Section: Anesthesiology

Original Research Article

A COMPARISON OF CLONIDINE AND FENTANYL AS AN ADJUVANT TO INTRATHECAL BUPIVACAINE FOR SPINAL ANAESTHESIA AND POSTOPERATIVE ANALGESIA IN PATIENTS UNDERGOING CAESAREAN SECTION

Bimal Prasad Sahu[1], Abhishek Patro[2], Lxmi Narayan Dash[3], Debadas Biswal[4]

[1]Assistant Professor, Department of Anesthesiology, SLN Medical College, Koraput, Odisha, India.
[2]Assistant Professor, Department of Surgery, SLN Medical College, Koraput, Odisha, India.
[3]Assistant Professor, Department of Anesthesiology, Bhima Bhoi Medical College, Balangir, Odisha, India.
[4]Associate Professor, Department of Anesthesiology, SLN Medical College, Koraput, Odisha, India.

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Corresponding Author:
Dr. Debadas Biswal,
Email: debadasbiswal@gmail.com

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Abstract

Background: Use of clonidine and fentanyl as adjuvant to bupivacaine in intrathecal block have been studied many times. Many variations are found about dose and efficacy of both adjuvants. Moreover, both adjuvants have their own side effects. Studies are on for the better adjuvant among both. The aim of this study is to evaluate the effects of clonidine and fentanyl as intrathecal adjuvant to bupivacaine heavy on duration and quality of spinal anaesthesia. **Materials and Methods:** A prospective randomised controlled trial of 80 patients of ASA grade I and II posted for elective lower segment caesarean section were divided into groups of 40 each. Group D received hyperbaric bupivacaine 10 mg(2ml) +50µg clonidine administered intrathecally. Group F received hyperbaric bupivacaine 10 mg (2ml) plus fentanyl 25µg administered intrathecally. Time of onset, the time to reach peak sensory and motor block, time taken for regression of sensory block to S2, motor block to Bromage 0 and duration of post-operative analgesia, haemodynamic parameters, side effects were recorded. **Result:** The addition of bupivacaine spinal block with 50µg intrathecal clonidine produces a significant longer duration of sensory (189.52±8.41 vs 155.16±4.55) (p value <0.001) and motor block (189.09±6.01 vs 180.31±4.58) (p value<0.001) than 25µg intrathecal fentanyl. Time for first dose of rescue analgesic was delayed in Group D (590.84±4.10) in comparison to group F (434.95±19.06) which was statistically significicant (p<0.001). Sedation was more in Group D than Group F (p value <0.001). Other side effects and haemodynamic characteristics were comparable in both groups. **Conclusion:** Clonidine provides a prolonged duration of analgesia, but fentanyl gives good analgesia with less sedation when used as an adjuvant to bupivacaine for intrathecal analgesia.

INTRODUCTION

Bupivacaine an amide local anaesthetic is commonly used in spinal anaesthesia. It has some limitations like it may be short and limited duration of action, need higher doses of rescue analgesia. Higher doses of bupivacaine can be used to avoid above limitations but with higher toxicity. Many studies have proven that adjuvant like opioids, dexmedetomidine, midazolam, clonidine prolong the effect of spinal anaesthesia.

Fentanyl is a commonly used opioid which produces selective spinal analgesia by acting on opioid receptors µ1 and µ2. It is 4 times more potent than morphine intrathecally. It is highly lipophilic and has rapid onset and short duration of action. It has little rostral spread which causes less respiratory depression. Side effects like bradycardia, hypotension, pruritus, urinary retention, respiratory depression, sexual dysfunction led to search for ideal non opioid adjuvants like clonidine. It is a partial α2 receptor agonist with prolonged sensory and motor block and post operative analgesia. It has

advantages like decreased post spinal shivering, emesis, anxiolysis, sedation, pruritus, and respiratory depression.

Studies have different results about efficacy of intrathecal clonidine and fentanyl prolonging postoperative analgesia. Clonidine is more potent in prolonging post operative analgesia. Khezeri et al, Bajwa et al, Chhabra et al.[1-3] 1st dose of rescue analgesia were comparable in study by Mahendru et al.[4] Bathari et al,[5] found that intrathecal fentanyl was better than clonidine in knee arthroscopy. As above studies differ in opinion about characteristics of sensory and motor block, the present study is carried to evaluate the effects of clonidine and fentanyl as adjuvant to hyperbaric bupivacaine in patients undergoing caesarean section. The prime aim is to compare and evaluate the sensory and motor action and time of 1st rescue analgesia in clonidine and fentanyl respectively. The secondary objectives are the haemodynamic status and side effects.

MATERIALS AND METHODS

A randomised control trial was carried out was carried out after obtaining approval from hospital ethics committee and written informed consent from the patients. Total 80 parturient between age of 20-35 years age of ASA Grade I and Grade II posted for elective lower segment caesarean section were selected. Patients with complicated pregnancy including PIH, placenta previa, abruptio placentae, severe systemic disorders like diabetes mellitus,hypertension and heart disease, allergy to bupivacaine, fentanyl or clonidine, all known contraindications for spinal anaesthesia such as spinal deformity, increased ICP, haemorrhagic diathesis were excluded from the study. They were divided randomly into 2 groups (n=40) using computer generated programme. The intrathecal drug formula was prepared by a separate anaesthesist and the anaesthesists who administered the drug were blinded to the group allocation.

Group D-Hyperbaric bupivacaine 10 mg(2ml) +50µg clonidine administered intrathecally.

Group F- Hyperbaric bupivacaine 10 mg(2ml) +fentanyl 25µg administered intrathecally.

Total volume was made 2.5 ml by addition of normal saline. All patients were kept nil per orally for 6 hours before surgery. Patients were premedicated with intravenous ondansetron 4mg. Preloaded with 500ml of ringer solution after securing intravenous cannula. Pre-operative parameters like pulse rate, oxygen saturation and blood pressure were recorded. Under all aseptic precaution spinal anaesthesia were performed at the level of L3-L4 intervertebral space in sitting position using midline approach by 25 G quincke needle. The drug was injected slowly over 10-15 seconds. Vitals were recorded every 2 min upto 10 min and every 5 min thereafter till 20 min. Beyond 20 min vitals were recorded every 20 min till time of discharge from PACU. Hypotension was defined as 20% decrease in baseline SBP, bradycardia when heart rate <60/min and treated with intravenous ephedrine and atropine respectively. The level and duration of sensory anaesthesia was tested by pin prick method and motor block by modified bromage scale.

Bromage 0-Patients able to move hip,knee and ankle.

Bromage 1-unable to move hip but able to move knee and ankle.

Bromage 2-unable to move hip and knee but able to move the ankle.

Bromage 3-Unable to move hip,knee and ankle.

The time to onset of analgesia at T10, time to maximum cephalad spread of analgesia and regression of analgesic level to S2 dermatome were measured. Motor block was measured from peak bromage 3 to regression to bromage 0. Duration of analgesia was recorded from intrathecal injection to 1st rescue analgesia administration. Side effects like nausea, vomiting, shivering, pruritus, sedation, hypotension, bradycardia, and respiratory depression were recorded. VAS (visual analogue scale) was used to access post-operative pain (0=no pain to 10=severe pain). Diclofenac sodium was given as rescue analgesic if VAS was more than 4.

Power analysis of 40 patients achieve a power of 80% and significance level 0.05 required to detect a difference. Interpretation of data was carried out by using Microsoft excel software and SPSS version 19. Data is represented as mean ± standard deviation for continuous data and frequency and median for non-parametric data. Analysis of variance were used to compare two groups, adverse effect by chi square test. $P<0.05$ was considered significant and $p<0.01$ was highly significant.

RESULTS

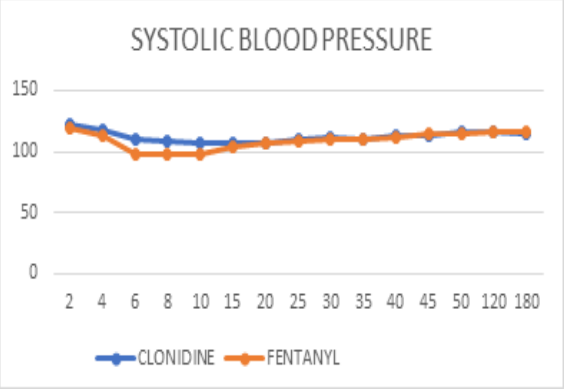

Figure 1: Change in Systolic, Diastolic and mean arterial blood pressure.

The SBP showed an initial decrease in both groups and there after it was stabilised but the changes were not statistically significant when compared at the corresponding intervals.

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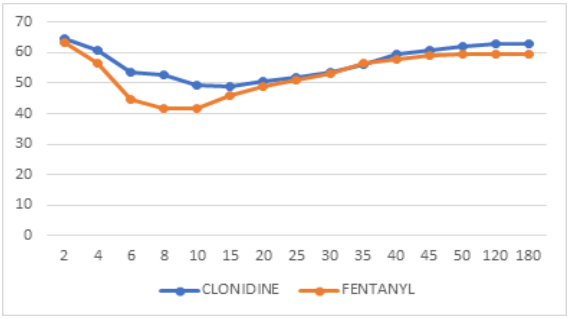

Figure 2: Diastolic Blood Pressure

Diastolic Blood Pressure - The preoperative DBP was 65±5.19 mm Hg,64.86±3.94 mm Hg in group D and F respectively. Variations in DBP was comparable and not statistically significant.

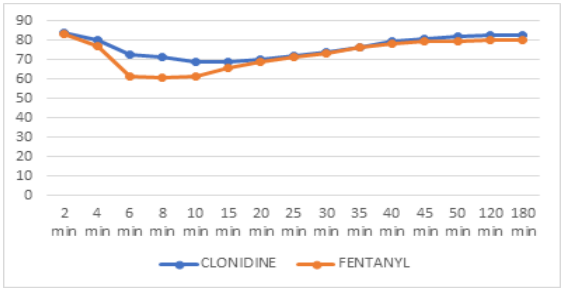

Figure 3: Mean Arterial Pressure

Mean arterial Pressure- The preoperative MAP was 85.58±5.24 mm Hg, 85.33±3.07 mm Hg in group D and F respectively. Variation in MAP was comparable in both the groups and was not statistically significant.

Table 1: Both groups were comparable with respect to their demographic profile.

Variables	Clonidine Group	Fentanyl Group	P Value
Age (in years)	27.60±3.92	26.99±3.97	0.574
Height(in cms)	147.98±4.58	148.65±4.18	0.816
Weight (in kgs)	60.74±4.84	64.97±8.21	0.006
Gestational age (in wks)	38.10±1.11	38.02±1.01	0.640
MAP (in mm of Hg)	84.96±4.96	84.84±3.01	0.795
HR (in Bpm)	83.50±5.50	82.22±5.12	0.457
BMI	27.62±2.87	28.88±3.69	0.019

Table 2: Comparison of factors related to delivery process.

Variables	Clonidine Group	Fentanyl Group	Chi-square value	P value
Gestational age <38 wks ≥38 wks	28(45.8) 12(52.4)	21(54.2) 20(26.2)	0.272	0.602
Duration of labour <5hr ≥5hr	19(43.9) 21(51.3)	22(56.1) 18(26.2)	0.436	0.509
Duration of surgery <50min ≥50 min	20(38.8) 20(61.3)	29(61.2) 11(38.7)	3.860	0.049
Blood loss <750ml ≥750ml	24(45.1) 16(51.7)	27(54.9) 13(48.3)	0.325	0.568

Table 3: The mean duration of labour, surgery and blood loss have no statistically significant difference.

Variables	Clonidine group	Fentanyl group	P value
Duration of labour	5.63±1.55	5.14±1.42	0.146
Duration of surgery	47.24±4.45	45.58±3.45	0.051
Blood loss	746.05±91.84	751.19±70.26	0.778

Table 4: Comparison of sensory, motor block and duration of analgesia.

Time	Clonidine Group	Fentanyl Group	P value
Onset of sensory block	0.93±0.14	0.88±0.14	0.193
Time for peak sensory block	6.95±1.30	6.73±1.17	0.431
Duration of sensory block	189.52±8.41	155.16±4.55	<0.001
Onset of G3 motor blockade	1.69±0.33	1.48±0.26	0.003
Duration of G0 motor blockade	189.09±6.01	180.31±4.58	<0.001
Rescue analgesia	590.84±4.10	434.95±19.06	<0.001

There was no statistically significant difference in onset of sensory block, grade 3 motor block, onset of peak sensory block but statistically significant difference was observed in duration of sensory block, weaning of motor block and 1st dose of rescue analgesia.

Table 5: Comparison of complications.

Variables	Clonidine Group	Fentanyl Group	Chi-square value	P value
Bradycardia NO YES	 33(45.1) 7(66.7)	 38(54.9) 2(33.3)	1.494	0.222
Hypotension NO	 31(44.6)	 36(55.4)	1.157	0.282

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YES	9(60.0)	4(40.0)		
Itching NO YES	 40(9.4) 0(0)	 37(50.6) 3(100.0)	2.820	0.093
Nausea/Vomiting NO YES	 37(46.2) 3(100)	 40(100.0) 0(0)	2.267	0.132
Resp. Depression NO	 40100)	 40(100)	_	---
Sedation No Yes	 30(40.8) 10(100.0)	 40(100) 0(0)	11.208	0.001

Hypotension-9 patients in group D and 4patients in group F developed hypotension which was not statistically significant upon intergroup analysis($p>0.05$). Bradicardia-7 patients in group D and 2 patients in group F had an episode of bradycardia. No significant difference was found. Respiratory Depression-No patients demonstrated any respiratory depression. Nausea and vomiting- 3 patients in group D and no patients in group F developed vomiting in perioperative period. No statistically difference was found. ($p>0.05$). Pruritus- No patients in group D and 3 patients in group F developed pruritus in perioperative period. Both groups are comparable without any significant statistical difference. Sedation- 10 patients in group D and no patients in group F was sedated which was statistically significant.

DISCUSSION

Mean time taken for sensory block to regress was significantly longer in group D (189.52±8.41 min) as compared to group F (155.16±4.55 min). Similarly, the mean duration of analgesia lasted significantly longer in group D (590.84±4.10 min) than in group F (434.95±19.06 min). This implies that both fentanyl and clonidine prolong the duration of postoperative analgesia and it is more with clonidine than fentanyl, Benhamou D et al.[6] In our study there was no significant difference in time to reach peak sensory block level in both groups. This can be explained due to larger volume of drugs (2.5ml) used. Duration of sensory block was comparable with Hunt et al. and Sethi et al.[7] All patients in our study demonstrated motor blockade grade 3 as per bromage scale. Time for 1st rescue analgesia consumption decreases in a dose dependant manner when intrathecal fentanyl was used in doses of 0.25µg/kg, 0.5µg/kg and 0.75 µg/kg by Belzarena.[8]

In our study no patient in group D and 3 patients in group F developed pruritus and was statistically insignificant. This is comparable with Shawagfeh et al who reported 6% incidence of pruritus. Lavand'homme et al showed higher incidence of hypotension and sedation with clonidine 150µg group than clonidine 75 µg.[9-11] 10 patients of group D and no patients of group F were sedated which was significant statistically. 9 patients in group D and 6 patients in group F developed hypotension which was statistically not significant after intergroup analysis. Our study is similar to Singh H10 who observed the effect of intrathecal bupivacaine alone and in combination with fentanyl in two different doses 12.5µg and 25µg of fentanyl respectively. Prolonged duration of analgesia due to fentanyl in our study was different to other studies. Similarly prolonged duration of analgesia due to clonidine in our study was also different to other studies. This was expected considering the different doses of clonidine, fentanyl or bupivacaine. Bajwa S J2 who used 9 mg of bupivacaine did not observe bradycardia with 45µg clonidine and Sethi BS7 who used 1µg/kg intrathecal clonidine had also very few incidences of hypotension and bradycardia requiring intervention. Biswas et al and Agrawal et al observed similar haemodynamic stability with 12.5µg and 25µg of intrathecal fentanyl. The overall haemodynamic stability in both groups throughout the surgical procedure in our study conforms this. Only two patients had significant bradycardia, one of which got corrected on its own and another patient with i.v atropine 0.6mg.

CONCLUSION

To conclude, Intrathecal addition of 50µg clonidine to bupivacaine gives longer duration of postoperative analgesia than 25µg of fentanyl but with higher degree of sedation. Fairly good analgesia is observed with less sedation with 25µg fentanyl, and it may be recommended as a better option when sedation is not desirable. When some amount of sedation is acceptable or required addition of 50 µg of clonidine which gives excellent analgesia with negligible haemodynamic complications may be recommended.

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