

Comparison of Levobupivacaine and Clonidine with Bupivacaine and Clonidine in Spinal Anaesthesia for Lower Segment Caesarean Section

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Abstract: Comparison Of Levobupivacaine And Clonidine With Bupivacaine And Clonidine In Spinal anaesthesia For Lower Segment Caesarean Section

Introduction: Intrathecal LevoBupivacaine is having similar clinical profile with less cardio-toxicity than Bupivacaine is used commonly for LSCS. Clonidine as an additive to LA provides effective, prolonged and dose dependent analgesia. In this study we compared effect of intrathecal Clonidine 30 µg and 0.5% isobaric Levobupivacaine 9 mg with Clonidine 30 µg and 0.5% hyperbaric Bupivacaine 9 mg for LSCS.

Material and method : In this study we want to compare onset, degree, maximum sensory level achieved, time required to achieve the maximum level of sensory blockade, duration of effective sensory blockade and onset and degree of effective motor blockade, its cardiac effect and effect on APGAR score of baby after intrathecal Clonidine 30 µg as an adjuvant to intrathecal 0.5% isobaric Levobupivacaine 9 mg and 0.5% hyperbaric Bupivacaine 9mg.

Observations: The mean time for the onset of motor blockade in patients in group B was 1.90 ± 0.54 min and in group L was 2.15 ± 0.47 min. Mean time required for maximum motor blockade was 4.70 ± 0.65 min for group B and 4.30 ± 0.59 min for group L. Time of onset of analgesia at T6 was 6.40 ± 0.81 in group B and 6.70 ± 0.84 min in L group. Time required to achieve maximum level of analgesia was 7.20 ± 1.21 min in group B and 7.33 ± 1.26 min in group L. Bradycardia was statistically significant in patients of group B as compared to that in group L. Two dermatome regression in group B was at 158.27 ± 5.01 min and in group L it was at 157.83 ± 3.49 min. The first rescue analgesic required in group B was at 167.68 ± 3.84 min and in group L was at 165.73 ± 4.65 min.

Conclusion: We observed that that isobaric Levobupivacaine with Clonidine has got comparable pharmacokinetic in onset and offset of sensory and motor block, less cardiovascular side effects, good intraoperative and postoperative analgesia without sedation and adverse effect on Apgar score so we conclude that Levobupivacaine with Clonidine is a better choice in LSCS than Bupivacaine with Clonidine.

Keywords: Levobupivacaine, Bupivacaine, Clonidine, LSCS

I. Introduction

Central neuraxial blockade is the most popular technique of anaesthesia for LSCS. It is having several advantages like economic, early onset, easy to perform and provides good quality of anaesthesia¹. It decreases blood loss, avoid risk of intubation and aspiration, provides early ambulation and early starting of breast feeding. Bupivacaine is most commonly used local anaesthetic drug for LSCS but cardio-toxicity is the limiting factor. Levobupivacaine having similar clinical profile with less cardio-toxicity than Bupivacaine is gaining popularity.¹ It has demonstrated less affinity and strength of inhibitory effect on the inactivated state of cardiac sodium channels than the Bupivacaine and faster protein binding rate².

To provide good quality of intra-operative anaesthesia with post-operative analgesia different additives like Opioids, Ketamine, Midazolam, Neostigmine and α_2 adrenergic agonist are used³. Opioids may cause pruritus, nausea, vomiting, urinary retention and respiratory depression either in mother and baby³. Neostigmine causes nausea, vomiting, bradycardia and hypotension. Midazolam causes neurotoxicity⁴. Clonidine is a selective partial α_2 adrenergic agonist provides effective, prolonged and dose dependent analgesia with a consequently decreased requirement of supplemental analgesics.⁵

This study was conducted in patients undergoing lower segment caesarean section to evaluate and compare the effect of Clonidine 30 µg as an adjuvant to intrathecal 0.5% isobaric Levobupivacaine 9 mg and 0.5% hyperbaric Bupivacaine 9 mg. Total volume of drug was 2 ml in both the groups.

II. Aims And Objectives

In this study our primary aim was to compare onset, degree, maximum level achieved, time required to achieve the maximum level of sensory blockade, duration of effective sensory blockade and onset and degree of

effective motor blockade after intrathecal Clonidine 30 µg as an adjuvant to intrathecal 0.5% isobaric Levobupivacaine 9 mg and 0.5% hyperbaric Bupivacaine 9 mg.

Our secondary aim was to compare effect of Clonidine 30 µg as an adjuvant to intrathecal 0.5% isobaric Levobupivacaine 9 mg and 0.5% hyperbaric Bupivacaine 9 mg. on vital parameters like pulse rate, mean arterial pressure, SpO₂ respiratory rate ,intraoperative side effects like nausea, vomiting, bradycardia, hypotension, sedation, respiratory depression, dry mouth ,effect on neonate (Apgar score) and time required for request of first rescue analgesic.

III. Material And Method

After approval from hospital ethics committee, detail clinical examination, investigations and written informed valid consent patients were posted for LSCS. Patients with ASA grade I and II, BMI<35 kg/m² with age 18-35 yrs. posted for emergency or elective LSCS were included in this study. Patients were kept NBM for 6 hours prior to the elective procedure. On arrival in the operating room patients were preloaded with ringer lactate solution at 10 ml/kg. Antiemetic prophylaxis was given using Injection Ondansetron 0.08 mg/kg , Injection Ranitidine 1mg/kg and Injection Metoclopramide 0.2 mg/kg. Patients were randomized into two groups with 30 each, on the basis of sealed envelope technique.

Under all aseptic precautions Lumbar puncture was performed in L3-L4 interspace in left lateral position by using 23 gauge pencil point spinal needle. After obtaining clear and free flow of CSF Group B patients received injection hyperbaric 0.5% Bupivacaine 9 mg and Clonidine 30 µg and Group L patients received 9 mg isobaric Levobupivacaine 0.5% and 30 µg Clonidine intrathecally over 10 seconds with total volume 2ml. Immediately supine position with wedge under right hip was given. Oxygen was administered through a face mask. Patient was monitored for pulse rate, mean arterial pressure, respiratory rate and sedation continuously. Hypotension defined as decrease in systolic pressure by more than 30% from baseline or decrease in mean arterial pressure more than 20% was treated with bolus intravenous dose of Injection Ephedrine 5-10 mg and intravenous fluids if required. Bradycardia defined as heart rate less than 50/min was treated with IV Atropine 0.6 mg.

Sensory level was determined by pinprick using 24gauge hypodermic needle. Onset of analgesia was defined as time interval from completion of subarachnoid injection to the loss of pinprick sensation at T6. Maximum dermatomal level was tested by pinprick in mid-clavicularline, every minute until the level is stabilized for two consecutive tests. After that sensory level was tested every 15 minutes until two segment regression. Time taken to achieve maximum sensory level, two segment regression and time for first analgesic required was noted.

Quality of analgesia was assessed by patients comfort and was graded as follows

- I.** Required general anaesthesia for completion of surgery
- II.** Pain that required addition of the analgesic drug.
- III.** Mild discomfort but did not required systemic analgesic.
- IV.** No discomfort at all during procedure

Onset of motor block was defined as the time from the injection of drug in subarachnoid space till the patient was unable to raise the extended legs. The degree of motor block was assessed with Bromage scale and graded as follows.

Grade

- 0** No motor block
- 1** Inability to raise extended legs
- 2** Inability to flex knee, able to flex the ankle
- 3** Complete motor block (Inability to flex the ankle)

Sedation was assessed by four point score and graded as follows:

- 0.** Awake and alert
- 1.** Mild sedation, easy to rouse
- 2.** Moderate sedation, unable to remain awake
- 3.** Difficult to arouse.

Incidence of side effects (nausea, vomiting, shivering, itching, pruritus, sedation, respiratory depression, bradycardia, dry mouth and hypotension) was recorded. Apgar score of baby at 1 and 5 minutes was recorded and graded as follows.

Sr. No. Sign 0 1 2

- 1** Respiratory efforts Absen Slow Irregula Good, crying
- 2** Heart rate Absent Slow(below100) Over 100
- 3** Muscle tone Flaccid Flexion of extremities Active body movements

4 Reflex irritability No Response Grimace Cry
5 Colour Blue, Pale Body pink, extremities blue Complete pink
Total score:10
No depression : 7-10
Mild depression : 4-6
Severe depression: 0-3

Onset of postoperative pain was considered when patient requests first rescue analgesic. If patient complains of pain before delivery of baby injection Ketamine 0.5 to 1 mg/kg IV was given as analgesic. If pain persists after Ketamine then general anaesthesia was given.

For analysis of this data SPSS (statistical software for social sciences) version 20 was used. Data was presented in visual impression by using bar diagram. Analysis of data was performed using student's unpaired t-test for finding the significance of difference between means of two independent samples. Comparisons between two qualitative variables were performed with Pearson's chi-square test. P value < 0.05 was considered to be statistically significant.

IV. Observations And Results

This prospective study was carried out on sixty women with singleton pregnancy ASA grade I - grade II, undergoing caesarean section under spinal anaesthesia. There was no statistical significant difference among both the groups as far as age, height and weight were taken into consideration. Mean age in Group B was 22.83 ± 2.61 yrs. while in Group L it was 23.3 ± 3.26 yrs. with $P=0.543$. Mean height was Group B was 150.53 ± 3.22 cm while in Group L it was 148.76 ± 4.79 with $P=0.098$. Mean age was Group B was 60.20 ± 4.97 kg while in Group L it was 62.30 ± 4.42 kg with $P=0.0089$.

The mean time for the onset of motor blockade in patients in group B was 1.90 ± 0.54 min and in group L was 2.15 ± 0.47 min with $p=0.087$. It indicates that the difference was statistically not significant. Mean time required for maximum motor blockade was 4.70 ± 0.65 min for group B and 4.30 ± 0.59 min for group L with $P=0.056$. The difference between both the groups was statistically not significant.

Time required for loss of pinprick sensation at T6 was almost similar in both the groups. In group B 6.40 ± 0.81 and 6.70 ± 0.84 min for L group with $P=0.164$ indicating that the difference between onset of analgesia was statistically not significant. Time required to achieve maximum level of analgesia was 7.20 ± 1.21 min in group B and 7.33 ± 1.26 min in group L with $P=0.676$ indicating that time required to achieve maximum level was comparable in both groups. 27 patients in B group had analgesia (grade IV) whereas 3 patients had mild discomfort for which no analgesic was required (grade III). 26 patients in L group had sensory analgesia (grade IV) whereas 4 patients had mild discomfort for which no analgesic was required (grade III). None of the patients from both the groups required general anaesthesia. The difference between the two groups was statistically not significant.

We observed that after 15 minutes of block 3 patients in group B and 4 patients in group L were mildly sedated after 15 minutes while after 45 minutes 6 patients in group B and 5 patients in group L were moderately sedated. 1 patient from each group was difficult to arouse. None had respiratory rate less than 12 and SPO₂ less than 95%. The difference between the two groups was statistically not significant. All babies had Apgar score > 9 at 1 and 5 minutes. The difference between the two groups was statistically not significant.

Bradycardia was statistically significant in patients of group B as compared to that in group L. Basal mean arterial pressure was comparable in both the groups ($p>0.05$). Hypotension was statistically significant in group B compared to group L.

The difference between the two groups was statistically not significant. Mean basal respiratory rate was 14.53 ± 1.36 per min in group B and 14.93 ± 1.04 per min in group L. The difference between the two groups was statistically not significant. Mean minimal respiratory rate was 13.10 ± 1.12 per min in group B and 13.47 ± 1.4 per min in group L. The difference between the two groups was statistically not significant. Mean basal SpO₂ Preoperative was 99.47 ± 0.51 % in the group B and 99.43 ± 0.05 in group L. Mean minimal intraoperative SpO₂ was 99.23 ± 0.73 % in group B and 98.93 ± 0.56 % in group L. Mean post-op SpO₂ was 99.47 ± 0.57 % in B group and 99.53 ± 0.51 % in group L. The difference between the two groups was statistically not significant.

Two dermatome regression in group B was at 158.27 ± 5.01 min and in group L it was at 157.83 ± 3.49 min. The difference between the two groups was statistically not significant. The first rescue analgesic required in group B was at 167.68 ± 3.84 min and in group L was at 165.73 ± 4.65 min. The difference between the two groups was statistically not significant.

Incidence of vomiting was same in both the groups .2 patients had intraoperative vomiting and 1 had postoperative vomiting. 3 patients in group B and 2 patients in group L had nausea intraoperatively .1 patient in each group had postoperative nausea. The difference between the two groups is statistically not significant. None of the patient had dry mouth or pruritus.

V. Discussion

Spinal anesthesia is most preferred technique of anesthesia for LSCS. In pregnancy dose requirement of local anesthetic is decreased due to physiological changes in epidural space and reduction in CSF protein concentration.^{6,7} We can further decrease the dose by adding an adjuvant to local anaesthetic. Intrathecal Clonidine is safe in pregnant females as it is not detected in the fetal circulation⁸.

Levobupivacaine is said to be less cardio-toxic and having more specific effects on sensory rather than motor nerve with shorter duration of analgesia and motor blockade.^{9,10,11} Misirlioglu K and et al and Feroz A. Dar et al compared efficacy of intrathecal 0.5% levobupivacaine with 0.5% bupivacaine and fentanyl 25 µg as an adjuvant. They noted that there was no significant difference in the quality of anesthesia and intraoperative side effects but time to complete regression of motor blockade was statistically lower in group L.^{12,13}

Clonidine blocks the conduction of C and A δ fibers and acts synergistically with local anaesthetics by its action of opening potassium channels.¹⁴ Intrathecal clonidine prolongs sensory as well as motor block of spinal anesthesia by activation of post synaptic α-2 receptor in substantia nigra of spinal cord.¹⁵ It decreases local anesthetic requirements and provides prolonged postoperative analgesia. Also it acts as antiemetic, anxiolytic, reduces post spinal shivering and provides sedation without respiratory depression.¹⁵ Bupivacaine acts mainly by blockade of voltage gated Na⁺ channel in the axonal membrane and presynaptic inhibition of calcium channels and a combination of these effects may explain the observed synergism between bupivacaine and clonidine.^{16,17,18}

This decreased dose of LA Reduction in spinal anaesthesia can decrease incidence of maternal hypotension, high spinal block, and prolonged motor block. Due to good postoperative analgesia after cesarean section with intrathecal Clonidine, the mother is better able to take care of her newborn, which immediately improves mother-baby relationship, decreases prelacteal feeds (feeding any other substance before first breastfeeding).¹⁹ The suggested optimal dose of clonidine is 37.5 µg for cesarean surgery, which allows reduction of up to 18% of the total dose of hyperbaric bupivacaine⁸.

In our study we observed that onset of analgesia was comparable in both groups. This indicates that Levobupivacaine and Bupivacaine are equipotent. Same findings were noted in different studies.^{20,12,21,22,23,13, 24} Gulen Guler²² et al reported longer onset of sensory blockade might be due to use of Fentanyl as an adjuvant. Maximum level of sensory blockade was up to T4-T6 dermatome and time to reach maximum level was comparable in both groups. Same findings were observed by Aygen Turkmen²⁵ et al. and Gulen Guler²² et al who used 10 mg of LA with 15 µg of Fentanyl. We noted that onset of motor blockade was comparable in both groups. Same findings were noted in previous studies by A. Mehta²³ et al and Feroz Dar¹³ et al while Rashmi Duggal²⁶ et al, Gulen Guler²² et al.

In our study sedation was not significant in both the groups. Sedation with Clonidine is due to central action produced due to hyper-polarisation of excitatory neurons localized in the nucleus coeruleus²⁷. Respiratory rate and SpO₂ was well maintained. None of the patients in both the groups required treatment. Drowsiness was noted in 25% patients by Bhavini Bhushan²⁸ et al who used 60 µg Clonidine and Anjali Bhure²⁹ et al observed increased incidence of side effects like sedation, bradycardia, and dry mouth after 75 µg Clonidine indicating sedation is dose dependent.

In LSCS if mother is awake after delivery of baby, she is able to take care of her newborn which improves mother baby relationship, decreases prelacteal feeds, which has harmful effects²⁹. Mean Apgar score at 1 min and at 5 min was comparable in both groups. Our findings are same with that of Ranju Singh³⁰ et al, Nikhil Kothari²⁰ et al, Bhavini Bhushan¹⁵ et al and Bajwa² et al, In Bupivacaine and Clonidine group.

Basal and maximal heart rate was comparable in both the groups. Statistically significant bradycardia was seen in Bupivacaine group. Our findings are similar to that of Rashmi Duggal²⁶ et al and, Gulen Guler²² et al. while Ashok Das³¹ et al observed that that incidence of bradycardia was same in both the groups. Bradycardia could be due to baricity of Bupivacaine. Hyperbaric Bupivacaine is characterized by early onset of action, greater cephalic distribution causing high level of block and subsequent bradycardia and hypotension³².

Bradycardia in spinal anaesthesia is believed to result from blockade of sympathetic cardio accelerator (T1 to T4) fibres and decreased venous return to the heart. The decrease in preload is believed to be the most important cause of decrease in heart rate⁸. Bupivacaine reduces the cardiac contractility by blocking the calcium transport. So higher sensory blockade and Bupivacaine's cardio depressant action might be responsible for bradycardia. Levobupivacaine has less cardiotoxicity due to less affinity and strength of inhibitory effect on cardiac sodium channels and faster protein binding rate².

There was more fall in mean arterial pressure in group B (27%) compared to group L (9%). Our observations are similar to of Rashmi Duggal²⁶ et al, Ashok Das³¹ et al and Richa Chandra²⁷ et al, while Mantouvalou³³ et al observed higher incidence of hypotension (42.5% in group B and 17.5% in group L). It might be due to use of higher dose of LA 15mg compared to 9 mg in our study.

Two dermatome regression in both the groups were comparable. While P. Gautier et al³⁴, Rashmi Duggal et al²⁶ and Gulen Guler²² et al. P. Gautier³⁴ used LA with Sufentanil and Gulen Guler²² et al used LA with 15 µg of Fentanyl found that 2 dermatome regression was shorter. This shows that addition of Clonidine increases time to two dermatome regression.

First rescue analgesic was needed at 167.68 ± 3.84 min in group B and in group L it was needed at 165.73 ± 4.65 min. Our findings are similar with that of Bajwa² et al while Rashmi Dugga²⁶ et al observed earlier requirement of rescue analgesic (in B group it was at 103.47 ± 10.18 min and in L group it was at 80.03 ± 8.12 min) with fentanyl as an additive indicates that Clonidine as an adjuvant provides prolonged postoperative analgesia than other additives.

Incidence of vomiting was same in both the groups. 1 patient in each group had postoperative nausea. None of the patient had dry mouth or pruritus.

From all our observation we can conclude that intrathecal isobaric Levobupivacaine with Clonidine is better alternative to Bupivacaine for LSCS as it provides good quality of sensory and motor blockade, better cardiac stability without sedation in mother and any effect on baby.

VI. Conclusion

We observed that that isobaric Levobupivacaine has got comparable pharmacokinetic in onset and offset of sensory and motor block, less cardiovascular side effects and comparable postoperative analgesia to hyperbaric Bupivacaine, so we conclude that Levobupivacaine with Clonidine is a better choice in LSCS than Bupivacaine with Clonidine.

It provides good quality of intraoperative and prolonged postoperative analgesia with reduced dose of LA (9 mg) and without sedation and adverse effect on Apgar score of baby. Drawback of our study is that we compared hyperbaric Bupivacaine with isobaric Levobupivacaine as hyperbaric Levobupivacaine preparation is not available in the market. So it needs to be further investigated.

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