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Original Research Article

Effect of Intrathecal Clonidine as Bupivacaine Spinal Anaesthesia Adjuvant in Caesarean Section: A Study

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ABSTRACT

Background: Pain in the perioperative period is common in parturient undergoing caesarean section under spinal anaesthesia. This study aims at evaluating the effect of intrathecal combination of clonidine and bupivacaine compared with bupivacaine alone on the block characteristic in elective caesarean section.

Methods: Sixty healthy parturient at term, scheduled for elective caesarean delivery were randomly allocated to receive intrathecally hyperbaric bupivacaine alone (Group B) or combined with 75µg of clonidine (Group C). The peak sensory block level(PSBL), time to reach peak block level (TPSBL) from injection, time to two segment regression (TTSR), side effects and time to the first analgesic request(TFAR)- after surgery were recorded and statistically analysed.

Results: Time to two segment regression was significantly prolonged in Group C (78.87±13.362 mins.) as compared to Group B (69.70±14.005 min) (P =0.012). There was significant prolongation of postoperative analgesia as seen by the time to first analgesic request after surgery in Group C (3.550±1.1013 hours) as compared to Group B (2.350±0.9016 hours) (P=0.000). There was increased incidence of hypotension and nausea in Group C compared to other two groups ($p< 0.05$).

Conclusion: Addition of 75 µg of clonidine to bupivacaine prolonged the perioperative analgesia; however, it was associated with increased side effects like nausea, vomiting & hypotension.

Key words: Intrathecal, clonidine, spinal anaesthesia, caesarean section

INTRODUCTION

One of the most important disadvantages of bupivacaine spinal anaesthesia is its relatively short duration of action, and the need for early analgesic intervention in the perioperative period. The use of two or more drugs to induce anaesthesia is termed as co-induction. Several studies have shown that clonidine has a substantial antinociceptive effect by its action on the alpha2-receptor in the dorsal horn of the spinal cord when administered in the epidural space or intrathecally [1,2] As an alpha2 agonist, spinal injected clonidine prolongs sensory and motor block, increases sedation and may potentiate hypotension and bradycardia. [3] However, this effect of clonidine is dose dependent and doses of more than 75µg intrathecal clonidine is

accompanied by excessive sedation, hypotension and bradycardia. [4]
So, this study was taken up to compare the effects of clonidine when administered intrathecally along with bupivacaine as regards the block characteristics of spinal anesthesia in elective caesarean section.

MATERIALS AND METHODS

Following institutional ethical committee approval and obtaining written informed consent 60 patients (ASA [5] I and II) of 18-45 yrs, undergoing elective caesarean section were recruited in this prospective randomized, double-blinded study. The study drug was prepared by an anaesthesiologist not involved in the study in a 5ml syringe in equal volume.

Based on the previous study of Benhamou D et al, [6] it was calculated that a sample size of 28 patients would be required per group to demonstrate a clinically significant difference between the groups, at $\alpha = 0.05$ with a power (1-β) of 80%. However, considering any dropouts, 30 (thirty) patients in each group were enrolled and randomly allocated into two groups by computer generated randomisation chart to receive the drugs during the study as follows:-

Group B (control): Inj. Bupivacaine 0.5% (2ml) + Normal saline 0.5 ml. (2.5 ml)

Group C (Clonidine): Inj. Bupivacaine 0.5% (2ml) + Clonidine 0.5 ml (75 µg) (2.5 ml)

Patients with a history of back injury, infection at injection site, coagulopathy, hypovolemia, increased intracranial pressure, neurological disease, spinal deformities and hypersensitivity to study drugs were excluded from the study.

In the lateral decubitus position, under strict aseptic and antiseptic precautions, spinal anesthesia was performed with a 25G Quincke needle at L_{3-4} & after free flow of cerebrospinal fluid, the drug was administered. The following parameters were observed viz. haemodynamic parameters, peak sensory block level, time to peak block level from injection, time to two segment regression, maximum degree of motor block, side effects, perioperative analgesic requirements(if any), time to the first analgesic request after surgery.

The parameters were recorded and statistical analysis was performed using statistical package for social sciences (SPSS) version 21 for windows and compared between the groups using chi square test for categorical variables, independent't' test for continuous variables. A *p*-value of < 0.05 was considered as statistically significant

RESULTS

The demographic profile which included the patients' age, weight, height and ASA physical classification were similar and no significant difference (P>0.05) was observed amongst the groups (Table 1).

Table 1: Demographic profile

Parameters	Group B (n= 30) (Mean±SD)	Group C (n= 30) (Mean±SD)	Statistical test value	*p-value*
Age (years)	29.83±6.438	28.23±5.697	Independent t test 0.402	0.312
Weight (kg)	65.87±6.475	64.87±10.231	Independent t test 5.707	0.657
Height (cm)	162.07±4.433	160.40±4.239	Independent t test 0.803	0.142
ASA (I:II)	16:14	10:20	Chi square(χ^2) 4.625	0.099

(*p* <0.05, considered significant)

Table 2: Showing the characteristics of the spinal block in the groups.

	Group B (n= 30) (Mean±SD)	Group C (n= 30) (Mean±SD)	Statistical Analysis	*p* value
TT $_{4\text{-}6}$* (min.)	8.10±3.255	6.25±2.137	Independent t test 0.011	0.199
PSBL	T4-T6/T2-T8 T4=27 , T6=3 , T8=0.	T4-T6/ T2-T8 T4=28 , T6= 2, T8 = 0	Chi square(χ^2) 10.854	0.093
TPSBL** (min.)	7.90±3.748	7.07±3.162	Independent t test 0.133	0.335
MBS***	Grade 1-Grade 2 (Grade 1-30 Grade 2-0 Grade 3-0 Grade 4- 0 Grade 5-0 Grade 6-0).	Grade 1- Grade 2 (Grade 1-29 Grade 2-1 Grade 3-0 Grade 4- 0 Grade 5-0 Grade 6-0).	Chi square test (χ^2) 2.022	0.364
TTSR**** (min) (mean±SD)	69.70±14.005	78.87±13.362	Independent t test 0.007	0.012
TFAR***** (hours) (mean±SD)	2.350±0.9016	3.550±1.1013	Independent t test 3.270	0.000

(*p* <0.05, considered significant)
*$TT_{4\text{-}6}$-Time to reach T4-6 level;
** TPSBL- Time to reach peak sensory block level;
***MBS- Modified Bromage scale;
****TTSR-Time to Two Segment Regression;
*****TFAR -Time to First Analgesic Request;

Peak sensory block level (PSBL) and time to reach peak sensory block (TPSBL) was similar in the two groups with *p* value 0.093 and 0.335 respectively. The time taken for two segment regression (TTSR) in Group B was 69.70±14.005 min., in group C it was 78.87±13.362 min. and it was statistically significant (p=0.012). The time for first analgesic request (TFAR) in Group B was 2.35±0.9016 hours, in group C - 3.55 ±1.1013 hours which is significant statistically (p=0.000). The overall quality of maximum motor blockade (MBS) was also similar in the two groups (p=0.364). The mean time to reach T4-6(TT4-6) segment (Group B/Group C=8.10±3.255 /6.25±2.137) was not statistically significant (p=0.199) (Table 2).

Table 3: Adverse effects:

Adverse effects	Group B (n= 30)	Group C (n= 30)	Chi square test	*p* value
Bradycardia	0	2	2.093	0.351
Hypotension	5	19	13.755	0.001
Nausea	2	16	15.556	0.000
Vomiting	0	3	4.028	0.133
Pruritus	0	0	15.181	0.001

(*p* <0.05, considered significant)

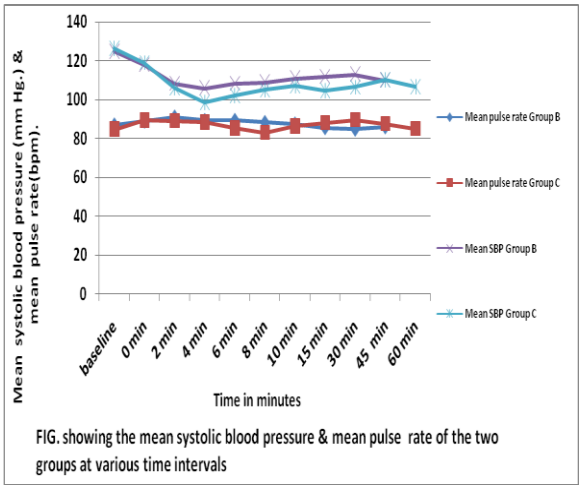

Fig 1. Showing the mean systolic blood pressure & mean pulse rate of the two groups at various time intervals

The incidence of side effects with higher incidence of hypotension (19/30; p=0.001), nausea (16/30; p=0.000) in the clonidine group (table 3), which was statistically significant. The systolic blood pressure (SBP) showed a decrease in the first 8 min. in the two groups and thereafter it was stabilised (Fig. 1) but the changes were not significant when compared at the corresponding time intervals. No significant

changes were observed in the pulse rate at the same time intervals in both the groups (Fig. 1).

DISCUSSION

Clonidine has been used as an anaesthetic adjunct in general and regional anaesthesia to provide increased perioperative cardiovascular and sympathoadrenal stability as well as sedation and analgesia. [2,7] It exerts its analgesic effects through activation of post synaptic α2 receptors in substantia gelatinosa of spinal cord. [8,9]

Workers like Paech et al. [10] and Filos et al. [11] used different doses of intrathecal clonidine combined with varying doses of bupivacaine. Enhanced side effects like sedation, hypotension, longer sensory and motor blockade were observed with increments of spinal clonidine doses. [11] However, postoperative analgesia was less with low doses of clonidine. [12,13]

Increased duration of the pain-free interval compared with only spinal local anaesthetics without causing any significant side effects was observed by Pederson et al. [14] when very small doses of intrathecal clonidine (25 µg) was used. On the other hand, Filos et al [11] observed that marked decrease in blood pressure is only observed with 150 µg dose of spinal clonidine and relative hemodynamic stability is maintained after larger doses (300-450 µg), which might be due to pressure effects at peripheral sites, but with marked sedation. This may be favourably compared with the findings of our study.

No significant difference in peak sensory block level and time to reach peak sensory block level in the two groups in our study, which may be explained by the comparatively large volume of drug (2.5 ml) used in this study. The time to two segment regression (min) was significantly higher in bupivacaine+clonidine group (78.87±13.362 mins) than bupivacaine alone group (69.70±14.005 mins). A longer two segment regression time was observed by Sethi BS et al. [12] Similarly, Benhamou D et al [6] reported two segment regression time of 95min. These findings may be correlated with our study where 78.87±13.62 min was observed in the clonidine group.

In the present study, the time to first analgesic to request was also significantly longer in and bupivacaine+clonidine group (3.550 ±1.1013 hours) (p=0.000). Similarly, Benhamou D et al. [6] observed that the time to first analgesic to request was 137±35 min in the control group 183±80 in the clonidine group.

Improved intraoperative spinal analgesia with 75 µg of clonidine was observed by Benhamou D et al [6] with no increase in the side effects with this dose. However, higher incidence of hypotension and sedation in clonidine 150 µg group then in clonidine 75 µg was observed by Lavand'homme et al. [15] Hence, the dose of clonidine was limited to 75 µg in our study to reduce the unwanted side effects and to increase the postoperative analgesia.

Increased intraoperative hypotension was observed in the clonidine group in our study which may be favourably compared with the findings Sethi BS et al. [12]

There were some limitations in the present study viz. no preloading or co loading was given to ameliorate hypotension; and different doses of the two study drugs and local anaesthetic could have been assessed.

CONCLUSION

Perioperative analgesia for caesarean section was prolonged by the addition of clonidine to bupivacaine; however, it was associated with unwanted side effects like nausea, vomiting & hypotension.

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