

Comparison of intrathecal clonidine and fentanyl in hyperbaric bupivacaine for spinal anesthesia and postoperative analgesia in patients undergoing lower abdominal surgeries

ABSTRACT

Background: There are many adjuvant used along with bupivacaine for subarachnoid block, but fentanyl and clonidine are commonly used as adjuvant to intrathecal bupivacaine for prolonging both sensory and motor blockade as well as postoperative analgesia in patients undergoing lower abdominal surgeries.

Objective: There is a paucity of studies comparing the efficacy of fentanyl and clonidine as adjuvant to intrathecal bupivacaine for improving intraoperative effect and postoperative analgesia in lower abdominal surgeries instigated us compare the effect of these drugs.

Methods: This prospective, randomized study is conducted on 100 American Society of Anesthesiologists I or II patients between 18 and 65 years of age divided into two groups of 50 each. The patients were given 2.5 ml of 0.5% hyperbaric bupivacaine with either 50 µg of clonidine (BC Group) or 25 µg of fentanyl (BF Group) intrathecally. The onset and duration of sensory and motor block, sedation score, hemodynamic parameters, total analgesia time, and potential side effects were recorded and compared.

Results: Both the groups were comparable in demographic data, onset and duration of sensory and motor blockade, hemodynamic parameters, but the duration of analgesia is significantly longer in clonidine group when compared with fentanyl group. Sedation score is more in clonidine group.

Conclusion: Addition of clonidine to intrathecal bupivacaine offers longer duration of postoperative analgesia than fentanyl but with higher sedation.

Key words: Bupivacaine; clonidine; fentanyl; intrathecal; postoperative analgesia

Introduction

Potential of the effect of subarachnoid block and prolongation of postoperative analgesia can be achieved by using adjuvants to local anesthetic agents such as midazolam, neostigmine, clonidine, and opioids.^[1-6] Wang *et al.* were the first to demonstrate the successful intrathecal administration

of morphine and since then almost all opioids were used as adjuvant to local anesthetic agent.^[7] Among all the opioids, fentanyl became the adjuvant of choice because of its potency, rapid onset and short duration of action with lower incidence of respiratory depression.^[3,8] Nevertheless, addition of opioids as adjuvant to local anesthetic agent is associated with side

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

How to cite this article: Bajwa BS, Singh AP, Rekhi AK. Comparison of intrathecal clonidine and fentanyl in hyperbaric bupivacaine for spinal anesthesia and postoperative analgesia in patients undergoing lower abdominal surgeries. Saudi J Anaesth 2017;11:37-40.

| Access this article online | |
|---|---|
| Website: www.saudija.org | Quick Response Code  |
| DOI: 10.4103/1658-354X.197337 | |

BALJIT SINGH BAJWA, ARWINDER PAL SINGH, ANGELINA K REKHI

Department of Anesthesia, PIMS Medical College, Jalandhar, Punjab, India

Address for correspondence: Dr. Baljit Singh Bajwa, Department of Anesthesia, PIMS Medical College, Jalandhar, Punjab, India.
E-mail: baljitbajwa7@gmail.com

effects^[9] such as nausea, vomiting, pruritus, urinary retention, herpes labialis activation, and respiratory depression directed the research in favor of nonopioid adjuvant which resulted in the introduction of clonidine as adjuvant to local anesthetic agent. Intrathecal clonidine is demonstrated to potentiate the effect of subarachnoid block as well as reduces the local anesthetic agent requirement.^[10] Intrathecal clonidine also offers prolonged postoperative analgesia,^[3-5,11,12] reduced shivering associated with subarachnoid block, and is devoid of side effects associated with intrathecal opioids. In this study, we have compared the intrathecal clonidine with intrathecal fentanyl as adjuvant to bupivacaine in terms of safety, efficacy, and postoperative analgesia in patients undergoing lower abdominal surgeries.

Methods

After approval from the Institutional Ethic Committee, this prospective, randomized study is conducted on 100 American Society of Anesthesiologists (ASA) I or II patients between 18 and 65 years of age planned for elective lower abdominal surgery and patients were divided into two groups of 50 each. From all the patients, informed consent was obtained. Exclusion criteria were severe systemic disorders such as diabetes mellitus, hypertension, heart disease with ASA grade more than II, allergy to study drugs, and all potential contraindications for spinal anesthesia, such as patient refusal, spine deformity, raised intracranial pressure, neurological disorders, bleeding disorders, or infection at the puncture site. The patients were randomized into two groups of 50 each, and patients were given 2.5 ml of 0.5% hyperbaric bupivacaine with either 50 µg of clonidine or 25 µg of fentanyl intrathecally. Premedication consists of glycopyrrolate 0.2 mg intravenous (IV) and ondansetron 4 mg IV, and sedatives were avoided as premedication, as well as during operative procedure. Preloading was done with ringer lactate 10–15 ml/kg. Monitoring parameters such as heart rate, oxygen saturation, and blood pressure were recorded. Under all aseptic precautions, subarachnoid block was given with 25 gauge Quincke needle in sitting position and depending upon the groups, either 25 µg fentanyl or 50 µg clonidine admixed with 2.5 ml of 0.5% hyperbaric bupivacaine resulting in total volume of 3 ml were injected intrathecally. Heart rate and blood pressure were recorded every 5 min, and all the heart rate and blood pressure variations more than 20% of baseline were recorded in both groups. Symptomatic hypotension and bradycardia are treated with mephentermine and atropine, respectively. Pinprick method was employed to check the sensory block. Modified bromage scale was used to assess the degree of motor blockade. Observations were recorded at T_0 = time of subarachnoid block administration,

T_1 = onset of sensory block time, T_2 = onset of motor block time, T_3 = peak sensory block time, T_4 = time of two segment regression of sensory level, T_5 = time of wearing off of motor block, and T_6 = time to first dose of postoperative rescue analgesia. Any potential side effects such as nausea, vomiting, shivering, pruritus, sedation, hypotension, bradycardia, and respiratory discomfort were recorded. Campbell Sedation Score was used to assess the degree of sedation and scoring. Campbell sedation score as (1) wide awake (2) awake and comfortable (3) drowsy and difficult to arouse (4) not arousable. Residual sensory blockade was monitored and its wearing-off time was noted using two segment sensory regression (sensation to pin-prick gets two dermatomal segments regression). Residual motor blockade was monitored and its wearing off time was noted when patient started to lift legs against gravity. Patients were monitored for degree of pain with the visual analogue scale (VAS). Postoperative rescue analgesia (intramuscular diclofenac 75 mg) was given when the VAS score was >5 and the time of injection of first analgesic drug was noted. This was taken as the time of wearing off of analgesia.

Statistical analysis was carried out using Mann–Whitney test, ANOVA, and Chi-square test and $P < 0.05$ is considered statistically significant.

Results

In our study, we observed that demographic data (age, height, weight, ASA grade, gender, and duration of surgery) were comparable with $P > 0.05$ (statistically not significant) [Table 1].

Similarly, in our study, there is no statistically significant difference in hemodynamic parameter (blood pressure and heart rate) is observed in both groups. Hypotension is not observed in any of the cases in both the groups. Incidence of bradycardia was similar in two groups, and only one patient in BC group developed bradycardia requiring treatment with injection atropine. Table 2 shows the comparison of blockade in terms of onset, duration, wearing off, and need of rescue analgesia. Both the group were comparable in terms of onset and offset of sensory and motor blockade,

Table 1: Demographic data

| Characteristics | BF group (n=50) | BC Group (n=50) |
|-------------------------------|-----------------|-----------------|
| Age in years | 42.53±15.43 | 44.76+ 14.20 |
| Height | 154.75±9.54 | 153.25+ -8.59 |
| Weight in kg | 64.54±12.50 | 61.80±8.38 |
| Sex of patients (male:female) | 16:18 | 18:16 |
| ASA grade | 1-2 | 1-2 |
| Duration of surgery | 120.47±54.63 | 128.65±7.10 |

Values are in mean±SD. $P > 0.05$ not significant. ASA: American Society of Anesthesiologists; SD: Standard deviation

peak of sensory blockade, regression of sensory blockade whereas the analgesic duration is prolonged in BC group as compared to BF group, and the time for the requirement of first analgesic dose is longer for BC group as compared to BF group ($P < 0.05$).

In our study, we observed more sedation in BC group as compared to BF group. On Campbell sedation score, we observed sedation score of 1 in 48 patients of BF group whereas only five patients in BC group has sedation score 1. Sedation score of 2 is observed in only two patients belonging to BF group, and it is contrary to BC group where 37 patients have sedation score 2. No patient in BF group demonstrated sedation score more than 2, whereas 8 patients in BC group showed sedation score of 3. From the above observation, we conclude that more patients are sedated in BC group as compared to BF and this difference is statistically significant ($P < 0.05$). Table 3 depicts the sedation scoring and percentage of patients in both the groups showing the sedation scores.

Apart from sedation, other complications and side effects are similar in both the groups and are not significant statistically ($P > 0.05$) and these complications are depicted in Table 4.

Discussion

Both clonidine and fentanyl when used in lower dose are safe and prolongs the postoperative analgesia of intrathecal bupivacaine, and there is a paucity of studies comparing the safety and efficacy of these two drugs. In our study, we compared intrathecal clonidine and fentanyl in terms of safety and efficacy, and to compare the efficacy, we used the effective analgesia duration measured in minutes for requirement of rescue analgesia. In consistent with several other studies,^[3-5,13,14] we found that both drugs are effective as adjuvants to intrathecal bupivacaine in prolonging the analgesia duration. Duration of analgesia was significantly higher in clonidine group (497.20 ± 139.78 min) than in fentanyl group (416.87 ± 105.67), ($P < 0.05$). Augmented analgesia duration due to fentanyl and clonidine in our study was different as compared to other studies^[3-5,13,14] but is consistent with the study conducted by Shidhaye *et al.*^[15] The reason for this may be because of the usage of doses of clonidine, fentanyl, or bupivacaine similar to those used by Shidhaye *et al.*^[15] Systemic side effects such as bradycardia, hypotension, or sedation are usually not associated with small dose of intrathecal clonidine or fentanyl and hemodynamic stability observed in both groups of our study confirms this. Only one patient had significant bradycardia requiring

Table 2: Comparison of blockade (onset and regression of sensory and motor block) and analgesic duration

| Parameters | Mean±SD | | P |
|---|-----------------|-----------------|--------|
| | BF group (n=50) | BC group (n=50) | |
| Time in min to onset of sensory blockade | 0.90±0.19 | 0.91±0.18 | 0.82 |
| Time in min to onset of motor blockade | 1.58±0.45 | 1.71±0.49 | 0.44 |
| Time in min for peak of sensory blockade | 7.34±0.96 | 7.56±1.78 | 0.94 |
| Two segment regression time in min for sensory blockade | 132±14.56 | 136.56±12.67 | 0.35 |
| Time in min for weaning offers motor block | 190.50±18.65 | 184.58±12.07 | 0.23 |
| Time in min for first dose rescue analgesia | 416.87±105.67 | 497.20±139.78 | 0.0004 |

SD: Standard deviation

Table 3: Campbell sedation score

| Sedation score | Group BF (n=50) (%) | Group BC (n=50) (%) |
|--------------------------------|---------------------|---------------------|
| Wide awake | 48 (96) | 5 (10) |
| Awake and comfortable | 2 (4) | 37 (74) |
| Drowsy and difficult to arouse | 0 | 8 (16) |
| Not arousable | 0 | 0 |

$P < 0.05$

Table 4: Other complications and side effects

| Side effects | BF group (n=50) | BC group (n=50) |
|------------------------|-----------------|-----------------|
| Nausea | 1 | 0 |
| Vomiting | 0 | 1 |
| Pruritis | 0 | 0 |
| Hypotension | 0 | 0 |
| Bradycardia | 0 | 1 |
| Respiratory depression | 0 | 0 |
| Shivering | 7 | 6 |

treatment with IV atropine. Similarly, Sethi *et al.*^[11] and Shah *et al.*^[12] observed very few incidences of hypotension and bradycardia by using 1 mcg/kg of intrathecal clonidine for nonobstetric surgeries, whereas Kothari *et al.*^[4] found the increased incidence of both hypotension and bradycardia in bupivacaine group than in bupivacaine with clonidine group. Bajwa *et al.*^[5] did not observe bradycardia by addition of clonidine even up to 45 µg in 9 mg of bupivacaine. Similar hemodynamic stability was observed by Biswas *et al.*^[16] and Agrawal *et al.*^[14] while using 12.5 µg and 25 µg of intrathecal fentanyl. In our study, both the groups are similar regarding onset, peak, and duration of sensory and motor block, but the duration of analgesia is significantly higher in clonidine group than in fentanyl group ($P < 0.05$). Sedation scores in our study were more in clonidine group than in fentanyl group ($P < 0.05$). Similarly, in consistent with our study, Kothari *et al.*^[4] reported 35–45% of patients drowsy by

addition of 50 µg of clonidine to bupivacaine but Bajwa *et al.*^[5] did not report any sedation by addition of up to 45 µg of clonidine to bupivacaine. From the above observation, we can make out that the sedation with clonidine is dose dependent. In our study, we observe no sedation in fentanyl group and these findings are consistent with study conducted by Biswas *et al.*,^[16] Dahlgren *et al.*,^[17] and Hunt *et al.*^[18]

Conclusion

Addition of 50 µg clonidine to intrathecal bupivacaine offers longer duration of postoperative analgesia than 25 µg of fentanyl but with higher sedation. Both the drugs offer similar surgical conditions and prolongs postoperative analgesia (clonidine more than fentanyl), so we suggest fentanyl as better choice when sedation is not desirable and clonidine is recommended where sedation is acceptable.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

- Prakash S, Joshi N, Gogia AR, Prakash S, Singh R. Analgesic efficacy of two doses of intrathecal midazolam with bupivacaine in patients undergoing cesarean delivery. *Reg Anesth Pain Med* 2006;31:221-6.
- Yoganarasimha N, Raghavendra T, Amitha S, Shridhar K, Radha M. A comparative study between intrathecal clonidine and neostigmine with intrathecal bupivacaine for lower abdominal surgeries. *Indian J Anaesth* 2014;58:43-7.
- Benhamou D, Thorin D, Brichant JF, Dailland P, Milon D, Schneider M. Intrathecal clonidine and fentanyl with hyperbaric bupivacaine improves analgesia during cesarean section. *Anesth Analg* 1998;87:609-13.
- Kothari N, Bogra J, Chaudhary AK. Evaluation of analgesic effects of intrathecal clonidine along with bupivacaine in cesarean section. *Saudi J Anaesth* 2011;5:31-5.
- Bajwa SJ, Bajwa SK, Kaur J, Singh A, Singh A, Parmar SS. Prevention of hypotension and prolongation of postoperative analgesia in emergency cesarean sections: A randomized study with intrathecal clonidine. *Int J Crit Illn Inj Sci* 2012;2:63-9.
- Elia N, Culebras X, Mazza C, Schiffer E, Tramèr MR. Clonidine as an adjuvant to intrathecal local anesthetics for surgery: Systematic review of randomized trials. *Reg Anesth Pain Med* 2008;33:159-67.
- Wang JK, Nauss LA, Thomas JE. Pain relief by intrathecally applied morphine in man. *Anesthesiology* 1979;50:149-51.
- Selvaraju KN, Sharma SV. Comparison of forced expiratory spirometric flow changes following intrathecal bupivacaine and bupivacaine with fentanyl. *South Afr J Anesth Analg* 2008;14:33-7.
- De Kock M. Site of hemodynamic effects of alpha 2-adrenergic agonists. *Anesthesiology* 1991;75:715-6.
- Bonnet F, Buisson VB, Francois Y, Catoire P, Saada M. Effects of oral and subarachnoid clonidine on spinal anesthesia with bupivacaine. *Reg Anesth* 1990;15:211-4.
- Sethi BS, Samuel M, Sreevastava D. Efficacy of analgesic effects of low dose intrathecal clonidine as adjuvant to bupivacaine. *Indian J Anaesth* 2007;51:415-9.
- Shah BB, Shidhaye RV, Divekar DS, Panditrao M, Panditrao MM, Suryawanshi C. Effect of addition of clonidine to bupivacaine used for patients undergoing spinal anaesthesia: A randomized, double blind, controlled study. *Sri Lankan J Anaesthesiol* 2011;19:17-21.
- Breen TW, Shapiro T, Glass B, Foster-Payne D, Oriol NE. Epidural anesthesia for labor in an ambulatory patient. *Anesth Analg* 1993;77:919-24.
- Agrawal A, Agrawal S, Asthana V, Payal YS, Sharma J, Gupta V. Comparison of intrathecal fentanyl and sufentanil in addition to bupivacaine for caesarean section under spinal anaesthesia. *J Anaesth Clin Pharmacol* 2009;25:154-6.
- Shidhaye RV, Shah BB, Joshi SS, Deogaonkar SG, Bhuvu AP. Comparison of clonidine and fentanyl as an adjuvant to intrathecal bupivacaine for spinal anaesthesia and postoperative analgesia in patients undergoing caesarian section. *Sri Lankan J Anaesthesiol* 2013;22:15-20.
- Biswas BN, Rudra A, Bose BK, Nath S, Chakrabarty S, Bhattacharjee S. Intrathecal fentanyl with hyperbaric bupivacaine improves analgesia during caesarean delivery and in early post operative period. *Indian J Anaesth* 2002;46:469-72.
- Dahlgren G, Hultstrand C, Jakobsson J, Norman M, Eriksson EW, Martin H. Intrathecal sufentanil, fentanyl, or placebo added to bupivacaine for cesarean section. *Anesth Analg* 1997;85:1288-93.
- Hunt CO, Naulty JS, Bader AM, Hauch MA, Vartikar JV, Datta S, *et al.* Perioperative analgesia with subarachnoid fentanyl-bupivacaine for cesarean delivery. *Anesthesiology* 1989;71:535-40.