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Research Article
Comparison of Analgesia Duration of Different Epidural Bupivacaine Volume for Lower Extremities Orthopedic Surgery

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Abstract

Background and Objective: Epidural analgesia is a technique of choice for reduction of acute pain due to surgery of the lower limb. This study aimed to compare the time of administration and side effects of intermittent bolus of bupivacaine 0.125% of volume 6, 8 and 10 mL in lower extremities procedure under epidural analgesia. **Materials and Methods:** This study was a single blind clinical experimental test. Samples were patients with 18-64 years of age, clinical criteria ASA PS I-II undergoing elective surgery of the lower limb. Randomization was done to obtain three groups with a sample size of 20 patients in each research group. The three groups were given a bolus of bupivacaine 0.125% 6, 8 and 10 mL, respectively. Data obtained were analyzed with one-way ANOVA and SPSS. Statistical analysis was done by using unpaired t-test, Chi-Square test and $p<0.05$ was considered significant. **Results:** Observation and recording time of onset of pain relief using numeric rating scale (NRS), with target of NRS<3 (mild pain). Pain relief of using 0.125% bupivacaine bolus increase as dose increase and the incidence of adverse events arising subsequently recorded. The time duration of intermittent bolus administration was shorter in 6 mL group (3 h, 50 min) than in 8 mL group (4 h, 56 min) and 10 mL (5 h, 17 min). Statistically, there was no significant difference between 8 and 10 mL group. Side effects were more common in the group of 10 mL compared to the 6 mL group and 8 mL group. **Conclusion:** It was concluded that administration of 8 mL, 0.125% bupivacaine has a better effect than 6 and 10 mL. The greater the volume that is used the greater the side effects that could occur.

Key words: Bupivacaine, intermittent bolus, epidural analgesia, lower extremities surgery, numerical rating scale

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Pain experienced by the patient after a surgery is a problem that is very important. Today knowledge of the mechanisms of postoperative pain has been much progress but management of post-surgical pain was not ideal yet and often neglected. As a result, pain that arises can affect physiology of the human body and emotional individuals who experience it. The response to the stress of pain involves the whole system of human organs, which then contributes to postoperative morbidity and mortality and can result in prolonged period of hospitalization. These conditions trigger aggressive and integrated management of post operative pain[1].

It was estimated that pain was not dealt adequately in half of all surgical procedures. Approximately 80% of patients who undergo surgery experience acute pain. Sommera *et al.*[2] reported the prevalence of postoperative pain at the University Hospital Maastricht Holland in 1490 patients who received postoperative pain management according to standard protocol, the result is 41% experience moderate pain and severe on days 1-4. The prevalence of postoperative abdominal pain group of moderate and severe pain on days 0-1 is 30-55%. Moderate and severe pain prevalence after lower extremities procedure on days 1-4 is 20-71% and 30-64% in spinal surgery, respectively[2].

Inadequate pain management can cause a variety of negative effects on the physiological functions of the body such as the respiratory system, cardiovascular, gastrointestinal, coagulation, renal, central nervous system and sympathetic. Tissue injury and pain can also trigger endocrine response with increased secretion of the cortisol, catecholamines and various other stress hormones. If the process continues, dysfunction, damage and even failure of the entire organ system involved can take place. Adequate analgetic can minimize the occurrence of physiological disorders[2,3].

Postoperative pain management as part of postoperative care was not only intended to reduce the suffering of patients due to postoperative pain but also to decrease the morbidity and mortality of acute pain post surgery. Services provided include multiple modalities in the treatment of acute pain. There are several modalities are used in the treatment of acute post operative pain, including: Patient control analgesia (PCA), Epidural analgesia with the provision of continuous or intermittent doses and TENS (Transcutaneous Electrical Nerve Stimulation). Pharmacological interventions include NSAIDs, opioids, antidepressants, neuroleptic agents, anticonvulsants, corticosteroids and a local anesthetic. Epidural analgesia can provide several benefits, including accelerated healing, decreased complication rate and improved patient outcomes such as quality of life and satisfaction. Furthermore, epidural analgesia provided with appropriate considerations can improve clinical outcomes, such as reduction in the incidence of pulmonary complications, myocardial infarction, deep vein thrombosis and pulmonary embolism[2,4].

Treatment of acute postoperative pain with epidural analgesia was one of the most widely done. Very lower extremities surgery with severe postoperative pain was generally managed with epidural analgesia. Epidural analgesia was now widely accepted as one of the management option for acute pain management techniques after surgery. Compared with parenteral opioid administration, in general, epidural analgesia provides superior analgesia and certain physiological advantages, namely reducing the neuroendocrine stress response secondary to surgical stress. Epidural analgesia is also superior to peripheral nerve block or PCA in terms of blunting the stress response in orthopedic surgery[4].

Previous study by Karnawat *et al.*[5], using 10 mL of 0.125% bupivacaine, obtained intermittent bolus duration on average 3 h, 50 min to provide adequate pain control after surgery. Ferdinand *et al.*[6], conducted a study that compares the intensity of acute pain after extremities surgery in patients receiving intermittent epidural bolus compared with continuous epidural dose, in which intermittent epidural dose of 8 mL bupivacaine 0.125% every 4 h provide good pain control results within 24 h after surgery[5,7].

This study aimed to compare the time of administration and side effects of intermittent bolus of bupivacaine 0.125% of volume 6, 8 and 10 mL in lower extremities procedure under epidural analgesia. The result of this study will help us in providing adequate analgesia in conditions where lack of resources to use continuous infusion protocol.

MATERIALS AND METHODS

Location and time research: This study was conducted in Dr. Wahidin Sudirohusodo Hospital and its network in Makassar starting from June, 2016 until required sample was achieved.

Design and research variables: The design of this research study was randomized single blind clinical trial. Variables consist of the independent variable (0.125% bupivacaine), the dependent variable (postoperative pain, side effects), control variables (ASA Physical Status (ASA PS), age, sex, body mass index (BMI)) and intermediate variable (lower limb surgery).

Population and sample: The population included in this study was patients undergoing elective lower extremities surgical procedures in the central operating theatre of Dr. Wahidin Sudirohusodo Hospital during the study. Study sample was a population that met the inclusion criteria and agreed to participate in the study.

Method of collecting data: Patients who meet inclusion criteria underwent elective surgery preparation procedures applicable. Patients underwent placement of epidural catheter at L2-L3 interspace or L3-L4 and epidural catheter was inserted cephalad, 3-4 cm of catheter was left in the epidural space. Test dose of 2% lidocaine 3 mL+adrenaline 1: 200,000 to locate the epidural catheter and assess the possibility of intravascular insertion. At the end surgery, patients were given epidural bupivacaine 0.125% dose according to their group. Pain intensity measure during after surgery. If there were complaints of discomfort in the area of operation or mild pain with NRS score≤3, intermittent bolus was given according to their groups. Adverse events and vital signs recorded.

Statistical analysis: Data obtained were processed using SPSS 18 for Windows. Statistical analytic method used based on types data obtained. Age, BMI and time to intermittent bolus was analyzed with one-way ANOVA test if it was distributed evenly or using Kruskal Wallis test if it is not. Times to intermittent bolus between two groups were done using unpaired t-test if it was distributed evenly or Mann Whitney test if not. Sex types, ASA PS, types of procedure and side effects was tested with Chi-Square if expected count was more than 5 or Fisher exact test if less. $p<0.05$ was considered significant.

RESULTS

A single-blind randomized clinical trial was done to compare the time of administration and side effects of intermittent bolus administration of 6, 8 and 10 mL of bupivacaine 0.125% in lower extremities surgery under epidural analgesia.

Comparison of time of intermittent bolus administration of 6 mL group and 8 mL group shows that there are statistically significant difference ($p<0.05$). Time to intermittent bolus administration of both groups were tested using unpaired t-test were ($p<0.05$) revealing significant result (Table 1).

Comparison of time of intermittent bolus administration at 8 and 10 mL group showed that there was no statistically significant difference ($p\geq0.05$). Time to intermitted bolus administration of both groups were tested using unpaired t test where ($p<0.05$) found significant difference (Table 2).

Table 1: Comparison of time of intermittent bolus of 6 and 8 mL bupivacaine

	Groups		
	Bupivacaine 6 mL (n=20)	Bupivacaine 8 mL (n = 20)	
Variables	Mean±SD	Mean±SD	p*
Time (h)	3.91 ± 0.76	4.93±0.61	
Time (min)	235±46	296±37	0.000

*Unpaired t-test, $p<0.05$ revealed significant

Table 2: Comparison of time of intermittent bolus of 8 and 10 mL bupivacaine

	Groups		
	Bupivacaine 8 mL (n = 20)	Bupivacaine 10 mL (n = 20)	
Variables	Mean±SD	Mean±SD	p*
Time (h)	4.93±0.61	5.29±0.92	
Time (min)	296±37	317±55	0.078

*Unpaired t-test, $p<0.05$ revealed significant

Table 3: Comparison of time of intermittent bolus of 6 and 10 mL Bupivacaine

	Groups		
	Bupivacaine 8 mL (n = 20)	Bupivacaine 10 mL (n = 20)	
Variables	Mean±SD	Mean±SD	p*
Time (h)	3.91±0.76	5.29±0.92	
Time (min)	235±46	317±55	0.000

*Unpaired t-test, $p<0.05$ revealed significant

Comparison of time of intermittent bolus administration of 6 mL group and 10 mL group showed that there were statistically significant differences ($p<0.05$). Time to intermittent bolus administration of both groups were tested using unpaired t-test where ($p<0.05$) and was found significant (Table 3).

Comparison of the 3 groups mean time, seen in 6 mL of bupivacaine group takes 3.91 h, the bupivacaine group 8 mL takes 4.76 h and the bupivacaine group 10 mL takes 5.29 h. It can be concluded that the fewer the number of drugs used, the less time until additional intermittent bolus was required and conversely if higher volume of drugs used it will take more time until rescue dose was required.

Comparison of adverse event in the 3 groups of showed that there are no patients who experienced adverse events at 6 mL bupivacaine group. About 1 patient (5%) of the 8 mL bupivacaine group experience hypotension and nausea, while 1 patient (5%) of bupivacaine 10 mL group experienced nausea and another patient (5%) experience nausea and hypotension. This shows that if larger the volume is given, the greater the side effects bias arises, albeit with a significant difference (Fig. 1).

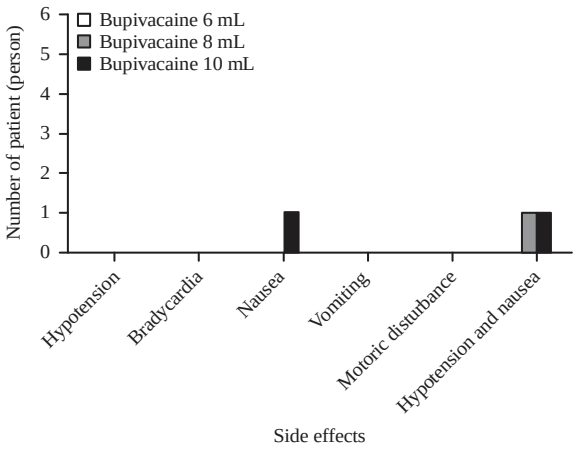

Fig. 1: Incidence of side effects in 3 groups

DISCUSSION

This study showed that the administration of 8 mL of 0.125% bupivacaine has a better effect than 6 and 10 mL. The greater the volume used, the greater the side effects that could occur. Based on the characteristics of the sample male was more prevalent than female in the study. Statistically, this difference was not significant ($p = 0.233$). This study was limited to the category of ASA PS 1 and 2. In the 3rd group of the samples showed the number of patient with higher ASA class. There was no statistically significant difference between the 2 groups in respect to PS ASA classification ($p = 1.000$). In the age and BMI of the three groups was not statistically significant with $p = 0.752$ on age characteristic and $p = 0.254$ on patient's BMI. In this study, there were 4 procedures, with Open Reduction Internal Fixation (ORIF) of femur being the most common procedure done on 18 patients and THA as the least common procedure with only 14 procedures done. There was no statistically significant difference ($p \geq 0.05$) in types of procedure in all 3 treatment groups, meaning homogenous sample was acquired.

Bupivacaine is generally used for the treatment of post-surgical pain of lower extremities through the epidural catheter. The concentration of 0.125% of bupivacaine was generally used because it does not cause motor blockade when given through lumbar epidural[5]. Bupivacaine was a widely used local anesthetic of potent amino amide class with long tenure. A series of 16 bupivacaine MIPs were studied[7].

Epinephrine combined with TTX prolonged blocks more than 10 fold, while reducing systemic toxicity. The TTX, formulated as Tectin, was in phase III clinical trials as an injectable systemic analgesic for chronic cancer pain[8]. Bupivacaine has a low therapeutic index, where the low dose of 50 mg can cause ventricular fibrillation if given intravenously in vulnerable patients. In adults, 1-2 mL of local anesthetic per segment for the block was generally used as a benchmark. Study by Ok *et al.*[9] found that a lipid emulsion reversed the vasodilation induced by bupivacaine during sodium orthovanadate induced contraction.

Usage of epidural anesthesia has been based on patient's clinical condition, it can either be used as primary anesthesia technique of as supplemental technique to general anesthesia. Bupivacaine maximum dose in the epidural, spinal, block infiltration and peripheral nerve is 3 mg kg^{-1} [5,6,10].

Based on the comparison of the time duration of drug administration showed a different time duration of the 3 groups. About 6 ml of bupivacaine have a shorter duration than 8 mL, where the 6 mL group obtained 3.91 ± 0.76 h and 8 mL groups obtained 4.93 ± 0.61 h. About 8 mL bupivacaine has a shorter analgesia time compared to 10 mL bupivacaine (5.29 ± 0.92). From research conducted by Ferdinand *et al.*[6], which uses 8 mL, 0.125% bupivacaine obtained the effect duration of intermittent bolus administration given every 4 h gave lower NRS (NRS 1-2) in which intermittent bolus administration every 4 h was capable of providing protection pain without giving rescue analgesics in patients. From the research, it has found that 8 mL group have a longer analgesia by approximately 1 h, in total of an average of 5 h (5.29 ± 0.92).

From research conducted by Karnawat *et al.*[5], using 10 mL 0.125% bupivacaine obtained that the analgesia duration of intermittent bolus administration an average was 3 h, 50 min and gave lower NRS score (NRS 1-3). While the research conducted by Bhattacayya and Dutta[11], which compares 10 mL of bupivacaine 0.125% with 10 mL 0.125% bupivacaine with adjuvant obtained that duration of bupivacaine 0.125% without adjuvant was 206.8 min or around 3 h, 40 min. In this study, use 10 mL bupivacaine 0.125% with analgesia duration on average for 5 h, 17 min (5.29 ± 0.92). The results of this study, the duration of 10 mL group was 1 h, 37 min longer than research conducted by Karnawat *et al.*[5] and Bhattacayya and Dutta[11]. Bupivacaine given to the epidural space will have 2 segments decrease of sensory block (two-segment regression) after 120-240 min of initial administration[11-13]. Total number of doses of local anesthetic and total volume determine the spread and quality of sensory block. Great concentration of local anesthetic produces greater motor block and sensory block. The amount of volume determines the number of segments blocked, use of higher volume will block more segments that allows longer analgesia even if there has been a regression of

sensory block of two segments. From theory suggested that epidural analgesia mechanisms focused on the number of nerve or segments blocked by local anesthetic.

In clinical observation 10 mL group provide longer duration than 6 and 8 mL bupivacaine, so it can be assumed that the increase in the drug volume affects the time duration of analgesia, where more volume was needed if longer duration required. However, volume difference among 8 mL group and 10 mL group in this study was statistically insignificant. The data obtained from this study shows that there are side effects that arise in the group of 8 and 10 mL bupivacaine. Statistically incidence of adverse events did not show significant differences in the three groups. In the group of 8 mL obtained side effects such as hypotension and nausea as much as 1 person and 2 person of study group given 10 mL exhibit side effects. Hypotension is a side effect that often occurs in epidural analgesia. The incidence of hypotension mainly depends on the altitude main blocks, especially when the block reaches a height T_1-T_5. Sympathetic blockade of the local anesthetic will cause peripheral vasodilation and increased peripheral blood capacity results in decreased venous return venous heart which may result in decreased cardiac output resulting in a decrease in blood pressure[12-15].

The incidence of nausea and vomiting may occur as a result of hypotension that occurs that causes a decrease in cerebral blood flow after loading local anesthetic agents. Hypotensive anesthesia adverse event can be prevented by administration of crystalloid or colloid fluids before epidural loading. At low dose (0.125%) rarely produce hypotension and bradycardia, it was consistent with the theory that the side effects can be reduced by reducing the dose. In this study, the side effects are not obtained on 6 mL groups, this proves that the greater the volume, adverse events are also likely to araise[5,13].

CONCLUSIONS AND RECOMMENDATIONS

It can be concluded that the 8 mL of 0.125% bupivacaine on epidural analgesia provide longer analgesia with intermittent bolus than the 6 and 10 mL. The greater the volumes used the longer the duration required but the greater the risk of side effects to occur. Researchers also suggested that the use of bupivacaine 0.125% 8 mL volume can be used in intermittent bolus administration with interval of every 5 h. Further research on pain management with postoperative epidural analgesia in digestive or obstetrics gynecology surgery is needed.

SIGNIFICANCE STATEMENT

This study discover that the pain relief of using 0.125% bupivacaine bolus increase as dose increase and the incidence of adverse events arising subsequently recorded that can be beneficial for the finding of the effective drug administration. In addition, this study applied a single blind clinical experimental test. Randomization was done to obtain three groups with a sample size of 20 patients in each research group.

REFERENCES

1. Kleinman, W., 2002. Regional Anasthesia and Pain Management. In: Clinical Anesthesiology, Kleinman, W. (Ed.)., Lange Medical Books, New York, pp: 289-323.
2. Sommer, M., J.M. de Rijke, M. van Kleef, A.G. Kessels and M.L. Peters *et al*., 2008. The prevalence of postoperative pain in a sample of 1490 surgical inpatients. Eur. J. Anaesthesiol., 25: 267-274.
3. Malhotra, N., R. Singh, S. Hooda, V. Singla and Kanika, 2016. Intermittent versus continuous epidural infusion technique for post operative analgesia. Northern J. Indian Soc. Anaesth., 1: 24-28.
4. Hanna, M.N., S.S. Liu and C.L. Wu, 2009. Effect of Epidural Analgesia on Postoperative Outcomes. In: Acute Pain Management, Raymond, S.S., O.A. de Leon-Casasola, B. Ginsberg and E.R. Viscusi (Eds.)., Cambridge University Press, Cambridge, pp: 637-45.
5. Karnawat, R., S. Chhabra, S. Mohammed and B. Paliwal, 2013. Comparison of effect of epidural bupivacaine, epidural bupivacaine plus fentanyl and epidural bupivacaine plus clonidine on postoperative analgesia after hip surgery. J. Anesth. Clin. Res., Vol. 4. 10.4172/2155-6148.1000373.
6. Ferdinand, T., D. Basuki and I. Isngadi, 2014. Comparison of acute pain intensity after surgery in patients with regional continuous epidural technique analgesia compared with intermitten techniques. J. Anestesiol. Indonesia.
7. Golker, K., B.C. Karlsson, A.M. Rosengren and I.A. Nicholls, 2014. A functional monomer is not enough: Principal component analysis of the influence of template complexation in pre-polymerization mixtures on imprinted polymer recognition and morphology. Int. J. Mol. Sci., 15: 20572-20584.
8. Berde, C.B., U. Athiraman, B. Yahalom, D. Zurakowski, G. Corfas and C. Bognet, 2011. Tetrodotoxin-bupivacaine-epinephrine combinations for prolonged local anesthesia. Mar. Drugs, 9: 2717-2728.

9. Ok, S.H., S.H. Lee, S.C. Kwon, M.H. Choi and I.W. Shin *et al*., 2017. A lipid emulsion reverses toxic-dose bupivacaine-induced vasodilation during tyrosine phosphorylation-evoked contraction in isolated rat aortae. Int. J. Mol. Sci., Vol. 18. 10.3390/ijms18020394.
10. Hadzic, A., 2009. Textbook of Regional Anesthesia and Acute Pain Management. McGraw-Hill Education, New York, ISBN: 9780071731973, Pages: 2000.
11. Bhattacharyya, R. and B. Dutta, 2007. Postoperative analgesia with local anaesthetic and opioid combinations, using double space CSE technique. Indian J. Anaesth., 51: 409-415.
12. Salinas, F.V., 2007. Pharmacology of Drugs Used for Spinal and Epidural Anesthesia and Analgesia. In: Spinal and Epidural Anesthesia, Wong, C.V. (Ed.)., McGraw-Hill Company, New York, pp: 76-109.
13. Doty, R. and R. Sukhani, 2007. Central Neuraxial Blockade for Lower Extremity Major Orthopedic Surgery. In: Spinal and Epidural Anesthesia, Doty, R. and R. Sukhani (Eds.)., McGraw-Hill Companies, New York, pp: 183-207.
14. Warren, D.T. and S.S. Liu, 2008. Neuraxial Anesthesia. In: Anesthesiology, Warren, D.T. and S.S. Liu (Eds.)., McGraw-Hill Company, New York, pp: 978-1008.
15. Arif, S.K., I. Amri and A. Mallongi, 2017. Comparison between the effect of the intravenous dexmedetomidine with fentanyl on the propofol induction dose requirement and the hemodynamic response due to laryngoscopy and tracheal intubation. Am. J. Drug Discov. Dev., 7: 39-47.