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RESEARCH ARTICLE

Comparison of Hyperbaric Lidocaine vs. Hyperbaric Bupivacaine-Morphine Spinal Anesthesia on Ephedrine Use and Neonatal Outcomes in C-Sections

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ABSTRACT

Spinal anesthesia using hyperbaric lidocaine or hyperbaric bupivacaine-morphine is common in C-sections, but research on ephedrine dose requirements and neonatal outcomes, like metabolic acidosis due to asphyxia, is limited. This study aimed to compare ephedrine dose requirements, APGAR scores, and umbilical cord pH and BE in C-sections using these two anesthetic drugs. This prospective analytical experimental study involved 26 subjects delivering via C-section at Universitas Airlangga Hospital, divided into hyperbaric lidocaine (HL) and hyperbaric bupivacaine-morphine (HBM) groups. Data on subject characteristics, ephedrine dose, and neonatal outcomes (APGAR scores at 1 and 5 minutes, umbilical cord pH, and base excess) were recorded and analyzed using SPSS with $p<0.05$ significance. The mean age of subjects who underwent SC delivery was 29.62±6.49 years. Ephedrine dose requirements and neonatal outcomes between HL and HBM groups showed variable results: Ephedrine (5.77±7.86mg vs 4.23±7.03mg, p=0.537), APGAR score minute 1 (7.62±0.96 vs 7.54±0.66, p=0.323), minute 5 (8.69±0.75 vs 8.62±0.51, p=0.338), pH (UC) (7.29±0.06 vs 7.32±0.09, p=0.303), and BE (UC) (-3.66±2.63 vs -0.65±2.47, p=0.006). Only APGAR minute 1 and BE were correlated (p=0.043, r=0.399). The use of hyperbaric lidocaine and hyperbaric bupivacaine-morphine did not show a different effect on either the maternal or the neonatal outcome of SC delivery.

INTRODUCTION

Sectio cesarean (SC) has become the preferred method of delivery in the last decade, with lower maternal and infant mortality rates (Verma et al., 2020). SC deliveries in Indonesia have increased from 4% of births in 1998 to 18.5% in 2017 (Al Farizi et al., 2022; Wyatt et al., 2021). Although this method of delivery is considered safer for newborns, SC delivery still carries risks that may affect neonatal outcomes (Sung & Mahdy, 2023). Several factors such as maternal, uteroplacental, and fetal factors affect fetal oxygenation, so any disruption or abnormality in these factors can lead to asphyxia and neonatal hypoxia (Krakauer & Gowen, 2023; Maheswara et al., 2023). Neonatal outcomes are also affected by intraoperative management during SC delivery, one of which is the choice of anesthetic technique and drug regimen during SC delivery (Ring et al., 2021).

Spinal regional anesthesia technique is a commonly used option for SC delivery compared to general anesthesia due to its advantages of rapid onset, dense block, no sacral sparing, and is associated with

better neonatal outcomes (Kim et al., 2019). The anesthetics lidocaine and bupivacaine in hyperbaric concentrations are standard regimens commonly used in spinal anesthesia for SC delivery. Both drugs act by inhibiting the flow of sodium ions through voltage-gated sodium channels in the neuronal membrane (Kim et al., 2019). This reduces the ability of neurons to transmit pain signals to the brain and produces a local analgesic effect (Taylor & McLeod, 2020). In addition, the addition of morphine to adjuvant anesthesia is often combined with hyperbaric bupivacaine to prolong the duration of anesthesia, provide a stronger analgesic effect, and reduce the dose of opioids after SC surgery (Jemal et al., 2022)

The choice of spinal regional anesthesia technique and drug regimen used for SC delivery has maternal side effects (hypotension) that can affect neonatal outcomes (asphyxia and hypoxia) (Šklebar et al., 2019). Ephedrine is a selective vasopressor with weak alpha-adrenergic and strong beta-adrenergic effects that is most commonly used to treat hypotension from spinal anesthesia by increasing cardiac output and blood pressure (Park & Choi, 2024). The incidence of hypotension during labor after the administration of spinal anesthesia correlates with the high dose of ephedrine required (Statler et al., 2023). In addition, a low APGAR score is an easy-to-use subjective parameter to rapidly determine the asphyxia status of neonates, although its use alone cannot be considered definitive evidence of asphyxia (Simon et al., 2023). Meanwhile, pH and base excess (BE) parameters obtained from the umbilical cord (UC) artery may be more objective predictors in assessing acid-base status of neonates (Bakare et al., 2023). Both APGAR score and umbilical blood gas analysis (pH and BE) can be predictors in assessing the risk of metabolic acidosis of neonates delivered under hyperbaric lidocaine and hyperbaric bupivacaine-morphine spinal anesthesia.

Currently, there are no studies that observe and compare ephedrine dose requirements and neonatal outcomes in SC deliveries using hyperbaric lidocaine and hyperbaric bupivacaine-morphine regimens. Therefore, this study aims to compare ephedrine dose requirements, APGAR score, pH (UC), and BE (UC) between the SC delivery groups receiving both anesthetic drug regimens. The results of this study are expected to provide insight into the use of these two spinal anesthetic drug regimens and their effects on maternal and fetal outcomes.

RESEARCH METHOD

This study is a prospective analytic experimental study with a randomized post-test only parallel group design that aims to analyze ephedrine requirements and infant outcomes in SC deliveries using hyperbaric lidocaine and hyperbaric bupivacaine-morphine spinal anesthesia. Subjects in this study were recruited according to specific inclusion and exclusion criteria. The inclusion criteria included: 1) willingness to be a research subject, 2) SC patients with a Physical Status (PS ASA) score of 1-2, and 3) pregnancy with a live, single, full-term, intrauterine fetus. While the exclusion criteria in this study included: 1) changes in anesthesia technique during SC surgery, 2) fetal distress prior to delivery, 3) neonates born with congenital anomalies, and 4) bleeding greater than 30% of estimated blood volume during SC surgery.

This study included a total of 26 subjects who delivered SC at Universitas Airlangga Hospital, Surabaya, Indonesia, according to the minimum sample size calculation and then equally and randomly divided into two intervention groups: hyperbaric lidocaine (HL) group and hyperbaric bupivacaine-morphine (HBM) group. In this study, subjects received SC delivery according to the standard protocol, but differed only in the anesthetic regimen used. The HL group received a hyperbaric lidocaine regimen consisting of 60 mg of lidocaine dextrose 5% 60 mg and 0.1 mg of adrenaline, while the HBM group received a hyperbaric bupivacaine 0.5% 7.5 mg regimen with 100 mcg of morphine as an adjuvant. In the event of hypotension (drop in systolic blood pressure ≤90 mm Hg) during surgery, intravenous ephedrine is administered at a dose of 5-10 mg. The number of ephedrine doses administered during surgery will be recorded on the anesthetic status.

Several data on subject characteristics were recorded, including MAP (mmHg), HR (x/min), RR (x/min), bleeding volume (mL), comorbid factors, and spinal block height. In addition, the neonates will receive

initial management according to the Neonatal Life Support Guidelines, depending on the clinical findings observed, and will then be assessed using the APGAR score at 1 minute and 5 minutes post resuscitation. After the umbilical cord was cut and the placenta delivered, an arterial blood sample from the umbilical cord and placenta was collected for umbilical artery blood gas analysis (UC-BGA) in the form of pH (UC) and BE (UC).

All data were processed and statistically analyzed using the Statistical Package for the Social Sciences (SPSS) software version 23 (Chicago, IL, USA) with a significance level of p-value <0.05. Data on characteristics are presented as descriptive statistics of mean and percentage. Meanwhile, data on the comparison of APGAR score, pH (UC), and BE (UC) between the two groups will be analyzed by Independent T-test if the data are normally distributed using Shapiro-Wilk test. If the data are not normally distributed, Mann-Whitney U test will be used. In addition, Spearman correlation test was performed to determine the relationship between APGAR score and UC-BGA in data that were not normally distributed. This study received ethical approval from Universitas Airlangga Hospital with registration number 003/KEP/2024.

RESULT AND DISCUSSION

Result

The distribution of data on the characteristics of the subjects of this study, including age, mean arterial pressure (MAP), heart rate (HR), respiratory rate (RR), amount of bleeding, comorbid factors, and spinal block height are presented in Table 1. The normality test results of these data between the HL and HBM groups showed a normal distribution (p > 0.05), so they were considered to have the same starting point.

Table 1. Distribution of Characteristic Data Based on Spinal Anesthesia Group

Variables	Group		Total (n = 26)	*p-value*
	HL (n = 13)	HBM (n = 13)		
Age (Years)				
Range	19 - 41	24 - 41	19 - 41	0.376*
Mean ± SD	28.46 ± 7.28	30.77 ± 5.66	29.62 ± 6.49	
MAP (mmHg)				
Range	85 - 120	85 - 119	85 - 120	0.099*
Mean ± SD	102.77 ± 10.76	95.77 ± 9.99	99.27 ± 10.78	
HR (x/min)				
Range	70 - 114	52 - 103	52 - 114	0.305*
Mean ± SD	83.92 ± 13.61	77.46 ± 13.22	80.69 ± 13.55	
RR (x/min)				
Range	18 - 20	19 - 20	18 - 20	0.126*
Mean ± SD	19.54 ± 0.78	19.92 ± 0.28	19.73 ± 0.60	
Blood Loss (mL)				
Range	150 - 500	100 - 700	100 - 700	0.853*

Variables	Group		Total (n = 26)	*p-value*
	HL (n = 13)	HBM (n = 13)		
Mean ± SD	292.31 ± 130.46	300.0 ± 148.61	296.15 ± 137.06	
Comorbidity				
Yes	8 (61.5%)	11 (84.6%)	19 (73.1%)	0.378*
No	5 (38.5%)	2 (15.4%)	7 (26.9%)	
Obesity	5 (38.5%)	9 (69.2%)	14 (53.8%)	0.238*
Hypertension	2 (15.4%)	4 (30.8%)	6 (23.1%)	0.645*
Preeclampsia	0 (0%)	2 (15.4%)	2 (7.7%)	0.480*
Gestational Diabetes	0 (0%)	2 (15.4%)	2 (7.7%)	0.480*
Anemia	1 (7.7%)	1 (7.7%)	2 (7.7%)	1000*
Subclinical Hypertiroid	0 (0%)	1 (7.7%)	1 (3.8%)	1000*
Spinal Block Height				
4 Th	2 (15.4%)	6 (42.6%)	8 (30.8%)	0.202*
6 Th	11 (84.6%)	7 (53.8%)	18 (69.2%)	

The results of the normality test of the main data of this study, including ephedrine dose, APGAR score (minutes 1 and 5), and pH (UC), showed no normal distribution ($p < 0.05$) in one or both intervention groups, so the comparison test at that time was continued non-parametrically using the Mann-Whitney U test. Meanwhile, the BE (UC) data showed normal distribution in the normality test, so the comparison test was continued parametrically using the independent t-test. The results of the APGAR score and UC-BGA comparison test between the HL and HBM groups can be observed in Table 2.

Table 2. Results of comparison between APGAR score and UC-BGA

Variables	Group		p-value
	HL (n = 13)	HBM (n = 13)	
Ephedrine Dose (mg)			
Range (Median)	0 - 25 (0)	0 - 20 (0)	0.537
Mean ± SD	5.77 ± 7.86	4.23 ± 7.03	
APGAR Score Minute 1			
Range (Median)	5 - 8 (8)	6 - 8 (8)	0.323
Mean ± SD	7.62 ± 0.96	7.54 ± 0.66	
APGAR Score Minute 5			
Range (Median)	7 - 9 (9)	8 - 9 (9)	0.338
Mean ± SD	8.69 ± 0.75	8.62 ± 0.51	
pH (UC)			
Range (Median)	7.14 - 7.36 (7.31)	7.12 - 7.42 (7.36)	0.303

Mean ± SD	7.29 ± 0.06	7.32 ± 0.09	
BE (UC)			
Range (Median)	-7,6 - 1,4 (-3,8)	-4,9 - 3,3 (-0,8)	0.006*
Mean ± SD	-3.66 ± 2.63	-0.65 ± 2.47	

The results of the correlation analysis between APGAR scores (minutes 1 and 5) with pH (UC) and BE (UC) using the Spearman correlation test showed varying results (Table 3). The findings of this study showed that APGAR score was found to have no significant relationship with pH (UC) ($p > 0.05$). Meanwhile, the relationship between APGAR score and BE (UC) showed variable results, where there was an association between APGAR score minute 1 and BE (UC) ($p = 0.043$; $r < 0.399$), while there was no similar relationship with APGAR score minute 5 ($p > 0.05$).

Table 3. Correlation results between APGAR score and UC-BGA

x	APGAR Score Minute 1 (n = 26)		APGAR Score Minute 5 (n = 26)	
	r	p-value	r	p-value
pH (UC)	0.297	0.141	0.275	0.174
BE (UC)	0.399	0.043*	0.386	0.051

DISCUSSION

SC delivery, using either hyperbaric lidocaine or hyperbaric bupivacaine-morphine spinal anesthesia, each had no significant difference in ephedrine dose requirements in managing maternal hypotension, as well as fetal outcomes including APGAR score and pH (UC). Only BE (UC) was found to have a significant difference between the HL and HBM groups. In general, as shown in Table 2, the ephedrine dose requirement was slightly lower in the HBM group, and the median pH (UC) and BE (UC) values were also found to be slightly better in this group. Meanwhile, the median of APGAR scores at 1 and 5 minutes were found to be similar in both intervention groups.

The results of this study are related to the differences in pharmacological properties between the two types of spinal anesthesia. Bupivacaine tends to give better results in spinal anesthesia than lidocaine due to several factors. Pharmacologically, bupivacaine has a longer duration of action and a stronger sympathetic blocking effect than lidocaine, resulting in better vasodilation and stabilization of tissue perfusion (Taylor & McLeod, 2020). In addition, bupivacaine has a slower metabolism and a stronger central nervous system depressant effect, resulting in better maternal physiologic stability (Shafiei et al., 2023). Although these differences occur in maternal physiological responses, changes in maternal acid-base balance may indirectly affect intrauterine environmental conditions and fetal well-being. Therefore, although differences in maternal physiological outcomes may affect fetal conditions, direct assessment of the effects of spinal anesthesia on the fetus is generally performed after delivery, including APGAR score, pH (UC), and BE (UC).

In certain cases, non-modifiable maternal factors such as history of hypertension (pre-eclampsia and eclampsia), BMI (obesity), diabetes, thyroid disease, and anemia may influence fetal outcomes (asphyxia and acidosis) after SC delivery (Gomaa et al., 2021). In this case, the interval between induction of spinal anesthesia and delivery and the management of hypotension after spinal anesthesia are modifiable factors to reduce the risk of neonatal acidosis (Ghidini et al., 2023). Prolonged operative time from induction of spinal anesthesia to delivery (>27 min) is known to affect the outcome of delivery in terms of neonatal acidosis (pH <7.2) (Hassanin et al., 2022).

This condition is also associated with hypotension induced by spinal anesthesia, which causes a decrease

in placental blood flow, disrupting fetal oxygenation and perfusion and leading to metabolic acidosis, which can be observed by APGAR score and pH (UC) (Ghidini et al., 2023; Kitaguchi et al., 2022). The longer this hypotension persists and is not treated promptly, the worse the fetal outcome. The incidence of hypotension after spinal anesthesia is estimated at 74% of planned SC deliveries and is associated with fetal acidosis when prophylactic vasopressor infusion is not used (Šklebar et al., 2019). Therefore, the choice of anesthesia method and type for SC delivery should consider several factors, including the indication for SC, emergency status, maternal status, and patient preference (Iddrisu & Khan, 2021). The effects of anesthetic agents on uterine blood flow and uterine vascular resistance can affect placental perfusion pressure, which has a direct impact on the fetus after birth (Iddrisu & Khan, 2021).

In Table 3, APGAR scores generally showed no significant association ($p > 0.05$) with pH (UC) and BE (UC) values, except between APGAR score minute 1 and BE (UC) ($p = 0.043$; $r = 0.399$). This could be due to various factors, including the clinical condition of the mother and medical interventions during labor. Furthermore, the APGAR score is a subjective parameter and has a high interobserver variability (Boos & Bührer, 2024). According to the American College of Obstetricians and Gynecologists, the use of APGAR score has limitations because there are several factors that can affect the results, such as maternal sedation or anesthesia, congenital malformations, gestational age, trauma, and inter-observer variability (Simon et al., 2023). In addition, pH (UC) and BE (UC) may be more objective predictors of fetal acid-base status (Bakare et al., 2023).

Several studies have also shown inconsistent results regarding whether there is an association between APGAR score and pH (UC) and BE (UC). The majority of studies mentioned that the association between APGAR score and pH (UC) was more frequently observed in high-risk pregnancies compared to low-risk pregnancies (Panahi et al., 2024). This proves that there are other variables such as maternal (obesity, hypertension, thyroid disease, and diabetes) and fetal (congenital anomalies, premature birth, and intrauterine growth restriction) factors in utero that also affect the outcome of APGAR and pH (UC). Meanwhile, BE (UC) values are considered more representative than pH (UC) values because they show a linear correlation with the degree of acidosis and are not affected by respiratory acidosis (Ghidini et al., 2023).

Despite its limitations, the APGAR score at 5 minutes is still recommended for neonatal assessment and is a widely used indicator of perinatal health (Boos & Bührer, 2024). However, a APGAR score at 5 minute of ≥ 7 may not be sufficient to verify newborn well-being as it may pose a risk of non-detection of some newborns with mild metabolic acidosis (Yılmaz et al., 2022). Therefore, umbilical artery blood gas analysis should be considered to monitor for possible metabolic acidosis even in the absence of signs of fetal distress and an APGAR score >7.

The results of this study showed that the use of hyperbaric lidocaine and hyperbaric bupivacaine-morphine generally did not have a significantly different effect on the mother or neonate born via SC delivery. However, this study has the limitation of not recording the induction time between the administration of spinal anesthesia and the completion of labor, as well as the duration of hypotension that occurs in pregnant women after the administration of spinal anesthesia. These factors may affect the outcome of the study and need to be considered for improvement in future studies.

CONCLUSION

In conclusion, the results of this study showed that there was no significant difference ($p > 0.05$) in ephedrine dose requirements and neonatal outcomes (APGAR score and pH) delivered by SC using hyperbaric lidocaine and hyperbaric bupivacaine-morphine spinal anesthesia. However, only the BE (UC) score was found to have a significant difference ($p < 0.05$) between the two groups, with the BE (UC) score in the HBM group being better than in the HL group. Overall, the use of hyperbaric lidocaine and hyperbaric bupivacaine-morphine did not show a significantly different effect on maternal and neonatal outcomes of SC delivery.

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Conflict of Interest

There is no conflict of interest in this research report.

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