

## A Comparative Study of Three Different Intrathecal Bupivacaine Doses During Combined Spinal Epidural Anesthesia for Cesarean Delivery

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**Abstract:** Background: Inadequate block, hypotension, nausea, and vomiting are common adverse effects of a single-shot spinal anesthetic used for cesarean deliveries. The study's goal: In this study, three distinct intrathecal (IT) hyperbaric bupivacaine 0.5% doses—5 mg, 7.5 mg, and 10 mg each—mixed with 25 µg of fentanyl were used to examine the anesthetic and side effects of combination spinal epidural anesthesia for cesarean birth. Methods: Each of the three groups was assigned at random to seventy-eight healthy women who were presenting for an elective cesarean birth. When combined spinal-epidural anesthesia was started, 5 mg (IT) of hyperbaric bupivacaine 0.5% was given to Group A, 7.5 mg to Group B, and 10 mg to Group C. IT bupivacaine was premixed with 25µg of fentanyl in each group. Following a full motor block of the lower limbs and the achievement or extension of the sensory level of T4 using epidural supplements, surgery started. When the amount of motor block reached Bromage level 3 and the full loss of feeling to ice reached the fourth thoracic dermatome T4, the IT block was considered successful. Results: There was no statistically significant difference in the three groups' preoperative data. 46.2% of group A, 80.8% of group B, and 92.3% of group C attained the best upper sensory block T4 (p-value = 0.003). Group A had the greatest rates of maternal intraoperative pain (69.2%), whereas groups B and C had lower and similar rates (26.9%). The effectiveness of epidural extension supplements in reducing patient discomfort was evident in all three groups: group A (65.4%), group B (19.2%), and group C (3.8%). The frequency of maternal hypotension was found to be greater with raising the dose of IT bupivacaine; 42 percent with group A 5mg, 73% in group B 7.5mg and 77% in group C 10 mg. Conclusion: When combined with 25µg fentanyl, intrathecal bupivacaine at doses of 5 mg, 7.5 mg, or 10 mg during CSE for cesarean delivery resulted in an effective block with a greater incidence of hypotension for 7.5 mg and 10 mg, whereas 5 mg of bupivacaine maintained maternal hemodynamic stability but was unable to produce sufficient anesthesia unless epidural extension took place prior to skin incision.

**Keywords:** spinal anesthesia - combined spinal epidural - t4 sensory block - bupivacaine - cesarean delivery.

### INTRODUCTION

Cesarean delivery is one of the most frequent major surgical interventions globally, its prevalence continuing to rise due to a multifactorial mix of obstetric, medical, and social factors (Lane, S. *et al.*, 2005). The anesthetic regimen for this procedure is of utmost significance, requiring a delicate balance between assuring profound surgical anesthesia and profound motor blockade of the surgeon while at the same time ensuring the maximum comfort and safety for the conscious mother and the hemodynamic stability so critical to fetal well-being (Biswas, B. N. *et al.*, 2002; Sowmya, N. *et al.*, 2016). Regional anesthesia, more specifically neuraxial techniques, has become the norm of practice for elective and most emergency cesarean deliveries, supplanting general anesthesia with its much superior safety record, including an extremely reduced risk of failed intubation, aspiration pneumonitis, and neonatal exposure to depressant drugs (Ali, M. A. *et al.*, 2018). Of these neuraxial techniques, combined spinal-epidural anesthesia (CSEA) has been a popular and highly utilized choice for its unique combination of

benefits; it offers the rapid onset, predictability, and block intensity of an intrathecal anesthetic, alongside the unparalleled flexibility, extensibility, and postoperative pain-controlling capability of an indwelling epidural catheter. This harmony positions CSEA in a singularly favorable position to address obstetrics' difficult situation, in which the time of operation can be unpredictable and the demand for prolonged postoperative analgesia is critical (Bogra, J. *et al.*, 2005).

The spinal component of CSEA is the basis for the initial block, and the choice of the local anesthetic agent is critical (Arzola, C., & Wieczorek, P. M. 2011). Within this realm, bupivacaine is the undisputed winner, so to speak, since it is prized for its long duration of action and its ability to produce a predictably dense sensory and motor block optimally suited to surgery. However, intrathecal bupivacaine administration is a practice also plagued by an underlying and persisting clinical dilemma: the search for the ideal dose (Gauchan, S. *et al.*, 2014). That dose must be sufficient enough to provide successful, fail-safe surgery without the need for urgency conversion to

general anesthesia, but not so great as to minimize to the lowest extent possible the dose-related side effects that can so profoundly influence the maternal experience and physiological state (Venkata, H. G. *et al.*, 2015; Gopichand, K., & Suresh, T. 2016). The most critical of these side effects is hypotension in the mother, a virtually universal consequence of sympathetic blockade caused by spinal anesthesia (Yesuf, K. A. *et al.*, 2017). The hypotension is not a benign phenomenon; it is associated with maternal symptoms of nausea, vomiting, and unpleasant dizziness, and more significantly, can result in uteroplacental hypoperfusion and fetal acidosis, jeopardizing neonatal outcomes. Thus, prophylactic and reactive hypotensive control—most often with vasopressors like phenylephrine and ephedrine—assumes a commanding priority for the anesthesiologist, often at the expense of other aspects of patient management (Ahmad, M. *et al.*, 2017; Nofal, W. H. *et al.*, 2017). The intensity and rate of such hypotension are both proportionate to the density and height of the sympathetic block, which itself is a function of the dose of intrathecal local anesthetic administered. Historically, 12 mg to 15 mg doses of hyperbaric bupivacaine were employed, with a very high rate of success but a very likely development of severe hypotension, requiring vigorous and quite complex vasopressor management (Unal, D. *et al.*, 2012). In response to this, a significant body of research has evolved over the past two decades exploring the efficacy of lower doses, often facilitated by the synergistic admixture of lipophilic opioids like fentanyl or sufentanil (Akanmu, O. N. *et al.*, 2013)

These adjuncts facilitate the sensory block, and with it, a marked decrease in the dose of local anesthetic can be tolerated without adversely affecting the patient's quality of anesthesia (Seyedhejazi, M., & Madarek, E. 2007). This has resulted in the widespread use of doses between 8 mg and 10 mg, which most studies have demonstrated to produce admirably safe surgical conditions with a clearly decreased incidence and severity of hypotension (Nahakpam, S. *et al.*, 2020). Therefore, the principal challenge in optimizing CSEA for cesarean section is to dose titrate the intrathecal bupivacaine to its therapeutic limit of successful anesthesia without lowering its most common and annoying side effect.

## PATIENTS AND METHODS

### Study Design

A sample of 78 healthy (ASA I and ASA II) full-term pregnant women who were taken to the obstetric operating rooms to an elective Cesarean section were chosen for this study after receiving parturient informed consent from the parturient and approval from the hospital research ethics committee. All pregnancies were singletons as well as uncomplicated. The study was conducted from November 2015 to April 2016 at Al Basra General Hospital. Women who had a central neuraxial block contraindication or an allergy to the research medications were not included. The following demographic information was gathered by looking through the enrolled patients' medical records:

Pre-block information includes name, age, height, and weight, parity, prior scar, arterial blood pressure, and heart rate.

Intraoperative information includes the highest degree of sensory block 15 minutes after intrathecal anesthetic agents were administered, maternal pain, changes in the mother's heart rate and blood pressure, ephedrine dosages, nausea, and vomiting.

### Materials

A standard epidural catheter equipped with a loss-of-resistance syringe (LOR) and Touhy's needle (gauge 18) (B BRAUN Germany). Spinal needle gauge 25 pencil point with introducer. (Hospital and home care device Co.Ltd, China). Bupivacaine HCL 0.5% solution with glucose for spinal anesthesia (Marcaine®, AstraZeneca). Bupivacaine HCL 0.5% solution without glucose for epidural (Inibasacaine®, Inibsa) anesthesia 2-Spinal needle gauge 25 pencil point with introducer (Hospital and homecare device Co.Ltd, China) . A 50 mic.gm/ml spinal fentanyl solution (Mercury Pharma).

### Procedure:

Following the patient's arrival in the anesthetic room, two intravenous, or IV, cannulas (20 gauge) were inserted, allowing each patient to receive a preload of 1000 ml of crystalloid fluid in the form of Ringer's lactate. Standard monitoring included noninvasive blood pressure using an electronic machine called the OMNI II, respiratory rate, SPO<sub>2</sub>, and ECG. Before the spinal block and every five minutes until the baby was delivered, the mean arterial blood pressure (MAP) as well as heart rate (HR) were measured. All of the women

were seated, and the combined spinal epidural sequential technique was carried out as explained by Cook, who introduced the spinal needle before the epidural (DST). In the classical DST, a traditional dural puncture is made in 1-2 lumbar segments distally employing a 25-gauge spinal needle after an epidural catheter is introduced through a Tuohy needle and a test dose is given. The spinal needle's stylet is replaced after a local anesthetic is injected at the site of insertion in the subarachnoid space at the intervertebral space beneath the Lumbar 2 vertebra under aseptic conditions, following cleaning and draping of the area. This is done while monitoring the free flow of cerebrospinal fluid. The LOR syringe, which is filled with 3 ml of air, is then linked to the epidural needle, which is then inserted gradually until the resistance to 2 ml of air disappears. The epidural needle is then introduced using the median method, regarding two segments above the spinal needle. The epidural needle was taken out once the catheter entered the epidural space (about 3 cm) through the Tuohy needle. The catheter was fixed into the patient's back after being adjusted. The spinal needle was then taken out, and the intrathecal medication (fentanyl and bupivacaine) was given.

Three equal groups of 26 women each were randomly selected from among the patients based on the spinal bupivacaine dosage:

In Group A, 5 mg of hyperbaric bupivacaine and 25µg of fentanyl were administered intrathecally (IT) and combined with isotonic saline to a total volume of 2.5 ml.

Group B was administered 7.5 mg of hyperbaric bupivacaine combined with 25µg of fentanyl, and the mixture was finished with 2.5 ml of isotonic saline.

Group C: Got 2.5 ml of IT, which included 10 mg of hyperbaric bupivacaine and 25µg of fentanyl.

The pregnant women were immediately positioned supine at a 15° left tilt following the administration of any spinal drugs. The degree of dermatomal sensory block, which is indicated by a total loss of sensation to ice, was assessed bilaterally in an ascending pattern beginning at the T10 and ending at the T4 dermatome, which is 5 cm from the midline. We estimated that it would take 15 minutes to achieve maximum sensory block in the T4 level. A sensory block that did not reach T4 bilaterally 15 minutes following an intrathecal block or that need epidural supplementation prior

to infant birth was considered inadequate anesthesia. 10 mL of isobaric bupivacaine 0.25% was administered epidurally as block supplementation if this was not accomplished after 15 minutes (up to a maximum of 15 mL). The degree of motor block was measured using the modified Bromage scale, and score three was judged to be reached. (0 = no impairment; 1 = mobility of the knees and ankles but inability to lift extended legs; 2 = incapacity to flex knees or raise extended legs but mobility of the feet; 3 = incapacity to flex ankles, knees, or hips). Every five minutes during the procedure, the patient's vital signs as well as any indications of pain, nausea, or vomiting were monitored. Every patient who experienced hypotension (MAP falling to 70 mmHg or below, or MAP declining by 20% below baseline blood pressure) received a 5 mg intravenous bolus dose of ephedrine. All patients received care at the recovery area following surgery. At 5-minute intervals, hemodynamic as well as block profile surveillance was maintained. When the sensory block level for cold had decreased to T10, along with the Bromage score was back to 2, the patients were deemed ready for release. Before the patient was released to the ward, the epidural catheter was taken out.

### Statistics Analyses

For all data, SPSS-20 was used. Categorical variables are represented as numbers and percentages, whereas continuous variables are represented as mean ± SD. The variation between variables was examined using the chi-squared ( $\chi^2$ ) test. Statistical significance was defined as P values below 0.05.

## RESULTS

Seventy-eight full-term pregnant women enrolled in the study were divided into three groups according to intrathecal dose of bupivacaine: group A (5mg), group B (7.5mg), and group C (10mg). Table 1 shows no statistically significant differences among the groups in their preoperative demographic data.

The dose-related sensory block following intrathecal bupivacaine & fentanyl injection is depicted in Table 2. In all, 27% of women failed the fourth thoracic dermatome T4, whereas 73% of all women experienced sensory block. The sensory block at the T4 dermatome was attained in around 92.3% of Group C, 80% of Group B, and 46.2% of Group A, indicating that Group C reacted more successfully over both Groups A and B.

**Table 1.** Demographic characteristics of the groups.

	Group A	Group B	Group C	P value
Age (yr)	30 ± 7.5	28 ± 7	29 ± 6	0.88
Weight (Kg)	78.3 ± 9.3	78 ± 15.7	83 ± 11.5	0.585
Height (cm)	156 ± 4	158.3 ± 4.8	158.7 ± 4.5	0.636
BMI (kg/m <sup>2</sup> )	31.2 ± 4	31.2 ± 5.2	33.1 ± 4.8	0.311
Base MAP	98.8 ± 13.2	96.3 ± 15.4	95.7 ± 13.7	0.383
Base HR	99.5 ± 20.3	89.7 ± 20.4	93.1 ± 14	0.416
Parity	3.3 ± 2.4	3 ± 2.4	3.1 ± 2.3	0.661

**Table 2.** Relationship between the dermatomes' sensory level and spinal dose.

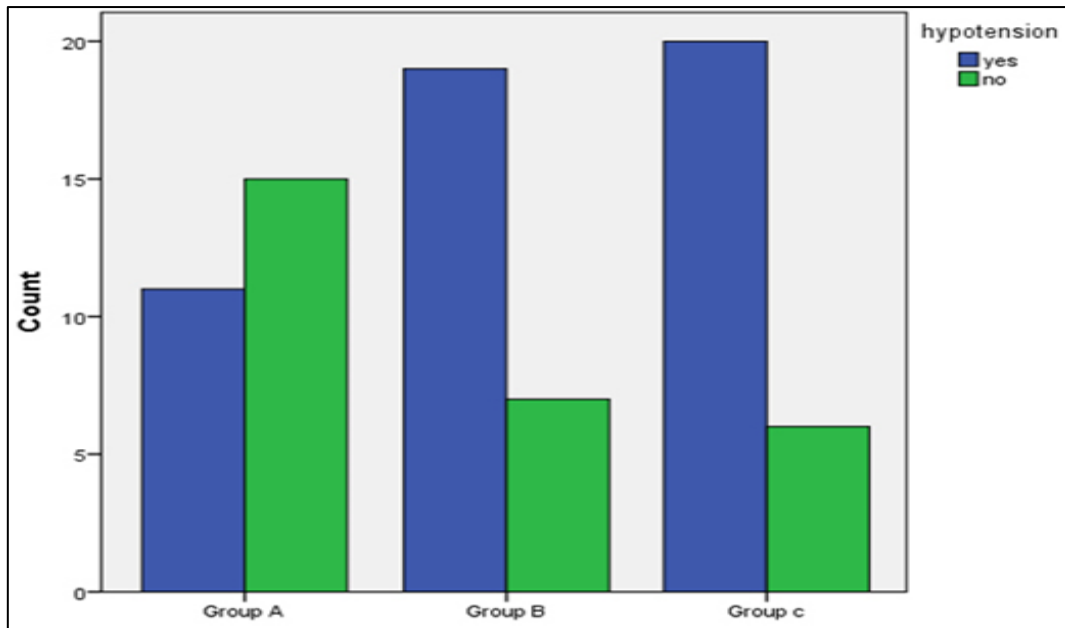
		Dermatomes sensory level			Total
		T4	T6	T8	
Group A 5mg bupivacaine	Frequency	12	12	2	26
	% within Group A	46.2%	46.2%	7.7%	100.0%
Group B 7.5mg bupivacaine	Frequency	21	5	0	26
	% within Group B	80.8%	19.2%	0.0%	100.0%
Group C 10 mg bupivacaine	Frequency	24	2	0	26
	% within Group C	92.3%	7.7%	0.0%	100.0%
Total	Frequency	57	19	2	78
	% within total	73.1%	24.4%	2.6%	100.0%

Following the intrathecal block, maternal hemodynamic instability is evident in both Table 3 and Figure. In all, hypotension affected 64% of the women across the three groups. In particular, women in group A exhibit the lowest rate of low blood pressure, at 42.3%, compared to 73.1% and 76.9% for, respectively, group B and group C.

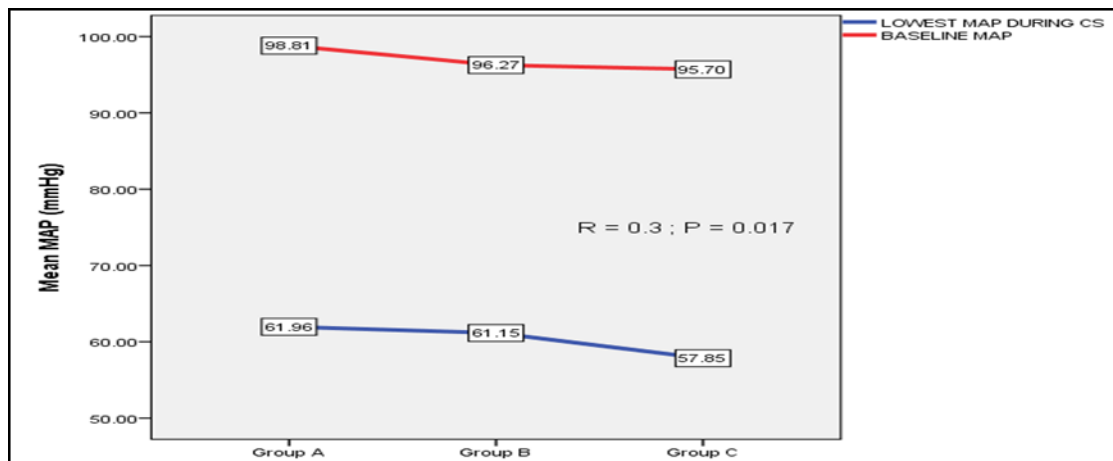
Since group C had the largest intrathecal bupivacaine dosage, it appears that they are more likely to experience maternal hypotension; in other words, there was a significant difference in maternal hypotension across all three groups (P value = 0.017).

**Table 3.** Frequency of maternal hypotension in all groups.

		Hypotension		Total n %
		Yes	No	
Group A 5mg bupivacaine	Frequency	11	15	26
	% within Group A	42.3%	57.7%	100%
Group B 7.5mg bupivacaine	Frequency	19	7	26
	% within Group B	73.1%	26.9%	100%
Group C 10 mg bupivacaine	Frequency	20	6	26
	% within Group C	76.9%	23.1%	100%
Total	Frequency	50	28	78
	% within Total	64.1%	35.9%	100%



**Figure 1:** Frequency of maternal hypotension in the group.



**Figure 2:** The least mean blood pressure (MAP) means versus their baselines in all groups.

The means of MAP for each patient in the three groups are compared before and after intrathecal bupivacaine injection in the plot diagram (Figure 2). After spinal block, the baseline MAP clearly decreased significantly in all three groups. But

group C had the biggest decline, going from 95.7 to 57.8 mmHg, followed by group B, which went from 96.27 - 61.15 mmHg, and group A, which went from 98.8 - 61.95 mmHg.

**Table 4.** Ephedrine consumption between the groups.

		Ephedrine				Total
		0	5mg	10mg	15mg	
<b>Group A</b> 5mg bupivacaine	Frequency	7	16	3	0	26
	% within Group A	26.9%	61.5%	11.5%	0.0%	100.0%
<b>Group B</b> 7.5mg bupivacaine	Frequency	1	13	11	1	26
	% within Group B	3.8%	50.0%	42.3%	3.8%	100.0%
<b>Group C</b> 10mg bupivacaine	Frequency	0	13	10	3	26
	% within Group C	0.0%	50.0%	38.5%	11.3%	100.0%
Total	frequency	8	42	24	4	78
	% within Total	10.3%	53.8%	30.7%	5.1%	100.0%

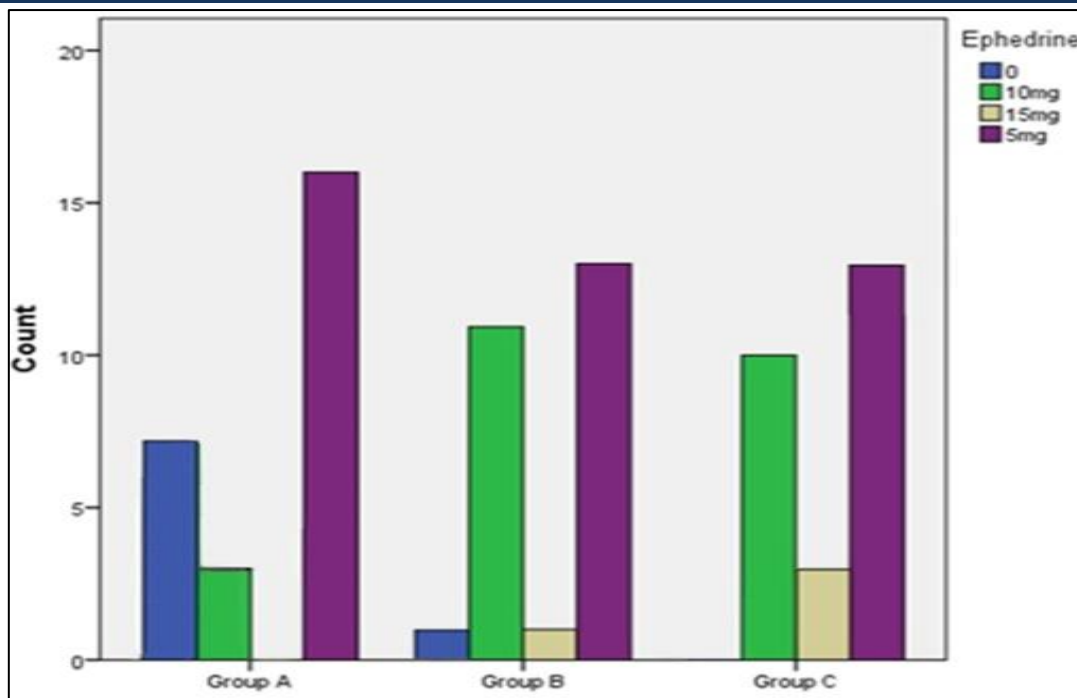


Figure 4: Ephedrine mg consumption in different groups.

Table 5. Incidence of nausea in all the groups.

		Nausea		Total
		No	Yes	
<b>Group A</b> 5mg bupivacaine	Frequency	17	9	26
	% within Group A	65.4%	34.6%	100.0%
<b>Group B</b> 7.5mg bupivacaine	Frequency	19	7	26
	% within Group B	73.1%	26.9%	100.0%
<b>Group C</b> 10mg bupivacaine	Frequency	15	11	26
	% within Group C	57.7%	42.3%	100.0%
Total	Frequency	51	27	78
	Total %	65.4%	34.6%	100.0%

The amounts of ephedrine needed to treat maternal hypotension in each group were shown in Figure 3 and Table 3. Overall, 10.3% of patients were hemodynamically stable along with did not require ephedrine; however, 89.7% of patients had hypotension and, depending on the severity of the hypotension, were given ephedrine in all three groups. The majority of patients in each of the groups received the lowest dose of ephedrine (5

mg), which was around 61.5% of group A, along with 50% of both group B and C. It is clear that group A had the greatest population who did not require ephedrine, followed by group B. Group C, however, had the highest consumption. Group A did not require the 15 mg dosages of ephedrine, group C mostly required them (11.5%), and group B required them 3.8%.

Table 6. Incidence of vomiting according to bupivacaine spinal dose

		Vomiting		Total
		No	Yes	
<b>Group A</b> 5mg bupivacaine	Frequency	23	3	26
	% within Group A	88.5%	11.5%	100.0%
<b>Group B</b> 7.5mg bupivacaine	Frequency	22	4	26
	% within Group B	84.6%	15.4%	100.0%
<b>Group C</b> 10mg bupivacaine	Frequency	21	5	26
	% within Group C	80.8%	19.2%	100.0%
Total	Frequency	66	12	78
	Total%	84.6%	15.4%	100.0%

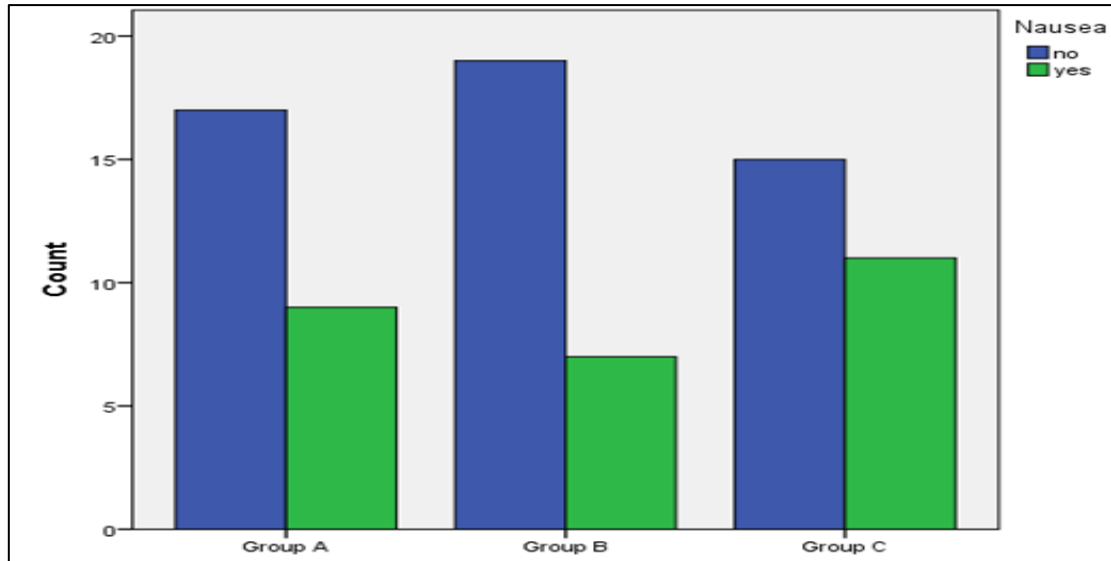


Figure 5: Frequency of nausea in all groups.

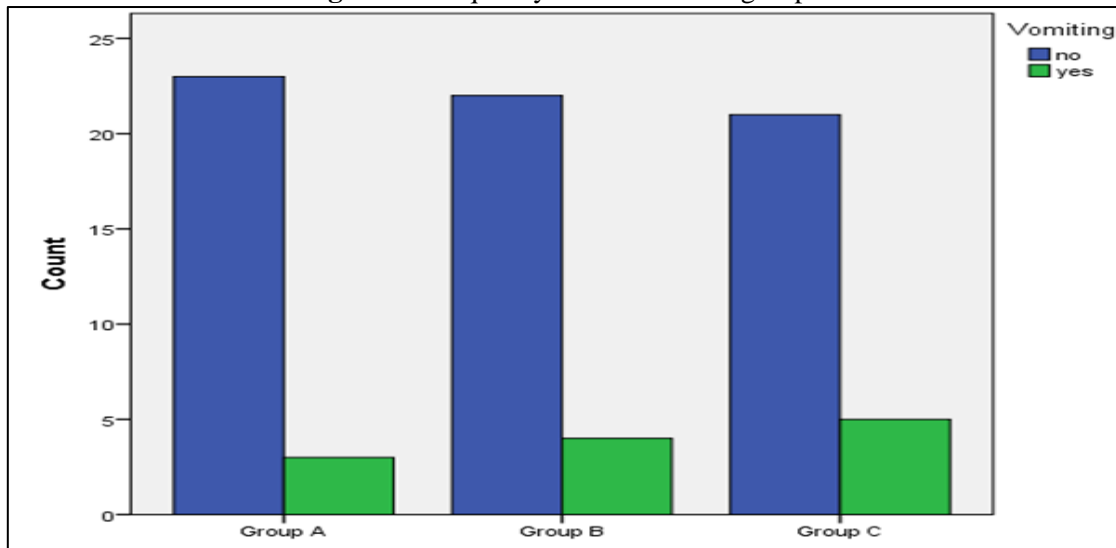


Figure 6: Frequency of vomiting in all groups.

The percentage of women who needed an additional epidural block to enhance spinal anesthesia is shown in both Tables 8 and Figure 6. About 30% of the patients required epidural supplements on average. However, the largest

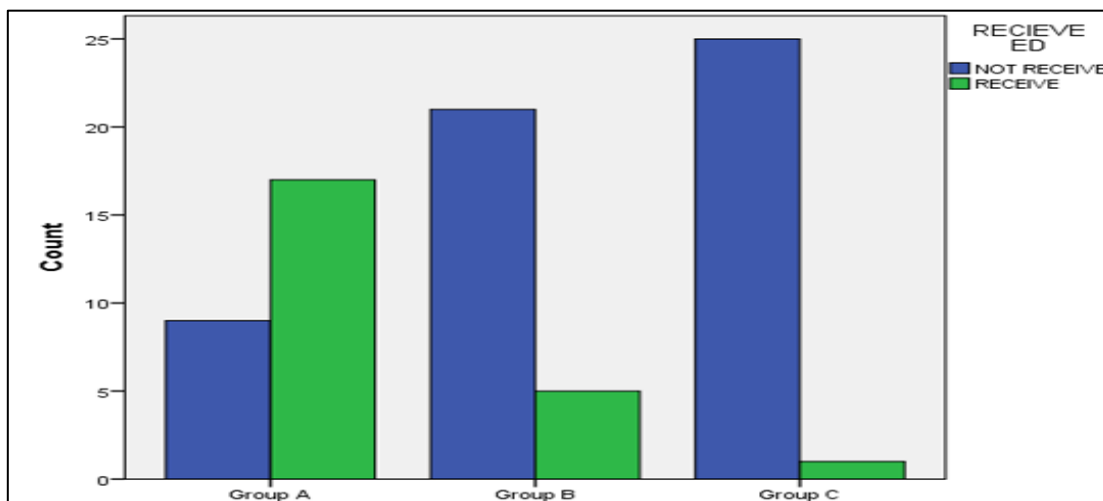
frequency of epidural extension supplements was required by women in Group A, who got the lowest dose of intrathecal bupivacaine (5 mg), as opposed to Groups B and C, who required 19.2% and 3.8%, respectively.

Table 7. Relationship between spinal dose and maternal discomfort

		Discomfort		Total
		no	Yes	
<b>Group A</b> 5mg bupivacaine	Frequency	8	18	26
	% within Group A	30.8%	69.2%	100.0%
<b>Group B</b> 7.5mg bupivacaine	Frequency	19	7	26
	% within Group B	73.1%	26.9%	100.0%
<b>Group C</b> 10mg bupivacaine	Frequency	19	7	26
	% within Group C	73.1%	26.9%	100.0%
Total	Frequency	46	32	78
	% within Total	59.0%	41.0%	100.0%

**Table 8.** Epidural supplement according to the bupivacaine spinal dose

		RECIEVEED		Total
		NOT RECEIVE	RECEIVE	
Group A 5mg bupivacaine	Frequency	9	17	26
	% within Group A	34.6%	65.4%	100.0%
Group B 7.5mg bupivacaine	Frequency	21	5	26
	% within Group B	80.8%	19.2%	100.0%
Group C 10mg bupivacaine	Frequency	25	1	26
	% within Group C	96.2%	3.8%	100.0%
Total	Frequency	55	23	78
	% within Total	70.5%	29.5%	100.0%



**Figure 7:** Frequency of epidural supplements in all groups.

**DISCUSSION**

Several prophylactic strategies have been tested to prevent spinal-induced hypotension. Crystalloid pre-loading, the use of vasopressors, and left lateral tilt have been shown to be partially effective (Nahakpam, S. et al., 2020). However, the incidence of hypotension can be minimized but cannot be eliminated (Seewal, R. et al., 2007). Most studies used doses of spinal bupivacaine of 9-15 mg, and many authors have mentioned that reducing the spinal dose to less than 7.5 mg of intrathecal bupivacaine may reduce the incidence and severity of hypotension. Several trials had reported a low incidence of hypotension when small doses of bupivacaine were used.

Some studies compared different doses and failed to demonstrate a beneficial effect of reducing the spinal dose (Mani, S. M. et al., 2016). However, it compared different bupivacaine doses and concluded that lowering the spinal dose significantly improved the maternal hemodynamic (Arikan, M. Ü. G. E. et al., 2016; Chavan, G. et al., 2014). Unfortunately, the trial by the Japanese study did not mix opioids with anesthetic drugs, resulting in a high incidence of inadequate anesthesia. (Weigl, W. et al., 2016; Belzarena, S.

D. 1992; Kotwani, M. B. et al., 2016) Numerous studies have reported that the addition of opioids improves anesthetic quality without causing hemodynamic instability.

The goal of our study is to determine the best intrathecal bupivacaine dosage with fentanyl to produce sufficient anesthetic with the fewest possible adverse effects. We will accomplish this by identifying the actions of 5 mg, 7.5 mg, and 10 mg of bupivacaine with 25 µg of fentanyl. Following spinal block, about 64% (50/78) of all women reported having hypotension; group A experienced the least amount of hypotension (42.3%), followed by group B (73.1%) and group C (76.9%; 20/26). Nonetheless, it is evident that the bulk of women who experienced lower blood pressure were those who received spinal bupivacaine dosages of more than 7.5 mg. As a result, depending on the degree of hypotension, hypotensive women need ephedrine during surgery. About 90% of all women needed ephedrine, while group A had the lowest amount of ephedrine supplementation. Common side effects of spinal anesthesia include nausea and vomiting, which are more common when the sympathetic blocking continues past the tenth

thoracic segment (Tyagi, A. *et al.*, 2008; Beale, N. *et al.*, 2005). Otherwise, other research indicated that the intrathecal administration of opioids may be the cause of nausea and vomiting. Although there is no evidence linking the dosage of spinal medications to the development of nausea and vomiting, in the current study, women who had nausea experienced vomiting in 34.6% of cases (27/78) and vomiting in 15.4% of cases (12/78).

The criteria for successful spinal anesthesia were different between some studies (Jain, G., & Singh, D. K. 2010; Teoh, W. H. L. *et al.*, 2006) performed which defined it as bilateral T4 sensory block to pinprick and modified Bromage score of 1 and 2 achieved within 15 minutes of intrathecal drug administration and/or no additional epidural analgesia was required during operation, while, who used sufentanil 2.5µg supplement considered successful block to T6 achieved within 10 minutes.

In our study we used fentanyl (25 µg) as a supplement and achieved T4 block with the least frequency with spinal bupivacaine 5mg and highest with 10mg, these result was similar of those of a study conducted in USA (Ntzoufras, I. 2011) and explained the highest rate of Intraoperative discomfort and more epidural supplements in the group A (5mg) compared to higher doses (Choi, D. H. 2000). Moreover, the presence of an epidural catheter provides the capability to extend and prolong an inadequate spinal block. The sequential CSE technique with spinal bupivacaine 5mg may be particularly advantageous in high-risk parturients who cannot tolerate rapid hypotension, especially when the sensory block is extended by epidural to T4 level before starting abdominal incision (Hughes, S. C. *et al.*, 2002).

## CONCLUSION

According to our findings, intrathecal bupivacaine at doses of 5 mg, 7.5 mg, or 10 mg, when combined with 25 µg fentanyl, produced an effective block with a higher rate of hypotension for doses of 7.5 and 10 mg. In contrast, 5 mg of bupivacaine maintained maternal hemodynamic stability but was unable to produce sufficient anesthesia unless epidural extension was carried out prior to skin incision.

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