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Co-administration of dexmedetomidine and levobupivacaine results in better onset and duration of epidural anesthesia in lower extremity orthopedic surgery

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ABSTRACT

Background: The goal of this study is to know the efficacy of the addition of 0.5 mcg/kg dexmedetomidine to 15 mL isobaric 0.5% levobupivacaine on the onset and duration of sensory and motor blockade of epidural anesthesia in lower extremity orthopedic surgery.
Methods: Randomized clinical double-blind trials were conducted in Dr. Mohammad Hoesin Hospital Palembang. A total of 34 patients underwent lower extremity surgery met the inclusion and exclusion criteria. Data were analyzed by independent t-test and Mann-Whitney test using SPSS 22.0 software.
Result: The onset of sensory block in group D was 5.41±1.84 minutes compared to 17.59± 2.65 in Group C (p <0.001), as seen in Table 2. The sensory block duration was 362.41±25.66 minutes in Group D compared to 215.82±15.69 in Group C (p <0.001). The onset of the motoric block in group D was 16.53±1.81 minutes compared to 26.12±2.78 in Group C (p <0.001), while the motoric block duration was 301.29±20.55 minutes in Group D compared to 167.35±17.24 in Group C (p <0.001).
Conclusion: The addition of 0.5mcg/kg dexmedetomidine to 15 ml isobaric 0.5% levobupivacaine in epidural anesthesia provide faster onset and prolonged duration in both motoric and sensory block in patients undergoing lower extremity surgery.

Keywords: *dexmedetomidine, levobupivacaine, epidural, sensory, motoric.*
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INTRODUCTION

Surgical procedures of the lower limb area can be facilitated by both general and regional anesthesia. Regional techniques such as epidural anesthesia provide many advantages over general anesthesia including maintained patient's awareness, produced adequate analgesia, reduced stress response, reduced intraoperative bleeding, reduced post-operative pain, earlier mobilization, and enhance rehabilitation.[1] Drugs that are often used in epidural techniques are the amide groups, such as bupivacaine, ropivacaine, and levobupivacaine. Bupivacaine is a local anesthetic of long-acting amide groups that have been used for more than 40 years. Since its introduction in 1957, this agent is associated with a number of side effects such as central nervous system and cardiovascular toxicity. This leads to further research for a newer and more secure local anesthetic agent.[2]

In recent years, levobupivacaine, the pure S (−)-enantiomer of bupivacaine, emerged as a safer alternative for regional anesthesia. Levobupivacaine pharmacokinetics has been compared with racemic bupivacaine in healthy humans, epidural administration and brachial plexus block with the same dose, there is no difference in pharmacokinetic parameters between these two agents.[3,4] The duration of analgesic effects of bupivacaine and levobupivacaine was longer than other local anesthetics. Both also showed the preferred motor and sensory blockade ratio. The enantio-selective properties of levobupivacaine exhibit affinity and inhibitory forces in the lower cardiac sodium channels as well as the blockade effect on cell firing in the central nervous system solitary tract nucleus.

The mean dose of levobupivacaine and bupivacaine that cause symptoms of the central nervous system in humans are approximately the same (56-58 mg for levobupivacaine and 48-65 mg for bupivacaine). At this dose, levobupivacaine exhibits the depression of myocardial contractility and less atrioventricular conduction than bupivacaine. With its advantages in pharmacokinetic profile and lack of side effects on the cardiovascular and central nervous system, levobupivacaine is an option in regional anesthetics compared to bupivacaine.[3,4]

Although some of the new local anesthetic agents above have better safety profiles, these agents still have a long-term onset of work and limited duration. Burlacu et al.[4] reported the average onset of sensory blockade was 8-30 minutes in 4-6 hours duration. To fasten the onset, the addition of other drugs (adjuvant) to local anesthetics is commonly practiced. These adjuvants include opioid, neostigmine, clonidine, and dexmedetomidine.[5,6]

Dexmedetomidine, an α2-adrenergic agonist group, was first introduced by the Food and Drug Administration (FDA) in 1999. Dexmedetomidine has antinociceptive effects that reduce hyperalgesia, prevent catecholamine release, and used as a sedative during surgery and postoperative periods.[6]

Schanabel *et al.*[6] showed that 1-2 mcg/kg dexmedetomidine as adjuvant local anesthesia in epidural anesthesia may accelerate the onset of the sensory blockade and increase the duration of sensory and motor blockade with no respiratory depression effect.

The effect of dexmedetomidine administration as adjuvant for regional anesthesia in both spinal and epidural anesthesia is potential to accelerate the onset of sensory blockade, prolong the duration of sensory and motor blockade, sedation effects, prolong postoperative analgesic administration, decrease the side effects of nausea and vomiting, no respiratory depression but bradycardia and hypotension can occur.[7-13]

PATIENTS AND METHODS

This study is a double-blind, randomized controlled trial. The study was conducted in the operating room of Dr. Mohammad Hoesin Hospital (Palembang, Indonesia) from January to April 2017. The study population is patients underwent lower limb orthopedic surgery in Dr. Mohammad Hoesin Hospital under epidural anesthesia. The study protocol was approved by the hospital's ethics committee. All involved subjects provided written informed consent to be included in this study.

The inclusion criteria were ASA (American Society of Anesthesiologist) I-II patient, aged 17-60 years, and scheduled for lower extremity surgery. Exclusion criteria were pregnancy, unsuitable condition for epidural anesthesia, and those who received sedative or analgesic medications 24 hours prior to surgery. Those who experienced epidural block failure after 30 minutes of epidural injection were excluded from the study.

The subjects were divided randomly into two groups. Group D received 0.5 μg/kg dexmedetomidine and 15 mL 0.5% levobupivacaine by epidural injection, and Group C received 15 mL 0.5% levobupivacaine + 1 mL 0.9% NaCl. The injection formula was put into the same 20 mL syringe so that the anesthetist performed the injection would not have known the exact composition. All other drugs and procedures were the same to both groups.

Pinprick test was used to assess the sensory block. Motor blockade was assessed using the Bromage scale. Systolic blood pressure, diastolic blood pressure, and pulse rate were assessed every 5 minutes after injection for 60 minutes and thereafter every 10 minutes during surgery with a Spacelabs monitor, model No. 91369.

Data were analyzed using SPSS 22.0 software. Descriptive analysis was used in the subject's characteristic. Shapiro-Wilk test was used in the normality test. Mann-Whitney test and independent t-test were used to compare the data between groups. A p-value of <0.05 was considered significant.

RESULTS

A total of 34 patients were enrolled in this study, divided into two study groups consist of 17 subjects each. General characteristics of research subjects are shown in table 1. The mean age in Group D

Table 1 Characteristics of the subjects

Characteristics	Groups	
	D	C
Age (year), mean±SD	34.00 ± 15.6	31.65 ± 14.03
Weight (kg), mean±SD	59.53 ± 9.06	56.59 ± 9.16
Height (cm), mean±SD	160.65 ± 7.43	160.53 ± 9.12
Duration of surgery (minute), mean±SD	172.77 ± 54.51	141.72 ± 29.75
Sex, n (%)		
• Male	9 (52.9)	9 (52.9)
• Female	8 (47.1)	8 (47.1)
ASA n (%)		
• I	11 (64.7)	14 (82.4)
• II	6 (35.3)	3 (17.6)

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Table 2 Profile of motoric and sensory block between the two groups (mean ± SD)

Variables	Group D	Group C	p-value
Sensory blockade onset (minute)	5.41 ± 1.84	17.59 ± 2.65	<0.001[a]
Regression of two segments (minute)	226.12 ± 20.45	118.18 ± 21.52	<0.001[b]
Sensory blockade duration (minute)	362.41 ± 25.66	215.82 ± 15.69	<0.001[b]
Motoric blockade onset (minute)	16.53 ± 1.81	26.12 ± 2.78	<0.001[b]
Motoric blockade duration (minute)	301.29 ± 20.55	167.35 ± 17.24	<0.001[b]

[a]Mann-Whitney test; [b] Independent t-test

was 34.00±15.6 years and in Group C was 31.65 ± 14.03 years. Normality test results showed that all data were normally distributed and comparable.

The onset of sensory block in group D was 5.41±1.84 minutes compared to 17.59± 2.65 in Group C (p <0.001), as seen in Table 2. The sensory block duration was 362.41±25.66 minutes in Group D compared to 215.82±15.69 in Group C (p <0.001). The onset of the motoric block in group D was 16.53±1.81 minutes compared to 26.12±2.78 in Group C (p <0.001), while the motoric block duration was 301.29±20.55 minutes in Group D compared to 167.35±17.24 in Group C (p <0.001).

DISCUSSION

This study found significant differences in onset and duration of both motoric and sensory blockade in epidural anesthesia between the two groups. These results were similar to the one reported by Bajwa *et al*[13] that found significant differences in sensory blockade onset, duration of sensory blockade and regression of two segments between groups given 1.5 μg/kg dexmedetomidine and 2 μg/kg clonidine. In this study, however, the onset of sensory blockade was faster (5.41±1.84 minutes) than in the Bajwa study (8.52±2.36 minutes). Likewise, the mean time of regression of two segments and the duration of the sensory blockade where the mean time of regression of two segments of the results obtained in the Bajwa study was shorter (136.46±8.12 minutes) than in this study (226.12±20.45 minutes) and the duration of the sensory blockade in the Bajwa study was shorter (342.88±29.16 minutes) than in this study (362.41±25.66 minutes).

This study also found similar results to Kaur *et al*[7] that reported significantly faster onset and longer duration of the motor blockade in subjects who were given 1 μg/kg dexmedetomidine. This study found a faster onset of the motor blockade (16.53±1.81 minutes) than the Kaur study (27.34 ± 5.97 minutes). The duration of the motor blockades in this study was longer (301.29 ± 20.55 min) than in the Kaur study (259.8 ± 15.49 min).

Dexmedetomidine is highly lipophilic, making it easier and faster to bind to a spinal cord that has the potential to affect local anesthesia.[13-16] The mechanism of dexmedetomidine binds to α2 receptors in the dorsal horn pre and post-synapse of the spinal cord lowers the stimulus of nociceptive substance in neuraxial use.[6,13,17-23]

Dexmedetomidine acts on the α2 adrenoceptor in the core and spinal cord locus. The mechanism of the presynapse is at the α2C and α2A receptors dorsal horn neurons which inhibits transmitter release of substance P and glutamate, and hyperpolarization of spinal interneuron-mediated through G protein produces a synergistic analgesia effect with local anesthetic agents.[24-26] This leads to an elongation of the duration of the sensory blockade. While on postsynapse, the mechanism of dexmedetomidine through α2B which produces vasoconstriction effect at the injection site thus slowing the absorption of local anesthesia.[27-28] This mechanism resulted in the prolongation of sensory and motor blockade of epidural anesthesia. The mechanism of action of analgesia from both α2 adrenergic agonist spinal and supraspinal is that modulate nociceptive transmission in the central nervous system, although α2 receptors in the periphery may also mediate antinociceptive.[5,6,13,29-32]

CONCLUSION

The addition of 0.5mcg/kg dexmedetomidine to 15 ml isobaric 0.5% levobupivacaine in epidural anesthesia provide faster onset and prolonged duration in both motoric and sensory block in patients undergoing lower extremity surgery.

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