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Research Article

The Effect of Addition of Clonidine to Low Dose Bupivacaine for Unilateral Inguinal Herniorraphy: A Randomised Double Blinded Study

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Abstract: Our study was aimed to see whether the addition of clonidine to small-dose bupivacaine for spinal anesthesia provided a sufficient degree of block that would be adequate for inguinal herniorrhaphy and whether it prolonged the duration of postoperative analgesia. We randomized 90 patients to 3 groups who received intrathecal hyperbaric bupivacaine 6 milligrams combined with 0.9% normal saline (Group A),with clonidine 15 micrograms (Group B) or clonidine 30 micrograms (Group C).All solutions were diluted with 0.9% normal saline to 3 milliliters .The duration of sensory block was the primary outcome measured. The mean upper level of sensory blockade on the dependent side was significantly higher (four to five dermatomes) in Groups B and C as compared with Group A. Two segment Regression time, time to request for first dose of analgesia, return of L1 sensation, and regression of motor block were significantly longer in Group B and C than in Group A. No differences were found among the groups in time to stand, walk and spontaneous urination. The addition of intrathecal clonidine 15 or 30 µg to small-dose bupivacaine increased the spread and duration of analgesia and produced an effective spinal anesthesia. This study has shown that use of clonidine 30 µg as adjuvant to small-dose (6 mg) bupivacaine is effective for ambulatory inguinal herniorrhaphy.
Keywords: ambulatory surgery, clonidine, spinal anaesthesia, post operative analgesia

INTRODUCTION

Spinal anaesthesia with hyperbaric bupivacaine provides rapid onset of action with effective sensory block and prolonged motor blockade. To make spinal anaesthesia suitable for ambulatory procedures, it is desirable to reduce the duration of motor blockade.

A small dose of hyperbaric bupivacaine produces a short duration of spinal anaesthesia, which may be clinically useful in ambulatory surgical procedures [1-3].

When only local anaesthetic is used, higher doses of postoperative opioids are required to provide adequate postoperative pain relief [4-5].The incidence of undesirable opioid side-effects such as pruritus or postoperative nausea and vomiting are very high.

The α2-adrenergic agonist Clonidine is known to potentiate the effect of local anaesthetics. It also prolongs the sensory blockade and reduces the quantity of local anaesthetic required to produce postoperative analgesia.Clonidine prolongs the duration of intrathecally administered local anesthetics and has potent antinociceptive effect by its action on the α2-receptor in the dorsal horn of the spinal cord [6-8].

Intrathecal clonidine produces dose-dependent analgesia [7-8]. Adding clonidine to intrathecal bupivacaine improves intraoperative analgesia and might prolong the duration of spinal analgesia, resulting in a sparing effect on postoperative opoid consumption [7-8]. The higher doses of intrathecal Clonidine (more than 150-450µg) are known to be associated with bradycardia, relative hypotension and sedation [9].

Our study was proposed to evaluate whether the addition of small dose of clonidine to smaller doses of bupivacaine for spinal anaesthesia provided analgesia that would be adequate for inguinal herniorrhaphy and also whether it prolonged the duration of postoperative

analgesia along with the ability to ambulate the patient early as required for day care surgeries.

METHODS

After obtaining the institutional ethical committee approval and informed written consent, 90 patients posted for inguinal herniorrhaphy, belonging to ASA physical status I–II and age group 20 to 40yr were selected for the study. Patients taking antihypertensive medications, showing dysrhythmias in the ECG, and who had a history of low back surgery, were excluded from the study. The patients were randomly allocated to one of three treatment groups, each comprising 30 patients.

Before conduct of spinal anaesthesia, all patients were preloaded with i.v. infusion of Ringer's lactate (500 ml).Standard intra operative monitoring consisted of [ECG, pulse oximetry and non-invasive blood pressure (NIBP)]. All patients received Inj midazolam 2 mg IV as premedication.

Patients were given spinal anaesthesia in a lateral decubitus position with operative side dependent. A midline lumbar puncture was performed at the L2-3 interspace by using a 27 gauge Quincke spinal needle.

All patients received 6 mg hyperbaric bupivacaine 0.5% for spinal anaesthesia at a rate of 1ml per 5 seconds. Group A patients received 6 mg hyperbaric bupivacaine 0.5% for spinal anaesthesia. Group B received clonidine 15 µgs along with 6 mg hyperbaric bupivacaine 0.5%. Group C clonidine 30 µgs along with 6 mg hyperbaric bupivacaine 0.5% mixed in the same syringe .All solutions were diluted with 0.9% normal saline to make 3ml. Patients were kept in the same position for next 10 minutes before turning them supine for surgery. The time at which the intrathecal injection was completed was considered as zero (t = 0).

Heart rate (HR), SpO_2 and ECG were recorded continuously and non-invasive arterial blood pressure was measured at every 5 min till recovery. Clinically relevant bradycardia was defined as a decrease in HR of < 50 bpm and was treated with Inj atropine 0.6 mg IV. Clinically relevant hypotension constituted a decrease of 20% or more in systolic blood pressure from baseline and was treated with Inj ephedrine 6 mg IV (repeated as and when required).

All patients were administered O_2 at the rate of 4 litres per minute by face mask.

The cephalic level of analgesia defined as the loss of pin prick sensation was recorded bilaterally. Data were registered at 5 minute intervals for the first 15 min, at 15 min intervals for 15-150 min, and later every 30 min. During the regression phase, time to two-segment regression and and time to full skin sensibility at the L1 segment were registered.

Motor block was measured bilaterally by using a modified Bromage scale (0–3) at the same time intervals. When the patients had a Bromage grade of 0 and full skin sensibility at the S1 segment and were alert, they were asked to stand and walk. The times to standing and walking were recorded.

Sedation was assessed with a four-point verbal rating scale (1=no sedation, 2 = light sedation, 3 = somnolence, 4 = deep sedation)

Inj fentanyl 50 µg IV was used as rescue analgesic. If the analgesia was inadequate or if the pain was not relieved by two doses of fentanyl, a General anaesthetic was administered and surgery was completed.

The time from intrathecal injection to request for the first dose of analgesic was considered as total duration of analgesia.

Time to spontaneous urination was noted and patients who did not pass urine after 6 hours of surgery were catheterized.

Adverse effects such as pruritus, postoperative nausea and vomiting (PONV), shivering, sedation, respiratory depression, postural hypotension and postdural puncture headache (on follow up after 48 hours) if any, were recorded.

The surgeon was asked to assess the quality of anaesthesia by using the following four-point scale: 4-excellent; 3- good; 2- inadequate; and 1- poor.

The data was analysed using software SPSS 15.0, Stata 8.0, medcalc 9.0.1 and Systat 11.0. Analysis of variance (ANOVA) has been used to find the significance of study parameters. Unless otherwise stated, results are expressed a Means +/- SD .values were taken as significant only when <0.05

RESULTS

The demographic variables were comparable among the three study groups (Table 1). The mean cephalic level of sensory blockade on the dependent side was significantly higher (4-5 dermatomes) in Groups C and B as compared to Group A $P<0.001$ (Table 2). The mean cephalic level of sensory block on the dependent side was T_7 in Group C, T_8 in Group B and T_{10} in Group A which was clinically significant. On the nondependent side it was T_{11}, T_{12} and L_1 in Group C,B and A respectively(Table 3).

The time to two-segment regression of sensory block on the dependent side was significantly prolonged in Group C(142.17±20.53) as compared with Group B (104.52 ±25..67) and Group A(50.16±11.65) (Table 4). This block on the nondependent side also was significantly prolonged in Group C(114.67±14.96) as

compared with Group B(83.71±22.84) and Group A(33.83±9.71) (Table 4).

Time to regression of spinal anaesthesia below level L1 was 204.83±29.26 in Group C, 144.84±30.64 in Group B and 72.67±22.19 in Group A (Table 4).

A complete motor blockade of the lower extremities on dependent side was observed in patients of all groups. On the nondependent side, both the incidence and the duration of motor block were significantly greater in Group C and B than in Group A.

The time to request for first dose of supplemental analgesia was significantly prolonged in Group C (202.50 ± 25.49) than Group B (144.84 ± 30.89) and Group A (67.83 ± 31.50) (Table 4). The return of Bromage Scale to Grade 0 on the dependent side was significantly longer in Group C (143.17±24.79) as compared to Group B (126.13±27.43) and Group A (61.67±18.99) (Table 4).

There were no differences found among the groups in time to stand, time to walk though spontaneous urination was delayed in Group B &C (Table 4).

Three patients in Group B and two patients in Group C required single dose of injection Ephedrine (6 mg) iv. No post operative hypotensive episode requiring intervention was recorded in any of the study groups.

No significant difference in sedation was found among the groups.
No respiratory depression or other side effects were observed during the intra and postoperative period in any Group.

The surgeon's rating of the operating conditions was excellent or good in all 30 patients in Group C, as compared to 28 in Group B only 8 in Group A

Table 1: Demographic variables were comparable among the three study groups

Sl. No.	Variables	Group A	Group B	Group C
1	Mean Peak sensory level,operated side	T 10(T10 to T12)9±6	T 8(T6 to T10)10±1	T7(T6 to T10) 12 ±1
2	Mean Peak sensory level,non operated side	L1(T10 to L4)6±2	T11(T10 t0 L2)8±1	T12(T8 to L2)9±2
3	Two segment regression time, operated side	50±13	107±26	142±21
4	Two segment regression time, non operated side	34±10	84± 23	115 ± 20
5	Return of Bromage score to 0, operated side (min)	62±19	126±27	145±20
6	Return of sensory level to L1	79±24	148±30	190±60
7	Return of sensory level to S1(pin pick)	170±30	199±49	245± 25
8	Time to standing (min)	218±71	244±46	247±28
9	Time to walking (min)	256±60	250±60	256±27
10	Time to spontaneous urination (mins)	259±57	316±41	318±33
11	Time to request for first dose of analgesia	61±20	147±30	204±26

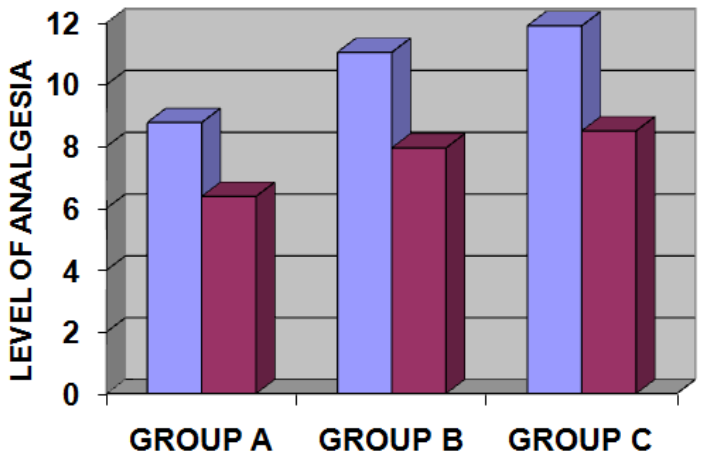

Fig. 1: Level of analgesia on operated (blue) and non operated (red) side

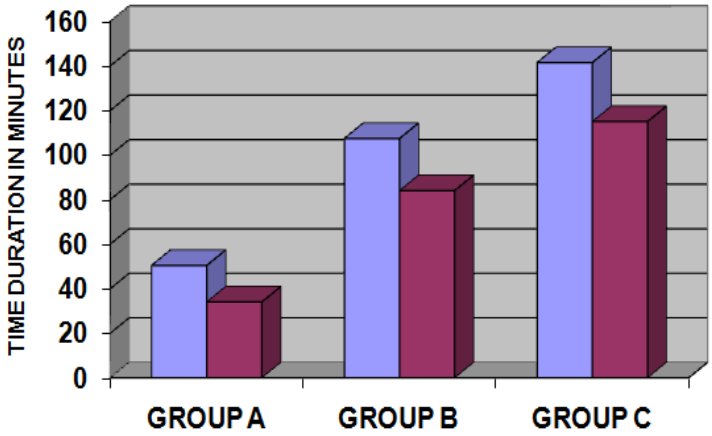

Fig. 2: Two segment regression time on operated (blue) and nonoperated (red) side

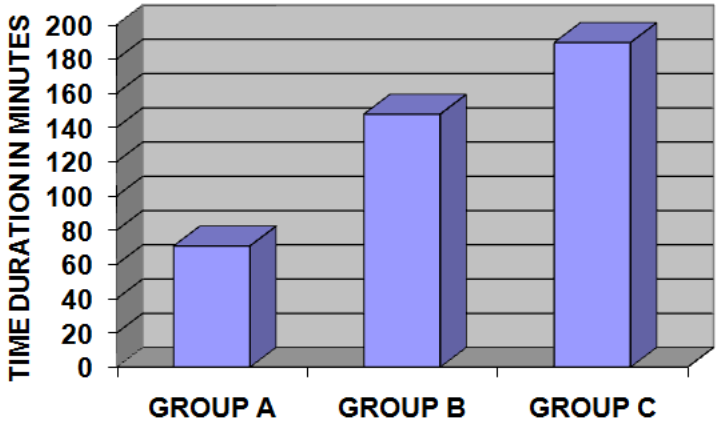

Fig. 3: Mean duration of return of sensory level to L1

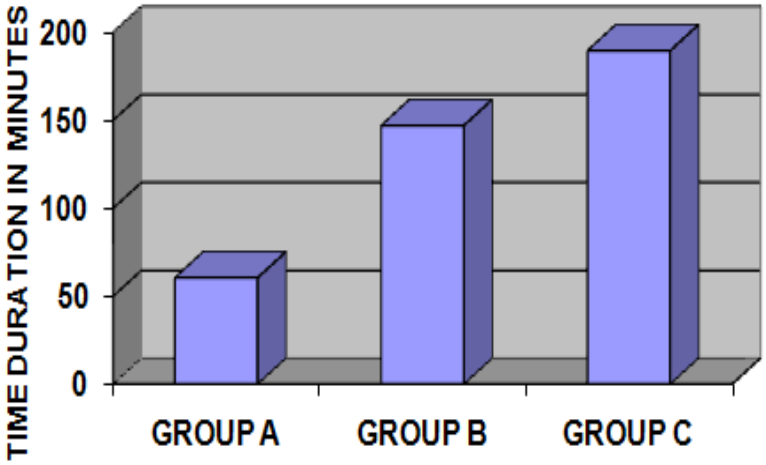

Fig. 4: Mean duration of request for first dose of analgesia

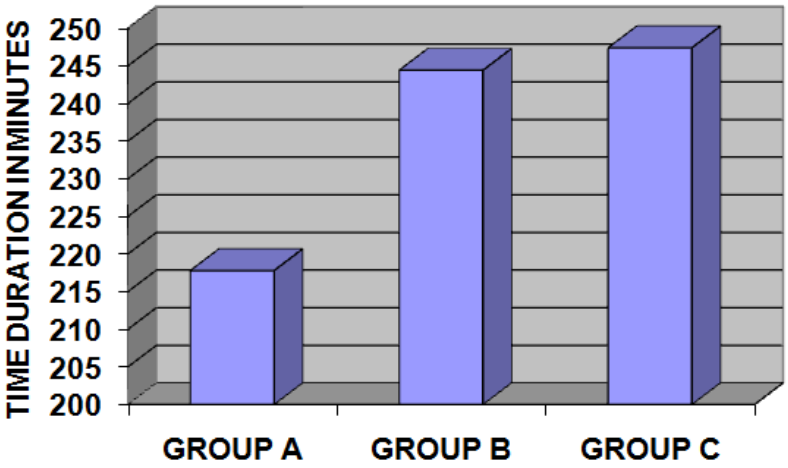

Fig. 5: Time to stand

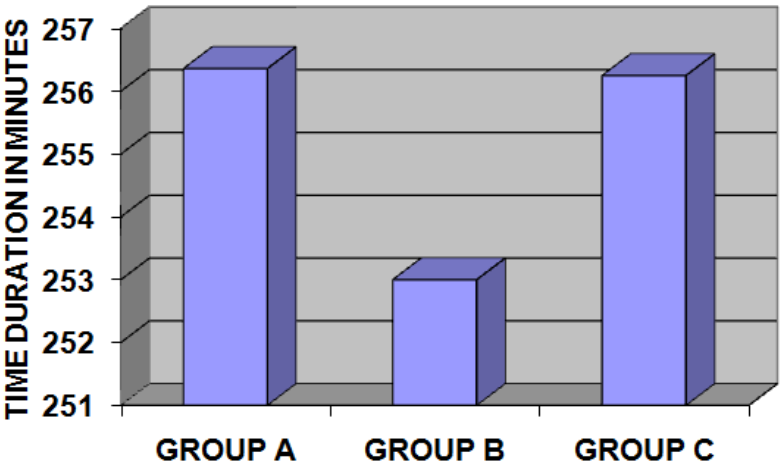

Fig. 6: Time to walk

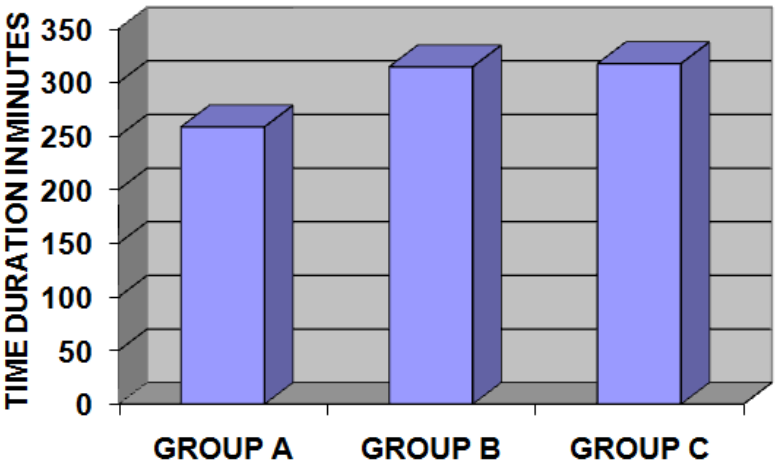

Fig. 7: Time to spontaneous urination

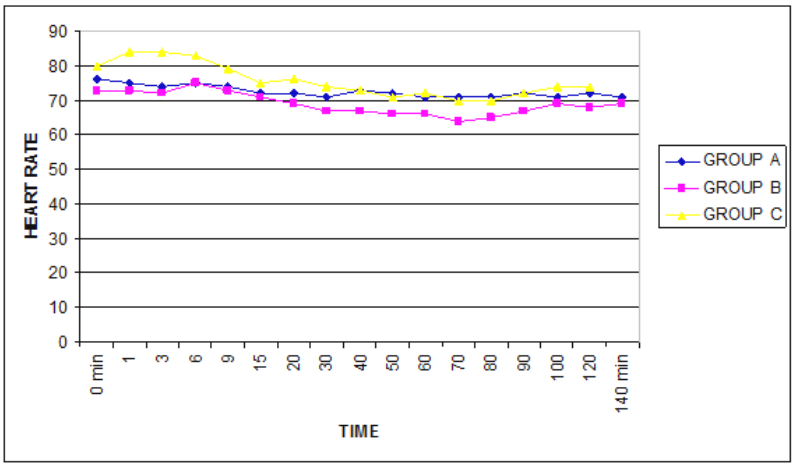

Fig. 8: Heart rate tracings in three study groups

DISCUSSION

Bupivacaine is a potent local anaesthetic with a long duration of action. The amount of local anaesthetic usually used for spinal anaesthesia is larger in relation to the minimum concentration required to block the various types of nerve fibers. Use of smaller doses of bupivacaine will reduce the duration of spinal block, but sometimes at the price of a small number of blocked dermatomes.

Our data from Group A suggests that 6 mg of bupivacaine alone produced inadequate analgesia for routine inguinal herniorrhaphy because of low level of sensory block. Thus, small dose of hyperbaric bupivacaine may be unpredictable, and the addition of adjuvant that increases the quality of analgesia would be desirable.

Intrathecal clonidine clearly increases the duration of both sensory and motor block [2-7], as well as post operative pain relief. The mechanism of clonidine-induced potentiation of sensory block in spinal anaesthesia is reported to be mediated by both presynaptic (inhibition of transmitter release) and postsynaptic (enhancing hyperpolarisation) effects.

Stephan Strebel *et al.* [1] found that the addition of intrathecal clonidine to 18 mgs hyperbaric bupivacaine prolongs both sensory blockade of spinal anaesthesia and time interval to first request for supplemental analgesia in a dose dependent manner with 150 µgs as optimal dose during orthopaedic procedures for lower limb.

Dobrydnjov *et al*. used 15 and 30 µgs of clonidine along with 6mg of 0.5% bupivacaine to prolong duration of spinal anaesthesia and recommended a dose of 15µgs of clonidine as optimal for supplementing spinal anaesthesia for unilateral herniorrhaphy [8].

However we observed that clonidine 30µgs acts as a better adjuvant to small dose bupivacaine as it significantly prolongs the analgesia and provides better operating conditions as compared to clonidine 15µgs. Increasing the dose of clonidine from 15 to 30µgs increases the duration of analgesia without prolonging the time until walking, voiding, recovery of sensory and motor block significantly.

A small dose of intrathecal Clonidine is not associated with clinical or statistically significant systemic side effects such as bradycardia, hypotension or sedation. The absence of severe hypotension could be explained due to usage of a smaller dose of local anaesthetic leading to fewer blocked segments so that the extent of sympathetic block is less.

CONCLUSION

In conclusion, the addition of intrathecal clonidine 15 or 30 µg to 6mg of 0.5% hyperbaric bupivacaine increase the cephalic spread of analgesia, increases the duration of analgesia and produces an effective anaesthesia for inguinal herniorrhaphy.

There is a dose dependent prolongation of post operative pain relief but without any significant delay in motor recovery.

In a dose of 15µg or 30µg, clonidine neither produced any significant hemodynamic disturbances in the patient nor caused any side effects.

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