Original Article

Comparative Study of Efficacy, Hemodynamic Stability and Safety of Fentanyl plus Hyperbaric Bupivacaine versus Fentanyl plus Hyperbaric Levobupivacaine in Spinal Anaesthesia for Elective Caesarean Sections

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ABSTRACT

Background: Spinal delivery of local anaesthetics is the preferred method for caesarean sections (CS), providing analgesia, anaesthesia, and motor blockade. The effectiveness of this method depends on the volume, concentration, and dosage of the local anaesthetic used. Hyperbaric bupivacaine is commonly utilized, but it carries risks such as hypotension and bradycardia. Levobupivacaine, a less cardiotoxic alternative, may offer benefits in terms of safety and efficacy.

Objective: To investigate the safety and efficacy of Fentanyl combined with Hyperbaric Bupivacaine compared to Fentanyl combined with Hyperbaric Levobupivacaine in spinal anaesthesia for elective caesarean sections.

Methods: An open-label randomized controlled trial was conducted at a tertiary care hospital in Bihar from January 2024 to December 2024. Informed consent was obtained from participants, and a sample size of 80 was calculated. Participants were randomly assigned to two groups: Group BF (Bupivacaine + Fentanyl) and Group LF (Levobupivacaine + Fentanyl). Various parameters, including sensory and motor block characteristics, hemodynamic stability, and adverse effects, were measured and analyzed statistically.

Results: Group BF had a faster onset of sensory block and reached T4 quicker than Group LF, but Group LF had a longer duration of sensory block. Group BF exhibited a faster onset and longer duration of motor block compared to Group LF. Group BF had a significantly longer duration of analgesia than Group LF. Group BF experienced higher rates of hypotension, bradycardia, nausea, and vomiting compared to Group LF.

Conclusion: Both levobupivacaine and hyperbaric bupivacaine are effective for spinal anaesthesia in elective CS. However, the combination of levobupivacaine and fentanyl offers advantages such as shorter motor block duration, reduced side effects, and improved hemodynamic stability, making it the preferred choice for elective CS.

Keywords: Spinal Anaesthesia, Caesarean Section, Hyperbaric Bupivacaine, Levobupivacaine, Hemodynamic Stability.

INTRODUCTION

The spinal delivery of local anaesthetics is the ideal method for caesarean section (CS) as it provides analgesia, anaesthesia, as well as motor blockade. This effect is contingent upon the volume, concentration, as well as dosage of the substance administered.[1, 2] 0.5% hyperbaric bupivacaine is predominantly utilized for spinal anaesthesia in caesarean sections. [3] Despite the impressive safety record of hyperbaric local anaesthetic treatments, their application is not entirely devoid of dangers.[4, 5, 6] To avert unilateral or saddle blocks, patients should transition swiftly from the lateral or sitting posture, and following patient movement, extension or early recurrence of the block may occur. Hyperbaric solutions can induce rapid cardiac arrest following spinal anaesthesia due to the prolongation of the sympathetic block. [7, 8] The utilization of genuinely isobaric solutions may demonstrate reduced sensitivity to positional discrepancies. Hyperbaric solutions may induce hypotension or bradycardia following movement, whereas isobaric solutions are preferred due to their reduced sensitivity to positional changes. [9]

Hyperbaric solutions frequently induce cephalad dispersion, obstructing cardiothoracic fibers and resulting in abrupt "bradycardia, hypotension, and cardiac arrest." Bupivacaine demonstrates a higher affinity for plasma proteins, binds more effectively to receptors, and is eliminated very slowly from isolated neurons, leading to an extended duration of the block. Bupivacaine traverses "the blood-brain barrier, and systemic absorption" or direct intravascular administration may result in CNS damage. Cardiotoxicity mostly results from the direct blockage of cardiac Na+ channels and the suppression of the autonomic nervous system. "Bradycardia, heart block, and hypotension" can result in cardiac arrest. The significant protein binding of bupivacaine hinders resuscitation efforts, particularly in pregnant instances. [10, 11]

Levobupivacaine is the enantiomeric S form of bupivacaine and may be utilized as a substitute for bupivacaine owing to its reduced cardiotoxicity as well as neurotoxicity. [12] The S (−) isomer demonstrates less effectiveness in inhibiting potassium channels, hence decreasing the probability of QTc interval lengthening. "Stereoselective binding to sodium and potassium channel" reduces inhibitory effects,

thereby diminishing overall toxicity potential relative to bupivacaine. It offers additional benefits due to its greater affinity for sensory fibers compared to motor fibers, resulting in a predictable distribution following spinal anaesthesia. [13]

The integration of low dosages of opioids with local anaesthetic agents throughout subarachnoid blockade mitigates the adverse effects linked to local anaesthetics and extends their duration of efficacy. [14] It offers analgesia during both the intraoperative and postoperative phases. Fentanyl may be incorporated as it prolongs the duration of action and aids in decreasing the dosage of local anaesthetic, hence minimizing its adverse effects. [15]

Fentanyl plus Hyperbaric Bupivacaine and Fentanyl plus Hyperbaric Levobupivacaine were compared for elective Caesarean sections for efficacy, hemodynamic stability, and safety. The main research question was if Fentanyl plus Hyperbaric Bupivacaine improve pain control, hemodynamic stability, and safety compared to Hyperbaric Levobupivacaine alone. The hypothesis was that adding Fentanyl to Hyperbaric Bupivacaine would improve analgesic efficacy and hemodynamic stability while preserving safety comparable to Levobupivacaine. The objective was to carefully investigate and determine the safest and most effective spinal anesthetic procedure for elective Caesarean sections to improve mother and fetal outcomes.

MATERIALS AND METHODS

This study was “an open label randomized controlled trial” conducted at the Department of Anaesthesiology of tertiary care hospital of Bihar from January 2024 to December 2024. “Informed consent” was obtained from all participants, with “a Participant Information Sheet” provided in their local language.

Sample Size: We utilized a formula for comparing two means with 95% power and 0.05 alpha to select the sample size for a trial comparing the efficacy and safety of Fentanyl with Hyperbaric Bupivacaine to Hyperbaric Levobupivacaine in spinal anaesthesia for elective Caesarean sections. Previous study indicate that Bupivacaine had a mean duration of analgesia of 196.35 ± 29.6 and Levobupivacaine had 170.46 ± 34.4.[10] We computed that each group needs 40 participants to attain statistical power and significance using these numbers.

Inclusion Criteria: The study comprised informed consenting pregnant women scheduled for elective Caesarean sections. Participants were classed as ASA Physical Status I or II, meaning they were healthy or had minimal systemic disease that did not affect everyday activities. Participants were 18–40 years old, had a singleton pregnancy, and had no spinal anaesthetic contraindications.

Exclusion Criteria: Participants with Fentanyl, Bupivacaine, or Levobupivacaine allergies or sensitivities were removed. Women with chronic pain, opioid misuse, or other substance abuse were excluded. Those with major cardiovascular, pulmonary, or neurological disorders and any condition that increased the chance of anaesthetic problems, such as coagulopathy or injection site infection, were also excluded. Women with numerous pregnancies, emergency Caesarean sections, or clinical trials within a month were excluded.

Intervention: Parturients were randomly divided into two groups. Group BF, comprising 65 patients, received "25 mcg (0.5 ml) of fentanyl and 10 mg 0.5% (2 ml) of hyperbaric bupivacaine." Group LF received "10 mg 0.5% (2 ml) hyperbaric levobupivacaine with 0.5 ml or 25 mcg fentanyl". Intrathecal drugs were delivered in 10 seconds. The parturients were supine and given 4 L/min oxygen.

Methodology:

The preoperative examination and preparation were carried out in accordance with the protocols of the department. Following the patient's transfer to the operating theater, baseline measurements such as blood pressure and heart rate were obtained. Intravenous access was achieved through the use of an 18G cannula, and all patients were pre-loaded with "1000 mL of Ringer Lactate" over the course of fifteen to twenty minutes prior to spinal anaesthesia commencement. Using a 26-gauge Quincke spinal needle, a lumbar puncture was conducted at the L3-4 interspace. Vital parameters were monitored throughout the procedure. When there was free flow of cerebrospinal fluid, the medicine that was being studied was given at a rate of 0.2 milliliters per second. After that, patients were placed in a supine position, and measurements of their hemodynamic parameters had been continuously monitored.[10]

Outcome Parameters:

Parameter	Details
Sensory Block	Time of onset, peak sensory block, and duration assessed using a 27-gauge needle and visual analogue scale.
Motor Block	Time to complete motor block and duration assessed using the modified Bromage scale.
Hemodynamic Parameters	Monitored at specified intervals post-block.
Complications	Hypotension (a fall in SBP or MAP below 20-30% of the baseline), bradycardia (HR <60/min), and respiratory depression (RR <8/min or SpO2 <85%).

Statistical Analysis: The study data was analysed using descriptive and inferential statistics. Results were presented as mean ± standard deviation (SD) for continuous variables including age, gestational age, BMI, surgery duration, sensory block onset, time to reach T10 and T4, total sensory block duration, motor block onset, maximum level, analgesia duration, SBP, and DBP. The independent t-test for normally distributed continuous variables was used to compare Fentanyl with Hyperbaric Bupivacaine and Levobupivacaine. Categorical variables like ASA I and II were

provided as frequencies and percentages. Where appropriate, the Chi-square or Fisher's exact test was used to compare groups for categorical variables. A p-value <0.05 indicated statistical significance. Analysis was done using SPSS or R. In addition, 95% confidence intervals were constructed to measure effect precision.

RESULTS

Table 1: Comparison of Baseline Demographic and Clinical Characteristics between Group Bupivacaine + Fentanyl (BF) and Levobupivacaine + Fentanyl (LF)

Parameters	Group BF (n = 40)	Group LF (n=40)	P-value
Age in Years, Mean ± SD	27.68 ± 5.07	27.94 ± 5.29	0.823018*
Gestational Age in Weeks,	38.06 ± 2.35	38.20 ± 2.50	0.797039*
BMI in kg/m^2,	23.46 ± 2.73	23.22 ± 2.45	0.680154*
Duration of Surgery,	64.15 ± 11.69	66.59 ± 10.13	0.321540*
ASA Status			>0.9999**
ASA I	18	19	
ASA II	22	21	

*Unpaired t-test **Fisher's Exact Test

There was no significant difference in age, gestational age, BMI, or surgical length between the two groups (all p-values > 0.05). The distribution of ASA I and II status amongst groups is also similar (p-value > 0.9999). [Table 1]

Table 2: Comparison of Sensory Block Characteristics between Group Bupivacaine + Fentanyl (BF) and Levobupivacaine + Fentanyl (LF)

Parameters in Minutes	Variables in ± Mean SD		P-value (Unpaired t-test)
	Group BF (n = 40)	Group LF (n=40)	
Onset of Sensory Block	1.85 ± 0.19	2.24 ± 0.18	<0.000001
Time to reach T10	4.50 ± 1.08	4.96 ± 1.93	0.192211
Time to reach T4	4.85 ± 1.21	5.94 ± 1.77	0.001897
Time for regression of 2 dermatomes	85.24 ± 15.63	80.45 ± 12.93	0.139354
Total duration of sensory block	113.55 ± 18.36	127.22 ± 13.62	0.000303

Group BF has a faster onset of sensory block (mean 1.85 ± 0.19 minutes) than Group LF (2.24 ± 0.18 minutes), with a significant p-value (<0.000001). Group BF reaches T4 faster (mean 4.85 ± 1.21 minutes) than Group LF (5.94 ± 1.77 minutes), with a significant p-value (0.001897). Time to reach T10 and time for regression of 2 dermatomes are not significantly different across groups, with p-values of 0.192211 and 0.139354. Group LF had a longer sensory block duration (mean 127.22 ± 13.62 minutes) than Group BF (mean 113.55 ± 18.36 minutes), with a significant p-value (0.000303). [Table 2]

Table 3: Comparison of Motor Block Characteristics between Group Bupivacaine + Fentanyl (BF) and Levobupivacaine + Fentanyl (LF)

Parameters in Minutes	Variables in ± Mean SD		P-value (Unpaired t-test)
	Group BF (n = 40)	Group LF (n=40)	
Onset of motor block	2.26 ± 0.61	3.95 ± 0.83	<0.000001
Time to reach the maximum level	6.84 ± 1.33	9.34 ± 2.09	<0.000001
Total duration of motor block	127.56 ± 10.97	101.67 ± 11.72	<0.000001

Group BF has a faster onset of motor block (mean 2.26 ± 0.61 minutes) than Group LF (mean 3.95 ± 0.83 minutes), with a significant p-value (<0.000001). Group BF reaches maximum motor block level faster (6.84 ± 1.33 minutes) than Group LF (9.34 ± 2.09 minutes), with a significant p-value (<0.000001). Additionally, Group BF had a significantly longer motor block duration (mean 127.56 ± 10.97 minutes) than Group LF (mean 101.67 ± 11.72 minutes), with a p-value <0.000001. [Table 3]

Table 4: Comparison of Time to Duration of analgesia between Group Bupivacaine + Fentanyl (BF) and Levobupivacaine + Fentanyl (LF)

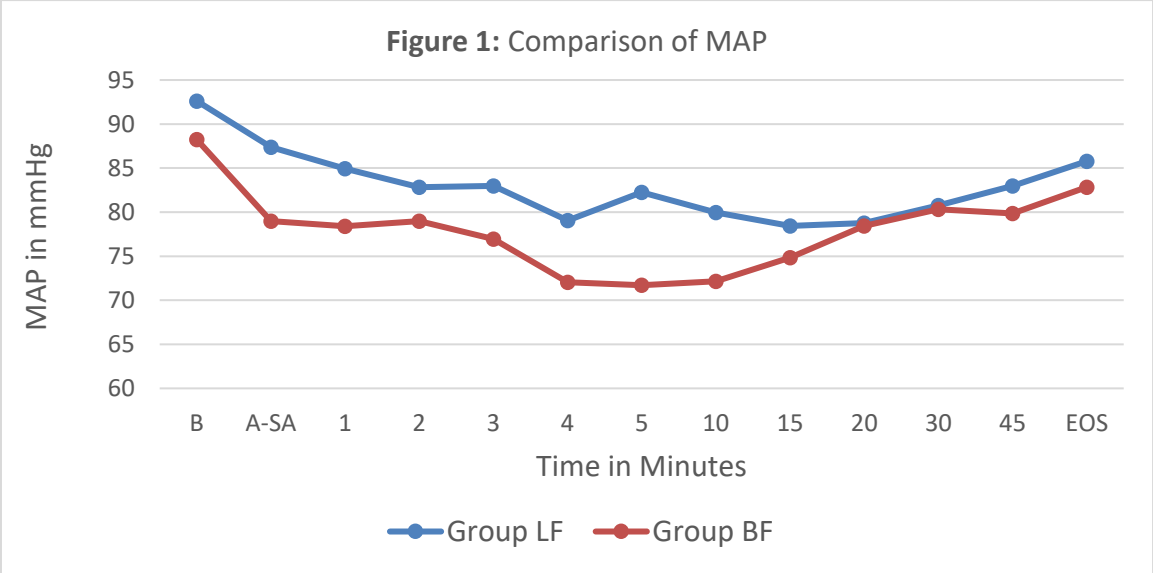
	Group BF	Group LF
Number of Patients (N)	40	40
Duration of analgesia in Minutes	195.46	172.55
Standard Deviation (SD)	30.16	33.47
Difference in Mean	22.9100	
95% CI of Mean Difference	8.7279 to 37.0921	
P-Value (Unpaired t test)	0.0019	

Compared to Group Levobupivacaine + Fentanyl (LF), Group BF has a significantly longer duration of analgesia. [Table 4]

Table 5: Comparison of Adverse Effects between Group Bupivacaine + Fentanyl (BF) and Levobupivacaine + Fentanyl (LF)

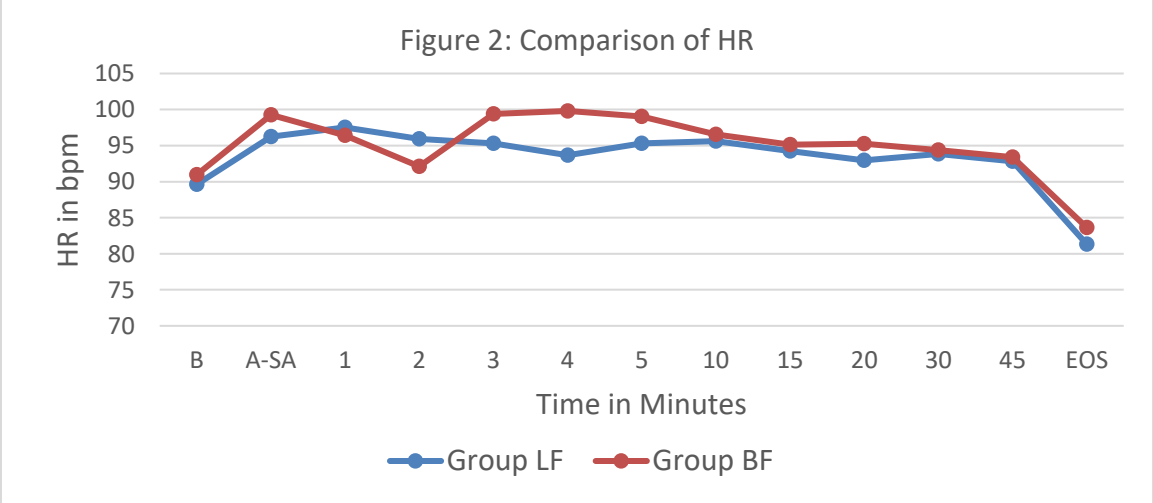
Adverse Effects	Group BF (n = 40)		Group LF (n=40)	
	Number of Patients	Percentage	Number of Patients	Percentage
Hypotension	27	67.5	11	27.5
Bradycardia	13	32.5	5	12.5
Headache	5	12.5	3	7.5
Backache	1	2.5	2	5
Nausea	24	60	5	12.5
Vomiting	11	27.5	5	12.5
Itching	3	7.5	3	7.5
Shivering	1	2.5	3	7.5

Hypotension (67.5% vs. 27.5%), bradycardia (32.5% vs. 12.5%), nausea (60% vs. 12.5%), and vomiting (27.5% vs. 12.5%) were higher in Group BF than Group LF. Group BF also had more headache (12.5% vs. 7.5%) and less backache (2.5% vs. 5%). [Table 5]



*B: Baseline, A-SA: After Spinal Anaesthesia, EOS: End of Surgery, MAP: Mean Arterial Pressure

MAP in Group LF gradually declines and stabilizes about 80 mmHg, while MAP in Group BF drops more to 70 mmHg before gradually increasing after surgery. [Figure 1]



*B: Baseline, A-SA: After Spinal Anaesthesia, EOS: End of Surgery, HR: Heart Rate, bpm: beats per minute

HR in Group LF declines gradually and stabilizes about 85 bpm, while HR in Group BF drops sharply to 80 bpm before slightly increasing at the end of surgery. [Figure 2]

DISCUSSION

In the current investigation, the combination of levobupivacaine and hyperbaric bupivacaine with fentanyl resulted in a comparable level of sensory blocking, as well as maternal hemodynamic and neonatal effects, in CS patients who were under spinal anesthesia. When delivered through the intrathecal route, the combination of fentanyl and levobupivacaine resulted in a lower level of motor blockage compared to hyperbaric bupivacaine.

There is a correlation between the addition of intrathecal opioids and an increase in the effectiveness of neuraxial local anesthetics. These combinations are typically associated with enhanced analgesia and anesthesia during the entire process. In addition to this, it makes it possible to provide very low dosages of local anesthetic, which helps to maintain more stable hemodynamic characteristics. [16-18]

Adding intrathecal fentanyl to low-dose local anaesthetics results in a synergistic effect, according to a study conducted by Goel et al. [19] This effect does not result in an increase in sympathetic blocking or a delay in the patient's departure from the hospital.

Two groups of researchers, Akcaboy et al.[20] and Hakan Erbay et al.[21], conducted a study to evaluate the efficacy of low-doses of 0.5% levobupivacaine and 0.5% bupivacaine, with dosages of 5 mg and 7.5 mg, respectively, when paired with 25 µg of fentanyl. When administered in greater doses, these regimens have been demonstrated to be successful in spinal anesthesia for the purpose of performing transurethral resection of the prostate. Levobupivacaine combined with fentanyl produced an efficient sensory blockade while producing a lower level of motor blockade than bupivacaine combined with fentanyl did in both of the tests.

Research has shown the impact of a combination of local anesthetic and opioid for regional anesthesia in cesarean sections, both extradurally and intrathecally; varying outcomes concerning the characteristics of sensory blockade between levobupivacaine and bupivacaine have been noted. [1, 11, 22-28] On the other hand, the majority of these research came to the conclusion that levobupivacaine results in a lower level of motor blockage compared to bupivacaine.

The current investigation found that variations in heart rate, as well as decreases in both systolic and diastolic blood pressure, were within acceptable levels. In the field of spinal anesthesia, Erdil et al. observed that low-dose levobupivacaine combined with fentanyl exhibited superior hemodynamic stability in comparison to low-dose bupivacaine combined with fentanyl.[26]

By comparing equipotent dosages of bupivacaine, levobupivacaine, and ropivacaine paired with sufentanil in patients receiving elective spinal cord stimulation with combined spinal–epidural anesthesia, Coppejans and Vercauteren were able to determine the effectiveness of these combinations. In spite of the fact that levobupivacaine was associated with a tendency toward improved systolic blood pressures and a reduced occurrence of severe hypotension, the researchers discovered that the hemodynamic values of the three groups were comparable. Levobupivacaine caused maternal hemodynamics to remain stable in the current trial as well, in contrast to hyperbaric bupivacaine, which caused hemodynamical instability.[22]

Bupivacaine's S-enantiomer, levobupivacaine, has a more stable haemodynamic profile. Scientists ascribe this to lower cardiotoxicity and neurotoxicity. Levobupivacaine is preferred in clinical settings due to its faster onset and extended sensory block. It causes fewer hemodynamic alterations such hypotension and bradycardia than bupivacaine, according to studies.[29, 30]

Clinically, levobupivacaine is safer for caesarean sections. It delivers efficient analgesia with fewer side effects, making it safer for mother and baby. Levobupivacaine's decreased cardiovascular and central nervous system toxicity makes anaesthesia more predictable and regulated. For mother and child safety, maternal hemodynamic stability is essential during caesarean sections.[31]

Bupivacaine induces more motor block than levobupivacaine. Caesarean sections benefit from faster healing and mobilization. Deep vein thrombosis and other problems of prolonged immobility are decreased by the reduced motor block. Levobupivacaine is better for caesarean spinal anaesthetic due to its consistent haemodynamic profile, safety, and lower motor block.[30]

The most significant disadvantage of our research is that it was limited to participants with ASA physical status I and II who were undergoing elective caesarean sections. This restricts the homogeneity of the sample and restricts the generalizability of the drug.

CONCLUSION

As a conclusion to our research, we would like to highlight that both levobupivacaine and hyperbaric bupivacaine are capable of inducing surgical anaesthetic for elective CS in a quick and efficient manner, and they do not have any negative effects on newborns. On the other hand, the combination of levobupivacaine and fentanyl results in a shorter motor block time, a reduction in the occurrence of side effects such as hypotension and bradycardia, and an improvement in hemodynamic stability, which in turn reduces the risk and allows for early mobility. For this reason, the combination of levobupivacaine and fentanyl ought to be the preferable approach for elective CSs.

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REFERENCES

1. Gautier P, De Kock M, Van Steenberge A, Miclot D, Fanard L, Hody JL. A double-blind comparison of 0.125% ropivacaine with sufentanil and 0.125% bupivacaine with sufentanil for epidural labor analgesia. Anaesthesiology. 1999;90:772–8. doi: 10.1097/00000542-199903000-00020.
2. Brizzi A, Greco F, Malvasi A, Valerio A, Martino V. Comparison of sequential combined spinal-epidural anaesthesia and spinal anaesthesia for caesarean section. Minerva Anestesiol. 2005;71:701–9.
3. Wiebke G. Spinal anaesthesia for obstetrics. Best Pract Res Clin Anaesthesiol. 2003;17:377–92. doi: 10.1016/s1521-6896(02)00116-7.
4. Hallworth SP, Fernando R, Columb MO, Stocks GM. The effect of posture and baricity on the spread of intrathecal bupivacaine for elective caesarean delivery. Anaesth Analg. 2005;100:1159–65. doi: 10.1213/01.ANE.0000149548.88029.A2.
5. Dobson PM, Caldicott LD, Gerrish SP. Delayed asystole during spinal anaesthesia for transurethral resection of the prostate. Eur J Anaesthesiol. 1993;10:41–3.
6. Køhler F, Sørensen JF, Helbo-Hansen HS. Effect of delayed supine positioning after induction of spinal anaesthesia for caesarean section. Acta Anaesthesiol Scand. 2002;46:441–6. doi: 10.1034/j.1399-6576.2002.460419.x.
7. Scull TJ, Carli F. Cardiac arrest after caesarean section under subarachnoid block. Br J Anaesth. 1996;77:274–6. doi: 10.1093/bja/77.2.274.
8. Løvstad RZ, Granhus G, Hetland S. Bradycardia and asystolic cardiac arrest during spinal anaesthesia: A report of five cases. Acta Anaesthesiol Scand. 2000;44:48–52. doi: 10.1034/j.1399-6576.2000.440109.x.
9. Povey HM, Jacobsen J, Westergaard-Nielsen J. Subarachnoid analgesia with hyperbaric 0.5% bupivacaine: Effect of a 60-min period of sitting. Acta Anaesthesiol Scand. 1989;33:295–7. doi: 10.1111/j.1399-6576.1989.tb02911.x.
10. A S S, Tk V, Alalamath S. Comparative Efficacy of Intrathecal Hyperbaric Levobupivacaine With Fentanyl Versus Hyperbaric Bupivacaine With Fentanyl in Elective Caesarean Section. Cureus. 2024 Sep 29;16(9):e70476. doi: 10.7759/cureus.70476. PMID: 39479058; PMCID: PMC11524607.
11. Goyal A, Shankaranarayan P, Ganapathi P. A randomized clinical study comparing spinal anaesthesia with isobaric levobupivacaine with fentanyl and hyperbaric bupivacaine with fentanyl in elective caesarean sections. Anaesth Essays Res. 2015 Jan-Apr;9(1):57-62. doi: 10.4103/0259-1162.150169. PMID: 25886422; PMCID: PMC4383120.
12. Foster RH, Markham A. Levobupivacaine: a review of its pharmacology and use as a local anaesthetic. Drugs. 2000;59:551–579. doi: 10.2165/00003495-200059030-00013.
13. Sundarathiti P, Sangdee N, Sangasilpa I, Prayoonhong W, Papoun S. Comparison of intrathecal bupivacaine, levobupivacaine for caesarean section. J Med Assoc Thai. 2014;97:710–716. Available from: https://pubmed.ncbi.nlm.nih.gov/25265769/
14. Di Cianni S, Rossi M, Casati A, et al. Spinal anaesthesia: an evergreen technique. Acta Biomed. 2008;79:9–17. Available from: https://www.mattioli1885journals.com/index.php/actabiomedica/article/view/1852
15. Goyal A, Shankaranarayan P, Ganapathi P. A randomized clinical study comparing spinal anaesthesia with isobaric levobupivacaine with fentanyl and hyperbaric bupivacaine with fentanyl in elective caesarean sections. Anaesth Essays Res. 2015;9:57–62. doi: 10.4103/0259-1162.150169.
16. Choi DH, Ahn HJ, Kim MH. Bupivacaine-sparing effect of fentanyl in spinal anesthesia for cesarean delivery. Reg Anesth Pain Med. 2000;25:240–5. doi: 10.1016/s1098-7339(00)90005-1.
17. Ben-David B, Miller G, Gavriel R, Gurevitch A. Low-dose bupivacaine-fentanyl spinal anesthesia for cesarean delivery. Reg Anesth Pain Med. 2000;25:235–9.
18. Chen X, Qian X, Fu F, Lu H, Bein B. Intrathecal sufentanil decreases the median effective dose (ED50) of intrathecal hyperbaric ropivacaine for caesarean delivery. Acta Anaesthesiol Scand. 2010;54:284–90. doi: 10.1111/j.1399-6576.2009.02051.x.
19. Goel S, Bhardwaj N, Grover VK. Intrathecal fentanyl added to intrathecal bupivacaine for day case surgery: A randomized study. Eur J Anaesthesiol. 2003;20:294–7. doi: 10.1017/s0265021503000462.
20. Akcaboy EY, Akcaboy ZN, Gogus N. Low dose levobupivacaine 0.5% with fentanyl in spinal anaesthesia for transurethral resection of prostate surgery. J Res Med Sci. 2011;16:68–73.
21. Hakan Erbay R, Ermumcu O, Hanci V, Atalay H. A comparison of spinal anesthesia with low-dose hyperbaric levobupivacaine and hyperbaric bupivacaine for transurethral surgery: A randomized controlled trial. Minerva Anestesiol. 2010;76:992–1001.
22. Coppejans HC, Vercauteren MP. Low-dose combined spinal-epidural anesthesia for cesarean delivery: A comparison of three plain local anesthetics. Acta Anaesthesiol Belg. 2006;57:39–43.
23. Guasch E, Gilsanz F, Díez J, Alsina E. Maternal hypotension with low doses of spinal bupivacaine or levobupivacaine and epidural volume expansion with saline for cesarean section. Rev Esp Anestesiol Reanim. 2010;57:267–74. doi: 10.1016/s0034-9356(10)70226-7.
24. Gunusen I, Karaman S, Sargin A, Firat V. A randomized comparison of different doses of intrathecal levobupivacaine combined with fentanyl for elective cesarean section: Prospective, double-blinded study. J Anesth. 2011;25:205–12. doi: 10.1007/s00540-011-1097-4.

25. Bouvet L, Da-Col X, Chassard D, Daléry F, Ruynat L, Allaouchiche B, et al. ED50 and ED95 of intrathecal levobupivacaine with opioids for Caesarean delivery. Br J Anaesth. 2011;106:215–20. doi: 10.1093/bja/aeq296.

26. Erdil F, Bulut S, Demirbilek S, Gedik E, Gulhas N, Ersoy MO. The effects of intrathecal levobupivacaine and bupivacaine in the elderly. Anaesthesia. 2009;64:942–6. doi: 10.1111/j.1365-2044.2009.05995.x.

27. Lirk P, Kleber N, Mitterschiffthaler G, Keller C, Benzer A, Putz G. Pulmonary effects of bupivacaine, ropivacaine, and levobupivacaine in parturients undergoing spinal anaesthesia for elective caesarean delivery: A randomised controlled study. Int J Obstet Anesth. 2010;19:287–92. doi: 10.1016/j.ijoa.2009.03.015.

28. Guler G, Cakir G, Ulgey A, Ugur F, Bicer C, Gunes I, et al. A comparison of spinal anesthesia with levobupivacaine and hyperbaric bupivacaine for cesarean sections: A randomized trial. Open J Anesthesiol. 2012;2:84–9.

29. Jagan G, Priyadharshini P, Divya S, Dhinesh Kumar C, Krishna Prasad T. Efficacy of Levobupivacaine in Regional Anaesthesia - A Narrative Review. Front Med Case Rep. 2024;5(5):1-12. DOI: http://dx.doi.org/10.47746/FMCR.2024.5504

30. Kaur K, Johar S, Kumar A, Jain M, Kumar P, Singh A. A comparative study of intrathecal bupivacaine and levobupivacaine for patients undergoing caesarean section. Int J Adv Med. 2019;6(6):1-12. DOI: https://doi.org/10.18203/2349-3933.ijam20195229.

31. Deori AK, Das A, Borgohain D, Bora D, Saikia A, Tiwari PK. A Comparative Study of Spinal Anaesthesia with Levobupivacaine and Hyperbaric Bupivacaine for Cesarean Sections. Int J Contemp Med Res. 2016;3(7):1902-1905. DOI: https://ijcmr.com/uploads/7/7/4/6/77464738/ijcmr_698_v1_jun_16.pdf.