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ORIGINAL ARTICLE

Low dose hyperbaric bupivacaine 5 mg combined with 50 mcg fentanyl for cesarean section in maternal heart disease

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ABSTRACT

Background & Aims: Most of the women with cardiovascular diseases suffer from worsening of their clinical condition during pregnancy. It is caused by cardiovascular physiological changes during pregnancy and increased demand of oxygen-metabolic system. Spinal anesthesia is the most commonly used technique in cesarean section (CS) patients, but there are concerns about sudden hemodynamic decrease. We aimed to investigate the use of low dose hyperbaric bupivacaine 5 mg combined with 50 µg fentanyl for caesarean section in patient with heart disease.

Methodology: This study is a retrospective study in 33 patients with maternal heart disease undergoing CS under low dose spinal anesthesia in Saiful Anwar Hospital Malang Indonesia from September 2017 until September 2018. The spinal regimen was administered with 5 mg bupivacaine heavy 0.5% combined with 50 µg fentanyl. We evaluated the hemodynamic preoperative, post injection of spinal anesthetics, post-delivery, and at the end of surgery. We also evaluated Bromage score, Apgar score of the baby, and satisfaction level by the obstetrician.

Results: Combination of low dose spinal and opioid for the CS delivery show no significant hypotension effects. Hemodynamic stabilization was achieved. Furthermore, target blocked was reached well in all cases, no significant changes in Apgar score of the baby, and obstetrician satisfied with motor relaxation.

Conclusion: Low dose spinal anesthesia using 5 mg of bupivacaine heavy 0.5% and adjuvant opioid fentanyl 50 µg can be successfully used for the performance of CS delivery satisfactory block, good fetal outcome, and impressive cardiovascular stability.

Key words: Anesthesiology; Bupivacaine; Caesarian section; Fentanyl; Heart disease; Pregnancy

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INTRODUCTION

Cardiac abnormalities during pregnancy are still the main non-obstetric factors causing morbidity and mortality in pregnant women.[1] In the United States, complications of heart disease are found in about 4% of all pregnancies. Maternal heart diseases have a mortality risk of (10%-25%).[2] Pregnant women with heart disorders due to congenital heart disease, acquired heart disease, and cardiomyopathy, require special attention and management, because of physiological changes during pregnancy will increase the workload on the heart, whereas the heart will have impaired ability to compensate and adapt to

imperfect pregnancy.[3] Every cardiac disease warrants some specific considerations, but the main goal in a patient with heart disease patient undergoing CS is same which is to maintain hemodynamic stability for the mother and baby by all means.

Spinal anesthesia is the most often used technique in cesarean sections (CS), but there are some concerns about use of spinal anesthesia in patients with cardiac disease. It has been contraindicated in some specific heart disease like mitral stenosis due to risk of hemodynamic instability. Recent studies, however, have proved hemodynamic changes in spinal anesthesia to be dose dependent. An inadequate dose might lead to inadequate block and maternal-fetal hemodynamic changes due to pain or discomfort. The addition of opioids could reduce the dose requirements of local anesthetics and prevent hemodynamic fluctuations and increase the effects of intraoperative and postoperative analgesia.

In this retrospective study, we evaluate the outcome of the low dose spinal anesthesia technique in pregnant patients with cardiac abnormalities undergoing CS. This study might prove to be useful in determining anesthetic techniques in pregnant patients with heart diseases.

METHODOLOGY

This retrospective, observational descriptive study evaluated maternal and fetal outcome parameters in the low dose spinal anesthesia technique during the lower segment CS in pregnant patients with cardiac abnormalities. The study was conducted at Saiful Anwar Malang Hospital in November 2018 by evaluation of the patients' one year medical record from September 2017 to September 2018. The pregnant patients with cardiac abnormalities, who underwent elective or emergency CS with a low dose spinal anesthesia technique employing hyperbaric bupivacaine 5 mg and fentanyl 50 µg were included. The exclusion criteria were conversion to general anesthesia (GA) or use of sedatives or vasopressors preoperatively, and patients with incomplete medical record. Medical records about the outcome of the mother and fetus were observed and recorded, such as:

1. Hemodynamic parameters (blood pressure and pulse rate) at 0, 3, 6, and 9 min after the anesthetic technique.
2. Apgar score of the baby.
3. Time to reach target Bromage score and block height and the time to regress.
4. Level of obstetrician's satisfaction with the anesthetic technique used.

The data obtained were analyzed using the SPSS 15.0. Data on hemodynamic changes (blood pressure and pulse) were analyzed for homogeneity and sample distribution. The homogeneous and normal distribution data were analyzed using one way ANOVA test. Other data were analyzed with Kruskal Wallis. The average Bromage score and block target were reached descriptively analyzed with the mean median. The infant Apgar score and obstetrician's satisfaction levels were analyzed descriptively with the mean median.

RESULTS

Patient characteristics:

A total of 33 pregnant patients with heart disease undergoing CS during the period of September 2017 - September 2018 were observed. Thirteen patients were primigravida and 20 were multipara. Age range was < 20 y (n = 3), 21-30 y (n = 18), and 31-40 y (n = 12). No patient was older than 40 y.

Heart abnormalities included mitral stenosis (n = 6), mitral regurgitation (n = 6), atrial septal defect (ASD) (n = 6), ventricular septal defect (VSD) (n = 3), patent ductus arteriosus (PDA) (n = 3), pulmonary hypertension (PH) (n = 3), tetralogy of Fallot (TOF) (n = 2), aortic regurgitation (n = 1), cardiomyopathy (n = 2), and other heart diseases (n = 4). Two medical records were excluded being incomplete.

Hypothesis testing and descriptive analysis:

Based on the normality testing of the observation results with the Kolmogorov Smirnov test, the patient's DBP and pulse data showed $p > 0.05$ which suggested that the data were statistically significant. Hence, the patient's DBP and pulse data were considered normal (Table 1). On the other hand, SBP and MAP data were not statistically significant ($p < 0.05$). Hence, it could be concluded that the systole and MAP data were not normally distributed. So

Table 1: Comparison of maternal hemodynamics

Maternal hemodynamics	Min				p value
	0	3	6	9	
DBP[A] (mmHg)	76.06 ± 18.3	68.70 ± 15.1	67.45 ± 13.8	69.45 ± 14.4	0.112
SBP[K] (mmHg)	134.97 ± 11.2	123.09 ± 14.3	122.21 ± 13.5	121.58 ± 13.6	0.071
Pulse rate[A] beats/min	95.21 ± 9.93	90.67 ± 11.74	89.88 ± 11.51	89.64 ± 13.13	0.178
MAP[K] (mmHg)	95.70 ± 20.7	86.83 ± 17.1	85.71 ± 16.1	86.83 ± 16.2	0.157

Notes: A = ANOVA analysis; K = Kruskal wallis

the analyses could not be subjected to ANOVA but was analyzed with the Kruskal wallis test. By using a Levene's test, the patient's DBP and pulse data were statistically significant ($p > 0.05$), so it can be concluded that the DBP and pulse rate data of these patients had homogeneous variances (Table 1).

Based on the maternal hemodynamic comparison table, it was evidenced that every minute showed differences for maternal hemodynamic parameters, where blood pressure (systolic and diastolic), pulse and MAP tended to decrease from 0, 3 and 6 min, but at the 9th min there was a slight increase (Table 2).

Table 2: Descriptive statistics of parameters of anesthesia block, infant hemodynamics and satisfaction of obstetrician about field relaxation

Parameter	Mean ±SD	Range
Anesthesia block (min)		
Bromage 2	1.45 ± 0.90	0.5 - 3
Bromage 3	2.85 ± 1.04	1.2 - 5
Bromage 0	119.85 ± 18.48	80 - 180
T10	2.33 ± 1.22	1 - 5
T6	3.87 ± 2.01	1.2 - 8
Hemodynamics of infant		
Apgar Score 1	6.52 ± 1.15	3 - 8
Apgar Score 2	8.36 ± 0.99	5 - 10
Obstetrician Satisfaction	7.59 ± 0.82	6 - 9.5

Based on the 4th average value of the observation time, then the *p* value of the ANOVA test results is 0.112 ($p > 0.05$), so it can be concluded that there were no significant differences in mean DBP at 0, 3rd, 6th or 9th min. In other words, the difference in the average DBP between the four periods of observation is relatively small, so it is not statistically significant.

The average for MAP at 0 min was 95.7 mmHg. However, it decreased till 6th min, finally at 9th it increased to 86.83 mmHg. Based on the 4th average value of the observation time, the *p* value of the Kruskal wallis test result is 0.157 which is greater than alpha 0.05 ($p > 0.05$). Hence it could be concluded that there were no significant differences in the average MAP at 0, 3rd, 6th and 9th min. In other words, the differences in the average of MAP values between the 4 periods of observation times were relatively small, so that it is statistically not significant.

At the 0 min, the average pulse of the 33 patients was 95.21 beats/ min, then decreased in the 3rd min to 90.67 beats/ min, the 6th min to 89.88 beats/ min, and in the min to -9 becomes 89.64 beats/ min. Based on the average pulse at the 4th observation time, the *p* value of the ANOVA test results is 0.178 which is greater than alpha 0.05 ($p > 0.05$), so it can be concluded that there was no significant difference in mean pulse at 0, 3rd, 6th and 9th min.

The next step was to process the existing data using the *post hoc* test method as multiple comparisons with the Tukey's test as one of the multiple benchmarking tests that has high enough sensitivity to test for differences between treatments in multiple comparisons. With this method multiple comparisons were made of the average data between the 4 points of observation, with the results, and there were no significant differences at 0, 3rd, 6th and 9th min.

Results in Table 2 show that Bromage score, the minimum time to reach T6 block and the time to reach T-10.

Apgar score at 1 min (AS-1) was 6.5, and at 2 min (AS-2) it was 8.36 ± 0.99. As for the score for satisfaction by obstetricians from 33 patients was 7.59 ± 0.82 (range 6-9.5).

DISCUSSION

Choice of the time and type of labor in parturients with heart disease depends on the condition of the mother and the fetus in the womb. Factors considered to determine the anesthetic technique include parturient's hemodynamic status, type of heart disease, previous drug use, and elective / emergency surgery.[4] GA is more widely used in patients that fall in a higher New York Heart Association (NYHA) class and have history of previous heart surgery.[5] GA is still an option in cases where regional anesthesia cannot be performed. Such as patients that are predicted to have heavy bleeding and hemodynamically unstable patients. However, GA has several risks including hemodynamic instability due to drug action, laryngoscope use, difficult intubation and risk of aspiration.[6] GA has been known to depress cardiac contractility, increase pulmonary vascular resistance through positive pressure ventilation and positive end-expiratory pressure (PEEP).

According to some studies regional anesthesia is contraindicated in patients with severe valve stenosis and the use of anticoagulants.[7] Patients with NYHA class III-IV should not receive spinal anesthesia but epidural techniques, because the block height can be adjusted easily. In some cases of CHD, regional anesthesia is a preferred option because hemodynamic stability can be well maintained.[8] However, if regional anesthesia is the chosen technique, the anesthetist must determine how to conduct the procedure with a single shot spinal, epidural, or combination of low-dose spinal followed by titration of epidurals.

A sudden decrease in preload and afterload due to spinal single shot is a condition that aggravates the patient's condition, so in some literature this

technique is contraindicated to use in patient with heart disease.[9] Administration of fluids and drugs as prophylaxis to prevent hypotension or bradycardia due to regional anesthesia can be a new problem for patients with low cardiovascular reserves.

There are several ways to reduce the incidence of post-spinal anesthesia hypotension, e.g., preloading/coloading fluids, uterine displacement, use of vasoconstrictors, and the use of a low dose bupivacaine technique. Spinal low dose technique can reduce the possibility of hypotensive events from regional anesthesia.[10] Several studies have revealed that hemodynamic changes in spinal anesthesia (especially hypotension) are caused by sympathetic block, the extent of which depends on the dose and concentration of local anesthetics used. Therefore, low-dose and low-concentration spinals (< 8 mg or lower concentrations below 0.25%) are expected to have minimal effects on hemodynamics of the mother and baby. The addition of opioids could reduce the dose requirements of local anesthetics and prevent hemodynamic fluctuations and increase the effects of intraoperative and postoperative analgesia.

The uterine blood flow is not autoregulated, so the uteroplacental perfusion is directly related to maternal blood pressure.[11] Hence, maternal blood pressure can be tolerated only by the mother but not by the fetus. One strategy to maintain both stable hemodynamics and adequate anesthesia block during spinal anesthesia in CS surgery is to use low-dose bupivacaine combined with opioid adjuvant.[12] In our study, low doses of hyperbaric bupivacaine (5 mg) combined with fentanyl 50 μg produced adequate blocks with minimal systemic side effects, including spinal hypotension and desaturation. No vasopressor (phenylephrine, nor ephinephrine, dopamine, ephedrine, etc.) needed to be used.

Spinal anesthesia works by inhibiting voltage-gated sodium channels on the spinal cord which will affect the motor and sensory impulses of afferent and efferent fibers.[13] This level of sensory and motor blocks depends on the technique, agent and the dosage used. Intrathecal opioids selectively produce an analgesic effect through interaction with opioid receptors in the dorsal horn of the spinal cord and thus can minimize the dosage and supraspinal effects of local anesthetics such as hypotension, respiratory depression, sedation and nausea and vomiting.[14] The main location of the opioid receptors is in the substantia grisea of the substantia gelatinosa. This is the basis of the anatomy of selective analgesia by intrathecal opioids.

Fentanyl works synergistically with bupivacaine in reducing the pain threshold without increasing sympathetic and motor blockade.[15] There have been many studies that prove the effectiveness of opioid use in spinal anesthesia especially in CS surgery. Previous studies have shown that lipophilic opioids, for example fentanyl, can accelerate the onset and extend the duration of bupivacaine blocks, and prolong the duration of postoperative analgesia.[16] The combination of both has a 5-min intrathecal onset speed and 10 min through the epidural and relatively has a shorter duration of action due to the presence of redistribution (2-4 intrathecal and epidural hours respectively). No active metabolites are found and the combination is 800 times more lipid soluble than morphine. This high solubility in fat will quickly bind it to opioid receptors in the dorsal horn; this rapid onset being beneficial both as analgesia in normal labor and in cases of emergency CS. The optimal doses of fentanyl for adjuvant spinal anesthesia are 12.5 µg - 50 µg. There is no more benefit in doses more than 50 µg.[17]

In patients with NYHA class III and IV, conventional doses of spinal anesthesia should not be used, given the risk of impaired hemodynamics.[18,19] In patients with stable hemodynamics, epidural anesthesia and low-dose epidural spinal combinations may be more preferable than GA.[20] GA is known to depress cardiac contractility, increase pulmonary vascular resistance through positive pressure ventilation.[21] Laryngoscopy and intubation are known causes of hemodynamic changes in patients undergoing GA.[22] Low-dose spinal bupivacaine combined with fentanyl adjuvant in some studies has been proved to produce minimally decreased hemodynamics with adequate anesthesia. Patient with cardiac heart disease are more susceptible to changes in cardiovascular function.[23] That's why we must avoid increase in cardiac workload and metabolic demands e.g., pain, hypovolemia, hypotension, shivering, etc. Therefore using the technique of low dose bupivacaine with minimal opioids can be used with advantage in patients with cardiac diseases.

CONCLUSION

The results of our study show that low dose hyperbaric bupivacaine 5 mg combined with fentanyl 50 µg can be considered as an anesthesia technique for cesarean delivery in parturients with heart diseases due to its rapid onset, adequacy of block level and the duration of the analgesia, good hemodynamic stability and favorable fetal outcome.

Conflict of interest: None declared by the authors

Authors' contribution:

DPH: Concept, Conduction of the work, Construction of manuscript

Il Sp.An: Concept, Conduction of the work

RH, Sp.An: Concept, Conduction of the work, Review of anuscript

ESP: Review of the manuscript content for publication

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