TO COMPARE ANALGESIC ACTIVITY OF INTRATHECAL CLONIDINE AND FENTANYL WITH HYPERBARIC BUPIVACAINE IN PATIENTS OF ANORECTAL SURGERY

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ABSTRACT

BACKGROUND

There are various adjuvants used along with bupivacaine but clonidine and fentanyl both prolong sensory and motor block and duration of analgesia. In this study we aim to evaluate the onset and duration of sensory and motor block, post-operative analgesia, and adverse effects of clonidine and fentanyl as an adjuvant with hyperbaric bupivacaine in patients of anorectal surgery.

METHODS

This prospective randomized controlled trial was performed among 60 patients of either sex, aged 18-60 years who belonged to ASA I to III. Group I (BF) received 0.5% hyperbaric bupivacaine (0.5 ml) and fentanyl (15 µg) and Group II (BC) received 0.5% hyperbaric bupivacaine (0.5 ml) and clonidine (30 µg). The onset and duration of sensory and motor block, post-operative analgesia, VAS score, hemodynamic parameters, sedation and adverse effects were recorded and analysed.

RESULTS

The onset of sensory block was comparable in group BF (8.83 ± 1.62) and group BC (8.16 ± 1.37). The onset of motor block was faster in group BC (8.90 ± 1.24) as compared to group BF (9.70 ± 1.66). The mean time for 2 segment regression, duration of sensory block and duration of motor block were significantly lower (<0.001) in group BC as compared to group BF.

CONCLUSIONS

Low-dose of intrathecal clonidine as an adjuvant to hyperbaric bupivacaine provided prolonged duration of sensory block and postoperative analgesia with more sedation as compared to intrathecal fentanyl.

KEY WORDS

Analgesia, Bupivacaine, Clonidine, Fentanyl, Postoperative

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BACKGROUND

Extensive advancement in ambulatory procedures requires changes in the clinical anaesthesia practice. The social and economic pressures have changed and so have views of surgeons and anaesthesiologists. About 60% to 70% of all elective procedures are currently performed in outpatient settings in the United States and some European countries.^[1,2] Now a days, spinal anaesthesia may not be used for such procedures due to extended lower limb motor block.^[3] So, anaesthesiologists must become familiar with techniques allowing fast spinal block recovery. Studies with low hypobaric bupivacaine doses have shown that this technique helps fast recovery.^[4,5] However, low spinal anaesthesia doses depend on individual response and some patients may not obtain adequate anaesthesia.

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In spinal anaesthesia, hyperbaric bupivacaine is frequently used local anaesthetic. Low doses of intrathecal bupivacaine will decrease the intensity and duration of sensory and motor block; as an adjuvant clonidine and fentanyl decreases the dose of bupivacaine and improves the quality of spinal anaesthesia.^[6-9]

The Intrathecal clonidine is an agonist for α_2 adrenoceptor. It is clearly increasing the duration of sensory and motor block of spinal anaesthesia. It decreases the requirements of local anaesthetics and increase the postoperative analgesia requirement.^[6-9] The adequate dose of intrathecal clonidine (1-2 µg/kg) as an adjuvant to local anaesthetics was significantly increase the intensity and duration of sensory and motor blocked.^[6] It is associated with sedation, bradycardia and relative hypotension. The low-dose intrathecal clonidine showed effectiveness with no systemic side effects.^[7,10]

Fentanyl is a μ_1 - and μ_2 -receptor agonist, has a more preferable drug as an adjuvant because of its fast onset, moderate duration (1-4 h), and minimal delayed respiratory depression risk. The recommended effective safe dose of spinal fentanyl is 10-25 mg.^[11] Previously, various studies have shown that low dose of fentanyl as an adjuvant to hyperbaric bupivacaine increases the sensory blockade and duration with low intensity of the motor blockade.^[12,13] In

present study, we have used a low dose of intrathecal clonidine (30 micro gm) and fentanyl as an adjuvant to establish its efficacy. The aim of this study to identify whether and low dose of intrathecal bupivacaine in combination with 15 µg fentanyl and 30 µg clonidine would provide adequate anaesthesia for anorectal surgery without increasing side-effects or delaying hospital discharge.

METHODS

This prospective randomized controlled trial was performed after getting approval from Ethical Committee and informed consent will be taken from all the patients. This study was performed in 60 patients of either sex, aged 18-60 years with belonged to American Society of Anaesthesiology (ASA) grade I to III. None of the patients had any contraindication for spinal anaesthesia. Patients scheduled for elective anorectal surgery will be enrolled in the study.

On the basis of previous study, difference in the mean duration of onset of sensory block ($\mu_1 - \mu_2$) was 0.95 in treatment group 1 (5.93) and group 2 (6.88) and the average population variance (σ^2) 1.14.^[14] The sample size (n) = 2 ($Z_{\alpha/2} + Z_{[1-\beta]}$)² × $\sigma^2 / (\mu_1 - \mu_2)^2$, assuming 80% power and 0.05 level significance, was 22 in each group. Considering any dropouts, we had enrolled 30 patients in each group. Patients were randomized into two groups using computer generated random number table-

- Group I (BF)-0.5% Hyperbaric bupivacaine (0.5 ml) and fentanyl (15 µg)
- Group II (BC)-0.5% Hyperbaric bupivacaine (0.5 ml) and clonidine (30 µg)

All patients were premedicated with oral midazolam (7.5 mg) 2 hours preoperatively. Ringer's lactate hydration solution (15 ml/kg), a midline spinal puncture will be performed by using a 26-gauge Quincke spinal needle using a 26-gauge Quincke spinal needle at L4/L5. The L4/5 interspace was identified by all patients had spinal anaesthesia according to a line between the upper borders of the iliac crest. Tachycardia and bradycardia have been defined as heart rate >100/min and <60/min. respectively. The level of sensory blockade was assessed bilaterally by pin prick method along midclavicular line. The time to achieve the peak level of sensory block and time to reach maximum block height for regression of two segments were noted. Motor blockade was assessed by using modified Bromage scale (0: no motor block; 1: inability to raise extended legs; 2: inability to flex knees; 3: inability to flex ankle and foot).^[7] Duration of anaesthesia was measured as the time interval from intrathecal injection to regression of the sensory block below L1. The time for first analgesic requirement for the first time following spinal anaesthesia was noted. The 10-point visual analog scale (VAS) score was used to assess the pain hourly for 24 hours. Rescue analgesia was given with i.v. tramadol 50mg. Sedation was measured hourly for 24 hours on a four-point scale (Grade 0, awake and alert; 1, mildly sedated, easily aroused; 2, moderately sedated, aroused by shaking; 3, deeply sedated, difficult to be aroused by physical stimulation).^[15]

Intraoperative complications was treated as follows: hypotension (<90 mmHg systolic blood pressure) was treated with increments of 5 mg ephedrine, bradycardia (<50 bpm heart rate) was treated with 0.3 mg of atropine, and oxygen

desaturation (pulse oximetry oxygen saturation <90% on room air) was treated with oxygen via Hudson's face mask. If a patient complained about discomfort or pain, midazolam 0.05 mg/kg and fentanyl 25 µg IV will be administered by the anaesthesiologist in incremental doses. Adverse events (hypotension, bradycardia, nausea, vomiting, sedation, shivering and pruritus) will be recorded during operation and recovery.

Statistical Methods

Statistical analysis was performed by using SPSS software 15. Sensory and motor block characteristics were compared using the student's t-test. The demographic data and proportion of side effects were compared using the chi-square test (χ^2) and statistical significance was observed at $p < 0.05$.

RESULTS

The demographic profile included age, gender, height, weight, ASA grade and duration of surgery were comparable in both groups as shown in table 1. The mean age of the patients in group BF and group BC were 43.90 ± 8.06 and 45.03 ± 7.54 years, respectively. In group BF and BC, 76.67% and 83.33% males were present. The mean height of patients were 164.97 ± 6.91 and 166.47 ± 7.05 (cm) in group BF and BC, respectively. The mean weight of patients in group BF and group BC were 65.70 ± 6.60 and 64.57 ± 7.13 (kg), respectively. Total 60.0% and 76.67% patients have ASA grade I and 40.0% and 23.33% patients have ASA grade II in group BF and group BC, respectively. The mean duration of surgery were 74.10 ± 13.98 and 75.43 ± 12.87 in group BF and group BC, respectively.

The onset of sensory block was 8.83 ± 1.62 and 8.16 ± 1.37 in group BF and group BC, respectively. The difference in onset of sensory block among the groups was comparable in both groups. Whereas the onset of motor block was 9.70 ± 1.66 and 8.90 ± 1.24 in group BF and group BC, respectively. The difference in onset of motor block among the groups was faster in group BC as compared to group BF. The mean time for 2 segment regression, duration of sensory block and duration of motor block were significantly lower (<0.001) in group BC as compared to group BF. The first-time analgesia requirement was significantly higher in group BC with mean 257.00 ± 28.67 min as compared to group BF with mean 350.17 ± 32.66 min as shown in Table 2.

The visual analog scale score (VAS) at 2 hrs and at the at first time rescue analgesic requirement are shown in Table 3. Vas score at first time rescue analgesic requirement was comparable in both group BF and group BC.

The mean heart rate of patients was shown in Fig. 1. The mean heart rate was 83.07 ± 5.87 and 82.12 ± 6.72 beats/min in group A at baseline (0 min). The baseline heart rate was comparable in both group BF and group BC (Fig. 1).

The mean atrial blood pressure (MAP) of patients was shown in Fig. 2. The mean MAP was 98.5 ± 10.01 and 97.0 ± 9.52 beats/min in group BF and group BC at baseline (0 min, respectively). The baseline heart rate was comparable in both group BF and group BC (Fig. 2).

The hemodynamic parameters (heart rate and MAP) are shown in Fig. 1 and Fig. 2. The heart rate and MAP did not show any significant change in both group BF and group BC, intraoperative.

Demographic Variables	Group BF	Group BC	p-Value
Age (Years) Mean±SD	43.90 ± 8.06	45.03 ± 7.54	0.576
Sex			
Male	23 (76.67%)	25 (83.33%)	0.527
Female	7 (23.33%)	5 (16.67%)	
Height (cm)	164.97 ± 6.91	166.47 ± 7.05	0.409
Weight (kg)	65.70 ± 6.60	64.57 ± 7.13	0.526
ASA Grade			
I	18 (60.00%)	23 (76.67%)	0.171
II	12 (40.00%)	7 (23.33%)	
Duration of Surgery (min)	74.10 ± 13.98	75.43 ± 12.87	0.647

Table 1. Patients Characteristics

Data are represented as mean, ± SD, and n (%). SD=Standard deviation

Parameters	Group BF	Group BC	p-Value
Onset of Sensory Block	8.83 ± 1.62	8.16 ± 1.37	0.90
Time for 2 Segment Regression	78.50 ± 8.58	130.77 ± 15.09	<0.001*
Duration of Sensory Block	143.77 ± 13.77	179.17 ± 12.74	<0.001*
Onset of Motor Block	9.70 ± 1.66	8.90 ± 1.24	0.039*
Duration of Motor Block	158.53 ± 18.78	195.13 ± 14.49	<0.001*
First Time Analgesia requirement	257.00 ± 28.67	350.17 ± 32.66	<0.001*

Table 2. Characteristics of Sensory and Motor Block

*=Significant (p<0.05)

Variable	Group BF	Group BC	p-Value
VAS score (2 hrs.)	0.0	0.0	-
VAS score (At first time rescue analgesic)	2.90 ± 1.06	2.80 ± 0.96	0.704

Table 3. Pain Score

	Group BF	Group BC	p-Value
Hypotension	4 (13.33%)	3 (10.00%)	0.694
Headache	2 (6.67%)	0 (0.00%)	0.155
Bradycardia	3 (10.0%)	1 (3.33%)	0.309
Nausea	2 (6.67)	0 (0.00%)	0.155
Vomiting	1 (3.33)	0 (0.00%)	0.321
Itching	4 (13.33)	0 (0.00%)	0.039*
Shivering	2 (6.67)	0 (0.00%)	0.155
Respiratory Depression	0 (0.00%)	0 (0.00%)	-
Sedation	0 (0.00%)	4 (13.33)	0.039*
Dryness of mouth	0 (0.00%)	3 (10.00%)	0.078
Pruritus	8 (26.67%)	0 (0.00%)	0.003*

Table 4. Complication

*=Significant (p<0.05)

Figure 1. Heart Rate (Beats/Min)

Figure 2. MAP (mmHg)

The incidence of hypotension, headache, bradycardia, nausea, vomiting, shivering, respiratory depression and dryness of mouth were comparable in both group BF and group BC as shown in Table 4. Itching and pruritus were significantly more in group BF as compared to group BC. The sedation was significantly greater in group BC as compared to Groups BF (p=0.039). Though, sedation never exceeded grade 2.

DISCUSSION

In these studies, we found that the duration of sensory block and duration of motor block, time to two-segment regression and analgesia effects were significantly greater in clonidine group as compared to fentanyl group. Similarly, Chopra and Talwar, (2014) reported that patients receiving 30 µg intrathecal clonidine with 0.5% hyperbaric bupivacaine had significantly greater duration of effective analgesia, duration of sensory block and duration motor block, and time to two-segment regression than those receiving 15 µg fentanyl with 0.5% hyperbaric bupivacaine.^[16] Another study also reported that the clonidine (45 µg) with 0.5% bupivacaine were significantly increased the duration of sensory block, motor block as compared to fentanyl (15 µg), in infra-umbilical surgery.^[17] Our results are supported by similar findings of previous study, in which the duration of sensory and motor block was significantly prolonged in group C (hyperbaric bupivacaine and 50 µg clonidine) compared to Group Fb (hyperbaric bupivacaine and 25 µg fentanyl) in lower limb orthopaedic surgery.^[14] The very low dose of intrathecal clonidine (15 µg) was increase the duration motor block.^[18] Whereas, Ahmed et al. (2017) did not find any effect of clonidine (25 µg) on the duration of motor block.^[19]

In our study we found that the addition of clonidine to intrathecal bupivacaine was significantly more increase the post-operative analgesia effects as compared to fentanyl to intrathecal bupivacaine. This finding is supported by several studies, which reported that the small dose of intrathecal fentanyl to bupivacaine increased the postoperative analgesia effects but less than clonidine with bupivacaine groups.^[19-22] The request of first time rescue analgesia was significantly longer in clonidine to bupivacaine group as compared to fentanyl.^[12] The fentanyl (12.5 µg) to intrathecal bupivacaine markedly increased the intraoperative anaesthesia, and significantly reduced the request for postoperative analgesia demand.^[23] The addition of clonidine (50 µg) to bupivacaine was significantly prolonged the time to first analgesic request.^[24]

In our study the heart rate and mean atrial blood pressure of patients were comparable in both clonidine and fentanyl groups. The overall haemodynamic stability was observed in both clonidine (30 µg) and fentanyl (15 µg) with in bupivacaine. The findings of our study is supported by Chopra and Talwar, 2014, who found that the incidence of sedation to be the highest with bupivacaine with clonidine than bupivacaine fentanyl groups.^[16] Similarly, the haemodynamic stability were observed in clonidine (60 µg) and fentanyl (25 µg) with in bupivacaine in patients undergoing caesarean section.^[25] Various other studies also reported that the haemodynamic stability with use of fentanyl and clonidine.^[26-28] Biswas et al. (2002) and Agrawal et al. (2009) also reported that the haemodynamic stability with 12.5 µg and 25 µg of intrathecal fentanyl.^[23,29] Chopra and Talwar, (2014) shows

that the intrathecal clonidine (30 µg) might not produce significant hemodynamic effects.^[16] Ahmed et al. (2017) reported that the intrathecal clonidine and fentanyl with hyperbaric bupivacaine are produce good hemodynamic stability in total abdominal hysterectomy.^[19]

In this study we found that the itching and pruritus were significantly more in fentanyl group whereas sedation was more in clonidine group. The incidence of hypotension, headache, bradycardia, nausea, vomiting, shivering, respiratory depression and dryness of mouth were comparable in both clonidine and fentanyl groups. Similarly, Routray et al. (2017) found that the more sedation in intrathecal clonidine (50 µg) as adjuvant to hyperbaric bupivacaine as compare to intrathecal fentanyl (25 µg).^[14] Perioperative analgesia was prolonged by the addition of 75 µg of clonidine and 25 µg fentanyl to bupivacaine, with increased side effects of nausea, vomiting and hypotension in the clonidine group.^[26] A small dose of intrathecal clonidine as well as fentanyl is not usually associated with systemic side effects such as bradycardia, hypotension, or sedation.^[25]

CONCLUSIONS

Low-dose of intrathecal clonidine (30 µg) as an adjuvant to hyperbaric bupivacaine provided prolonged duration of sensory block and postoperative analgesia with more sedation as compared to intrathecal fentanyl (15 µg). Impartially excellent analgesia with few sedations with negligible haemodynamic complication was observed with 30 µg clonidine and it may be suggested.

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