Optimal Dose of Spinal Bupivacaine on Maternal and Fetal Outcomes in Parturients Undergoing Combined Technique for Labor Analgesia: A Randomized Double Blinded Prospective Study

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ABSTRACT

Study Objectives: Maternal hypotension and fetal bradycardia (FB) are recognized complications of combined spinal epidural. Our purpose was to ascertain which of 3 common doses of spinal bupivacaine results in optimal analgesia with minimal side effects, assuming the lowest dose fills all criteria.

Design: Prospective, randomized clinical trial.

Setting: Labor and Delivery Unit of 514-bed urban teaching hospital.

Patients, Interventions and Measurements: Patients were assigned to receive an intrathecal dose of 20 mcg of fentanyl with either 2.5 mg, 1.66 mg, or 1.25 mg of isobaric bupivacaine. Visual Analog Scale (VAS) Pain Score, fetal heart rate (FHR), maternal blood pressure (BP), number of hypotensive episodes, doses of vasopressors, nitroglycerin and mode of delivery were recorded at various time points.

Main results: 164 patients were enrolled: 66 receiving 1.25 mg, 50 in the 1.66 mg group and 48 in the 2.5 mg. At 6 and 10 minutes, we recorded in the 1.66 mg group: 4.7% and 4.6%, 18.9% and 23.9% fewer hypotensive episodes compared with the 1.25 mg and the 2.5 mg groups respectively and significantly more hypotensive episodes in the 2.5 mg group ($p = 0.025$ and 0.019 respectively). There was no statistical difference in vasopressors use, mode of delivery or FB. The VAS decreased equally by an average of 7–10 points among all groups.

Conclusion: The 1.66 mg spinal dose was associated with the least hypotensive episodes and equivalent pain relief as the 2.5 mg. The 1.25 mg and 1.66 mg doses allowed for adequate BP and FHR stability.

Clinical Trial: Study registered on the ClinicalTrial.gov website under the NCT number NCT02159807.

INTRODUCTION

Severe pain associated with childbirth has led to the widespread use of neuraxial techniques for labor analgesia. Combined spinal epidurals (CSE) are one of the techniques frequently administered and are safe, simple, and efficient. Their placement, however, can lead to transitory maternal hypotension (MHT) and fetal bradycardia (FB) following the rapid onset of pain relief as shown by Lee et al. [1] The authors compared safety and efficacy of 1.25 mg of bupivacaine spinal to 2.5 mg with 25 mcg of fentanyl. The 2.5 mg group had a larger incidence of hypotensive episodes within the first 10 minutes following spinal, longer duration of analgesia, with a higher incidence of motor block, but no significant difference in analgesia quality, suggesting 1.25 mg was safer and equally effective. They found all subjects, regardless of the bupivacaine dose, had VAS pain scores of 0 at 10 minutes post-administration. Identification of an effective bupivacaine dose that minimizes these adverse effects is the stimulus for this study.

Previous studies have determined that the intrathecal bupivacaine ED95 for labor analgesia was 1.66 mg when combined with fentanyl 15 mcg [2, 3, 4]. Whitty et al. [2] conducted a "dose-finding" study for spinal bupivacaine in CSE comparing 1.5 mg and 1.75 mg of bupivacaine, both with 15 mcg fentanyl. Response rate was defined as a verbal numeric pain score < or = 1 within 10 minutes of administration and was 85% for the 1.5 mg group and 100% for the 1.75 mg group. An effective dose in 95% of the population (ED95) of 1.66 mg of intrathecal bupivacaine was calculated, however the accuracy of this estimate must be considered in the context of its wide confidence interval (CI 1.50–482.5 mg). The effects of other commonly used doses on maternal and fetal indices or delivery outcome are still not as well explored.

Also, the incidence of FB has been linked to higher doses of intrathecal bupivacaine but more importantly to the addition of opioids in the spinal portion of the labor analgesia procedure [7]. The occurrence of FB at lower doses of bupivacaine, even with opioids added, is not well documented in the literature. The prediction was that the incidence of FB will be reduced with lower doses of spinal bupivacaine with opioids. The decision to use 20 mcg of fentanyl was related to the current practice of our anesthesiologists at the time of the study's design.

The primary goals of this study were to identify whether three widely used doses of bupivacaine, with a set amount of fentanyl, would decrease the risk of MHT and FB while providing adequate analgesia. The three doses of bupivacaine chosen for this study are commonly used at our institution: One higher than the reported ED95 at 2.5 mg, the reported ED95 at 1.66 mg, and one lower than the ED95 at 1.25 mg. The secondary outcomes of interest included cumulative usage of vasopressors to treat hypotension, nitroglycerine to treat uterine tetany, and mode of delivery.

MATERIALS AND METHODS

STUDY DESIGN

This study was approved by the Icahn School of Medicine at Mount Sinai's Institutional Review Board and written informed consent was obtained from all participants. The trial was registered at ClinicalTrials.gov prior to enrollment with NCT number 02159807.

This randomized, prospective, double-blinded study's primary outcomes included incidence of MHT and FB in patients receiving CSE for labor analgesia, and quality of analgesia, using the VAS pain score. The VAS was used as a highly reliable [8] evaluation of pain. It allowed us to compare results to previous studies using VAS to guide clinical practice [9], with a VAS score of <1 considered adequate analgesia [10, 11]. In our clinical experience, patients had adequate analgesia with a VAS score <3, which is what we chose as a cutoff. Secondary measures included cumulative usage of vasopressors, nitroglycerine, and mode of delivery.

This study took place at Mount Sinai West, a 514-beds urban teaching hospital with a level IV maternity.

Any patient admitted to the Labor and Delivery Unit at Mount Sinai West between April 24, 2015 and December 29, 2017, ASA 2, 18 or older, with a gestational age (GA) between 37 and 42 weeks, requesting labor analgesia was invited to participate. Exclusion criteria were pregnancy-

induced hypertension, contraindication to neuraxial anesthesia, and non-reassuring fetal heart rate (FHR) tracings including baseline fetal tachycardia.

The discussion regarding participation in the trial occurred at the time of request for labor analgesia, the usual first meeting between patients and anesthesia team at our institution. After explanation of risks and benefits of both the procedure and the study, written informed consent was obtained and the medication for spinal administration was removed from the Pyxis machine.

Randomization, Allocation, and Study Medications

To avoid errors in preparing and labelling the syringes, the pharmacy staff decided to have only one set of dosage (either 1.25, 166 or 2.5 mg) made daily and to rotate each dose every day. This randomization process was performed by pharmacy staff daily rather than being done for each patient enrolled. For the patients selected, we used a consecutive sampling technique as we included all the patients who met criteria and agreed to participate in the study. The patients were assigned to receive the dose of bupivacaine available in the Pyxis on that particular day. Four syringes labeled "bupivacaine study" were prepared daily under sterile conditions, identified with a serial number and placed by our pharmacy in the Pyxis. Each syringe contained either 1.25 mg, 1.66 mg, or 2.5 mg of bupivacaine, mixed with a fixed dose of 20 mcg of fentanyl, and had a fixed volume of 1.4 cc for all groups, to prevent any identification based on volume.

At the end of each day, unused study syringes were discarded by the pharmacy staff and new syringes prepared the next day. The study representative from the pharmacy, as well as the pharmacist mixing the medication, were the only individuals aware of the content of each syringe and kept a log of the serial numbers with the corresponding dose of bupivacaine. The participating anesthesia team and the patient were blinded to the dosage, and the log was only disclosed at the completion of the study when data was ready for analysis.

Protocol

Unless otherwise indicated all elements followed our standard unit protocol. The FHR tracing was recorded with an external continuous heart rate monitor, prior to placing the CSE. We did not require assessment by an obstetrician as we looked at the change in FHR rather than a change in category tracing which we felt was more subjective. We followed the American college of Obstetricians and gynecologists' (ACOG) definition of fetal bradycardia as a FHR below 110 bpm [5]. All providers involved were OB anesthesia-fellowship trained, with a reliable knowledge of FHR tracing readings.

Patients were placed in the sitting position for the initiation of the neuraxial procedure. Blood pressure (BP) cuff and pulse oximeter were placed on the patient. An initial BP and pain score on a scale of 0 to 10 were recorded as the baseline. CSE was placed under sterile conditions at L3-L4 or L4-L5 by locating the epidural space using the loss of resistance (LOR) with air or saline technique. Then a 27G Pencan spinal needle was introduced through the Tuohy needle and the spinal dose was administered after confirmation of CSF return. A flexible, multi-orifice catheter was introduced through the epidural needle and left 5 cm into the epidural space, and the epidural needle then removed. The time of the spinal injection was recorded. Following the procedure, the patient was immediately placed on her side for left uterine displacement, and our standard patient controlled epidural analgesia, with a continuous infusion of 0.0625% bupivacaine with 2 mcg/cc of fentanyl was initiated at a rate of 12 cc/hr, with a demand dose of 8 cc every 10 minutes.

We defined hypotension as a systolic BP decrease of 20% from the baseline BP. If hypotension occurred, as pre-defined in the study protocol, the patient was treated with phenylephrine, unless maternal bradycardia (heart rate below 60 beats per minute) necessitated using ephedrine.

VAS scores were recorded before spinal dose, 8 minutes, and 60 minutes post spinal. If the patient did not report pain improvement by 8 minutes, additional epidural bupivacaine was titrated to effect, as we wanted to ensure our patients were getting adequate pain relief.

If FB occurred after CSE placement, the patient was assessed for tetanic uterine contraction through abdominal tone and contraction monitor, and intrauterine resuscitation performed with change in maternal position, supplemental oxygen administration and intravenous nitroglycerin. The doses used to treat both hypotension and uterine tetany were left to the discretion of the provider in charge; those doses (phenylephrine 100 mcg, ephedrine 5 mg and nitroglycerine 100 mcg bolus at a time) are usually standardized among the providers in our clinical practice.

DATA COLLECTION

Data were collected by one of the co-investigators available each day on the Labor and Delivery Unit and consisted of demographic information including patient's age, gestational age (GA), cervical dilation in centimeters at time of neuraxial request, gravidity, parity as well as the presence of labor, induction, or augmentation with oxytocin.

Maternal BP was documented at baseline, every 2 minutes for 20 minutes then every 15 minutes, following the spinal bupivacaine dose, as well as a final BP at 60 minutes. Continuous FHR monitoring was performed per standard protocol, and recorded with the same schedule as the maternal BP. Patients were asked to quantify pain relief by recording their VAS Pain Score at 8 minutes following spinal medication, as this is theoretically the time to full effect of the spinal dose, though some patients experience relief sooner [6], and at 60 minutes, when the spinal dose wears off and is relayed by the epidural analgesia.

Cumulative ephedrine, phenylephrine, or nitroglycerin use was calculated after recording dose and timing of each administration. Delivery outcomes were accounted for as normal spontaneous vaginal delivery, vacuum or forceps assisted vaginal delivery, or caesarean delivery.

SAMPLE SIZE DETERMINATION AND STATISTICAL ANALYSIS PLAN

Sample size determination was based on results of a previous, prospective study of estimation of the minimal local analgesic dose of intrathecal bupivacaine in labor [3]. Assuming power set at 82% with a 0.05 two-sided Chi-square test of trend in proportions based on the logistic model, we calculated that the study required 60 patients per group to detect a difference in proportions of having at least one episode of FB or MHT in the first 10-minute window, assuming the rates are 50%, 30% and 20% for the 2.5 mg, 1.66 mg, and 1.25 mg groups, respectively. Published data estimated the incidence of MHT after spinal bupivacaine was twice as pronounced at the higher 2.5 mg bupivacaine dose with 25 mcg of fentanyl compared with a lower dose of 1.25 mg with 25 mcg of fentanyl [1].

When analyzing the data, we decided to look at each of the parameters both as a specific time point and as a time window. Specific time point information looks at data punctually such at 2, 4, or 6 minutes. A time window is the average up to a certain time point. The time window system accounts for cumulative data. Our statistician helped extract time intervals and categorical values.

All tests were 2-sided and a p-value of <0.05 was considered statistically significant. Descriptive data were presented as mean (SD) and N (%). For comparisons among the three groups, we employed the ANOVA or Kruskal-Wallis's test for continuous data, and Chi-square, Fisher's exact test and/or Cochran-Armitage trend test for categorical data, as appropriate. P-values were not adjusted for multiple comparisons for different time points in order to avoid increasing the risk of making type II error.

RESULTS

Over two and a half years, 164 patients were enrolled, 66 in the 1.25 mg bupivacaine group, 50 in the 1.66 mg group and 48 in the 2.5 mg group. We deliver about 4500 patients a year with a 94–95% epidural rate, which gives us an enrollment rate of about 1.6%, knowing that this study was mostly conducted during the daytime on week days due to logistics' constraint. Five patients were excluded from the study after enrollment: Two (one in the 2.5 mg and one in the 1.66 mg group) for difficult neuraxial placement with no cerebral spinal fluid obtained, one in the 2.5 mg group for maternal hypertension, one in the 1.25 mg group for inadvertent wet tap

where no spinal dose was given, and one for a vaso-vagal episode during the procedure in the 2.5 mg group. This brought the total for data analysis to 159: 65 in the 1.25 mg, 49 in the 1.66 mg, and 45 in the 2.5 mg group.

There was an uneven number of patients enrolled in the 3 groups since randomization was at the machine level and not by subject. However, we did not find any significant difference regarding the demographic data (age, weight, body mass index BMI, gestational age, gravity, parity and dilation for which the mean at the time of epidural placement was 3.2 cm +/– 1.9 for the 1.25 m group, and 3.1 cm +/– 1.7 for the 2 other groups) among the 3 groups (Table 1).

	BUPIVACAINE DOSE 1.25 MG	BUPIVACAINE DOSE 1.66 MG	BUPIVACAINE DOSE 2.5 MG	SIGNIFICANT DIFFERENCE
Age (years)	32.3 ± 5.4	32.9 ± 4.6	32.4 ± 4.7	P = 0.839
Weight (kg)	78.5 ± 14.3	76.2 ± 11.7	74.8 ± 10.5	P = 0.584
BMI	28.9 ± 5.2	27.8 ± 4.4	28.6 ± 4.4	P = 0.364
Gestational age (weeks)	39.3 ± 1.2	39.3 ± 1.5	39.7 ± 1.1	P = 0.269
Gravity	2.2 ± 1.3	1.8 ± 1.1	1.9 ± 1.1	P = 0.318
Parity	0.5 ± 0.7	0.5 ± 0.9	0.4 ± 0.8	P = 0.596
Dilation (cm)	3.2 ±1.9	3.1 ± 1.7	3.1 ± 1.7	P = 0.994

Table 1 Demographic Data showing the mean ± standard deviation.

Tables 2 and 3 show the results for MHT at various time points. In bold and highlighted, are the value differences when the data were analyzed by time point (e.g., at 10 minutes) vs. time window (e.g., from 0 to 10 minutes). Of importance, the earliest onset of hypotension was associated with the 2.5 mg bupivacaine group (Table 2). At 6 minutes, the risk of hypotensive episodes increased in all three groups. Overall, the incidence of hypotensive episodes was highest for the 2.5 mg throughout the entire time course, and lowest for the 1.66 mg bupivacaine group.

FHR means at different time points were not statistically different among the three groups (Table 4). Only 1 case of FB happened at 8 and 12–16 minutes in the 2.5 mg group.

BUPIVACAINE DOSE	0 (MIN)	2 (MIN)	4 (MIN)	6 (MIN)	8 (MIN)	10 (MIN)
1.25 mg	0	0	3 (4.6%)	11 (16.9%)	16 (24.6%)	15 (23.0%)
1.66 mg	0	1 (2%)	2 (4.1%)	6 (12.2%)	12 (24.5%)	9 (18.4%)
2.5 mg	0	3 (6.7%)	3 (6.7%)	14 (31.1%)	19 (42.2%)	19 (42.2%)
P value (Fisher's Exact test)	None	0.069	0.906	0.099	0.175	0.599
(Cochran-Armitage trend test)	None	0.636	0.636	0.059	0.090	0.050
(Chi-square test of comparing 2.5mg vs. (1.25mg+1.66mg)	None	0.575	0.575	0.025	0.065	0.019
BUPIVACAINE DOSE	**12 (MIN)**	**14 (MIN)**	**16 (MIN)**	**18 (MIN)**	**20 (MIN)**	**60 (MIN)**
1.25 mg	15 (23.1%)	21 (32.3%)	20 (30.8%)	17 (26.1%)	21 (32.3%)	19 (29.2%)
1.66 mg	14 (28.6%)	12 (24.5%)	12 (24.5%)	11 (22.4%)	10 (20.4%)	7 (14.3%)
2.5 mg	16 (35.5%)	17 (37.8%)	18 (40.0%)	14 (31.1%)	13 (28.9%)	9 (20.0%)
P value (Fisher's Exact test)	0.465	0.403	0.322	0.689	0.354	0.134

Table 2 Time Points: Number and percentage of hypotensive episodes at different times (time points) per dose used.

BUPIVACAINE DOSES	0 (MIN)	2 (MIN)	4 (MIN)	6 (MIN)	8 (MIN)	10 (MIN)
1.25 mg	0	0	3 (4.8%)	*12 (18.7%)*	*18 (28.1%)*	22 (34.4%)
1.66 mg	0	1 (2.0%)	2 (4.0%)	6 (12.0%)	12 (24.0%)	*15 (30.0%)*
2.5 mg	0	3 (6.2%)	3 (6.2%)	14 (29.2%)	*22 (45.8%)*	25 (52.1%)
P value (Fisher's Exact test)	None	0.069	0.906	*0.113*	*0.052*	*0.063*
Bupivacaine dose	**12 (min)**	**14 (min)**	**16 (min)**	**18 (min)**	**20 (min)**	**60 (min)**
1.25 mg	*26 (40.6%)*	*28 (43.7%)*	*30 (46.1%)*	*31 (48.4%)*	*35 (53.8%)*	*35 (54.7%)*
1.66 mg	*18 (36.0%)*	*20 (40.0%)*	*20 (40.0%)*	*20 (40.0%)*	*21 (42.0%)*	*21 (42.0%)*
2.5 mg	*26 (54.2%)*	*26 (54.2%)*	*26 (54.2%)*	*27 (56.2%)*	*27 (56.2%)*	*29 (60.4%)*
P value (Fisher's Exact test)	*0.173*	*0.336*	*0.374*	*0.285*	*0.332*	*0.159*

Table 3 Time Windows : Number and percentage of hypotensive episodes up to the different times (time windows) per dose used. Bolded and italicized are the value differences when the data were analyzed by time point vs. time window.

BUPIVACAINE DOSE	BASELINE	2 (MIN)	4 (MIN)	6 (MIN)	8 (MIN)	10 (MIN)
1.25 mg	141.1 (12.3)	138.4 (10.5)	137.8 (11.5)	134.6 (11.4)	134.9 (11.0)	135.7 (12.8)
1.66 mg	136.4 (9.6)	137.7 (12.4)	137.3 (13.2)	132.9 (21.9)	136.4 (9.4)	134.4 (11.0)
2.5 mg	135.3 (9.4)	136.4 (11.4)	138.0 (13.0)	134.9 (11.8)	132.4 (11.9)	132.7 (10.4)
P-value	0.010	0.675	0.954	0.790	0.162	0.400
BUPIVACAINE DOSE	**12 (MIN)**	**14 (MIN)**	**16 (MIN)**	**18 (MIN)**	**20 (MIN)**	**60 (MIN)**
1.25 mg	136.0 (12.1)	134.5 (10.1)	134.9 (11.0)	133.5 (13.0)	135.4 (11.3)	134.7 (10.9)
1.66 mg	133.7 (14.7)	134.2 (8.7)	135.1 (8.6)	136.3 (10.6)	134.6 (10.5)	137.6 (10.3)
2.5 mg	133.3 (12.1)	132.0 (12.8)	132.8 (13.2)	132.4 (8.8)	133.5 (9.1)	135.6 (10.2)
P-value	0.483	0.429	0.518	0.200	0.664	0.337

Table 4 Fetal Heart Rate means (standard deviations) at different times points per dose.

The parametric p-value is calculated by ANOVA for numerical covariates and chi-square test for categorical covariates.

There was an increased use of vasopressors in the 2.5 mg group but without a significant difference (Table 5). The occurrence of uterine tetany was exceedingly rare with only one patient in the 2.5 mg group (p = 0.502) having an episode requiring nitroglycerine bolus.

	BUPIVACAINE DOSE	N	DOSE AMOUNT				USAGE	
			MEDIAN	Q3	MAXIMUM	P-VALUE*	% OF PATIENTS	P-VALUE**
Pheny lephrine	1.25 mg	65	0	100	500	0.414	32.3%	0.544
	1.66 mg	49	0	100	400		28.6%	
	2.5 mg	45	0	200	700		40.0%	
Ephe drine	1.25 mg	65	0	0	10	0.905	7.7%	0.931
	1.66 mg	49	0	0	15		6.1%	
	2.5 mg	45	0	0	20		8.9%	

Table 5 Pressor Amount and Usage for Treatment of Hypotension.

 * Based on the Kruskal-Wallis's test.

 ** Fisher's exact test.

Results pertaining to pain relief at 8 and 60 minutes, showed no difference among the 3 groups with a similar degree of pain relief in all groups (Table 6).

BUPIVACAINE DOSE	BASELINE	8 MIN	60 MIN
1.25 mg	9.0 [7.0–10.0]	0.0 [0.0–1.0]	0.0 [0.0–0.0]
1.66 mg	8.3 [7.0–10.0]	0.0 [0.0–0.0]	0.0 [0.0–0.0]
2.5 mg	9.0 [8.0–10.0]	0.0 [0.0–0.0]	0.0 [0.0–0.0]

Table 6 Visual Analog Scale Scores for pain (Median/IQR), across three doses and measured time points.

Finally, there was no difference (p = 0.410) among the 3 groups (Table 7) regarding the mode of delivery.

DELIVERY MODE	BUPIVACAINE DOSE			TOTAL
	1.25 MG	**1.66 MG**	**2.5 MG**	
NSVD	54 (83.1%)	34 (69.4%)	37 (82.2%)	125
VAVD	3 (4.6%)	6 (12.2%)	4 (8.9%)	13
CD	8 (12.3%)	9 (18.4%)	4 (8.9%)	21
Total	65	49	45	159

Table 7 Mode of Delivery: NSVD**:** Normal Spontaneous Vaginal Delivery. VAVD**:** Vacuum-Assisted Vaginal Delivery. CD: Caesarean Delivery p-value 0.410.

DISCUSSION

This randomized clinical trial examined safety and efficacy of three commonly used spinal dosages of bupivacaine, 1.25 mg, 1.66 mg, and 2.5 mg, combined with 20 mcg of fentanyl for CSE, with the primary goal of showing equal analgesic efficacy of the lower dose with a lower incidence of maternal hypotension and fetal bradycardia.

We had an uneven number of patients in each group. The number of patients requesting epidural varied each day so the higher number of patients in the 1.25 mg group is likely due to a higher number of patients requesting epidural analgesia and consenting to the study on the days that dose was loaded in the Pyxis machine.

The 2.5 mg bupivacaine group had more hypotensive episodes compared to the two lower doses as anticipated: 31.1% versus 16.9% and 12.2% at 6 minutes and 42.2% versus 24.6% and 24.5% at 10 minutes, for the 2.5, 1.25 and 1.66 mg doses respectively).

There were no significant differences found among the 3 groups in terms of the other parameters assessed.

Our results for hypotension were consistent with those of Lee et al. [1] The 2.5 mg group had the highest incidence of hypotensive episodes at 8 and 10-minute time points, the 1.66 mg group at 8 and 12- minute time points, and the 1.25 mg group at 14 and 16- minute time points. The dose of bupivacaine impacted the time to onset of hypotension, with higher doses leading to earlier onset. Interestingly, the lowest rate of hypotensive episodes was not in the 1.25 mg bupivacaine group as anticipated, but the 1.66 mg group. We do not believe this resulted from differences in demographics or any labeling error of the syringes.

Similarly to Lee et al., we found no differences in pain measured by VAS among the groups. This suggests analgesia can be achieved with lower doses of bupivacaine in combination with fentanyl, knowing that combining opioids with local anesthetics for the spinal allows for synergy of action hence lower doses of each medication [8]. All study groups had an average VAS <1 at 8 minutes post-spinal administration. Time points were guided by theoretical optimal analgesia onset, and duration of analgesia provided by the spinal. All patients achieved and maintained effective analgesia throughout the study duration. Patients may have different pain tolerances; however, the randomization process should account for these differences. We did not record the dose of oxytocin patients were given but relied on the initial VAS pain score and adequate pain relief post CSE, both similar for all 3 groups.

In our study, FB was a rare event. Prudent evaluation and treatment of MHT or uterine tetany likely prevented this complication. MHT was treated quickly with hydration, lateral decubitus position, and use of vasopressors, upon witnessing a systolic BP drop of more than 20% from baseline or the patient complaining of nausea or dizziness.

Incidence of MHT and FB lead us to question the use of higher doses of bupivacaine in the spinal portion of CSE due to its risk-benefit balance. Our results were consistent with the findings of Lee et al. and Whitty et al., suggesting lower dosages of bupivacaine (1.25 and 1.66 mg), when combined with fentanyl, are as effective clinically as higher dosages, evidenced by the analgesia satisfaction rate.

One of the strengths of this research is its design. The double-blinded, randomized by machine/medication preparation, controlled trial allowed for a non-biased early treatment of MHT. Knowing which group the patient belonged to might have biased the investigator into more aggressive prevention of hypotension in the highest dose groups, but we established strict parameters to initiate treatment. This protocol has strengths over a similar, previously conducted study comparing only two doses [1] as we compared clinical differences across three commonly used bupivacaine doses.

We recognize the potential limitations of randomizing our patients to one fixed dose daily based on what medication was loaded into the Pyxis machine on that day. Our staff treated MHT early and aggressively, halting the downstream complication of FB. We did not consider the use of non-pharmacologic labor pain management methods, such as labor support (doula), baths, maternal movement, hypnosis, and positioning [12, 13]. Literature has shown these methods may reduce labor pain and improve satisfaction, however the quality of evidence is poor due to the lack of homogeneity of the trials [14], and we believe this would have a minor effect on the results. We did not look at the height of the patient which might play a role in the extent of the block and the degree of hypotension. While this parameter has been well studied in spinal for cesarean delivery (CD), little data is found in its effect regarding labor analgesia and it might not be as relevant in this case.

The lower rates of FB due to lower dosages of bupivacaine, and proactive treatment of hypotension, may allow researchers and clinicians to safely investigate higher dosages of intrathecal opioids, with the benefit of more complete sacral dermatomal coverage. Further trials might investigate the safety and efficacy profiles of larger dosages of fentanyl (25 or 30 mcg) with 1.66 mg or 1.25 mg of bupivacaine for the spinal portion of a CSE.

Our investigation found a higher rate of maternal hemodynamic changes in the high dose bupivacaine group without significant differences in VAS scores. This suggests the optimal doses of bupivacaine, to minimize complications without compromising analgesia, are the lower doses (1.25 and 1.66 mg) in combination with fentanyl 20 mcg. This study showed that the lower doses of bupivacaine were associated with less hypotensive episodes with a superiority of the 1.66 mg dose over the 1.25 mg dose.

CONCLUSION

This investigation found a statistically significant higher rate of hypotensive episodes for the 2.5 mg bupivacaine group within the first 10 minutes following placement of a CSE compared to the two lower dosage groups. There was no difference in VAS scores among the three groups.

These findings suggest using lower doses, either 1.25 mg or 1.66 mg bupivacaine with fentanyl 20 mcg, for initiation of CSE for labor analgesia have clinically equivalent analgesic effects as the higher dose, without the increased risk of MHT or FB.

COMPETING INTERESTS

The authors have no competing interests to declare.

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