Biological and Clinical Sciences Research Journal
eISSN: 2708-2261; pISSN: 2958-4728
www.bcsrj.com
DOI: https://doi.org/10.54112/bcsrj.v2023i1.431
*Biol. Clin. Sci. Res. J., Volume, **2023**: 431*
Original Research Article

ISOBARIC LEVOBUPIVACAINE VERSUS HYPERBARIC BUPIVACAINE IN PREGNANT WOMEN UNDERGONE CESAREAN SECTIONS: A RANDOMIZED CONTROLLED TRIAL

AMJAD A[1], SADIA H[2], SAAD M[2], ALI A[1], NAEEM A[2], NAEEM H[1], AHMED M[3]

[1] *Department Of Anesthesia, MTI-Lady Reading Hospital, Peshawar, Pakistan*
[2] *Khyber Medical College, Peshawar, Pakistan*
[3]*Department of Dermatology, MTI-Lady Reading Hospital, Peshawar, Pakistan*
Corresponding author email address: afnanamjad27@yahoo.com

(Received, 5th August 2023, Revised 29th August 2023, Published 1st October 2023)

Abstract *To compare isobaric levobupivacaine versus hyperbaric bupivacaine for pregnant women who have undergone cesarean sections. In this randomized controlled trial, 70 patients with ASA physical status I-II, scheduled i.e for elective lower segment cesarean section (LSCS), were divided into two equal-sized groups (n = 35 each). Group A was treated with 2.5 ml of isobaric levobupivacaine, while Group B was treated with 2.5 ml of hyperbaric bupivacaine. Both groups' sensory and motor block features were evaluated using the pinprick test and the Bromage scale. Additionally, any instances of hypotension and potential side effects were meticulously recorded. Subsequently, the collected data underwent statistical analysis employing appropriate tests. The initiation of sensory blockage was observed to be slower, and the regression duration for two segments was extended while using isobaric levobupivacaine ($p < 0.001$). Nevertheless, it generated sufficient surgical anesthetic with a reduced duration of motor blocking and fewer side effects compared to hyperbaric bupivacaine. This study concludes that single-shot spinal anesthesia with different local anesthetics is effective for prompt surgical anesthesia induction in elective cesarean section procedures. Among these options, levobupivacaine is a superior choice due to its smaller duration of motor block, reduced side effects, and lower risk of hypotension, making it particularly well-suited for such procedures.*

Keywords: Caesarean section; Bupivacaine; Spinal anesthesia; Comparison

Introduction

Cesarean section (CS) is a frequent surgical intervention worldwide, especially among pregnant women with specific medical indications or those who opt for elective CS (Antoine and Young, 2021). Ensuring optimal pain management and minimizing complications during and after CS is of paramount importance, not only for the mother's well-being but also for the safe delivery and postoperative care of the newborn. Regional anesthesia techniques, particularly spinal anesthesia, have gained widespread acceptance for CS due to their effectiveness, rapid onset, and minimal fetal exposure to anesthetic agents. In this context, selecting the local anesthetic and its formulation plays a crucial role (Horlocker et al., 2010; Jelting et al., 2017). Spinal anesthesia is considered the preferred approach for CS as it provides a dense and reliable block, allowing for adequate surgical anesthesia with minimal systemic effects on both the mother and the fetus (Fakherpour et al., 2018). Bupivacaine, a long-acting local anesthetic, has been widely used for decades in obstetric anesthesia due to its established safety and efficacy profile (Goffard et al., 2022). Traditionally, hyperbaric bupivacaine has been the choice for spinal anesthesia in CS, primarily because its heavy density leads to a predictable spread of anesthesia, ensuring adequate surgical anesthesia with a lower dose (Manassero and Fanelli, 2017). However, hyperbaric bupivacaine can lead to profound motor block and cause maternal hypotension more frequently than desired, potentially compromising maternal and fetal well-being (Durodola et al., 2021). While hyperbaric bupivacaine provides reliable sensory and motor blockade, its association with hypotension can necessitate additional interventions, which may have their own risks (Manouchehrian et al., 2022). Isobaric levobupivacaine, on the other hand, is an emerging alternative to hyperbaric bupivacaine for spinal anesthesia in CS (Maheshwari et al., 2019). Isobaric levobupivacaine, which has a density similar to cerebrospinal fluid, avoids the predictable and sometimes excessive motor block associated with hyperbaric solutions. This property may lead to less motor impairment, earlier ambulation, and improved maternal satisfaction, which are important considerations for postoperative care and maternal recovery (Atalay et al., 2018; Sreekanth and

[Citation Amjad, A., Sadia, H., Saad, M., Ali, A., Naeem, A., Naeem, H., Ahmed, M. (2023). Isobaric levobupivacaine versus hyperbaric bupivacaine in pregnant women undergone cesarean sections: a randomized controlled trial. *Biol. Clin. Sci. Res. J.*, **2023***:* 431. doi: https://doi.org/10.54112/bcsrj.v2023i1.431]

Totawar, 2018). The choice concerning isobaric levobupivacaine, and hyperbaric bupivacaine for spinal anesthesia in CS remains a subject of ongoing research and debate. Previous literature has investigated their comparative efficacy and safety, with varying results. This research work aimed to compare "outcome of isobaric levobupivacaine versus hyperbaric bupivacaine for pregnant women who had undergone cesarean sections". This study will investigate the evidence to provide a comprehensive analysis of both options' relative efficacy and safety in pregnant women undergoing cesarean sections.

Material and methods

A total of seventy participants, aged 18-40 years, who met the ASA physical status I or II standards and had a gestational age > 36 weeks, were included in this investigation (Randomized Controlled Trial). This study was conducted for one-year duration, from January 2021 to January 2022, at Lady Reading Hospital Peshawar and received approval from the institutional ethical committee. The exclusion criteria included individuals who were experiencing obstetric problems, had concurrent medical illnesses such as heart disease, anemia, pregnancy, gestational diabetes, and hypertension, had any contraindications related to the spinal anaesthetic, or had a previous known history of sensitivity to the medications being studied. A thorough pre-anesthetic assessment was performed for all female patients in the late evening before the surgical intervention, and documented agreement was acquired. As a component of premedication, all patients were administered a dosage of 150 mg of ranitidine the evening before the surgical procedure. Following this, they were positioned in the left lateral orientation for transit to the operating room. The study population was randomly separated into two groups, consisting of 35 patients in each group. The allocation was performed using the shuffled sealed opaque envelope method. All participants received a 500 ml infusion of Ringer lactate solution 30 minutes prior to undergoing spinal anesthesia. Additionally, measures were taken to prevent acid aspiration before the surgical procedure. The lumbar puncture procedure was performed on the individuals when they were positioned in the right lateral decubitus posture, namely at the L3-L4 interspace level. A midline approach was utilized, and a 25G Quincke spinal needle was employed in experimental groups. The administration of the research medication was after that performed through injection into the theca using the following procedure:

Group A was administered isobaric levobupivacaine (2.5 ml of 0.5%).

Group B was administered 2.5 ml of hyperbaric bupivacaine at a concentration of 0.5%.

A non-participating anesthesiologist administered the test medicines by loading them into a 3 ml syringe. The subarachnoid block was administered by an anesthesiologist who maintained blinding of the observer and subjects regarding the composition of the study medicines. Following this, the patients were shifted supine with the wedge placed below the right hip, and additional oxygen was administered via face mask. The sensory blockade was supervised continuously, using a blunt 27G hypodermic needle, with observations made at 15-second intervals until the onset of sensory blockage was detected. Following this, evaluations were carried out every 2 minutes till the highest level of sensory blocking was attained. Afterward, assessments were undertaken at 5-minute intervals within the first 30 minutes, at 15-minute intervals between 30 and 120 minutes, and then at 30-minute intervals until full sensory recovery. The commencement of surgical intervention occurred with the expansion of the sensory level to encompass the T6 dermatome. The duration from the administration of the study drug to the point at which the maximal sensory blockade was reached is considered the time required to reach the highest level of sensory blockade. The term "two-segment sensory regression time" denotes the period that elapses from the point at which the maximal sensory block is achieved to the point at which feeling regresses by two segments. The measurement of sensory blockage duration commenced at the time of study medication delivery and concluded when sensation had fully restored to the S1 dermatomal level. The assessment of motor block quality was performed utilizing the modified Bromage scale. The onset of motor blockage i.e, operationally determined as the duration between administration of the study medication and the point at which the subject displayed Bromage-1. The time required to attain the maximum motor blockade was labelled as the interval between the administration of the study drug and the point at which the maximum motor blockade was reached. The complete length of motor blockade was assessed starting from the moment of injection until the individual achieved full motor recovery, indicated by a Bromage score of 0. The hemodynamic parameters were measured at intervals of 2 min in the first 10 minutes, followed by at intervals of 5 min until 40 minutes, and finally at intervals of 10 min until the completion of the surgical process. The study diligently recorded the comprehensive documentation of adverse effects, such as hypotension (a decrease in systolic blood pressure exceeding 20% from the initial value or systolic blood pressure falling below 90 mmHg), along with symptoms of nausea, vomiting, and headache. The data underwent statistical analysis using SPSS version 24. The Independent Samples T-test was utilized to compare numerical variables,

[Citation Amjad, A., Sadia, H., Saad, M., Ali, A., Naeem, A., Naeem, H., Ahmed, M. (2023). Isobaric levobupivacaine versus hyperbaric bupivacaine in pregnant women undergone cesarean sections: a randomized controlled trial. *Biol. Clin. Sci. Res. J.*, **2023***:* 431. doi: https://doi.org/10.54112/bcsrj.v2023i1.431]

while the Chi-Square test was implemented to evaluate connections among categorical variables. Statistical significance was determined at a p-value of 0.05.

Results

The baseline characteristics of the patients in both groups are presented in Table 1. The mean time of onset of sensory block in group A was 113.11±6.98 sec, while in group B it was 97.34±9.38 sec (P = 0.0001). The mean time for two-segment regression in group was 69.20±3.72 sec while in group B it was 76.11±5.25 sec (P = 0.0001). The mean time for complete sensory recovery in group A was 155.91±8.83 min; in group B, the mean time for complete sensory recovery was 167.29±5.85 min (P = 0.0001). Regarding the motor block characteristics we found that the mean time to onset of motor block was 140.26±6.58 sec in group A while it was 91.46±6.6 sec in group B (P = 0.0001). The duration of motor block in group A was 120.26±4.83 min while the duration of motor block was 141.03±6.65 min in group B (P = 0.0001). The occurrence of hypotension was notably higher in group A in comparison to group B (P = 0.04). Regarding the side effects, we observed that in group A 5.7% of patients had postoperative nausea, vomiting in 2.9% while in group B 14.3% of patients had nausea, vomiting 8.6%, and headache in 5.7% of patients, however, we could not find any statistical difference in both groups in terms of postoperative side effects (P = 0.16).

Table 1 Baseline characteristics

Groups		Age (Years)	Gestational age (Weeks)	Duration of surgery (Mins)
Group A (Isobaric levobupivacaine)	Mean	25.31	38.63	50.69
	N	35	35	35
	Std. Deviation	4.751	1.031	6.272
Group B (Hyperbaric bupivacaine)	Mean	25.77	38.94	51.14
	N	35	35	35
	Std. Deviation	5.065	1.136	6.170

Table 2 Comparison of characteristics of sensory block between both groups

Sensory block characteristics	Groups	N	Mean	Std. Deviation	P-value
Time to Onset of Sensory Block (Sec)	Group A (Isobaric levobupivacaine)	35	113.11	6.986	0.0001
	Group B (Hyperbaric bupivacaine)	35	97.34	9.381	
Time for Two Segment Regression (sec)	Group A (Isobaric levobupivacaine)	35	69.20	3.724	0.0001
	Group B (Hyperbaric bupivacaine)	35	76.11	5.257	
Time for Complete Sensory Recovery (min)	Group A (Isobaric levobupivacaine)	35	155.91	8.836	0.0001
	Group B (Hyperbaric bupivacaine)	35	167.29	5.854	

Table 3 Comparison of motor block characteristics between both groups

Motor block characteristics	Groups	N	Mean	Std. Deviation	P-value
Time to Onset of Motor Block (Sec)	Group A (Isobaric levobupivacaine)	35	140.26	6.586	0.0001
	Group B (Hyperbaric bupivacaine)	35	91.46	6.604	
Time for Duration of Motor Block (min)	Group A (Isobaric levobupivacaine)	35	120.26	4.835	0.0001
	Group B (Hyperbaric bupivacaine)	35	141.03	6.653	

Table 4 Comparison of side effects between both groups

		Side effects				Total	P value
		Nausea	Vomiting	Headache	No side effects		
Groups	Group A (Isobaric levobupivacaine)	2	1	0	32	35	0.16
		5.7%	2.9%	0.0%	91.4%	100.0 %	
	Group B (Hyperbaric	5	3	2	25	35	

[Citation Amjad, A., Sadia, H., Saad, M., Ali, A., Naeem, A., Naeem, H., Ahmed, M. (2023). Isobaric levobupivacaine versus hyperbaric bupivacaine in pregnant women undergone cesarean sections: a randomized controlled trial. *Biol. Clin. Sci. Res. J.*, **2023***:* 431. doi: https://doi.org/10.54112/bcsrj.v2023i1.431]

bupivacaine)	14.3%	8.6%	5.7%	71.4%	100.0 %
Total	7	4	2	57	70
	10.0%	5.7%	2.9%	81.4%	100.0 %

Discussion

To alleviate maternal discomfort during cesarean section, it is crucial to provide dermatomal analgesia extending to the T4 level. Nevertheless, attaining such an elevated spinal level can trigger hypotension and influence placental perfusion. Decreasing the number of local anesthetic agents as a preventive measure for hypotension could potentially lead to the experience of visceral pain during medical treatment and a decrease in the effectiveness of postoperative pain relief. As a result, opioids such as buprenorphine have been utilized as intrathecal adjuvants to mitigate the intraoperative visceral pain that parturients may encounter during uterine manipulation . The intrathecal administration of fentanyl offers extended postoperative analgesia and the possibility of decreasing the dosage of local anesthetics. This combination improves hemodynamic stability due to a synergistic impact without increasing sympathetic blockade (Jenkins and Khan, 2003; Rao et al., 2020). Nevertheless, it is important to acknowledge that the administration of intrathecal lidocaine has been linked to temporary neurological irritation and the development of cauda equina syndrome. Bupivacaine 0.5% is widely employed as an intrathecal local anesthetic as it has a lengthy motor and sensory blockage period. It is significant to note that the cardiotoxicity of commercial bupivacaine can be attributed to the presence of the dextro enantiomer (Bajwa and Kaur, 2013). Levobupivacaine is distinguished by its exclusive S(-) enantiomer composition, unlike the racemic precursor compound. It shares pharmacodynamic characteristics with bupivacaine, but demonstrates a reduced occurrence of systemic toxicity. In modern obstetric care, the primary approach preferred by the majority of anesthesiologists, owing to its procedural simplicity, consistent effectiveness, and prompt initiation of sensory and motor block, is spinal anesthesia (Agarwal and Kishore, 2009). Nevertheless, it is imperative to allocate careful and thorough attention to prevent possible difficulties and guarantee the well-being of both the mother and the neonate. Although hyperbaric local anesthetics have demonstrated a remarkable safety record in obstetric anesthesia, their employment is not wholly without dangers (Rao et al., 2020). At a temperature of 37 degrees Celsius, it is seen that all concentrations of bupivacaine without additives are classified as hypobaric. On the other hand, levobupivacaine without additives can be accurately characterized as isobaric concerning cerebrospinal fluid in pregnant women, as specific gravities are closely matched. The isobaric property of levobupivacaine has the potential to result in a more reliable and consistent spread of spinal anesthesia. In theory, the maximum level of dermatomal analgesia that isobaric local anesthetics may achieve must not be influenced by the position of the subject or gravitational forces. Additionally, the distribution of isobaric levobupivacaine in term women is not shown to be affected by gravitational factors (Bidikar et al., 2017; Rao et al., 2020). Moreover, the coadministration of local anesthetics and opioids has been linked to enhanced anesthesia and analgesia. The concurrent administration of intrathecal fentanyl alongside low-dose local anesthetics leads to synergistic outcomes without any noticeable impact on sympathetic blocking or an increase in the duration of hospitalization. This methodology enables the utilization of diminished quantities of local anesthetics, resulting in enhanced hemodynamic outcomes (Bidikar et al., 2017; Rao et al., 2020). In our study, we observed the mean time for onset of sensory block in group bupivacaine was 97.34±9.38 sec, and that for levobupivacaine was 113.11±6.98 sec; the difference was statistically significant. Similar results have been demonstrated by a study that showed that in the group bupivacaine the mean time for onset of sensory block was shorter than group levobupivacaine.[18] We noted that the time for two segment regression in levobupivacaine group was considerably shorter than the bupivacaine group, this is also in comparison with the aforementioned study (Lee et al., 2009; Rao et al., 2020). Time for complete sensory recovery was significantly shorter in levobubivacaine group in comparison to bupivacaine, this is again comparable with the above study (Lee et al., 2009). The motor block features, including onset, maximum grading, and total length, were superior and prolonged in the bupivacaine group compared to the levobupivacaine group. These results align with previous studies conducted on the subject matter (Deori et al., 2016; Rao et al., 2020). Administration of isobaric levobupivacaine results in a shorter motor block, which is effective for performing cesarean sections. Additionally, this approach promotes early postoperative ambulation, reducing the risk of postoperative sequelae such as deep vein thrombosis (DVT) and thromboembolic events. Hypotension was found to be higher in bupivacaine group in comparison to levobupivacaine group (P = 0.04); we also observed that side effects like vomiting, nausea, and headache also had a higher prevalence in bupivacaine group; our results

[Citation Amjad, A., Sadia, H., Saad, M., Ali, A., Naeem, A., Naeem, H., Ahmed, M. (2023). Isobaric levobupivacaine versus hyperbaric bupivacaine in pregnant women undergone cesarean sections: a randomized controlled trial. *Biol. Clin. Sci. Res. J.*, **2023***:* 431. doi: https://doi.org/10.54112/bcsrj.v2023i1.431]

are in agreement with the aforementioned study (Bidikar et al., 2017; Deori et al., 2016).

Conclusion

This study determined that the administration of single-shot spinal anesthesia using various local anesthetic medications yields prompt and efficient induction of surgical anesthetic in elective cesarean section procedures. Levobupivacaine, which exhibits a shorter duration of motor block, fewer side effects, and a lower incidence of hypotension, presents itself as a superior alternative for cesarean section procedures.

Declarations

Data Availability statement

All data generated or analyzed during the study are included in the manuscript.

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Funding

Not applicable

Conflict of Interest

Regarding conflicts of interest, the authors state that their research was carried out independently without any affiliations or financial ties that could raise concerns about biases.

References

Agarwal, A., and Kishore, K. (2009). Complications and controversies of regional anaesthesia: a review. *Indian Journal of Anaesthesia* **53**, 543.

Antoine, C., and Young, B. K. (2021). Cesarean section one hundred years 1920–2020: the Good, the Bad and the Ugly. *Journal of Perinatal Medicine* **49**, 5-16.

Atalay, C., Karaca, M., Naldan, M. E., Soyalp, C., and Kursad, H. (2018). Fentanyl with low dose bupivacaine (isobaric and hyperbaric) and levo bupivacaine for combined spinal-epidural technique in cesarean section. *Medicine Sci* **7**, 494-98.

Bajwa, S. J. S., and Kaur, J. (2013). Clinical profile of levobupivacaine in regional anesthesia: A systematic review. *Journal of anaesthesiology, clinical pharmacology* **29**, 530.

Bidikar, M., Mudakanagoudar, M. S., and Santhosh, M. (2017). Comparison of intrathecal levobupivacaine and levobupivacaine plus fentanyl for cesarean section. *Anesthesia, essays and researches* **11**, 495.

Deori, A. K., Das, A., Borgohain, D., Bora, D., Saikia, A., and Tiwari, P. K. (2016). A comparative study of spinal anaesthesia with levobupivacaine and hyperbaric bupivacaine for cesarean sections. *International Journal of Contemporary Medical Research* **3**, 1902-5.

Durodola, A. O., Adekola, O. O., Agbamu, P. A., Akinwilliams, O. O., and Olatosi, J. O. (2021). Maternal hypotension and fetal outcome: effect of height-adjusted and weight-adjusted dose versus fixed dose of 0.5% intrathecal hyperbaric bupivacaine. *Research & Opinion in Anesthesia & Intensive Care* **8**.

Fakherpour, A., Ghaem, H., Fattahi, Z., and Zaree, S. (2018). Maternal and anaesthesia-related risk factors and incidence of spinal anaesthesia-induced hypotension in elective caesarean section: A multinomial logistic regression. *Indian journal of anaesthesia* **62**, 36.

Goffard, P., Leloup, R., Vercruysse, Y., Fils, J.-F., Gautier, P. E., and Kapessidou, Y. (2022). Comparison of equipotent doses of intrathecal hyperbaric prilocaine 2% and hyperbaric bupivacaine 0.5% for elective caesarean section: A prospective, randomised, controlled, two-centre clinical trial. *European Journal of Anaesthesiology| EJA* **39**, 227-235.

Horlocker, T. T., Wedel, D. J., Rowlingson, J. C., Enneking, F. K., Kopp, S. L., Benzon, H. T., Brown, D. L., Heit, J. A., Mulroy, M. F., and Rosenquist, R. W. (2010). Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines. *Regional Anesthesia & Pain Medicine* **35**, 64-101.

Jelting, Y., Klein, C., Harlander, T., Eberhart, L., Roewer, N., and Kranke, P. (2017). Preventing nausea and vomiting in women undergoing regional anesthesia for cesarean section: challenges and solutions. *Local and regional anesthesia*, 83-90.

Jenkins, J., and Khan, M. (2003). Anaesthesia for Caesarean section: a survey in a UK region from 1992 to 2002. *Anaesthesia* **58**, 1114-1118.

Lee, Y. Y., Kee, W. D. N., Fong, S. Y., Liu, J. T., and Gin, T. (2009). The median effective dose of bupivacaine, levobupivacaine, and ropivacaine after intrathecal injection in lower limb surgery. *Anesthesia & Analgesia* **109**, 1331-1334.

Maheshwari, N., Gautam, S., Kapoor, R., Prakash, R., Jafa, S., and Gupta, R. (2019). Comparative study of different doses of clonidine as an adjuvant with isobaric levobupivacaine for spinal anaesthesia in patients undergoing caesarean section. *Journal of Obstetric Anaesthesia and Critical Care* **9**, 9-13.

Manassero, A., and Fanelli, A. (2017). Prilocaine hydrochloride 2% hyperbaric solution for intrathecal injection: a clinical review. *Local and regional anesthesia*, 15-24.

Manouchehrian, N., Rahimi-Bashar, F., Pirdehghan, A., and Shahmoradi, F. (2022). Comparison between 10 and 12 mg doses of intrathecal hyperbaric (0.5%) bupivacaine on sensory

block level after first spinal failure in cesarean section: A double-blind, randomized clinical trial. *Frontiers in Medicine* **9**, 937963.

Rao, D. G., Anand, S., and Pasha, N. (2020). Comparative study of isobaric levobupivacaine and hyperbaric bupivacaine for subarachnoid block in elective cesarean sections. *Anaesthesia, Pain & Intensive Care* **24**, 215-222.

Sreekanth, R., and Totawar, S. R. (2018). Comparison of the effects of lateral and sitting position during induction of spinal anaesthesia with plain levobupivacaine in caesarean section. *Indian Journal of Clinical Anaesthesia* **5**, 86-91.

Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licen ses/by/4.0/. © The Author(s) 2023