ORIGINAL RESEARCH PAPER | Medical Science | Volume : 6 | Issue : 7 | July 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 74.50

To Evaluate the Effect of Addition of Clonidine and Fentanyl to Hyperbaric Bupivacaine 0.5% Intrathecally in Patients Undergoing Lower Segment Caesarean Section.

KEYWORDS: Clonidine, fentanyl, lower segment Caesarean section, spinal anaesthesia.

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ABSTRACT *BACKGROUND: The aim was to compare clonidine and fentanyl as additives to hyperbaric bupivacaine 0.5% intrathecally in patients undergoing lower segment Caesarean section with regard to their efficacy and safety for spinal anaesthesia, and post operative analgesia. MATERIAL AND METHOD: Sixty parturients of ASA grade I and II posted for elective and emergency Caesarean section were chosen for this prospective double blind study and randomly allocated into three equal groups of twenty each. Group A received 0.5 ml of clonidine (75 µg), Group B received 0.5 ml of fentanyl (25 µg), Group C received 0.5 ml of normal saline, as an adjuvant to 2 ml hyperbaric bupivacaine 0.5 % (10 mg) intrathecally. Block characteristics such as time of onset, sensory, motor levels, duration of analgesia, need of rescue analgesia, maternal side effects and foetal outcome were evaluated. For rescue analgesia injection tramadol 100 mg was given. RESULTS: There was no statistical significance (P>0.05) for sensory and motor onset and peak sensory and peak motor effect among the groups. Time of rescue analgesia was significantly prolonged in clonidine group (677.7±179.3 min) than fentanyl group (345 ± 62.8 min) and lowest in control group (160±20.1). No significant change on baby's APGAR score in either group. Side effects like hypotension and bradycardia were observed more in clonidine group than fentanyl and control groups. CONCLUSION: Adding clonidine or fentanyl to bupivacaine prolongs the duration of spinal anaesthesia and analgesia. With clonidine, more prolonged duration of analgesia than fentanyl, without severe side effects, was observed.*

INTRODUCTION

Spinal anaesthesia has increasingly become the technique of choice for lower segment Caesarean section.[1] It offers the advantages of simplicity of technique [2,3], rapid onset and dense nerve blockade, producing uniform sensory and motor blockade as compared to epidural anaesthesia.[4,5,6] This regional anaesthesia is preferred as it allows the mother to be awake and interact immediately with her baby.[7] Advantages of regional anaesthesia include the absence of risks of general anaesthesia like pulmonary aspiration of gastric contents and accidental oesophageal intubation. [8] Its main disadvantage is related to its limited duration of action and hence lack of long lasting post operative analgesia. Spinal anaesthesia and analgesia can be prolonged by using adjuvants to local anaesthetics like adrenaline, midazolam and neostigmine. Intrathecal opioids, like fentanyl citrate are very potent adjuvants. Fentanyl has rapid onset and short duration of action with less incidence of respiratory depression [9], pruritis, nausea, vomiting, activation of herpes labialis, urinary retention and other side effects of opioids. Clinical studies have suggested that intrathecal clonidine (α_2 adrenoceptor agonist) prolongs sensory as well as motor block of spinal anaesthesia and provides post operative analgesia.[10] Other beneficial effects are anti-emesis, reduced post spinal shivering, anxiolysis and sedation. In this study, we evaluated the effects of addition of intrathecal clonidine and fentanyl to bupivacaine in patients undergoing Caesarean section, and effects on newborns by assessment of APGAR score; observed intra-operative quality of block, post-operative pain relief and noted any maternal and fetal side effects.

MATERIAL AND METHOD

After obtaining approval from the institutional ethical committee, along with written and informed consent, 60 parturients of age group between 18-35 years, ASA Grade I and II posted for lower segment Caesarean section under subarachnoid block, were enrolled in this prospective, randomized and double blind study. Exclusion criteria were complicated pregnancy including pregnancy induced hypertension, placenta praevia, abruption placenta, severe systemic disorders including diabetes, hypertension, heart disease, allergy to bupivacaine or clonidine and all known contraindications for spinal anaesthesia, such as spine deformity, increased intracranial pressure, neurological disorders, haemorrhagic diathesis, or infection at puncture site.Selected patients were secured with 20G venous cannula and routine monitors (pulse oximetry, non-invasive blood pressure, electro-cardiography) were attached before performing the procedure. The study medication was prepared by personnel not involved in the study to ensure blinding of the anaesthesiologist. Investigator who collected post-operative data was also blinded to the study drug administered.All these patients were pre-medicated with inj. ondansetron 4 mg intravenously prior to spinal anaesthesia. Patients were preloaded with Lactate Ringer solution 10-15 ml/kg body weight. Pre-operative parameters like pulse rate, blood pressure, oxygen saturation and respiratory rate were noted. Spinal anesthesia was given with 26G Quincke's needle in sitting position.

Under all aseptic precautions and depending upon the groups, respective agents were given intrathecally.

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GROUP A (STUDY GROUP)
In this group, patients were given 2.0 ml of hyperbaric bupivacaine 0.5% (10 mg) with 0.5 ml of clonidine (75 µg) intrathecally.

GROUP B (STUDY GROUP)
In this group, patients were given 2.0 ml of hyperbaric bupivacaine 0.5% (10 mg) with 0.5 ml of fentanyl (25 µg) intrathecally.

GROUP C (CONTROL GROUP)
In this group, patients were given 2.0 ml of hyperbaric bupivacaine 0.5% (10 mg) with 0.5 ml of normal saline intrathecally.

Pulse and blood pressure was measured at 5, 10, 15 minutes and then every 15 minutes till 45 minutes.Sensory block was tested by pinprick method. Degree of motor blockade was assessed by modified Bromage scale[11] (0 = no impairment, 1 = unable to raise extended legs but able to move knees and ankles, 2 = unable to raise extended legs as well as flex knees, able to move feet, 3 = not able to flex ankle, feet, or knees).

In the intra-operative period, patients were closely monitored for pulse rate, respiratory rate, SpO2, blood pressure and blood loss. Whenever needed, blood loss was replaced with whole blood. Any side effects such as nausea, vomiting, pain, shivering, pruritus, sedation, hypotension, bradycardia and respiratory discomfort was noted, and treated with appropriate drugs. Ringer lactate & 5% Dextrose with normal saline were used for i.v. infusion throughout.

After the delivery, neonates were assessed by using APGAR score at 1, 5 minutes. Oxytocin 20 units was added to Dextrose with normal saline after the delivery of the anterior shoulder.

Residual sensory blockade was monitored and its wearing off time was noted (when sensation to pinprick regressed by two dermatomal segment). Residual motor blockade was monitored and its wearing off time was noted (when patient starts to lift legs against gravity). Post-operative analgesic drugs were given when patients VAS score reaches >7. (This will be taken as the time of wearing off of analgesia), and the time of injection of first analgesic drug (i.e., inj. tramadol 50 mg iv) was noted.

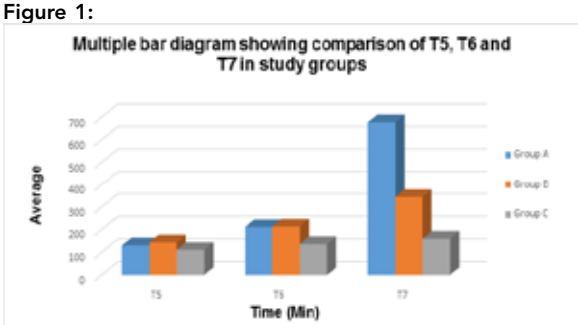
Following observations were made:
T0 = Time of Spinal Anesthesia
T1 = Time of onset of Sensory Block
T2 = Time of onset of Motor Block
T3 = Time to reach maximum sensory level
T4 = Time to reach maximum motor level
T5 = Time to two segment regression of sensory level
T6 = Time of wearing off of motor block
T7 = Time of first dose of post-operative rescue analgesia
Baby APGAR score was monitored at 1, 5 minutes using APGAR score reading.
At the end of study, results in all the three groups were tabulated and subjected to statistical analysis by applying Statistical Package for Social Sciences (SPSS) software version 11 by the Analysis Of Variance (ANOVA) test. The ANOVA test can be used in cases where there are more than two groups. The F-test was used for comparisons of the components of the total deviation. Finally, the results in the three groups were compared to draw the conclusion.

RESULTS
There was no statistically significant difference between the three groups with respect to age, weight, ASA grade, pulse rate and SpO_2.There was no statistical significance (P>0.05) for sensory and motor onset, and peak sensory and peak motor effect among the groups. For 2-segment sensory regression in Group A- Clonidine at 131.15±28.23 min, Group B- Fentanyl at 143.7±23.49 min, Group C- Control at 111±1539 min (P<0.0001), there is highly significant difference between the groups. It is implying that Group B- Fentanyl took maximum time while Group C- Control took the least amount of time for regression of 2 segments. (Table 1)For wearing off of motor block in Group A- Clonidine at 211.3±59.53 min, Group B- Fentanyl at 213.5±38.94 min, Group C- Control at 136.55±13.13 min (P<0.0001), there is highly significant difference between the groups. It is showing that Group B- Fentanyl took maximum time while Group C- Control took the least time for motor regression. (Table 1)For time to rescue analgesia in Group A- Clonidine at 677.7±179.3 min, Group B- Fentanyl at 345±62.8, Group C- Control at 160±20.1 min (P<0.0001), there is highly significant difference between the groups. It is implying that Group A- Clonidine is most effective while Group C- Control is the least effective as an analgesic. (Table 1)

Table 1:

Time (min)	Group AMean±SD (n=20)	Group B Mean±SD (n=20)	Group C Mean±SD (n=20)	F Value	P Value
T5	131.15±28.23	143.7±23.49	111±15.39	10.30	<0.0001
T6	211.3±59.53	213.5±38.94	136.55±13.13	22	<0.0001
T7	677.7±179.3	345±62.8	160±20.1	113.14	<0.0001

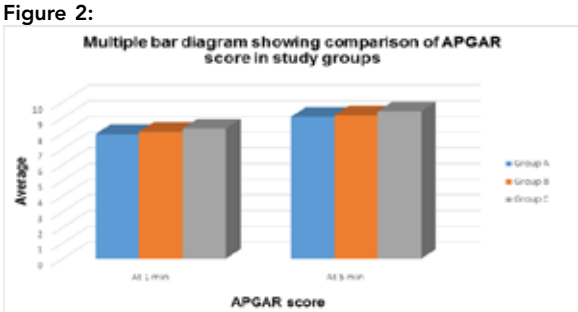
Figure 1:



There is no significant difference in APGAR score amongst the groups for 1 and 5 minutes. (Table 2)
Table 2:

APGAR score	Group A Mean±SD (n=20)	Group B Mean±SD (n=20)	Group C Mean±SD (n=20)	F Value	P Value
At 1 min	7.95±0.76	8.1±0.79	8.3±0.80	1.01	>0.05
At 5 min	9.05±0.76	9.15±0.74	9.4±0.50	1.41	>0.05

Figure 2:



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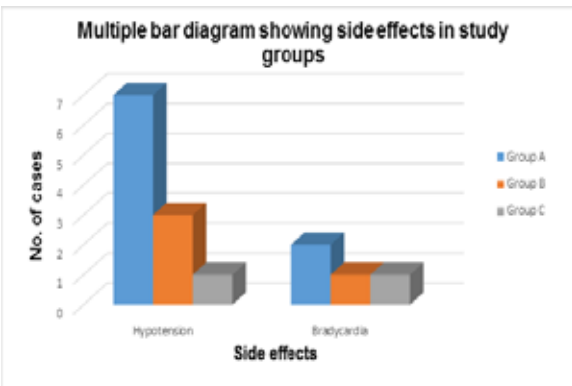
Hypotension was observed in 7 out of 20 cases in Group A- Clonidine, 3 out of 20 cases in Group B- Fentanyl, and 1 out of 20 cases in Group C- Control group. It is implying that Group A- Clonidine had more incidences of hypotension and the difference is statistically significant (P<0.05). Considering bradycardia, no statistical association was seen amongst the groups. (Table 3)Other side effects sedation, nausea, vomiting and pruritus were not observed.

Table 3:

Side Effects	Group A (%)	Group B (%)	Group C (%)	P Value
Hypotension	7 (35)	3 (15)	1 (5)	<0.05
Badycardia	2 (10)	1 (5)	1 (5)	>0.05

Figure 3:



DISCUSSION

Spinal anaesthesia is the safest regional anaesthesia technique for LSCS. But its effects on analgesia are limited. Many adjuvants like adrenaline, midazolam, neostigmine have been used with local anaesthetics for prolonging intra-operative and post-operative analgesia. But they have their own side effects.In our study, we used clonidine (75 µg) and fentanyl (25 µg) as an adjuvant with 0.5% bupivacaine. Fentanyl citrate (synthetic opioid) is a µ receptor agonist. It produces profound dose dependent analgesia, due to its action on both supraspinal and spinal opioid receptors.Clonidine is a partial α_2 adrenoceptor agonist drenoreceptor agonist used intrathecally and has well established record of efficacy and safety.[12] The local anaesthetic acts by blocking sodium channels, whereas α_2 adrenoceptor agonist produces analgesia by depressing the release of C fibre transmitters by hyperpolarization of post-synaptic dorsal horn neurons.[13,14] Its other benefits are anti-emetic effects, reduced post-spinal shivering, anxiolysis and sedation.In 2006, Bano F, Sabbar S, Zafar S, Rafeeq N et al15 conducted a study to compare the effect of intrathecal fentanyl added to hyperbaric bupivacaine on the onset, duration and quality of spinal anesthesia. Sixty parturients undergoing elective caesarian section were randomly divided in two groups by using 0.75% hyperbaric bupivacaine 1.5 ml with 0.25 ml normal saline or 0.75% hyperbaric bupivacaine 1.5 ml with 0.25 ml fentanyl (12.5 µg).They found that the time taken to achieve highest sensory level was significantly shorter in fentanyl group in comparison to bupivacaine group, while the duration of complete analgesia lasted significantly longer in fentanyl group. Duration of effective analgesia was also prolonged in fentanyl group than bupivacaine group and there was no significant difference in incidents of side effects of both groups. They concluded that addition of fentanyl to intrathecal bupivacaine results in faster onset with improved peri-operative anesthesia without increasing the side effects.In 2010, Joshi N, Sharma CS, Saxena AK16 compared the postoperative analgesic efficacy of intrathecal clonidine and intrathecal midazolam as adjuvant to bupivacaine in patients undergoing elective LSCS. 60 patients were randomly allocated into three groups: Group BC got 2 ml of hyperbaric bupivacaine and 60 µg of clonidine, Group BM received 2 ml of bupivacaine and 2 mg of midazolam and Group BS received 2 ml of bupivacaine and 0.4 ml of normal saline. They concluded that addition of intrathecal midazolam to bupivacaine and clonidine to bupivacaine prolongs the post- operative analgesia in patients undergoing LSCS as compared to bupivacaine alone.The results of our study are in accordance with the above studies. This implies that both Clonidine and Fentanyl when compared to Bupivacaine prolong the duration of analgesia, with Clonidine being most effective as an analgesic in the post-operative period (rescue analgesia required after 677.7±179.3 min) and without any significant adverse effects on the mother or the neonate.

CONCLUSION

The present study indicates that adding clonidine or fentanyl to bupivacaine as adjuvants, improves quality of block, gives good post operative analgesia and provides satisfactory intra operative anaesthesia. Clonidine provided much prolonged post operative analgesia compared to fentanyl without any significant maternal or foetal side effects.

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