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A Comparative Study of Intrathecal Clonidine with Hyperbaric Bupivacaine Administered As A Mixture and Sequentially in Cesarean Section

Krishna Diddi[1], Putta Vinod Kumar[2]

[1,2]Assistant Professor, Department of Anaesthesia, Government Medical College and Hospital, Mahabubnagar, Telangana 509001, India.

Abstract

Context: Adjuvants and hyperbaric bupivacaine are mixed in a single syringe before injecting the drugs intrathecally. Their densities may be altered by mixing them in a single syringe, thus affecting their spread. Administering local anesthetic and the adjuvant separately minimizes the effect of changes in densities. *Aims:* To compare efficacy of intrathecal clonidine with hyperbaric bupivacaine administered as a mixture and sequentially and to assess the onset and duration of sensory and motor blockade and postoperative analgesia. *Settings and Design:* Group M received mixture of clonidine (75 mcg) and hyperbaric bupivacaine 0.5% (10 mg) and Group S received clonidine (75 mcg) followed by hyperbaric bupivacaine 0.5% (10 mg) through separate syringes. *Materials and Methods:* 60 full term parturients of elective cesarean section were divided into two groups based on the technique of intrathecal drug administration. *Statistical analysis used:* Quantitative data was analyzed by student's '*t*' test and qualitative data was analyzed by Chi-square test. *Results:* Duration of analgesia was significantly longer in Group S (474.33 ± 20.79 min) than in Group M (337 ± 18.22 min). The time to achieve highest sensory block and complete motor block was significantly less in Group S. *Conclusions:* When clonidine and hyperbaric bupivacaine were administered in a sequential manner, block characteristics improved significantly compared to the administration of the mixture of the two drugs.

Keywords: Bupivacaine; Clonidine; Postoperative analgesia; Spinal anesthesia.

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Introduction

Subarachanoid block is a widely used method providing a fast onset and Effective sensory and motor blockade. It has definitive advantages like profound analgesia which can be produced in a large part of the body by relatively simple injection of small amount of local anesthetic agent. Spinal anesthesia has been widely used for Cesarean Section (CS) deliveries because of greater maternal safety, fetal benefits, higher parental Satisfaction, and consumer demand.[1] Bupivacaine is the local anesthetic most commonly used. In order to extend intraoperative analgesia into postoperative period a number of spinal adjuvants like opioids are added to improve the block quality and provide postoperative

Corresponding Author: **Krishna Diddi,** Assistant Professor, Department of Anaesthesia, Government Medical College and Hospital, Mahabubnagar, Telangana 509001, India.

E-mail: drkrish3.0@gmail.com

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pain relief, examples include morphine, fentanyl, diamorphine or buprenorphine.[2] Central neuraxial opioids, intrathecal as well as epidural, offer the benefit of analgesia but however, the related side-effects include sense of dizziness, nausea, vomiting, pruritus, urinary retention and even cases of respiratory depression have been reported.[3] Clonidione, a selective partial agonist for alpha-2 adrenoreceptors, is an attractive alternative to commonly used opioids, and is known to increase both sensory and motor block of LA.[4,5] Several studies have shown that clonidine also has antihyperalgesic effect and thus, reduces the postoperative analgesic requirement.[6] Commonly, adjuvants are mixed with LA in a single syringe before injecting the drugs intrathecally. Mixing of these drugs changes the density of both drugs, thus affecting their spread in the Cerebrospinal Fluid (CSF).[7] Density is known to influence the spread of LA, but the effect of adjuvant solution density on its movement in the CSF has not been studied extensively.[8,9]

Therefore, we hypothesized that if we administer LA and the adjuvants separately, it may minimize the effect of the changes in densities and their actions. We compared block characteristics, intraoperative hemodynamics and postoperative pain relief in patients undergoing CS under Subarachnoid Block (SAB), after administering Hyperbaric Bupivacaine (HB) and clonidine as a mixture in single syringe and sequentially in two syringes.

The main objectives of the study are:

1. To compare efficacy and safety of intrathecal clonidine with hyperbaric bupivacaine administered as a mixture and sequentially.
2. To assess the onset and level of blockage.
3. Duration of sensory and motor blockade and postoperative analgesia.

Materials and Methods

This clinical study was conducted on 60 ASA Grade 1 and 2 patients aged 18–40 years undergoing elective cesarean section at our institute from November 2018 to November 2019.

Patients were divided into two groups of 30 patients each.

Group M (Mixture group) patients received intrathecal mixture of 0.5% hyperbaric bupivacaine 10 mg and clonidine 75 mcg;

Group S (Sequential group) patients received intrathecal clonidine 75 mcg followed by 0.5% hyperbaric bupivacaine 10 mg.

Inclusion Criteria

1. ASA Grade 1 and 2 patients;
2. Age group of 18–40 Years.

Exclusion Criteria

1. Patients belonging to ASA Grade 3 and 4;
2. Patient's on opioids and α_2 agonist like clonidine;
3. Patients allergic to any of the drugs mentioned above;
4. Patients with other comorbidities.

Methods of Study

Preanesthetic check up was carried out preoperatively with a detailed history, general physical examination, systemic examination and laboratory investigations. Airway assessment and spinal column examination were done.

Procedure

Patient was shifted to the OT table; IV access was obtained on the forearm with 18 gauge IV cannula and lactated Ringer's solution 500 ml was infused intravenously before the block. The monitors connected to the patient included noninvasive BP, pulse oximeter and ECG. Baseline PR, BP and RR, SpO_2 were recorded. Under strict aseptic precautions, lumbar puncture was performed in left lateral or sitting position by midline approach using disposable Quince spinal needle (25 G) at L3-L4 intervertebral space, after free flow of CSF study drugs were injected according to group. Patients were monitored continuously using non invasive blood pressure, pulse oximeter and electrocardiogram. After spinal anesthesia, Oxygen (4L/min) was given by facemask. Lactated Ringer's solution (10 ml/kg/hr) was given.

Results

A total of 60 ASA Grade 1 and 2 patients aged 18–40 years posted for elective cesarean section was selected and were divided into two groups of 30 patients each:

Group M (Mixture group) patients received

intrathecal mixture of 0.5% hyperbaric bupivacaine 10 mg + clonidine 75 mcg.

Group S (Sequential Group) patients received intrathecal clonidine 75 mcg followed by 0.5% hyperbaric bupivacaine 10 mg separately.

The mean time for onset of sensory block in Group M was 126.4 ± 5.51 seconds and Group S was 120.2 ± 5.55 seconds. The onset of sensory block in Group S was faster compared to Group M and is highly significant with $p < 0.001$. The mean time for onset of motor block in Group M was 242 ± 38.92 seconds and Group S was 168 ± 40.36 seconds.

Table 1: Onset time of sensory and motor block

	Group M	Group S	*p* - value	Result
Sensory block onset	126.4 ± 5.51	120.2 ± 5.55	< 0.001	HS
Motor block onset	242 ± 38.92	168 ± 40.36	< 0.001	HS

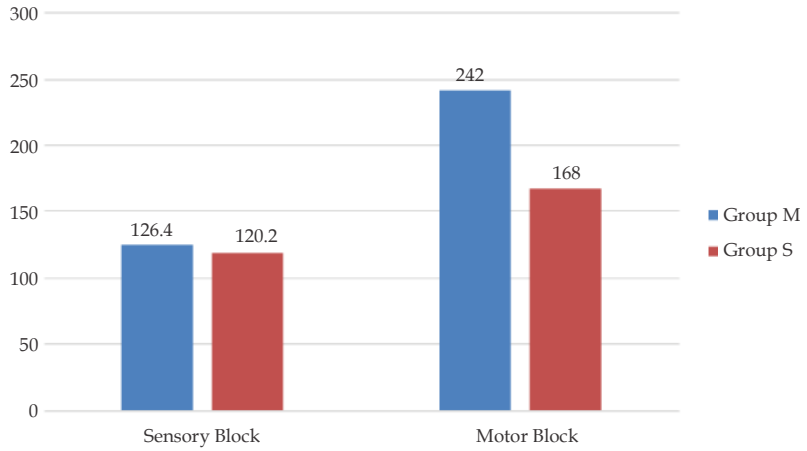

Fig. 1: Onset time of sensory and motor block.

The mean time for peak sensory block in Group M was 467.33 ± 32.92 seconds and 424.833 ± 41.26 seconds in Group S with $p < 0.001$, which was statistically highly significant.

Table 2: Time to peak sensory block

	Group M	Group S	*p* - value	Result
Peak sensory block (secs)	467.33 ± 32.92	424.83 ± 41.26	< 0.001	HS

Ten percent of patients attained T8 level blockade, 43% patients attained T6 level blockade and 47% patients attained T4 level blockade in Group M where as in Group S 3% patients attained T8 level, 33% patients attained T6 level and 63% attained T4 level blockade. Group S achieved higher level of sensory block.

Table 3: Highest level of sensory block

	Group M (*n* %)	Group S (*n* %)
T4	14 (46.67)	19 (63.33)
T6	13 (43.33)	10 (33.33)
T8	3 (10)	1 (3.33)

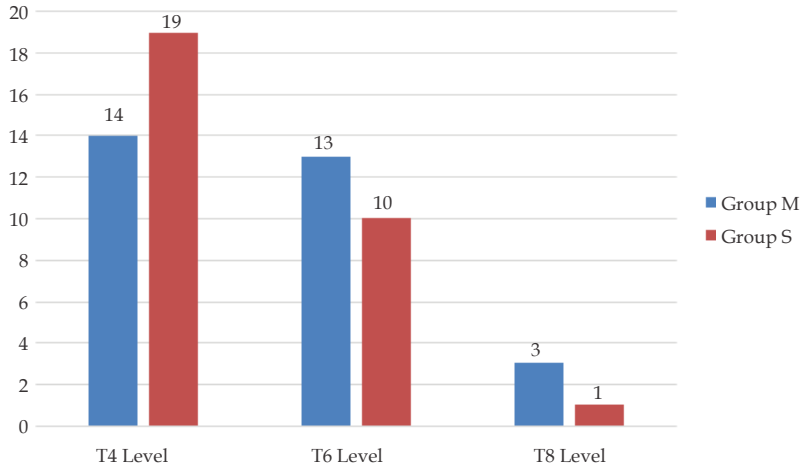

Fig. 2: Highest level of sensory block.

Mean duration of complete analgesia, effective analgesia in Group S higher than Group M which was statistically highly significant ($p < 0.001$). The time for first request for rescue analgesic postoperatively in Group M was earlier than in Group S which was statistically highly significant ($p < 0.001$).

Table 4: Duration of Analgesia

	Group M	Group S	*p* - value	Result
Duration of complete analgesia (minutes)	262.67 ± 85.14	387.67 ± 63	< 0.001	HS
Duration of effective analgesia (minutes)	371.33 ± 108.9	560.33 ± 78.32	< 0.001	HS
Time to first pain medication (minutes)	426.53 ± 94.91	604.00 ± 97.23	< 0.001	HS

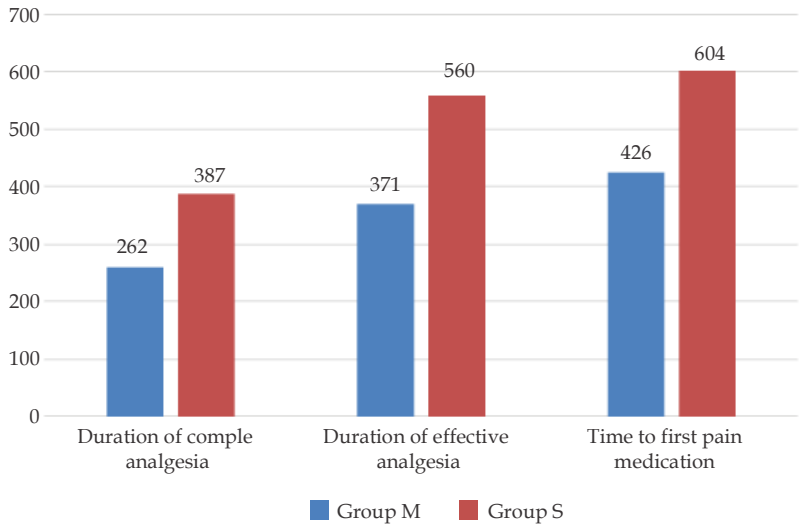

Fig. 3: Duration of analgesia

In our study, in Group M 10% patients had hypotension whereas in Group S 13.3% patients had hypotension. There was no bradycardia, mouth dryness and respiratory distress in either groups.

Table 5: Perioperative Complications

Cases	Hypotension	Vasopressor used	Bradycardia	Respiratory distress	Mouth dryness
Group M	3	1	0	0	0
Group S	4	2	0	0	0

VAS at the end of three hours was 0.7 ± 0.75 and 0.17 ± 0.38 ($p < 0.001$), at the end of six hours it was 2.9 ± 0.89 and 1.3 ± 0.3 ($p < 0.001$) and at the end of twelve hours it was 5.27 ± 0.58 and 4.2 ± 0.41 ($p < 0.001$) respectively in Group M and Group S. VAS was statistically significant at 3,6, and 12 hours in both groups but Group S had better pain relief (lower VAS) in the postoperative period than in Group M.

Table 6: Visual analog scale (VAS) score

Time (Hrs)	Group M	Group S	*p* - value	Result
3	0.7 ± 0.75	0.17 ± 0.38	0.001	HS
6	2.9 ± 0.89	1.3 ± 0.6	< 0.001	HS
12	5.27 ± 0.58	4.2 ± 0.41	< 0.001	HS

Discussion

The present study was carried out to compare efficacy and safety of intrathecal clonidine with hyperbaric bupivacaine administered as a mixture and sequentially during spinal anesthesia in patient posted for elective cesarean section. Our study design, consisted of 60 patients aged between 18 and 40 years, ASA physical status I/II were randomly divided into two groups after taking informed consent. The study has demonstrated that the sequential administration of bupivacaine with clonidine in spinal anesthesia significantly decreases the onset time, prolongs the duration of sensory, motor blockade and postoperative analgesia than in mixture group.

Onset of sensory and motor blockade

In our study, there was statistically highly significant difference with regard to onset of sensory and motor block between the groups with faster onset in Group S than Group M.

Gurudatta et al.[10], concluded that the mean time for onset of sensory blockade was faster in Group BC (Clonidine Group) compared to Group B (Bupivacaine Group) and the mean time for onset of motor blockade was also faster in BC Group compared to Group B.

Jyoti Pushkar et al.[11], in their study found rapid onset of both sensory & motor block, delayed sensory block regression & motor block resolution as well as prolonged postoperative analgesia in Sequential Group compared to Mixed Group.

Sachan et al.[12], observed that the mean onset time of sensory and motor block was similar in both groups.

Time for peak sensory level and highest sensory level blockade

In our study, the mean time to achieve peak sensory level in Group S was faster compared to Group M was (467.33 ± 32.92 seconds *vs* 424.83 ± 41.26 seconds).

In Group S, more percentage of patients attained T4 level block (63.33%) when compared to Group M (46.67%).

Desai et al.[7] in their comparative study observed that the time to reach highest level of block was less when morphine and fentanyl were administered sequentially with hyperbaric bupivacaine than given as a mixture.

In the study of Jyoti Pushkar et al.[11] the mean time to reach maximal sensory height and complete the motor block were less in Group S compared to Group M.

In the study of Sachan et al.[12] time to reach maximum sensory block height and maximum motor block was significantly less in Group B (sequential drugs) than Group M (mixed drugs).

Duration of analgesia

The duration of complete analgesia and effective analgesia was longer in Group S compared to Group M. The time for first request of rescue analgesic postoperatively was considerably prolonged in Group S by 160–175 minutes compared to Group M,

thereby, reducing the requirement of analgesics in the early postoperative period. The quality of analgesia was better as the VAS was lower in Group S than in Group M.

In the study of Jyoti Pushkar et al.[11] the mean time taken for sensory block to regress to T10 level was significantly longer in Group B (240.67 ± 18.47 min) than in Group M (153.83 ± 13.11 min). Similarly, the mean duration of analgesia lasted significantly longer in Group B (474.33 ± 20.79 min) than in Group M (337 ± 18.22 min), depicting significant prolongation of analgesic effect in the group receiving drugs in a sequential fashion.

Desai et al.[7], in their comparative study observed that dextrose in a HB solution slowed the movement of morphine molecules in the CSF, reducing the exposure of supraspinal centers to morphine. Clonidine also being hypobaric drug acting on both spinal and supraspinal receptors, might exhibit similar properties.

Dobrydnjov et al.[13] observed that the quality of intraoperative analgesia was better in Clonidine Group when compared to Bupivacaine Group.

Postoperative analgesia

In our study VAS scores were statistically significant at 3, 6, and 12 hours in both groups but Group S had better pain relief (lower VAS) in the postoperative period than Group M.

BS Sethi et al.[14] in their study found that the duration of effective analgesia was significantly prolonged with addition of clonidine (614 mins) compared to bupivacaine alone (223 mins).

No patient in the Clonidine Group required additional intraoperative analgesics compared with 17.6% in the Bupivacaine Group alone. There was improved patient comfort and reduced need for intramuscular and intravenous analgesia in the immediate postoperative period.

Side-effects

In our study, in Group M 10% patients had hypotension, where as in group S13.33% patients had hypotension. Hypotention was managed by intravenous fluids and vasopressors. There was no bradycardia, mouth dryness, urinary retention or respiratory depression in either groups. Sachan et al.[12] observed hypotension in 13% patients in Group M and 16% in Group B and none of the patients had bradycardia.

In the study of Jyoti Pushkar et al.[11] one patient in Group M & two in Group S had bradycardia. They observed hypotension in 13.24% in Group M & 16.63% in Group S. Dobrydnjov et al.[13] in their study concluded that small dose of intrathecal clonidine is not usually associated with systemic side-effects such as bradycardia, hypotension or sedation.

Conclusion

On the basis of the present clinical comparative study, we can conclude that sequential administration of clonidine 75 mcg with 0.5% hyperbaric bupivacaine 10 mg in spinal anesthesia posted for elective cesarean section decreases the onset time of sensory and motor block and prolongs the duration of analgesia with no significant postoperative complications when compared to the administration of drugs as mixture with no difference in neonatal outcome.

Key Messages: It is an old age practice to mix adjuvants with hyperbaric bupivacaine in a single syringe before injecting the drugs intrathecally but administering local anesthetic and the adjuvant separately improved block characteristics like duration of analgesia and the time to achieve highest sensory block and complete motor block significantly.

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