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ORIGINAL ARTICLE

Comparative evaluation of addition of either fentanyl or clonidine to bupivacaine in spinal anesthesia – a randomized controlled trial

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ABSTRACT

Background: Single dose subarachnoid anesthesia is a commonly used anesthetic technique for pelvic and lower limb surgeries. Various adjuvants, e.g. opioids, alpha 2 agonists, neostigmine, midazolam etc. have been used to counter some of the shortcomings of the technique. Synthetic lipid soluble opioids like fentanyl for hemodynamic stability or clonidine for prolongation of duration have been used. We wanted to compare both the drugs with a control when used in conjunction with local anesthetics in lower abdominal and pelvic surgeries with regard to sensory and motor block with early postoperative analgesia along with their side effect profile.

Methodology: One hundred and fifty adult patients of ASA status I and II, posted for lower abdominal and pelvic surgeries, were randomly divided into three groups. Group BC (bupivacaine + clonidine) received 50 µg clonidine while BF (bupivacaine + fentanyl) received 50 µg of fentanyl, the third group received equal volumes of normal saline (Group NS, bupivacaine + normal saline) for subarachnoid block. The duration of anesthesia, analgesia, motor blockade and side effects like sedation, bradycardia and hypotension were noted and subjected to statistical analyses with ANOVA (analysis of variance) and Kruskal-Wallis test as and when appropriate.

Results: All of the 150 patients completed the study. The duration of surgical anesthesia was not significantly higher in the experimental groups. But the duration of analgesia was higher in BC than BF which in turn was higher than the Group NS [281.26 ± 97.57, 237.80 ± 58.49 min and 190.48 ± 61.94 min respectively]. The sedation and the intraoperative motor blockade were similar, in Group BC, L1 regression time was 232.76 ± 94 min which was higher compared to Group BF (202.34 ± 60 min) and Group BN (172.28 ± 56 min) but statistically insignificant. The hemodynamic instability with regard to hypotension was more in Group BC than BF.

Conclusion: Addition of 50 µg of clonidine to intrathecal bupivacaine produces prolonged duration of analgesia in surgical anesthesia. The onset of hemodynamic imbalance was from forty minutes in Group BC which prompts for an additional monitoring in those cases. There is no excess sedation with the above said dose of clonidine.

Key words: Anesthesia; Intrathecal; Bupivacaine; Adjuvants; Clonidine; Fentanyl

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INTRODUCTION

Single dose intrathecal anesthesia is a commonly used anesthetic technique for pelvic and lower limb surgeries. Usually hemodynamic disturbances, early recovery and patient discomfort are encountered frequently in clinical practice. To overcome these hiccups, certain adjuvants are added to local anesthetics in the subarachnoid space. Opioids,

clonidine, midazolam, neostigmine and ketamine are some of them[1-4]. Natural opioids like morphine when introduced as intrathecal adjuvant can produce dangerous complications like late respiratory depression even it produces significant analgesia[5]. Neostigmine, an anticholinesterase[6], is associated with excessive nausea while ketamine can produce hallucinations. Synthetic opioids like fentanyl is lipid soluble and hence a cephalad migration like morphine to cause problems are rare. The newer class of alpha 2 agonists which include clonidine is said to prolong the duration of action of subarachnoid local anesthetics while causing hemodynamic disturbances[1]. Hence with this background we wanted to compare the effects and side effects of two different adjuvants, namely clonidine or fentanyl with Bupivacaine in subarachnoid block for lower abdominal and pelvic surgeries

The primary objective was to assess the characteristics of spinal anesthesia (Sensory level, , degree of motor blockade, duration of spinal block) between the two groups. The secondary objectives were to compare the respiratory and cardiovascular effects, early post operative analgesia and any other significant side effects.

METHODOLOGY

The study was conducted at our Institute during the period from August 2008 to August 2010. After getting an ethics committee approval (MGMCRI 2008 PGMD/MS institute ethics committee), 150 adult patients between 18 – 75 years of age belonging to American Society of Anesthesiologists (ASA) physical status class I or II of either sex, who were admitted for elective lower abdominal, and pelvic surgeries were recruited for the study. Patient with previous spinal surgeries, spinal deformities, haemorrhagic disorders and cardio respiratory co morbidities were excluded from the study. During the pre anesthetic evaluation patients were explained about the study purpose, merits and demerits of the intervention and instructed to demand analgesia whenever they felt pain at the operated site in the postoperative ward. All patients were premedicated with tablet Diazepam 10 mg the night before and the morning of surgery. The morning sedative drug was given four hours prior to anesthesia with sips of water in all patients After establishing the monitoring systems in the operating room, and recording the base line parameters, the patients were randomized in to one of the three groups of fifty each (BC – bupivacaine + clonidine, BF – bupivacaine + fentanyl, BN – bupivacaine + normal saline) by the sealed envelope technique. After a standard preloading of 10 ml/kg Ringer lactated solution, Spinal anesthesia was administered under aseptic precaution in horizontal left lateral position at L3 – L4 inter space using 25 gauge Quincke spinal needle. The local anesthetic mixture was prepared in the operating room at 22^{o} C according to the group in which the patient was allocated (0.5% Hyperbaric bupivacaine 2.5 ml was added with clonidine 50 μg (Group BC) or fentanyl 50 μg (Group BF) or normal saline (Group BN) made up to total volume of 3.5 ml) and the spinal solution was given to the anesthesiologist who was blinded about the drug mixture. The anesthesiologist did not take part in the study there after. The sensory level and analgesic levels were assessed 5 minutes after the spinal anesthesia by applying constant pressure with a blunted needle in each dermatome starting from the area of 'no sensation' and moving cephalad. The dermatome at which the patient felt the pressure but no pain was taken as level of total sensory blockade. The dermatome where the patient felt both pressure and pain was taken as analgesic level. The motor blockade was assessed at 5 minutes after the spinal injection with Bromage scale (0 - no paralysis, 1 – inability to raise extended leg, 2 – inability to flex the knee, 3 – inability to flex the ankle). The sedation level was analyzed with Ramsay sedation scale (1 – anxious and agitated, 2 – cooperative, oriented and tranquil, 3 – responding to command only, 4 – brisk response to light glabellar tap, 5 – sluggish response to light glabellar tap, 6 – no response to light glabellar tap.the duration of anesthesia was defined as a regression to a level of L1. The time at which patient complained of pain was noted as time to first analgesic (TFA) and intravenous tramadol 1 mg/kg was used as rescue analgesic. As we resorted to fentanyl, we did not give routine antiemetic in all cases.

Statistical analysis: A 10 % increase in the duration and a similar percentage of hemodynamic variations due to addition of clonidine when compared to fentanyl along with the previous studies calculated the sample size to be 135 with a total of three groups with alpha of 0.05 and a power of 80 %.all the parametric data were analyzed with analysis of variance (ANOVA) and Kruskal-Vallis test was used for ranking data. A p value of less than 0.05 was taken as significant.

RESULTS

All the 150 patients completed the study. There were no drop outs. All the surgeries were satisfactorily completed within the spinal time and none needed conversion to general anesthesia. Even though the

age groups showed some differences, it was statistically insignificant (Table 1). The mean weight and heights were comparable between the three groups (Table 2). The sensory and motor levels were comparable between the two groups. The pulse rate, respiration and oxygen saturation remained similar between the three groups without any untoward change. There was a significant fall in both systolic and diastolic blood pressure in the Group BC when compared to others (Figures 1 and 2).

The mean duration of analgesia for Group BF was 237.80 ± 58.49 min, Group BC 281.26 ± 97.57 min and for Group BN 190.48 ± 61.94 min respectively (Figure 3). Even though there was an extended pain relief with addition of fentanyl, the prolongation with clonidine was statistically significant. Considering the duration of spinal block, in Group BC, L1 regression time is 232.76 ± 94 min which was higher compared to Group BF (202.34 ± 60 min) and Group BN (172.28 ± 56 min) but statistically insignificant. The intraoperative motor blockade was similar in all the Groups. As mentioned earlier, patients of Group BC had more episodes of hypotension to receive vasopressors frequently. The sedation scores were comparable in all the three groups. Majority of the patients in all groups were between scores two and three in the Ramsay sedation scale. Even though there were minor differences with regard to shivering, bradycardia, there was no significance. All the patients were discharged comfortable and the perioperative course was uneventful.

Table 1: Age-wise distribution of patients in various groups

Age (years)	Groups			p-value
	BF	BC	NS	
18-39 (Young adults)	14	20	5	0.1
40-59 (Adult)	31	24	6	
> 60 (Elderly)	5	6	8	

Table 2: showing the mean height and weight between the three groups

Variable	Groups			p-value
	BF	BC	NS	
Weight (Kg)	54.86	54.54	55.90	0.747
Height (cm)	159.28	158.34	161.54	

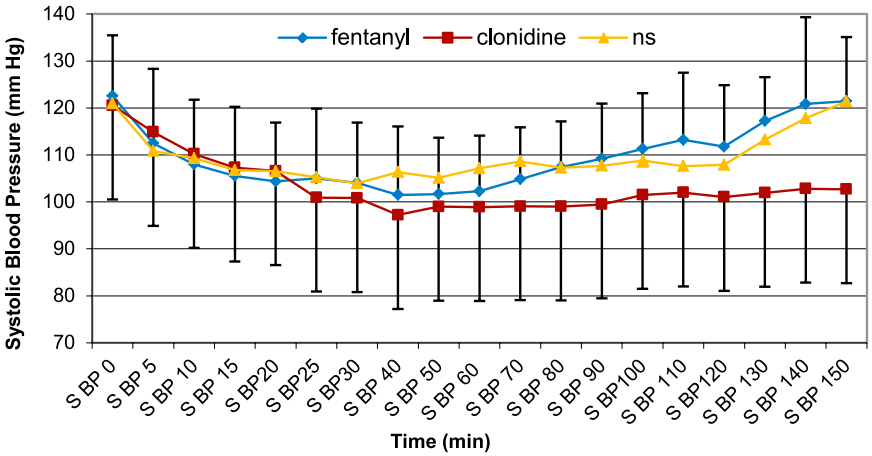

Figure 1: Comparison of systolic blood pressure in the groups

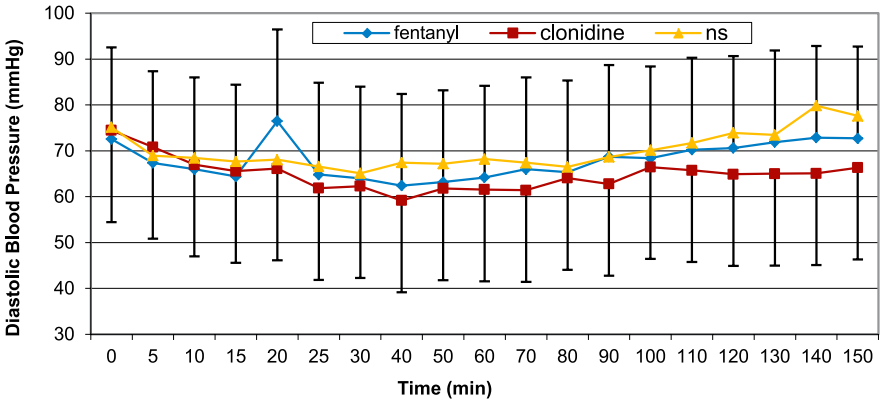

Figure 2: Comparison of diastolic blood pressure in the groups

DISCUSSION

The concept of intrathecal adjuvants is becoming a necessary armamentarium in day to day anesthesiology practice. The addition of alpha 2 agonists has been proved to increase the duration of anesthesia. Almost

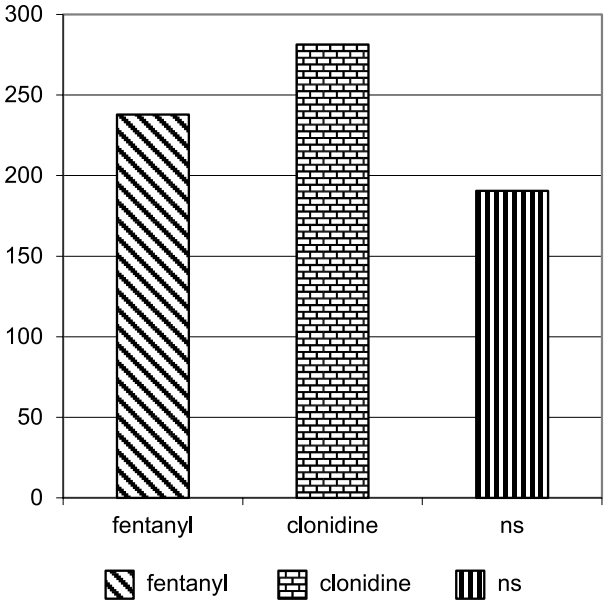

Figure 3: Comparative duration of analgesia in the groups

all the researchers have identified a prolongation of surgical anesthesia and analgesia in patients receiving additional clonidine in different doses[7,8,9], but in our study the prolongation of L1 regression was not statistically significant with 50 μg of additional clonidine. The duration of analgesia was significantly higher with clonidine in our study which goes along with others. Even addition of 12.5 μg has increased the duration of subarachnoid block[10]. Strebel et al.[11] have found that addition of 37.5 μg prolonged the duration without significant hemodynamic disturbances. In our study the duration of analgesia and post operative analgesic requirement is prolonged in clonidine group as compared to fentanyl group which correlates with the study of Bajwa et al.[12] In most of the studies[13,14] using intrathecal clonidine, the onset of hypotension was around twenty minutes after the block, while in our case, it was forty minutes. This assumes significance in surgeries which finish before sixty minutes and continued hemodynamic monitoring is essential upto 150 min in patients receiving intrathecal clonidine. Fentanyl, when added intrathecally with bupivacaine produces stable haemodynamics.[15] Bogra et al.[16] administered graded dose of bupivacaine (8, 10, 12.5 mg) alone and similar doses of bupivacaine along with 12.5 μg dose of fentanyl, studied the synergistic effect of intrathecal fentanyl and bupivacaine in spinal anesthesia for 120 obstetric patients scheduled caesarean section.[15] He demonstrated the abolition of visceral pain and better hemodynamic stability with addition of fentanyl. In our study, a similar observation is made with regard to stable hemodynamics with the addition of 50 μg of fentanyl. Addition of fentanyl prolongs duration of analgesia than the control group without any side effects, even though the prolongation is less than that caused by clonidine. This makes clear that fentanyl may be considered for such cases where a mild prolongation is suffice with stable hemodynamics.[16] The motor blockade was similar in the initial times especially intraoperative time while there is an extended motor blockade with the addition of clonidine. This was not found in the BF group. This finding suggests that addition of clonidine may be considered in whom we want an extended relaxation of the muscles. This finding is in contrast to earlier studies where intra operative motor blockade is better with clonidine[17]. Shah BB et al. have suggested the dose of clonidine as adjuvant as 60 μg which nearly goes along with our results.[18] The sedation was not significant in any of the groups to indicate that addition of 50 μg of clonidine which is just less than 1 μg/kg for a mean weight of 55 kg in our study patients is less than the dose in studies which give sedation as a side effect with the use of clonidine. As such addition of 1 μg/kg may be extremely difficult in patients with variable weights like 54 kg and 48 kg etc. Hence we resorted to a fixed 50 μg of both the drugs which can be given with relative ease when we combine with bupivacaine rather than 1 μg/kg as a precise dose. This study may look like establishing an old well known fact, yet it's the analgesia which is provided by clonidine lasted longer with an extended hemodynamic disturbance. Hence we suggest a need for a closer prolonged monitoring in cases where clonidine is added.

CONCLUSION

Addition of 50 μg of clonidine to intrathecal bupivacaine produces prolonged duration of analgesia more than either addition of fentanyl or the control group. The hemodynamic instability was more with clonidine group which occurred forty minutes after the block. There was no extended motor block or excess sedation with clonidine. Addition of fentanyl gives a mild prolongation of analgesia with stable hemodynamics than the control group. Prolonged vigilance on hemodynamics is mandatory if we add clonidine.

Conflicts of Interest: None of the authors involved in this study have reported any conflicts of interest.

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Author contribution:
RD - Done the study
SP - Concept, statistics, write up
NK - Overall supervision

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