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Comparative Study of the Effects of Addition of Intrathecal Fentanyl and Clonidine Added To 0.5% Hyperbaric Bupivacaine for Lower Segment Caesarean

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Abstract

Background: To compare the analgesic activity of fentanyl and clonidine combined to Bupivacaine for caesarean section spinal anaesthesia. To compare hemodynamics, post-operative sedation, and newborn outcome. **Material and Methods:** 150 patients undergoing elective or emergency caesarean section were studied at Area Hospital, Dhone, Nandyal, Andhra Pradesh, India from October 2021 to September 2022. Randomly dividing patients into 3 groups of 50 each for injections. Physiological and demographic data, the start of analgesia, the peak of cephalic spread, the upper level of sensory block, and the grade of motor block were observed during surgery. The additional results' mean and SD were calculated. Statistical significance was determined using Anova tables. **Results:** Statistics showed that groups' greatest sensory levels were exceedingly highly significant (P 0.001). After five minutes in SBP, there were no significant differences between the three groups (P>0.05). At 15 minutes, group A considerably differed from groups B and C. (P 0.001). B&C, however, did not differ from one another significantly (P>0.05). At 30 minutes, A&B had a considerable difference (P 0.05). Sedation level 1 was associated to groups A and B. The second sedation level was tied to Group C. The aforementioned associations were statistically quite strong (P 0.001). **Conclusion:** Both intrathecal clonidine and the clonidine fentanyl combination improved the efficacy of intraoperative analgesia. Clonidine and fentanyl together significantly improved the intraoperative analgesic effects and sustained postoperative analgesia compared to clonidine alone. The operating room's hemodynamics were steady. Unexpectedly, the analgesia persisted longer. The medication's synergistic benefits virtually ever resulted in any side effects. The course of the developing foetus was unaltered.

Keywords: Sensory block, Spinal anestheia, Hemodynamic effect, Bromage.

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Introduction

Ralph Waters once said that pain relief is always acquired at a cost. Because only relief from pain can bring about all the enjoyment that people are capable of. John Dyrden The goal of anesthesiology as a science is to temporarily eliminate pain. This goal first began with pain relief during surgeries and has since expanded to include post-operative pain relief, treatment from chronic pain, and relief from cancer pain.[1-3] Within the operating room and occasionally into the recovery period, spinal anaesthetic is crucial for reducing discomfort. The most significant advancement in spinal anaesthesia was made possible by Corning's needle's penetration into the subarachnoid space in 1885. "Be the density of this observation," he said, "whatever it may have seemed to me overall worth recording.[3,4]

The prelude for the word "spinal anaesthesia" was thus opened. The substance that was initially tested on dogs was cocaine. The first spinal anaesthesia in males was performed by "August Bier" on 16.8.1898 using 3 ml of cocaine as a 0.5% solution. Matas in America and Tuffier in France then performed the procedure. For caesarean sections, spinal anaesthesia has traditionally been popular because it prevents pulmonary aspiration complications and the

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challenges associated with tracheal intubation that can arise with general anaesthetic.[5,6] This method's dependability, speedy start, and simplicity are further benefits. Interest in the intrathecal injection of opiates has grown since Yaksh and Rudy (1976) showed that the substantia gelatinosa of the spinal cord contains opiate receptors. Ezzaz Aboulesish et al. pioneered the use of intrathecal morphine to relieve postoperative pain following caesarean surgery in the year 1988. Opioids delivered via neuraxial injection have an advantage over neuraxial local anaesthetics in that they provide segmental analgesia that is powerful, persistent, and selective without causing motor blockage or sympathetic dysfunction.[6]

The term "subarachnoid block" refers to the temporary stoppage of nerve conduction within the spinal cavity caused by the injection of medications there. Preganglionic fibres, temperature, pain, proprioception, and ultimately motor fibres are the first senses to be blocked. Factors affecting the depth and length of anaesthesia The most crucial factor is the solution's specific gravity. the patient's position before and right after the injection, location of injection, Volume and concentration of the solution: Extending the impact by increasing the dose and concentration patient characteristics, such as age, height, and pregnancy, cardiovascular system effects. Due to the combined effects of autonomic denervation and vagal nerve innervation at higher levels, the CVS is the physiological response to spinal anaesthesia that is most significant. If a significant number of thoracic segments are blocked, betafibres are more sensitive than alphafibres, resulting in a stronger sympathetic block (zone of differential blockade) and a reduction in blood pressure. The Bainbridge reflex causes the blood pressure to drop, which causes bradycardia. Another component that contributes to bradycardia is blockade of the cardiac sympathetic fibres, which ranges from T1 to T4.[6,7]

Normal breathing is not inhibited. Intercostal muscles may become paralysed as a result of high spinal levels, but the phrenic nerve, maximal inspiratory volume, negative intrapleural pressure, and resting tidal volume remain unaffected. Hypoxia may accompany hypotension, which can be treated with a face mask of oxygen.[7,8] Spinal anaesthesia prevents the body's hormone and metabolic systems from reacting to pain signals coming from the surgical site. It reduces the release of rennin, aldosterone, catecholamines, cortisol, and other stress-related hormones. Antidiuretic hormone secretion and postoperative negative nitrogen balance are suppressed. In direct proportion to the drop in blood pressure, the hepatic blood flow falls. Hepatic oxygen extraction may be increasing. Autoregulation keeps renal blood flow constant, and it doesn't fall until mean arterial pressure falls below 50 mmHg. Vasodilation causes heat to escape to the chilly environment, resulting in hypothermia.[8]

The bladder's sphincters are not loosened, and the tone of the ureters is not significantly changed. Due to the paralysis of the nerve-erigentes, the penis frequently becomes engorged and flaccid (S2, 3). Since L2 and L3 contain little automatic fibres and their paralysis lasts longer than that of the bigger sensory and motor fibres, postspinal retention of urine may be moderately protracted. During pregnancy, uterine tone is unaffected. Spinal anaesthesia has no impact on the progression of labour or uterine blood flow in the absence of hypotension. The preganglionic fibres in the intestine are inhibited from T5 to L4. In sympathetic blocking, the small intestine therefore contracts with relaxed sphincters and peristalsis continues to function normally. Since the vagus is not inhibited, handling viscera causes discomfort and bradycardia.[8,9]

Administering opioids and local anaesthetics simultaneously has a powerful synergistic analgesic effect. Intrathecal opiates improve analgesia from subtherapeutic local anaesthetic doses and enable the successful induction of spinal anaesthesia with otherwise insufficient doses of local anaesthetic. More than 100 years have been spent using the 2 adrenergic pathway. While veterinarians have utilised 2 agonists for regional analgesia for a long time, human experience with these drugs is only around ten years old.[8,9] In 1984, Tamsen and Gordh administered a parenteral formulation of the 2 agonist clonidine, epidurally, to two

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patients with chronic pain following the testing of neurotoxicity in animals. Since then, a thorough toxicologic analysis of animal research has indicated that intrathecal administration of clonidine is safe.[9]

Material and Methods

After obtaining informed consent from each patient and discussing the operation, a randomised prospective trial including 150 patients undergoing elective or emergency caesarean sections was conducted at the Area Hospital, Dhone, Nandyal, Andhra Pradesh, India from October 2021 to September 2022. Three groups of 50 patients admitted each were randomly assigned to the patients. A- Injection in the Control Group (0.5%) 0.4 ml NS and 1.8 ml of buprenorphine Study group 1 injuries (0.5%) in B 0.2 ml NS plus 1.8 ml of bupivacaine and 30 g of clonidine. Study group 2 Inj (0.5%), C Bupivacaine 1.8 ml, 30 g of clonidine, and 10 g of fentanyl. Patient evaluation and data recording A subarachnoid block's onset time was noticed. The timing of analgesia's onset, the greatest cephalic spread, the upper degree of sensory block, and the grade of motor block determined using the Bromage motor scale were all observed. The mean and standard deviation were used to express the results. The Anova table was used to determine statistical significance.

Inclusion criteria

Term, parturient, and ASA I am an ASA IE who is between the ages of 18 and 35 and is healthy enough to have a caesarean section.

Exclusion criteria

1. Patients with placental dysfunction and medical and obstetric problems.
2. Patients who underwent general anaesthesia conversion.

Results

Table 1: Matching of three groups according to their demographic characteristics

Variables	Group	N	Mean	S D	ANOVA 'F'	Df	Significance
Age	A	50	24.6	4.4		2,117	
	B	50	24.1	3.6	1.092		P>0.05
	C	50	25.4	3.8			
Weight	A	50	58.5	5.0		2,117	P>0.05
	B	50	59.4	8.3	0.319		
	C	50	59.6	7.2			
Height	A	50	155.8	6.1			
	B	50	154.2	4.2	2.021	2,117	P>0.05
	C	50	156.8	6.4			

Age, weight, and height comparisons between the three groups are provided in [Table 1]. They did not differ significantly from one another (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	50	85.2	5.8	1.466	2,117	P>0.05
	B	50	87.3	7.2			
	C	50	85.2	5.9			
Base	A	50	121.5	9.6	0.015	2,117	P>0.05

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SBP	B	50	121.6	10.2			
	C	50	121.2	7.9			
Base RR	A	50	18.4	1.0	2.831	2,117	P>0.05
	B	50	19.0	1.0			
	C	50	18.6	0.9			
Base SPO2	A	50	97.2	0.9	3.748	2,117	P>0.05
	B	50	96.9	1.0			
	C	50	96.6	0.8			

The above [Table 2] matches and lists the physiological traits of the three groups. Regarding their fundamental physiological parameters, there were no discernible variations between groups (P>0.05).

Table 3: Comparison of sensory level between three groups

Max Sensory level	**GROUPS**				**$\chi 2$**	**df**	**Significance**
	A	**B**	**C**	**Total**			
T4	5	9	10	24	76.795	8	P<0.001
T 5.	11	21	27	59			
T 6.	15	20	13	48			
T 7.	18	0	0	18			
T 8.	1	0	0	1			

The three groups' top sensory levels are correlated in [Table 3] above. T7 was associated with the group A, T6 with the group B, and T5 with the group C. The correlations mentioned above were statistically extremely strong (P<0.001).

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	50	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	50	3.6	0.7				
C	50	4.3	0.8				

The sensory time between the groups were compared in the [Table 4]. The mean time of A was 3.8±0.8 minutes with mean time of B (3.6±0.7) and C (4.3±0.8) not differed significantly (P>0.05). But there was a significant difference between the averages of B (3.6±0.7) and C (4.3±0.8) (<P0.01).

Table 5: two segment regression time (minutes) to attain Sensory level between groups.

Groups	**n**	**Mean**	**SD**	**ANOVA 'F'**	**d.f**	**Significance**	**Significantly differed groups**
A	50	69.4	8.6	177.952	3,117	P<0.001	A,B&C were differed significantly between Them.
B	50	89.5	5.7				
C	50	101.1	8.1				

In [Table 5] above, the two segment regression times for the various groups were contrasted. Three groups' means varied significantly from one another (P<0.001)

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Table 6: Comparison of pulse rates between groups at different intervals:

Interval	Group	n	Mean	SD	ANOVA 'F'	df	Significance	Significantly differed groups
5 Min	A	50	88.2	7.6	4.370	3,117	P<0.01	A vs. B Significant AvsC, and BvsC not significant
	B	50	93.5	9.1				
	C	50	90.6	7.5				
15 Min	A	50	92.5	9.1	2.107	3,117	P>0.05	A,B & C were not significant
	B	50	95.5	8.5				
	C	50	91.8	8.3				
30 Min	A	50	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	50	94.2	7.6				
	C	50	89.4	6.1				

The pulse rate is displayed in the previous [Table 6] at several intervals, such as at 5 minutes, 15 minutes, and 30 minutes. At 5 minutes, group A significantly differed from group B (P<0.05), but group C did not statistically differ from both group A and group C (P > 0.05). There was no discernible difference between the three groups after 15 minutes (P>0.05). At 30 minutes, B and C had a substantial difference (<P0.01), but A&A and A&C had no difference (P>0.05).

Table 7: Comparison of SBP between groups at different intervals

Interval	Group	n	Mean	SD	ANOVA 'F'	df	Significance	Significantly differed groups
5 Min	A	50	120.6	11.4	2.136	3,117	P>0.05	Three groups were not differed significantly
	B	50	116.2	13.5				
	C	50	120.9	8.8				
15 Min	A	50	102.4	12.4	14.357	3,117	P<0.001	Significant. differed with B & C. but B & C not differed.
	B	50	115.8	9.9				
	C	50	112.2	12.0				
30 Min	A	50	105.9	12.5	7.838	3,117	P<0.01	A&B differed Sig. A&C and B&C not differed.
	B	50	115.1	9.7				
	C	50	110.8	8.4				

The SBP at various intervals between the groups were displayed in [Table 7] above. Three groups did not significantly differ from one another after five minutes (P>0.05). A significantly differed from groups B and C at 15 minutes (P<0.001). B&C, however, did not significantly differ from each other (P>0.05). A&B had a significant difference at 30 minutes (P<0.05). A vs. C and B vs. C, however, did not differ substantially (P>0.05).

Table 8: Comparison of pain free time (minutes) between the groups.

Groups	n	Mean	SD	ANOVA 'F'	d.f	Significance	Significantly differed groups
A	50	125.8	23.1	177.955	3,117	P<0.001	All were differed significantly between them
B	50	178.2	14.4				
C	50	221.6	28.4				

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In [Table 8] above, the groups' pain-free times were contrasted. The means for the three groups were, respectively, 125.8±23.1, 178.2±14.4, and 221.6±28.4. They significantly varied from one another (P<0.001).

Table 9: Comparison of sedation between three groups

Sedation level	GROUPS				$\chi 2$	Df	Significance
	A	B	C	Total			
0	27	8	0	35	96.092	6	P<0.001
1	23	26	11	60			
2.	0	16	28	44			
3	0	0	11	11			
Total	50	50	50	150			

Three groups' sedation levels were correlated in [Table 9] above. Groups A and B were connected with sedation level 1. Group C was connected to the sedation level 2. The correlations mentioned above were statistically extremely strong (P<0.001).

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	50	7.6	0.5	0.122	3,117	P>0.05	All were not significant
	B	50	7.5	0.6				
	C	50	7.5	0.7				
5 Min	A	50	9.1	0.5	4.790	3,117	P<0.05	A & B only significant. Others NS
	B	50	8.8	0.5				
	C	50	9.0	0.3				

[Table 10] compares the Apgar scores at 1 and 5 minutes for the three groups. The difference in group Apgar scores at 1 minute was not significant (P>0.05). There was a significant difference between the groups A and B's Apgar scores (P<0.05). A&C and B&C were not statistically significant (P>0.05) for the other two.

DISCUSSION

Age, height, weight, pulse, SBP, respiration, and SPO2 measurements were matched between the three groups prior to randomization, and it was discovered that there was no significant difference between them (P>0.05). As a result, the groups were similar to one another. A group 1 (2.5%), B group (2%) and C group (10%) all attained the sensory level T4. The aforesaid achievement of group C was significantly higher than that of groups A and B (P 0.001). C had a much longer mean time than B (4.3±0.8 > 3.6±0.7), whereas A and C had the same mean time (4.3±0.8>3.8±0.8). The two segment regression time was significantly longer for the C group than the B group and the same for the B group as the A group.[10,11] (101.1±8.1 > 89.5 ± 5.7 > 69.4 ±8.6 and P<0.001). The B group's pulse rate at 5 minutes was noticeably higher than that of the A and C groups. (93.5±7.6 > 88.2±7.6 & 90.6±7.5), whereas the A group C group had an equal score (88.2±7.6 = 90.6±7.5). Three groups' pulse rates were roughly equal at 15 minutes. (92.5±9.1 = 95.5±8.5 = 91.8=8.3 and P>0.05). At 30 minutes, the C group's pulse rate was lower than the B group's (89.4±6.1<94.2±7.6 and P<.0.01). Both A versus. B and A vs. C had roughly comparable results (91.2±6.7 = 94.2±7.6 and 91.2±6.7 = 89.4±6.1, P>0.05).[11,12]

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Three groups' SBPs at 5 minutes were 120.6 ±11.4, 116.2 ±13.5, and 120.9±8.8 minutes, respectively. There was no discernible difference in the means (P>0.05). At 15 minutes, the mean SBP of the A group was 102.4 ±12.4; this value was substantially lower than that of the B and C groups (102.4 ±12.4 <115.8 ±9.9 & 112.2 ±12.0, respectively, and P <0.01). At the 30-minute mark, the mean SBP of the B group was noticeably higher than that of the B group (115.1 ±9.7 > 105.9 ±12.5, P0.01).[13-15] A vs. C and B vs. C's mean SBP comparisons were not statistically different (P>0.05). B group considerably outlasted A group in terms of pain-free time (221.6 ±25.4 > 178.2± 14.4 > 125.8± 23.1 and P <0.001), while C group significantly outlasted B group. Levels 1 and 2 of sedation were related with the a (57.5%), b (70%) and c (72.5%) groups, respectively. The enhancement had a very high level of significance (P <0.001).[16,17]

The difference in Apgar scores between the three groups was not significant at 1 minute, but at 5 minutes, the A group had significantly better results than the B group (9.1±0.5 > 8.8±0.5 and P<0.05), while the differences between the A and C groups (9.10.5 = 9.00.3) and the B and C groups (8.8±0.5 = 9.0±0.3) were not significant (P>0.05). According to the aforementioned findings and discussions, the C group administration performs better than the two other groups, A and B groups, above.[17,18] The post-operative period has better analgesia quality, there is little variation in analgesia onset, consistent with studies, two segment regression took longer (C>B>A), consistent with studies, and analgesia duration increased (C>B>A).

CONCLUSION

The abovementioned study found that intrathecal clonidine and the clonidine fentanyl combination equally enhanced the quality of intraoperative analgesia, and that the combination of the two greatly sustained postoperative analgesia compared to clonidine alone. Hemodynamics within the operating room were stable. The analgesia lasted longer than expected. There were hardly any negative effects brought on by the medications' synergistic effects. Result for the foetus was unaffected.

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