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Original Research

An Observational Study Of Clonidine And Fentanyl As Adjuvants To 0.5% Hyperbaric Bupivacaine In Spinal Anaesthesia In Elective Lower Abdominal Surgeries

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Abstract:
Background: Regional anaesthesia is the preferred anaesthetic technique in lower extremity, anorectal, urologic, obstetric, and lower abdominal surgeries. Adjuvants such as Morphine, Fentanyl, Clonidine and Dexmedetomidine have been used to supplement intrathecal local anesthetics providing possible advantages.

Aim: The aim of this observational study was to evaluate whether intrathecal clonidine and fentanyl could prolong the duration of sensory and motor block during spinal anesthesia and duration of analgesia.

Methods: A total of 90 patients of (ASA) physical status I-II of both sexes, aged between 18 and 70 years, were randomly allocated to two groups. Each group consists of 45 patients. Group A: 2.5ml of 0.5% hyperbaric bupivacaine and 50ug of clonidine in 0.5ml of normal saline. Group B: 2.5ml of 0.5% hyperbaric bupivacaine and 25ug of fentanyl in 0.5ml of normal saline. The time of onset and duration of sensory block, highest dermatome level of sensory block, time of onset of motor block, time to complete motor block recovery and duration of spinal anesthesia, intraoperative and postoperative hemodynamics and side effects if any were recorded. VAS, total number of patients who were administered supplemental analgesic in each group and the total amount of supplemental analgesic administered in the next 24 h was quantified and documented.

Results: The time of onset of sensory block (min) in groups A and B was 9.10 ± 1.40, and 10.50 ± 1.50 respectively, thus onset of sensory block was not statically significant. Similarly, onset of motor block was also statically insignificant among the study groups. Time of requirement of supplemental analgesia was 212.80 ± 26.32 min and 198.20 ± 21.92 min in group A and B respectively. Duration of analgesia was significantly longer in clonidine group when compared with fentanyl group. Sedation score was more in clonidine group.
Conclusion: We conclude that the addition of clonidine in doses of 50 µg and 12.5 µg to low-dose bupivacaine and bupivacaine fentanyl prolongs the sensory and motor block while increasing the duration of postoperative analgesia without significant side-effects.

Key words: Subarachnoid block, Intrathecal clonidine, spinal adjuvants, fentanyl, post operative analgesia.

INTRODUCTION:

Subarachnoid block has become increasingly popular technique in many countries over the last few decades. Subarachnoid block (Spinal anaesthesia), is the preferred anaesthetic technique in lower extremity , anorectal, urologic, obstetric, and lower abdominal surgeries.[1] Compared to general anaesthesia Subarachnoid block (Spinal anaesthesia) has

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decreased incidence of cardiovascular morbidity, deep venous thrombosis and pulmonary embolism , blood loss, pain, and length of hospital stay. It is also known that Subarachnoid block improves rehabilitation compared to general anaesthesia.[2,,3,4]

Various additives have been evaluated in the quest for an ideal adjuvant, which can enhance the quality of analgesia and prolong the duration of spinal anesthesia with minimal adverse effects. However, success with many additives has been variable, especially with regards to side-effects such as hypotension, bradycardia, pruritus, respiratory depression, nausea, vomiting, and urinary retention.[5]

Subarachnoid blockade with 0.5% hyperbaric bupivacaine provides sensory and motor blockade for surgeries lasting for about 2 hours but co-administration of spinal adjuvants allow reduction in the required dose of local anesthetics with the advantage of generating the same degree of analgesia. Several adjuvants such as opioids and alpha-2 agonists are used to enhance the onset and duration of spinal anesthesia and sedation along with their ability to provide enhanced post-operative analgesia. [6]

Adjuvants such as Morphine, Fentanyl, Clonidine and Dexmedetomidine have been used to supplement intrathecal local anesthetics providing possible advantages, such as delayed onset of pain and reduced analgesic requirements.[3] Fentanyl is μ receptor agonist 80 times more potent than morphine as an analgesic added to spinal 0.5% heavy bupivacaine improves quality of spinal analgesia, reduces visceral and somatic pain. However their addition may have side effects like pruritus, respiratory depression, urinary retention, postoperative nausea and vomiting which limits their use.[4,7] Dexmedetomidine is a highly selective α2-adrenergic agonist, used intrathecally, found to have antinociceptive action for both somatic and visceral pain.[8] In present study we aimed to compare dexmedetomidine and fentanyl as adjuvants to 0.5% hyperbaric bupivacaine in spinal anaesthesia in elective lower abdominal surgeries at a tertiary hospital.

METHODS:

The present study was conducted in the department of anesthesiology in Government medical collage Srinagar over a period of eighteen months for 90 patients of (ASA) physical status I-II of both sexes, aged between 18 and 70 years, equally divided in to two groups, Group A (n=45), Group B (n=45), scheduled for elective lower abdominal surgeries.

After getting approval from Institutional Ethical Committee, written informed consent was obtained from all the patients before surgery. Patients with any moderate to severe systemic disorders, patients unwilling to accept regional anesthesia, patients with any contraindication for spinal anesthesia, were excluded from the study.

A detailed history was noted and a complete general and systemic examination was done. Procedure was explained to patients and a written informed consent was taken. In surgical theatre monitors attached to record ECG, NIBP, SpO2, HR and RR. The baseline readings were noted.

Group A: received 2.5ml of 0.5% hyperbaric bupivacaine and 50ug of clonidine in 0.5ml of normal saline.

Group B: received 2.5ml of 0.5% hyperbaric bupivacaine and 25ug of fentanyl in 0.5ml of normal saline.

The procedure began by identifying anatomic landmarks. The patient was placed in the sitting position and the line joining the superior aspect of the iliac crests posteriorly (Tuffier's line) was palpated. When the Tuffier's line crossed an interspinous space, the spinal level was identified as L3–L4 interspace. According to this land-mark, the L2–L3 interspace was identified as one inter-space above. Identification of lumbar interspaces was performed separately by a junior and senior anesthesiologist and if there was any discrepancy in the identification of lumbar interspace, the patient was excluded from the study.

All patients were then placed supine and administered air/oxygen mixture (60%: 40%) via facemask. During the procedure an electrocardiogram, the heart rate and pulse oximetry were monitored continuously. Non-invasive blood pressure was taken before the conduct of spinal anesthesia and every 5 minutes after the intrathecal injection until the end of surgery. Hypotension was defined as a decrease in the mean arterial blood pressure, more than 20% from baseline within a 5 min interval. Hypotension was treated with either fluid boluses or aliquots of intravenous mephentermine 6 mg since the efficacy of mephentermine) was recognized in earlier studies. Bradycardia was defined as heart rate less than 50 beats min^{-1} and was treated with i.v. injection of atropine 0.5–1 mg. The quality of anesthesia was assessed by testing severity of intra operative pain using a 10 cm VAS, where VAS 0 meant no pain and VAS 10 worst pain imaginable. VAS was evaluated every 5 min from the time of skin incision until the end of surgery. The use of VAS had previously been explained to each patient before surgery. VAS 1–3 was considered as mild pain, VAS 4–6 as moderate, VAS 7, 8 as severe and VAS 9, 10 as unbearable pain. Five minutes thereafter, the VAS was assessed. The height of sensory block was also noted. The level of sensory block was determined by the loss of pinprick sensation and was performed using a 22 G hypodermic needle. Sensory block level was tested every 5 minutes during the first 30 minutes after the intrathecal injection. The surgeon started all operations 30 minutes after intrathecal injection in every patient. No sensory testing was performed during surgery.

Intraoperative parameters:

The following parameters were studied in the intra operative period.

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01. Onset and duration of sensory block: The onset at T10 of sensory block was assessed by pinprick test performed at 2, 5, 10, 15, 20, and 30 min and total duration of sensory block was noted.
02. Quality of intraoperative anaesthesia: Using a "four Grade scale". This was graded as:
Excellent: No supplementary sedative or analgesia required.
Good: Only sedative required.
Fair: Both sedative and analgesic required.
Poor: General anesthesia and tracheal intubation required.
03. Motor blockade: This was assessed by Modified Bromage Scale as under:
Grade 0: No paralysis
Grade 1: Unable to raise extended leg.
Grade 2: Unable to flex knee.
Grade 3: unable to flex ankle (complete block).
04. Alteration in vital parameters like heart rate and blood pressure.
05. Other undesirable sequelae like nausea, vomiting or any other Complication.
06. Sedation was assessed by modified Ramsay sedation score.
Modified Ramsay Sedation score.
1. Patient anxious, agitated or restless.
2. Patient cooperative, oriented and tranquil.
3. Patient responds to commands only.
4. Patient exhibits brisk response to light glabellar tap or loud auditory stimulus.
5. Patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus.
6. Patient exhibits no response.

Postoperative period:
Patients were evaluated for 24 hours regarding total duration of analgesia, postoperative analgesia requirements and other sequelae. Postoperatively, the pain was recorded by using visual analogue scale (VAS) between 0 and 10 (0= no paon,10= most severe pain), initially every 1 hourly for two hours, then every 2 hourly for the next 8 hours and then after every 4 hourly till 24 hours. Injection Diclofenac (75mg) was given intramuscularly as rescue analgesia when visual analogue scale was > 4.

Conflict of interest: Nil

Funding: Nil

RESULTS:

The treatment groups were comparable with respect to age, weight, height, sex distribution, and duration of surgery [Table 1].

Table 1: Patient demographic characteristics:

Parameters	Group A n=45	Group B n=45
Age(years)	42.6±14.58	44.73±15.08
Weight(kg)	61.50±8.87	62.50±10.99
Height(cm)	160.3±6.49	169.2±6.07
Gender(M/F)	25/20	27/18
ASA status I/II	34/11	32/13
Duration of surgery	97.66±13.70	94.66±14.45

Values in the table are mean ± SD or absolute numbers (percentage). SD = Standard deviation, ASA = American Society of Anesthesiologists.

The mean time of onset of sensory block in group A was 9.10 ± 1.40 min and in Group B 10.50 ± 1.50 min respectively. No, statistically significant differences were observed between study groups ($P > 0.05$). The mean time of onset of motor block in group A was 13.45±1.40 min and 15.20±1.50 min in group B respectively. Intergroup comparison did not reveal any statistically significant difference between the groups [Table 2].

Table 2: Characteristics of spinal block:

Parameters	Group A	Group B
Time of onset of sensory block (min)	9.10±1.40	10.50±1.50
Time of onset of motor block (min)	13.45±1.40	15.20±1.50

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Duration of sensory block (min)	**126.10±12.80**	**122.00±10.50**
Duration of motor block (min)	**110.50±8.50**	**109.20±6.48**

Values in the table are mean ± SD or absolute numbers (percentage). All times are in calculated from time of intrathecal injection. SD = Standard deviation.

The quality of intraoperative anesthesia remains excellent in among the study groups and statistical difference between the Groups was not significant (p=0.851) [Table 3].

Table 3: Quality of Intra operative anesthesia:

Quality of Intra operative anesthesia	Group A	Group B
Excellent	**41**	**42**
Good	**03**	**02**
Fair	**01**	**01**
Poor	**0**	**0**
Total	**45**	**45**

The requirement of rescue analgesic was significantly higher in group B as compared to group A at 2 h and 3 h postoperatively (*P* = 0.04 and *P* = 0.007). At 4 h postoperatively, groups B required more analgesic when compared to groups A and the difference was statistically significant [Figure 1].

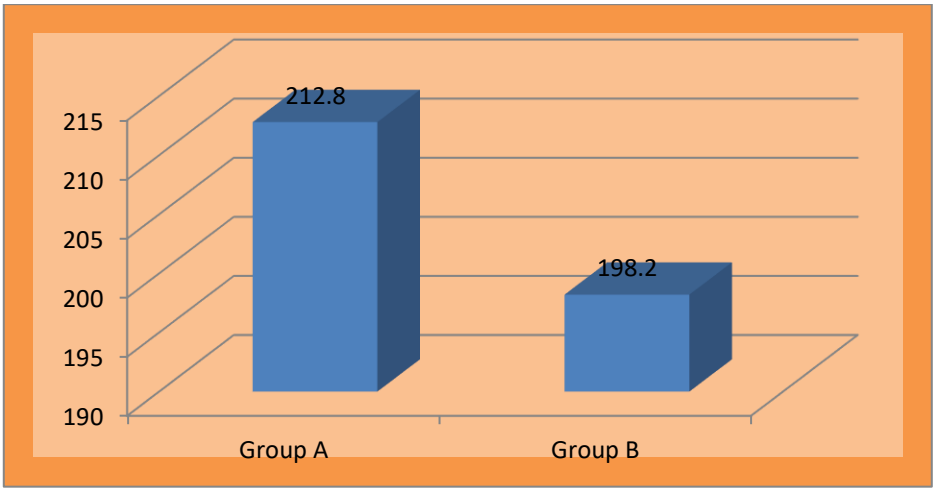

Fig 1

The requirement of total analgesic dose in first 24 hours was 142.159 in Group A and 175.5 mg in Group B. The statistical difference was significant among the study Groups (p<0.005) [Fig 2].

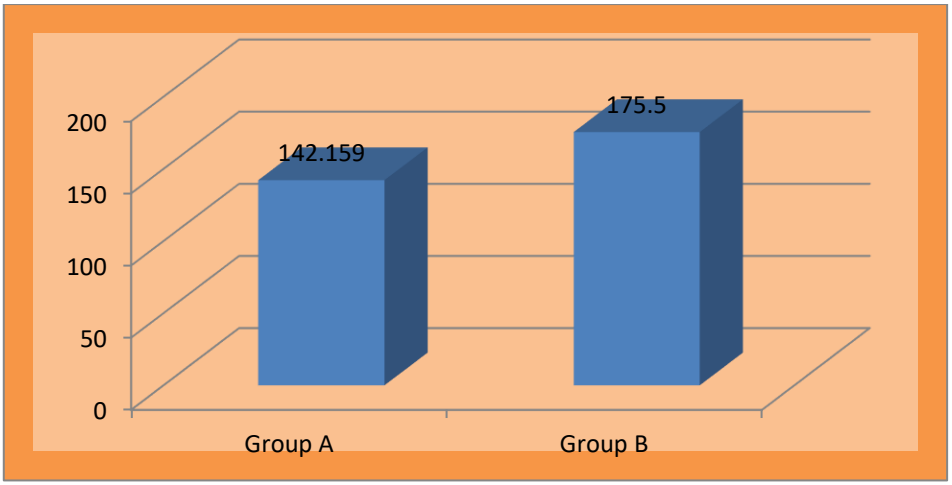

Fig 2

The adverse effects observed among the two study Groups. When compared statistically, the results were found not significant with a p value of > 0.05 [Fig 3].

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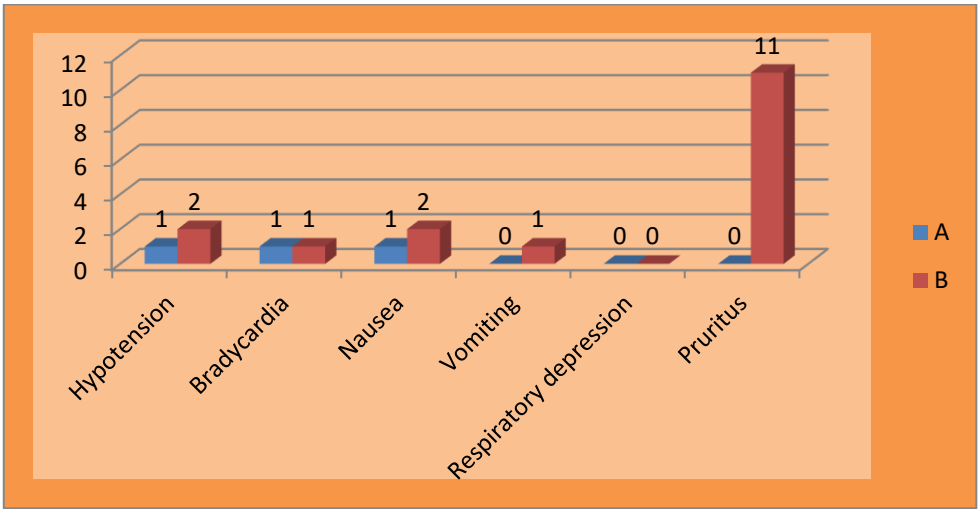

Fig 3

DISCUSSION:

Subarachnoid block is commonly used regional anesthetic technique for patients who require surgical anesthesia for lower extremities, perineum, pelvic girdle or lower abdomen. It may be useful in patients with difficult airway or suffered from co-morbidities of severe respiratory disease. Spinal anesthesia covering the mid-thoracic level yields a contracted small intestine to provide superior surgical conditions in combination with profound muscle relaxation of abdominal muscles.[9] Many previous studies have used intrathecal clonidine combined with opioids and local anesthetics for labour analgesia and orthopedic surgery.[10,11,12] Gautier and colleagues recommend 15 to 45 µg of clonidine as optimal for supplementing spinal anesthesia;[13] in keeping within this range, we chose 25 µg as optimal. Clonidine (15-30 µg) significantly prolongs sensory blockade and improves postoperative analgesia for gynecological operations,[14] knee arthroscopy and ambulatory inguinal herniorrhaphy.[15] The data match with our results concerning the duration of sensory block-postoperative analgesia. Our results showed that the addition of a small dose (25 µg) of clonidine increased the spread (onset-T9) and duration of sensory block, thereby prolonging postoperative analgesia. According to some previous studies, intrathecal clonidine alone, even at doses above 450 µg, does not cause muscular weakness and motor blockade, [16] but combined with local anesthetics it significantly enhances the intensity and duration of motor blockade.[17,18] In our study, however, we found a significant difference in the TAMB between the two groups, in favour of the clonidine group, but we failed to achieve statistical significance in the duration of the motor block. The higher doses of clonidine have been reported to cause important decreases in arterial pressure and marked sedation.[19,20,21] However, as our results demonstrate, a small dose of intrathecal clonidine is not usually associated with systemic side effects, such as bradycardia, hypotension or sedation.[13]

Clonidine has been used intrathecally in different doses. The dose of clonidine used in the present study corresponds to that of van Tuijl *et al*. who administered intrathecal clonidine in a dose of 25 mcg/kg.[22] The results of our study demonstrates that that the addition of clonidine in doses of 25 µg to Bupivacaine (7.5 mg) and 25 µg to bupivacaine (7.5 mg) plus fentanyl (12.5 µg) truncates the time of onset of sensory and motor block. Similar results were observed by Strebel *et al*.[23] and Gecaj-Gashi *et al*.[24] who reported shorter onset of sensory and motor block in patients receiving intrathecal clonidine. Grace *et al*., however observed prolonged time to onset of motor block in pethidine-clonidine group which is in contrast to the results of our study.[5] The difference in the result could be due to the fact that higher doses of pethidine 0.75 mg/kg was used in this study. It is possible that the higher dose of intrathecal pethidine could mask the effect of intrathecal clonidine.

The time of duration of motor block was similar in the both groups. Similar results were reported by Nazareth *et al.* [25] who obtained corresponding duration of motor block in the intrathecal clonidine group and in a group where combination of intrathecal clonidine and fentanyl were administered.

Postoperatively, lower VAS scores were observed for 12h and significantly reduced cumulative 24h supplemental analgesic consumption was noted in group receiving intrathecal clonidine, indicating good postoperative analgesic effect. The results of our study are comparable to those of Strebel *et al*.,[23] Merivirta *et al*.,[26] and Benhamou *et al*.[27] where addition of clonidine intrathecally resulted in significantly reduced VAS scores and significant reduction in postoperative analgesic consumption.

Intrathecal clonidine has been reported to result in intraoperative hypotension.[28,29] However, we observed stable hemodynamics among the two groups without any incidence of respiratory depression. This could be explained by adequate preloading which was performed in all the patients prior to subarachnoid block. In addition, the dose used in our study was small, and the mean level of anesthesia achieved was T8-9. Our results are similar to those of Singh *et al*. who

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observed no significant difference in HR and blood pressure in patients receiving 50 μg and 75 mcg of clonidine intrathecally Undergoing cesarean section.[30]Similarly, Nazareth *et al*. also reported stable hemodynamic parameters in the groups receiving intrathecal clonidine and fentanyl combination.[25] However, Dobrydnjov *et al*. reported significant decreases in patients receiving clonidine and fentanyl intrathecally. The difference could be explained by the fact that they used 3.5 ml of hyperbaric bupivacaine and clonidine as compared to the present study, accounting for higher level of sensory blockade achieved and thus explaining hypotension.[31]

Patients in groups A were sedated as evidenced by higher sedation scores. However, sedation never exceeded grade 2 and did not cause any problems in any of the patients. Singh *et al*.[30] and Nazareth *et al*.[32] also reported mild to moderate degree of sedation in the clonidine groups. Clonidine is known to cause sedation, and this hypnotic response is believed to be mediated via locus coeruleus where alpha-2- adrenergic receptors are abundant.[29]

A potential limitation of our study design relates to small sample size. Secondly, we did not attempt dose-response effect by using various doses of clonidine. Recently, there are few studies which report beneficial effects of using 30 or even 15 mcg of intrathecal clonidine with minimal adverse effects. Possibly, further reducing the dose of clonidine could have elucidated dose-response relationship.

CONCLUSION:

To conclude, our study demonstrated that the use of intrathecal fentanyl and clonidine in combination as adjuvant to hyperbaric bupivacaine in very low dose in surgical procedures provides good quality of intraoperative analgesia, hemodynamic stability, minimal side effects and excellent quality and duration of postoperative analgesia.

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