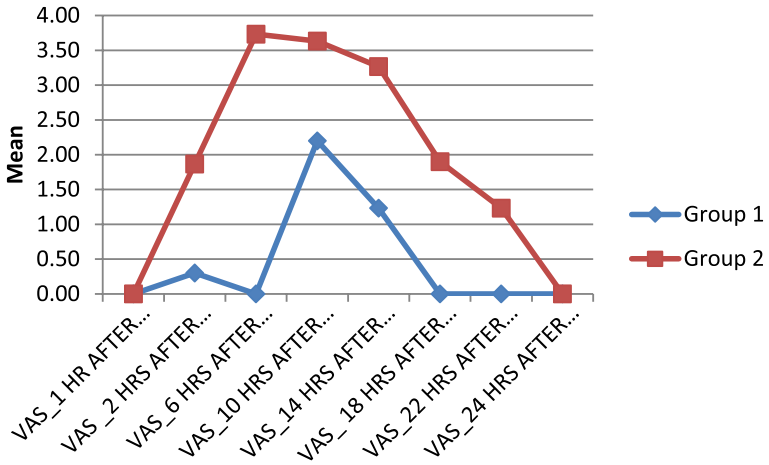

Fig. 2 Mean VAS Score distribution of both the groups. VAS: visual analogue scale

Table 3 Mean amount of drug given in both the groups

	Group PCEA	Group IBEA	*Z* value	*P* value
Mean amount of drug given in ml	131 ± 6.88	250 ± 0.00	− 7.131	0.000

Table 4 Likert scale distribution in both the group

Likert scale	Score	GroupPCEA	GroupIBEA	Total	Chi-square value	*P* value
Undecided	3	0	20	20	36.00	0.000
Somewhat satisfied	4	15	10	25		
Very much satisfied	5	15	0	15		
Mean ± S.D		4.50 ± 0.51	3.33 ± 0.48			

Table 5 Rescue analgesia distribution in both the groups

Rescue analgesia	GroupPCEA	GroupIBEA	Total	Chi-square value	*p* value
No	28	20	48	6.667	0.021
Yes	2	10	12		

fentanyl is preferred as it has rapid onset, clearance, and less respiratory depression. Bupivacaine alone can cause sympathetic and motor block. Adding fentanyl to bupivacaine prolongs the analgesia and decreases dose requirement so that low concentration of the drug is required to achieve effective analgesia with minimal side effects (Brodner J et al. 1999).

We have selected very low concentration of bupivacaine (0.0625%) with fentanyl (1.5 μ/ml). Most of the studies done earlier are done with higher concentration of drug such as fentanyl (2–3 μg/ml) and bupivacaine (0.125–0.25) (Duncan La et al. 1998; El Sayed and Mokbel E 2014). So, we conducted a prospective randomized

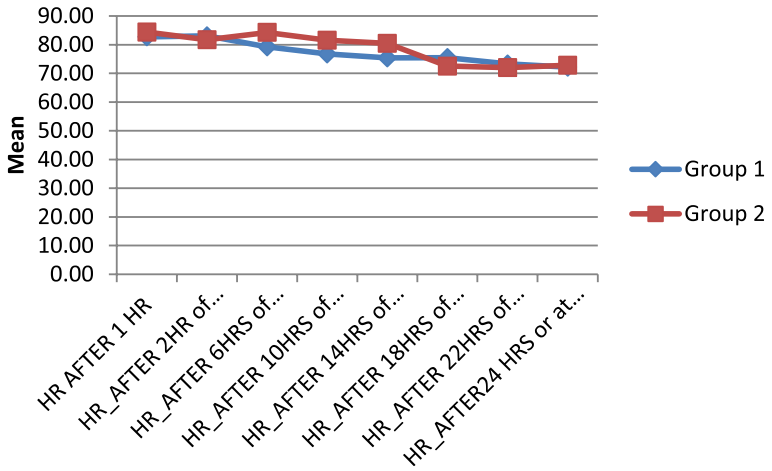

Fig. 3 Mean heart rate distribution of both the groups. HR: heart rate

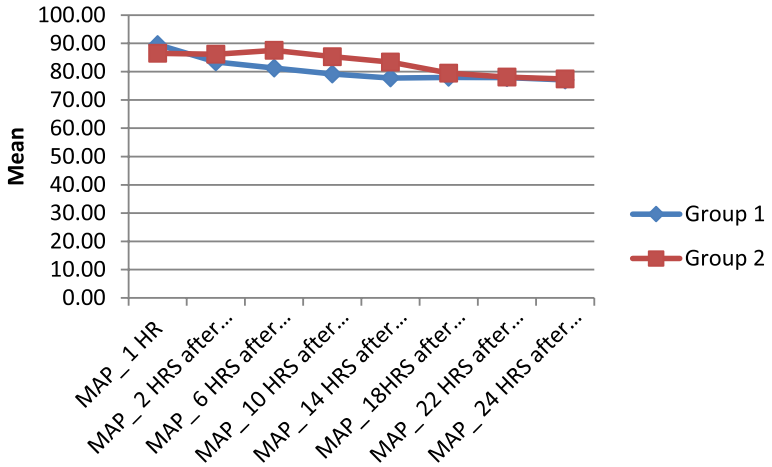

Fig. 4 Mean arterial pressure distribution in both the groups

Table 6 Comparison of post- operative side effects in both the groups

Complications	Group PCEA		Group IBEA		Chi-square value	*p* value
	Number	%	Number	%		
Nausea	4	13.33	10	43.33	3.354	0125
Vomiting	0	0	5	16.66	5.455	0052
Pruritus	0	0	3	10	3.158	0.237
Respiratory depression	0	0	0	0		
Parasthesia	0	0	0	0		

study to compare PCEA with conventional IBEA using bupivacaine and fentanyl for analgesia in lower limb orthopedic surgeries postoperatively.

In the present study, we have used the same concentration of local anesthetic plus opioids in both groups. Some studies compared intermittent epidural bolus at one rate and concentration with continuous epidural infusion at different concentration and rate (Pitimana AS et al. 2005; Bhasin S et al. 2018). We compared the visual analogue score, parameters, amount of drug consumption, patient satisfaction regarding postoperative analgesia technique, and postoperative complications among both the groups.

The demographic profile and ASA physical status were comparable in both PCEA and IBEA group.

The VAS score (mean)was less than 3 in PCEA group and IBEA group. At 1st hour VAS score was comparable in PCEA group and IBEA group. This could be because of residual effect of spinal anesthesia or due to bolus amount of analgesia given as loading dose. In group IBEA there was significant increase in VAS at 2, 6, 10, 14, 18, 22, and 24 h after catheter activation compared to group PCEA (p value < 0.05) which could be because of reduced time between patient demand and onset of action of the analgesic drug. Jan Maca et al. in their study found that group I (PCEA) had lower intensity of pain than group II (non-PCEA) (Maca J et al. 2020). The VAS score(mean) was less than 2 in PCEA group and non PCEA group and was comparable. El Sayed Moawad H et al. stated that PCEA group had less pain than PCIA group at 2, 8, and 12 h which was significant. Immediate postoperatively PCIA had significantly less NPRS score than PCEA and at 24th hours pain scale was comparable at both groups (El Sayed and Mokbel E 2014).

We administered rescue analgesia I/V diclofenac 75 mg if VAS scores were found to be ≥ 4. Rescue analgesia was given to 2 patients in group PCEA and to 10 patients in group IBEA which was significant (p value = 0.021). More patients received rescue analgesia in intermittent bolus group this could be due to tachyphylaxis of local anesthetics, which occur more in intermittent epidural bolus group. Malhotra et al. also found that rescue analgesia was given in less number of patients in continuous epidural infusion than in intermittent epidural bolus group (Malhotra N et al. 2016). Behera B K et al. gave I/V fentanyl 0.5 μg/kg and found more patients in I/V PCA group received rescue analgesia than in PCEA group (Behera BK et al. 2008).

The total analgesic consumption is clinically important as high doses of opioids have potential adverse effects. Also, decreased analgesic dose leads to decreased treatment costs. In our study, mean amount of analgesic consumption in PCEA group was significantly less in 24 h than in the intermittent bolus epidural group similar to the study done by Standl T et al. who also found a statistically significant difference in PCEA (BS) group and in non PCEA (BS) group (Standl T et al. 2003). Antok E et al. in their study in children found that analgesia with PCEA group was obtained at half dose of ropivacaine than in the non PCEA group (Antok E et al. 2003). Both these studies are in accordance with our study.

Pain relief is better when control is with the patient because they know the severity of pain and their own tolerance to pain. Patient controlled analgesia (PCA) reduces the time between analgesics and improves patient satisfaction (Brodner G et al. 1999). In our study, we used Likert scale (5-point version) to evaluate patient satisfaction during postoperative pain management. The mean satisfactory score distribution in PCEA group was better significantly than in IBEA group. The study done by Gambling DR et al. evaluated the patient satisfaction using vertical visual analogue scale (0–10) and concluded that PCEA group are more satisfied than intermittent epidural to up (p < 0.05) (Gambling DR et al. 1990). Similar to study by Jan Maca et al. and El Sayed Moawad H et al. also found that the mean satisfactory score of PCEA group was more than in PCIA group (Maca J et al. 2020; El Sayed and Mokbel E 2014).

The hemodynamic parameters were comparable in PCEA group and IBEA group at different time points similar to the study done Malhotra et al. (Malhotra N et al. 2016).

In our study, the adverse effects are very low and comparable between the two groups because we have used a low concentration of bupivacaine (0.0625%) with fentanyl (1.5 μg/ml) for postoperative analgesia. In group II, 10 patients had nausea, 5 patients had vomiting and 3 patients had pruritus where as in group I, 4patients had nausea, none had vomiting and pruritus. None of the patients in both the groups had respiratory depression and paraesthesia which is in accordance with the study done by (Maca J et al. 2020; El Sayed and Mokbel E 2014; Malhotra N et al. 2016; Antok et al. 2003). A retrospective analysis of adverse effects of PCEA in 2435 young and elderly patients found that different PCEA regimens should be followed for young and elderly patients to minimize side effects (Jae Chul Koh et al. 2017).

There are a few limitations of this study.First a fixed volume of the drug combination was used irrespective of weight and height of the patients in intermittent epidural bolus group. Second we did not compare the VAS score at rest and on movement. Lastly, the anesthetist involved in collection of data postoperative was not blinded to the intervention used and hence a bias cannot be ruled out.

Conclusions

In conclusion, this study showed that patient controlled epidural analgesia (PCEA) is better than intermittent bolus epidural analgesia (IBEA) group as postoperative analgesic technique in orthopedic lower limb surgeries as it provides better analgesia with less analgesic consumption and more patient satisfaction. There is maintenance of hemodynamic stability and adverse effects are less in both the groups.

Abbreviations

ASA	American Society of Anaesthesiologists
E.C.G	Electrocardiogram
SpO_2	Saturation of O_2

HR	Heart rate
Bp	Blood pressure
MAP	Mean arterial pressure
PCIA	Patient controlled intravenous analgesia
VAS	Visual analogue scale

Acknowledgements
Not applicable.
Authors' contributions
BR: study design, manuscript drafting, revised the literature, final revision of the manuscript. TVG: patient enrolment, data collection intraoperative and postoperative, performed the procedure. DKS: manuscript drafting, data analysis, critically revised the manuscript, revised the literature. All the authors read and approved the final version of the manuscript.

Funding
None.

Availability of data and materials
The data is available on request.

Declarations

Ethics approval and consent to participate
Ethical approval was taken from Institute Ethical Committee vide MMIMSR, MMU, Mullana, IEC Project No. 1205 and a written informed consent was taken from all the participants. The study was registered in UMIN-CTR vide ID number UMIN000044487.

Consent for publication
Not applicable**.**

Competing interests
The authors declare that they have no competing interests.

Received: 28 September 2022 Accepted: 2 June 2023
Published online: 16 June 2023

References

Aitkenhead A. Acute Pain Management (1987) Edited by Cousins M. J. and Phillips G. D. Published by Churchill Livingstone, New York.; indexed; illustrated. British Journal of Anaesthesia 59:811

Antok E, Bordet F, Duflo F, Lansiaux S, Combet S, Taylor P et al (2003) Patient-controlled epidural analgesia versus continuous epidural infusion with ropivacaine for postoperative analgesia in children. Anesthesia Analgesia 97(6):1608–11

Behera BK, Puri GD, Ghai B (2008) Patient-controlled epidural analgesia with fentanyl and bupivacaine provides better analgesia than intravenous morphine patient-controlled analgesia for early thoracotomy pain. J Postgrad Med 54(2):86–90

Bhasin S, Dhar M, Sreevastava DK, Nair R, Chandrakar S (2018) Comparison of efficacy of epidural ropivacaine versus bupivacaine for postoperative pain relief in total knee replacement surgeries. Anesth Essays Res 12:26–30

Brodner G, Mertes N, Van Aken H, Pogatzki E, Buerkle H, Marcus MA et al (1999) Epidural analgesia with local anesthetics after abdominal surgery: earlier motor recovery with 0.2% ropivacaine than 0.175% bupivacaine. Anesth Analg 88(1):128–33

Bullingham A, Liang S, Edmonds E, Mathur S, Sharma S (2018) Continous epidural infusion vs programmed intermittent epidural bolus for labour analgesia: a prospective, controlled, before and after cohort study of labour outcomes. Br J Anaesth 121(2):432–437

Cuschieri RJ, Morran CG, Howie JC, Mc Ardle CS (1985) Postoperative pain and pulmonary complications: comparison of three analgesic regimens. Br J Surg 72(6):495–8

Duncan LA, Fried MJ, Lee A, Wildsmith JA (1998) Comparison of continuous and intermittent administration of extradural bupivacaine for analgesia after lower abdominal surgery. British J Anaesth 80(1):7–10

El Sayed MH, Mokbel E (2014) Postoperative analgesia after major abdominal surgery: Fentanyl–bupivacaine patient controlled epidural analgesia versus fentanyl patient controlled intravenous analgesia. Egypt J Anaesth 30:393–397

Gambling DR, Mc Morland GH, Yu P, Laszlo C (1990) Comparison of patient-controlled epidural analgesia and conventional intermittent "top-up" injections during labor. Anesth Analg 70(3):256–61

Koh Jae Chul, Song Young, Kim So Yeon, Park Sooyeun, Ko Seo Hee, Han Dong Woo (2017) Postoperative pain and patient –controlled epidural analgesia related adverse effects in young and elderly patients: a retrospective analysis of 2435 patients. Journal of Pain Research 10:897–904

Kang S, Jeon S, Choe JH, Bang SR, Lee KH (2013) Comparison of analgesic effects of programmed intermittent epidural bolus and continuous epidural infusion after total knee arthroplasty. Korean J Anesthesiol 65(6 Suppl):S130–S131

Maca J, Neiser J, Grasslova L, Trlicova M, Streitova D, Zoubkova R (2020) Patient-controlled epidural analgesia versus conventional epidural analgesia after total hip replacement - a randomized trial. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub 164:108–114

Malhotra N, Singh R, Hooda S, Singla V, Kanika (2016) Intermittent versus continuous epidural infusion technique for post operative analgesia. Northern Journal of ISA 1:24–28

Patil SS, Kudalkar AG, Tendolkar BA (2018) Comparison of continuous epidural infusion of 0.125% ropivacaine with 1μg/ml fentanyl versus 0.125% bupivacaine with 1μg/ml fentanyl for postoperative analgesia in major abdominal surgery. J Anaesthesiol Clin Pharmacol 34(1):29–34

Pennington P, Caminiti S, Schein JR, Hewitt DJ, Nelson WW (2009) Patients assessment of the convenience of fentanyl hcl intophoretic transdermal system(ITS) versus morphine intravenous patient controlled analgesia(IV PCA) in management of postoperative pain after major surgery. Pain Manag Nurs 10(3):124–33

Pitimana AS, Visalyaputra S, Komoltri C, Muangman S, Tiviraj S, Puangchan S et al (2005) An economic evaluation of bupivacaine plus fentanyl versus ropivacaine alone for patient-controlled epidural analgesia after total-knee replacement procedure: A double-blinded randomized study. Reg Anesth Pain Med 30:446–545

Renck H, Edstrom H, Thoracic epidural analgesia III (1976) Prolongation in the early postoperative period by intermittent injections of etidocaine with adrenaline. Acta Anaesthesiologica Scandinavica 20:104–110

Rutberg H, Hakanson E, Anderberg B, Jorfeldt L, Martensson J, Schildt B (1984) Effects of the extradural administration of morphine, or bupivacaine, on the endocrine response to upper abdominal surgery. Br J Anaesth 56(3):233–8

Small C, Laycock H (2020) Acute postoperative pain management. Br J Surg 107:70–80

Standl T, Burmeister MA, Ohnesorge H, Wilhelm S, Striepke M, Gottschalk A et al (2003) Patient-controlled epidural analgesia reduces analgesic requirements compared to continuous epidural infusion after major abdominal surgery. Can J Anaesth 50(3):258–64

Wheatley RG, Schug SA, Watson D (2001) Safety and efficacy of postoperative epidural analgesia. Br J Anaesth 87:47–61

Publisher's Note