Original Research Article

Comparative evaluation of the effects of addition of intrathecal fentanyl and clonidine added to 0.5% hyperbaric bupivacaine for lower segment caesarean section

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Abstract

Introduction: Spinal anesthesia plays an important role in alleviating pain intraoperatively, extending sometimes into the postoperative period also. Spinal anesthesia for cesarean section has always enjoyed popularity as it eliminates the complication of pulmonary aspiration and avoids the problem of difficult tracheal intubation observed with general anesthesia. Opioids and local anesthetics administered together have a potent synergistic analgesic effect. Intrathecal opioids enhance analgesia from a subtherapeutic dose of local anesthetic and make it possible to achieve successful spinal anesthesia using otherwise inadequate doses of local anesthetic.

Aim of the study: To evaluate the effects of fentanyl and clonidine added to Bupivacaine, for cesarean section in spinal Anesthesia and to evaluate the hemodynamic effects, postoperative sedation, and neonatal outcome between the two groups.

Materials and methods: This prospective study was conducted at Laksha Hospitals, Royapettah, Chennai in the year 2019-2020. 120 patients undergoing elective or emergency cesarean section after getting informed consent from each patient and explaining the procedure were included. This was a randomized prospective comparative study. 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%) Bupivacaine 1.8 ml + 0.4 ml NS, B- Study group 1 inj. (0.5%) Bupivacaine 1.8 ml + Clonidine 30 μg) + 0.2 ml NS, C- Study group 2 Inj. 0.5% Bupivacaine (1.8 ml) + Clonidine (30 μg) +fentanyl (10 μg).

Results: There were no significant differences were observed between groups in respect of their base Physiological characteristics (P>0.05). Group A was associated with T_7, B was associated with T_6, and C was associated with T_5. The above associations were statistically very highly significant (P<0.001). The mean time of A was 3.8±0.8 minutes with a mean time of B (3.6±0.7) and C (4.3±0.8) not differed significantly (P>0.05). But the means of B (3.6±0.7) and C (4.3±0.8) were differed significantly (P<0.01). Group A significantly differed from group B (P<0.05) and C was not significantly differed with groups A and C (P>0.05) at 5 minutes. At 15 minutes no significant difference was observed between the three groups (P>0.05). At 30 minutes B significantly differed with C (P<0.01) and at the same time A & B and A&C were not significantly different (P>0.05). The means of the three groups were 125.8±23.1, 178.2±14.4, and 221.6±28.4 respectively. They were significantly differed between them (P<0.001). Sedation level 1 was associated with groups A and B. The sedation level 2 was associated with group C. The above associations were statistically very highly significant (P<0.001). The Apgar score at 1 minute and 5 minutes were compared between the three groups in table 10. At 1 minute the Apgar was not significant between groups (P>0.05). At the Apgar scores of groups, A&B was significantly differed (P<0.05). The others A&C and B&C were not statistically significant (P>0.05).

Conclusion: Intrathecal clonidine and the clonidine fentanyl combination, both improved quality of Intra Operative analgesia. The combination of clonidine with fentanyl increased the intraoperative analgesic efficacy and significantly prolonged postoperative analgesia compared with clonidine alone. Stable Intra Operative hemodynamics was obtained. The duration of analgesia was prolonged. The incidence of side effects due to additive effects of the drugs was minimal. The fetal outcome was not altered.

Key words

Intrathecal Fentanyl, Clonidine, 0.5% Hyperbaric Bupivacaine, Lower Segment Caesarean Section.

Introduction

Spinal anesthesia for cesarean section has always enjoyed popularity as it eliminates the complication of pulmonary aspiration and avoids the problem of difficult tracheal intubation observed with general anesthesia. Other advantages of this technique are its simplicity, rapid onset, and dependability [1]. The advantages of neuraxial opioids over neuraxial local anesthetics are that it produces prolonged, intense, selective, segmental analgesia without motor blockade and sympathetic dysfunction. Opioids and local anesthetics administered together have a potent synergistic analgesic effect. Intrathecal opioids enhance analgesia from a subtherapeutic dose of local anesthetic and make it possible to achieve successful spinal anesthesia using otherwise inadequate doses of local anesthetic [2]. Although they ensure superior quality of analgesia, they are associated with many side effects such as pruritis, nausea, vomiting, urinary retention, and especially late and unpredictable respiratory depression. This has directed the research toward the use of newer and better local anesthetic additives for SA such as neostigmine, ketamine, midazolam, and clonidine [3]. Clonidine is an α_2 adrenergic agonist. As with lipophilic opioids, it is possible to achieve analgesia from systemic, epidural, or intrathecal administration of clonidine. Adding clonidine to intrathecal (IT) bupivacaine provides effective, prolonged, and dose-dependent analgesia with a consequently decreased requirement for supplemental analgesics [4]. It

has been used successfully as a sole analgesic for pain relief in labor and also as a sole analgesic for pain relief after cesarean section. As per the available literature, different dosages of clonidine, ranging from 30 to 150 μg have been used in SA for cesarean sections producing a variable duration of postoperative analgesia. No ideal dose has yet been found that can produce optimum analgesia with minimum side effects. Therefore, the present study has been planned to investigate whether the addition of two different dosages (50 and 75 μg) of IT clonidine to hyperbaric bupivacaine increases the duration of post-cesarean analgesia as compared to the addition of fentanyl [5].

Materials and methods

This prospective study was conducted at Laksha Hospital, Royapettah, Chennai. 120 patients undergoing elective or emergency cesarean section after getting informed consent from each patient and explaining the procedure were included. This was a randomized prospective comparative study. 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%) Bupivacaine 1.8 ml + 0.4 ml NS, B- Study group 1 inj. (0.5%) Bupivacaine 1.8 ml + Clonidine 30 μg) + 0.2 ml NS, C- Study group 2 Inj 0.5% Bupivacaine (1.8 ml) + Clonidine (30 μg) +fentanyl (10μg). The term, parturient, ASA I, and ASA IE who were fit to undergo spinal anesthesia for cesarean section, age between 18-35 yrs., was selected. Patients with medical and obstetrical complications and impaired placental function were excluded; patients who were converted to general anesthesia were also excluded from the study. 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. On arrival at the operation theatre, basic monitoring was applied to all patients and basic pulse rate, blood pressure, oxygen saturation, and respiratory rate were recorded. An intravenous line with an 18 g cannula was established and preload of 250-300 ml of crystalloid was given to all patients. Boyles machine with an oxygen source, laryngoscope, and appropriate size blades, suction apparatus, vasopressors (Ephedrine), naloxone, and other emergency drugs. The subarachnoid block was performed in the right lateral position with a 23 G spinal needle through L3, 4 space. Free flow of CSF was ensured before introducing the drug. Drugs were measured in a sterile tuberculin syringe.

Statistical method

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 SPO_2 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 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 conditions.

Results

The three groups were namely A (Bupivacaine only), B (Bupivacaine + intrathecal clonidine), and C (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.

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

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			

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			
BaseSBP	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			

Table – 3: Comparison of sensory level between three groups.

Max Sensory level	GROUPS				χ^2	df	Significance
	A	B	C	Total			
T4	1	2	10	13	76.795	8	P<0.001
T 5.	3	13	21	37			
T 6.	14	25	9	48			
T 7.	19	0	0	19			
T 8.	3	0	0	3			

Table – 4: Duration of time (minutes) to attain sensory blockade or level between groups.

Groups	n	Mean	SD	ANOVA 'F'	d.f	Significance	Significantly differed groups
A	40	3.8	0.8	8.003	2,117	P<0.01	C differed with B and not differed with A. A & B not differed.
B	40	3.6	0.7				
C	40	4.3	0.8				

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

Table – 5: Two- segment regression time (minutes) to attainsensory level between groups.

Groups	n	Mean	SD	ANOVA 'F'	d.f	Significance	Significantly differed groups
A	40	69.4	8.6	177.952	3,117	P<0.001	A B & C were differed significantly between them.
B	40	89.5	5.7				
C	40	101.1	8.1				

Table – 6: C omparison of pulse rates between groups at differentintervals.

Interval	Group	n	Mean	SD	ANOVA 'F'	df	Significance	Significantly differed groups
5 Min	A	40	88.2	7.6	4.370	3,117	P<0.01	A vs. B Significant A vs C, and B VS c not significant
	B	40	93.5	9.1				
	C	40	90.6	7.5				
15 Min	A	40	92.5	9.1	2.107	3,117	P>0.05	A B & C were not significant
	B	40	95.5	8.5				
	C	40	91.8	8.3				
30 Min	A	40	91.2	6.7	5.012	3,117	P<0.01	A vs. B Not Signify, B vs. C significant, A vs. C Not Signify
	B	40	94.2	7.6				
	C	40	89.4	6.1				

Table – 7: Comparison of SBP between groups at differentintervals.

Interval	Group	n	Mean	SD	ANOVA 'F'	df	Significance	Significantly Differedgroups
5 Min	A	40	120.6	11.4	2.136	3,117	P>0.05	Three groups have not differed significantly
	B	40	116.2	13.5				
	C	40	120.9	8.8				
15 Min	A	40	102.4	12.4	14.357	3,117	P<0.001	Significant. differed with B & C. but B & C not differed.
	B	40	115.8	9.9				
	C	40	112.2	12.0				
30 Min	A	40	105.9	12.5	7.838	3,117	P<0.01	A&B differedSig. A&C and B&C not differed.
	B	40	115.1	9.7				
	C	40	110.8	8.4				

Table – 8: Comparison of pain-free time (minutes) between thegroups.

Groups	n	Mean	SD	ANOVA 'F'	d.f	Significance	Significantly differed groups
A	40	125.8	23.1	177.955	3,117	P<0.001	All were differed significantly between them
B	40	178.2	14.4				
C	40	221.6	28.4				

Table - 3 associates the maximum sensory level of three groups. Group A was associated with T_7, B was associated with T_6, and C was associated with T_5. The above associations were statistically very highly significant (P<0.001).

Table – 9: Comparison of sedation between three groups.

Sedation level	Groups				χ^2	Df	Significance
	A	B	C	Total			
0	17	2	0	19	96.092	6	P<0.001
1	23	28	3	54			
2	0	10	29	39			
3	0	0	8	8			
Total	40	40	40	120			

Table – 10: Comparison of apgar scores at 1 minute and 5minutes.

Time	Groups	n	Mean	SD	ANOVA 'F'	Df	Significance	Significantly differed groups
1 Min	A	40	7.6	0.5	0.122	3,117	P>0.05	All were not significant
	B	40	7.5	0.6				
	C	40	7.5	0.7				
5 Min	A	40	9.1	0.5	4.790	3,117	P<0.05	A & B only significant. Others NS
	B	40	8.8	0.5				
	C	40	9.0	0.3				

The sensory time between the groups was compared in the **Table - 4**. The mean time of A was 3.8±0.8 minutes with a mean time of B (3.6±0.7) and C (4.3±0.8) not differed significantly (P>0.05). But the means of B (3.6±0.7) and C (4.3±0.8) were differed significantly (P<0.01).

The two-segment regression time between the groups was compared in the **Table - 5**. The means of the three groups differed significantly between them (P<0.001).

Table - 6 shows the pulse rate at different intervals like at 5 minutes 15 minutes and 30 minutes. Group A significantly differed from group B (P<0.05) and C was not significantly differed with groups A and C (P>0.05) at 5 minutes. At 15 minutes no significant difference was observed between the three groups (P>0.05). At 30 minutes B significantly differed with C (P<0.01) and at the same time A&B and A&C were not significantly different (P>0.05).

The SBP at the different interval between the groups were shown in the **Table - 7**. At 5 minutes, three groups were not significantly differed between them (P>0.05). At 15 minutes A significantly differed from the groups B and C (P<0.001). But B&C was not significantly differed between them (P>0.05). At 30 minutes A&B differed significantly (P<0.05). But A vs C and Bvs. C was not significantly different (P>0.05).

The pain-free time between the groups was compared in **Table - 8**. The means of the three groups were 125.8±23.1, 178.2±14.4, and 221.6±28.4 respectively. They significantly differed between them (P<0.001).

The sedation levels of the three groups were associated in the **Table - 9**. Sedation level 1 was associated with groups A and B. The sedation level 2 was associated with group C. The above associations were statistically very highly significant (P<0.001).

The Apgar score at 1 minute and 5 minutes were compared between the three groups in **Table - 10**. At 1 minute the Apgar was not significant between groups (P>0.05). At the Apgar scores of groups, A&B was significantly differed (P<0.05). The others A & C and B & C were not statistically significant (P>0.05).

Discussion

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, their groups were comparable. 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 the C group was significantly greater than the other A& B groups (P<0.001) [6]. 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 the 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) [7]. 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 A group C group was equal (88.2±7.6 = 90.6 ±7.5). At 15 minutes, the pulse rates of the 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 the C group was lesser than the B group (89.4 ±6.1<94.2 ±7.6 and P<.0.01). 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) [8]. The SBP at 5 minutes of three groups was 120.6 ±11.4, 116.2±13.5, and 120.9 ± 8.8 minutes respectively. The means were not significantly different (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) [9]. At 30 minutes, the mean SBP of the B group was significantly higher than the group (115.1± 9.7 > 105.9 ±12.5 and P<0.01). The mean SBP of A vs. C and B vs. C were not significant (P>0.05) [10]. The pain-free time of the C group was significantly greater than the B group and the B group was significantly greater than the A group (221.6±25.4 >178.2±14.4 >125.8±23.1and P<0.001) [11]. The sedation level of A (57.5%) and B (70%) groups was associated with level 1 and C (72.5%) was associated with the level. The improvement was very highly significant (P<0.001) [12]. The Apgar score between the three groups was not significant at 1 Minute, But at 5 minutes, A group was significantly improved than B (9.1±0.5 > 8.8 ±0.5 and P<0.05). The A vs. C (9.1±0.5 = 9.0±0.3) and B vs. C (8.8 ±0.5= 9.0±0.3) were not significant (P>0.05) [13, 14, 15].

Conclusion

The above study bears out the following facts. Intrathecal clonidine and the clonidine fentanyl combination, both improved quality of Intra Operative analgesia. The combination of clonidine with fentanyl increased the intraoperative analgesic efficacy and significantly prolonged postoperative analgesia compared with clonidine alone.

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