

A Comparative Study to Evaluate the Effects of Addition of Intrathecal Fentanyl with Clonidine To 0.5% Levo-Bupivacaine for Patients Undergoing LSCS.

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Abstract

Aim: To evaluate the effects of fentanyl and Clonidine added to levo-bupivacaine, for caesarean section in spinal Anaesthesia 2. To evaluate the duration of analgesia by comparing two groups. 3. To evaluate the hemodynamic effects, post-operative sedation and neonatal outcome between the two groups.

Materials and methods: Following approval by the institutions ethical committee, this prospective study was done at Dr SMCSI Medical College, Karakonam on 120 patients undergoing elective or emergency caesarean section after getting informed consent from each patient and explaining the procedure. This is a randomized prospective comparative study.

Statistical Analysis: The Randomization of three groups was done by matching their age, height, and weight of their demographic factors and base Physiological factors such as pulse rate, SBP, respiration rate and SPO2 by ANOVA (Analysis of Variance). The differences between them were interpreted by the Post hoc test of Bonferroni. Similarly, the time for maximum loss of sensation, the 2 segment regression time, pain free time and Apgar score

at 1 minute and 5 minutes were compared between groups by ANOVA.

Conclusion: 1. Intrathecal clonidine and the clonidine fentanyl combination, both improved quality of Intra Operative analgesia 2. An amalgamation of clonidine and fentanyl accentuated the intra operative analgesic potency and remarkably lengthened the post-operative analgesia in comparison with just mere clonidine. 3. Stable Intra Operative hemodynamics was obtained. 4. Duration of analgesia was prolonged.

Keywords: Clonidine, Levobupivacaine, hemodynamics; delivery.

Introduction

The aim of anesthesiology as a science is the removal of pain temporarily started initially with pain relief for surgeries, extending now to post operative pain relief, relief of chronic pain and cancer pain. Spinal anesthesia plays an important role of alleviating pain intraoperatively(1), extending sometime into postoperative period also. The entry of Corning's needle in 1885-into the subarachnoid space paved the way for the greatest leap into spinal anaesthesia. His words "Be the

density of this observation, what it may have seemed to me on the whole, worth recording (2).

This opened the prologue for the word “spinal anaesthesia”. Cocaine was the drug first used experimentally in dogs(3). In men the first spinal anaesthesia was conducted by “August Bier” on 16.8.1898 with cocaine 3 ml as 0.5% solution followed by Matas in America and Tuffier in France(4-6). Spinal anaesthesia for caesarean section has always enjoyed popularity as it eliminates the complication of pulmonary aspiration and avoids the problem of difficult tracheal intubation observed with general anaesthesia. Other advantages of this technique are its simplicity, rapid onset and dependability. The demonstration of opiate receptors in substantia gelatinosa of spinal cord (Yaksh and Rudy 1976) has created interest in the intrathecal administration of opiates(7).

The use of intrathecal morphine for providing postoperative pain relief in caesarean section was started in the year 1988 by Ezzaz Aboulesish et.al. The advantages of neuraxial opioids over neuraxial local anaesthetics are that it produces prolonged, intense, selective, segmental analgesia without motor blockade and sympathetic dysfunction(8-10). Opioids and local anaesthetics administered together have a potent synergistic analgesic effect(11). Intrathecal opioids enhance analgesia from sub therapeutic dose of local anaesthetic and make it possible to achieve successful spinal anaesthesia using otherwise inadequate doses of local anaesthetic(12,13,14).

The α_2 adrenergic mechanism have been exploited for more than 100 yrs. Veterinarians have used α_2 agonist for many years for regional analgesia, but the experience with these agents in humans, dates back only slightly more than 10 years(15). In 1984 Tamsen, Gordh after testing neurotoxicity in animals and then injected a parenteral

preparation of α_2 agonist clonidine, epidurally in two patients with chronic pain. Since then the complete toxicologic assessment in animal studies has suggested that clonidine is safe for Intrathecal use (4).

Materials and Methods

Following approval by the institutions ethical committee, this prospective study was done at Dr SMCSI Medical College, Karakonam on 120 patients undergoing elective or emergency caesarean section after getting informed consent from each patient and explaining the procedure. This is a randomized prospective comparative study.

Inclusion Exclusion Criteria

Term, parturient, ASA I an ASA IE who were fit to undergo spinal anaesthesia for caesarean section, age between 18-35 yrs., are selected. Patients with medical and obstetrical complications and impaired placental function were excluded; patients who were converted to general Anaesthesia were also excluded from the study.

Preoperative Preparation

Preoperatively all patients were seen by the anesthetist. The procedure was explained in detail and informed consent was obtained. No premedication was given. Patients were randomly allocated into 3 groups of 40 each.

- A- Control Group - Injection (0.5%) Levo-Bupivacaine 1.8 ml + 0.4 ml NS
- B- Study group 1 inj. (0.5%) Levo-Bupivacaine 1.8 ml + Clonidine 30 μ g) + 0.2 ml NS.
- C- Study group 2 Inj (0.5%) Levo-Bupivacaine 1.8 ml + Clonidine (30 μ g) +fentanyl (10 μ g)

Procedure

On arrival to operation theatre, basic monitoring was applied to all patients and basic pulse rate, blood pressure, oxygen saturation and respiratory rate were recorded (16).

TM

Intravenous line with 18 g cannula was established and preload of 250-300 ml of crystalloid was given to all patients. TM

Following resuscitative measures were kept ready before the start of the procedure: Boyles machine with oxygen source, laryngoscope and appropriate size blades, suction apparatus, endotracheal tubes, connectors, vasopressors (Ephedrine), naloxone and other emergency drugs. TM

The subarachnoid block was performed in right lateral position with 23 G spinal needle through L3, 4 space. Free flow of CSF was ensured before introducing the drug. The drug injected was according to the group assigned.

A- Injection (0.5%) Levo-Bupivacaine 1.8 ml + 0.4 ml NS

B- B- inj. (0.5%) Levo-Bupivacaine 1.8 ml + Clonidine 30 µg) + 0.2 ml NS.

C- C-Inj (0.5%) Levo-Bupivacaine 1.8 ml + Clonidine (30 µg) + fentanyl (10µg)

Drugs were measured in a sterile tuberculin syringe. Thorough aseptic precautions were taken during the addition of injection and making the final injection. Immediately after the intrathecal injection the patients were gently turned to supine position with leftward tilt by a wedge under right buttock. 100% oxygen was given through Magills breathing system till the delivery of baby (17).

Assessment of Patient and Recording of Data

Time of subarachnoid block was noted. Following observations were made

1. Time of onset of analgesia
2. Time of maximum cephalic spread
3. Upper level of sensory block.
4. Grade of motor block obtained according to bromage motor scale.

Bromage motor scale

0- No paralysis 1- Inability to raise extended legs. 2- Inability to flex the knee joint 3- inability to flex the ankle joint After the establishment of an adequate level of analgesia, the surgeons were allowed to operate and the time of beginning of surgery was noted.

Blood pressure, pulse rate, respiratory rate and Spo2 were monitored intraoperatively every 2 minutes for the first 10 minutes and every 5 minutes till the end of surgery. Patients were watched for side effects like hypotension, bradycardia, and vomiting, itching and respiratory depression.

Any hypotension (30 % fall from base line) was treated with oxygen, intravenous fluid and inj. ephedrine. Any bradycardia (pulse rate <60bpm) was treated with Inj.Atropine(18).

Nausea and vomiting were treated with inj. Metaclopramide.

Pruritis if complained was treated with inj. chlorpheniramine maleate.

Two segment regression time

Time to decrease from maximum sensory level to 2 segments below that level was noted. Sedation state was assessed by Brain and Ready sedation score 1. Awake and alert 2. Drowsy 3. Sleepy but easily arousable on call. 4. Sleepy but difficult to arouse. In the postoperative period, any complications to the mother and baby, especially that is attributed to opioids like respiratory depression, nausea, vomiting, pruritus were noted (one of the expected complication i.e., urinary retention could not be studied as all the patients were invariably catheterized).

Total duration of analgesia was taken as the period from the time of giving subarachnoid block till the patient's first requirement of analgesic medication. Pain was evaluated using 10 cm linear visual analogue scale (VAS)

with 0 for no pain and 10 for worst pain. If VAS was more than 6, supplementary analgesia was given and the study was assumed to be concluded at that point.

Foetal Outcome

Immediately after delivery, foetal well being was assessed by 1 mt. and 5 mt. Apgar score. During the postoperative period, the well being of the baby whether exclusively sedated or not and the nature of cry were noted. Reflexes like sucking reflex, rooting reflex and moro reflex were tested. Presence of seizures, if any, was also noted. All mothers and their babies were followed up till their discharge.

Statistical Method

Results were expressed as mean ± standard deviation. Statistical significance was determined by Anova table.

Observations And Results

The Randomization of three groups was done by matching their age, height, and weight of their demographic factors and base Physiological factors such as pulse rate, SBP, respiration rate and SPO2 by ANOVA (Analysis of Variance). The differences between them were interpreted by the Post hoc test of Bonferroni. Similarly, the time for maximum loss of sensation, the 2 segment regression time, pain free time and Apgar score at 1 minute and 5 minutes were compared between groups by ANOVA.

The intra and post-operative pulse rate and SBP at different intervals were compared between groups by ANOVA and interpreted the difference by Post hoc test of Bonferroni. The sensation level and sedation score were analyzed and interpreted by χ^2 test (Chi- square). The above statistical procedures were performed by the statistical package IBM SPSS statistics 20. The P - values less than 0.05 (P<0.05) were treated as significant in two tail condition.

Results

Randomization by group matching

The three groups were namely A (Levo-Bupivacaine only), B (Levo-Bupivacaine + intrathecal clonidine) and C (Levo-Bupivacaine + intrathecal fentanyl + Clonidine). Each group 40 Caesarean Sections were selected and data were collected before, during and after surgery. For Randomization the three groups were matched according to their selected and related demographic characteristics and base level Physiological characteristics.

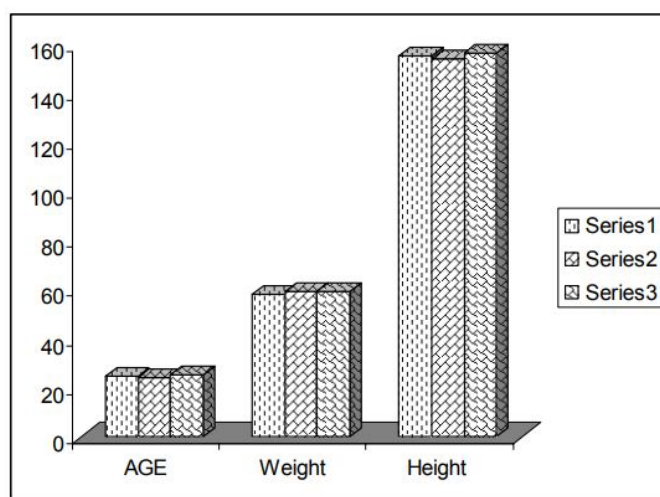


Table-1. Matching of three groups according to their demographic characteristics

Variables	Group	N	Mean	S D	ANOVA 'F'	Df	Significance
Age	A	40	24.6	4.4	1.092	2,117	P>0.05
	B	40	24.1	3.6			
	C	40	25.4	3.8			
Weight	A	40	58.5	5.0	0.319	2,117	P>0.05
	B	40	59.4	8.3			
	C	40	59.6	7.2			
Height	A	40	155.8	6.1	2.021	2,117	P>0.05
	B	40	154.2	4.2			
	C	40	156.8	6.4			

The three groups were matched in respect of their age, weight and height and shown in the table -1. They were not significantly differed between them (P>0.05).

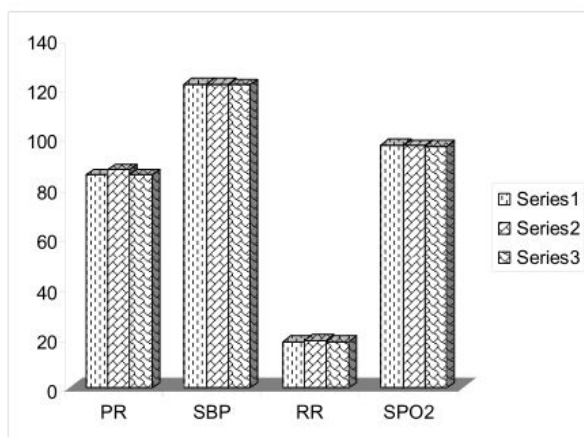


Table - 2 matching of three groups according to their Physiological characteristics

Variable	Group	n	Mean	SD	ANOVA 'F'	Df	Significance
Base PR	A	40	85.2	5.8	1.466	2,117	P>0.05
	B	40	87.3	7.2			
	C	40	85.2	5.9			
Base SBP	A	40	121.5	9.6	0.015	2,117	P>0.05
	B	40	121.6	10.2			
	C	40	121.2	7.9			
Base RR	A	40	18.4	1.0	2.831	2,117	P>0.05
	B	40	19.0	1.0			
	C	40	18.6	0.9			
Base SPO2	A	40	97.2	0.9	3.748	2,117	P>0.05
	B	40	96.9	1.0			
	C	40	96.6	0.8			

The Physiological characteristics of three groups were matched and stated in the above table -2. There was no significant differences were observed between groups in respect of their base Physiological characteristics (P>0.05).

Post-Operative Complications

Nausea and vomiting occurred in 5% of patients in group A and group B and 2.5% in group C and they were treated with inj. Metaclopramide.

Pruritus occurred in 2.5% of patients in group B and 7.5% of patients in group C and they were treated with inj.chlorpheniramine maleate.

For Randomization, the three groups were matched with their age, height, weight, pulse, SBP, respiration and SPO2 and found that there was no significant difference

between them (P>0.05). Hence, those groups were comparable groups. The sensory level T4 was obtained by A group 1(2.5%), B group 2(5%) and C group 10 (25%). The above attainment by C group was significantly greater than the other A& B groups (P 3.6±0.7) and A and C were equal (4.3±0.8 = 3.8±0.8). The two segment regression time for C group was significantly more than B and the same for B was significantly more than A.(101.1±8.1 > 89.5 ± 5.7 > 69.4 ±8.6 and P<0.001). The mean time of C was significantly greater than B (4.3±0.8 > 3.6±0.7) and A and C were equal (4.3±0.8 > 3.8±0.8). The two segment regression time for C group was significantly more than B and the same for B was significantly more than A.(101.1±8.1 > 89.5 ± 5.7 > 69.4 ±8.6 and P<0.001).

The Pulse rate at 5 minutes of B group was significantly greater than A and C groups. (93.5 ±7.6 > 88.2±7.6 &90.6 ±7.5) and that A group & C group was equal (88.2±7.6 = 90.6 ±7.5). At 15 minutes, the pulse rates of three groups were more or less equal. (92.5±9.1 = 95.5±8.5 = 91.8±8.3 and P>0.05). At 30 minutes the pulse rate of C group was lesser than B group (89.4 ±6.10.05).

The same of A vs. B and A vs. C were more or less equal (91.2±6.7 = 94.2 ±7.6 and 91.2 ±6.7 = 89.4±6.1 and P>0.05).

The SBP at 5 minutes of three groups were 120.6 ±11.4, 116.2 ±13.5 and 120.9 ± 8.8 minutes respectively. The means were not significantly differed (P>0.05). At 15 minutes, the mean SBP of A group was 102.4 ± 12.4 and the same was significantly lower than B and C groups (102.4 ± 12.4 < 115.8 ± 9.9 & 112.2 ±12.0 and P<0.01). At 30 minutes, the mean SBP of B group was significantly higher than 72 B group (115.1± 9.7 > 105.9 ±12.5 and P>0.05).

Hemodynamics

- There is less incidence of hypotension and Bradycardia, consistent with studies by Cang Fc, Chang PG et al. 73
- No respiratory depression occurred in any of these patients, consistent with study conducted by Lan et al (19).
- Pruritus developed in 12.5% in Group C, consistent with the study conducted by Cang Fc, Tsai YC et al.(20)

Fetal Outcome Low dose opioids do not have adverse effects on fetus and neonates (Ohen S, Arn et al) (Fernado F, Bonello E et al) (6).

Conclusion

The above study bears out the following facts.

1. Intrathecal clonidine and the clonidine fentanyl combination, both improved quality of Intra Operative analgesia.
2. An amalgamation of clonidine and fentanyl accentuated the intra operative analgesic potency and remarkably lengthened the post-operative analgesia in comparison with just mere clonidine.
3. Stable Intra Operative hemodynamics was obtained.
4. Duration of analgesia was prolonged.
5. The incidence of side effects due to additive effects of the drugs was minimal.
6. Fetal outcome was not altered.

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