Original Research Article

A study of intrathecal bupivacaine with fentanyl and intrathecal bupivacaine with clonidine with respect to sedation and intraoperative and postoperative analgesia in patients undergoing lower abdominal and lower limb surgeries

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Abstract

Background: Spinal anesthesia is a preferred choice of anesthesia in lower abdominal and lower limb surgeries. Various drugs have been used as adjuvants along with bupivacaine for subarachnoid block, but fentanyl and clonidine are commonly used for prolonging both sensory and motor blockade as well as postoperative analgesia. In present study, we tried to study sedation and analgesic effectiveness of intrathecal clonidine heavy bupivacaine combination with intrathecal fentanyl heavy bupivacaine for lower limb and lower abdominal surgeries. **Material and Methods:** This prospective, randomised double-blind, controlled study consisted of 90 patients scheduled for lower abdominal and lower limb surgeries. Patients were randomly allocated in 3 equal groups. Group A patients received 0.5% hyperbaric bupivacaine with preservative free normal saline, Group B patients received 0.5% hyperbaric bupivacaine with 0.5µg/kg clonidine and Group C patients received 0.5% hyperbaric bupivacaine with 0.5 µg/kg fentanyl. Assessment of pain was done using Visual Analogue Scale and Sedation was judged by Ramsay Sedation Scale. **Results:** Mean sedation score in group C (2.20±0.4) was significantly higher than group A (1.93±0.25). There was no significant difference in group B and group C. Duration of analgesia in group B (269.30±12.13) was significantly higher than group A (201.6±11.67) and group C (240.73±9.4). Also it was significantly higher in group C compared to group A. **Conclusion:** Clonidine and fentanyl seems to be an attractive alternative as an adjuvant to spinal bupivacaine. Clonidine when compared with fentanyl, offers a better additive with bupivacaine owing to earlier onset and prolonged duration of sensory and motor blockade as well as longer duration of analgesia.

Key Words: Lower abdominal surgeries, bupivacaine, clonidine, fentanyl, sedation, post-operative analgesia.

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Received Date: 06/06/2017 Revised Date: 28/07/2017 Accepted Date: 20/08/2017
DOI: https://doi.org/10.26611/1015326

Access this article online	
Quick Response Code:	Website: www.medpulse.in
	Accessed Date: 22 August 2017

INTRODUCTION

Pain is an inevitable component of post-operative period. It is a sense of damage, hurt, fear and punishment to the patient. Apart from obvious humanitarian reasons, post-operative pain is also associated with various systemic adverse responses all contributing to increased post - operative morbidity and mortality. Hence, an effective pain relief after surgery is essential for optimal care of surgical patients. The gate theory of pain has had considerable influence on the anesthesiologist's management of pain by focusing attention on the unique

How to cite this article: Keshav Gutte, Surekha Shinde, Kalpana Kelkar. A study of intrathecal bupivacaine with fentanyl and intrathecal bupivacaine with clonidine with respect to sedation and intraoperative and postoperative analgesia in patients undergoing lower abdominal and lower limb surgeries. *MedPulse International Journal of Anesthesiology.* August 2017; 3(2): 80-84.
http://medpulse.in/Anesthsiology/index.php

pharmacology of the dorsal horn of the spinal cord. By using intrathecal and epidural injections, anesthesiologists have learned to suppress nociceptive transmission at the first synaptic relay in the spinal cord[1]. The technique has implications in acute and chronic pain therapy because neuraxially administered drugs can provide analgesia without some of the systemic side effects of intravenously administered drugs. A typically modern view of perioperative pain is to view it as an impediment to recovery. Aggressive methods are often used to minimize pain and facilitate rapid return to normal functional activity. Lower abdominal and lower limb surgeries may be performed under local, regional (spinal or epidural) or general anesthesia. But, spinal anesthesia is a preferred choice of anesthesia in lower abdominal and lower limb surgeries since long time because of its rapid onset, superior blockade, low risk of infection[2]. In a patient receiving spinal anesthesia, with local anesthesia agents like bupivacaine, addition of an adjuvant drug intrathecally that will increase the efficacy of neuraxial block is a logical choice. Various drugs such as midazolam, neostigmine, clonidine, and opioids have been used as adjuvants to local anaesthetic agents intrathecally and epidurally for prolongation of post-operative analgesia. 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[3,4].Intrathecal clonidine is demonstrated to potentiate the effect of subarachnoid block as well as reduces the local anesthetic agent requirement[5]. Intrathecal clonidine also offers prolonged postoperative analgesia reduced shivering associated with subarachnoid block, and is devoid of side effects associated with intrathecal opioids[3,6,7]. In present study, we tried to study sedation and analgesic effectiveness of intrathecal clonidine heavy bupivacaine combination with intrathecal fentanyl heavy bupivacaine for lower limb and lower abdominal surgeries.

MATERIAL AND METHODS

This study is a prospective, randomised double-blind, controlled, single centre study. The study was conducted in a Tertiary care level institute and a clinical research organization. Patients were examined one day prior to surgery and baseline recordings of pulse, blood pressure and other vitals were recorded. Informed written consent was obtained from the patients prior to joining the study. Description of the measures taken to minimize / avoid bias randomization.

Randomization: Randomization was done in the block of 3 as per a computer- generated code from http://www.randomization.com.

Blinding: To facilitate the double-blinding method, the medication was prepared according to the randomization chartby an anaesthesiologist who was not be involved in the study. The randomization code was sealed in an envelope. The code number of each individual was also sealed in the envelope.

All the study drugs were sourced from the same manufacturer.

Study population: The study consists of 90 patients in the age group 18-55 yearsbelonging to ASA grade I and II scheduled for lower abdominal and lower limb surgeries. Patients were randomly allocated in 3 groups. Each group consisted of 30 patients.

Group A: Control Group

Patients received 0.5% Hyperbaric bupivacaine 3cc (15 mg) +0.5ml preservative free normal saline.

Group B: Patients received 0.5% hyperbaric bupivacaine 3cc (15mg) + 0.5 ug/kg Clonidine diluted with preservative free normal saline making it 0.5 ml.

Group C: Patients received 0.5% hyperbaric bupivacaine 3cc (15mg) + 0.5 ug/kg Fentanyl diluted with preservative free normal saline making it 0.5 ml.

All patients received volume of 3.5 ml intrathecal drug.

Inclusion Criteria: Patients of both sexes between age group of 18-55 years and weighing 45-75 Kgs with ASA I and II scheduled for lower limb and lower abdominal surgeries.

Exclusion Criteria: Patient having heart disease (using adrenergic receptor antagonist, calcium channel blockers, Angiotensin converting enzyme inhibitors), dysarrythmias on ECG, respiratory, renal, hepatic and CNS disease, metabolic and bleeding disorders. Patients with diabetes mellitus, acid peptic disorder, local infection of spinal area, known allergic to any of the study medication, uncooperative patient.

Patients under study had undergone thorough preoperative assessment including detailed case history, clinical examination and all necessary investigations. Pre-operative investigations such as routine haemogram, Liver and kidney function tests were done along with chest X-ray and ECG. After thorough pre-anaesthetic assessment and obtaining consent patient satisfying inclusion criteria undergoing lower abdominal surgeries were randomly assigned into one of the following groups. Drug which was prepared and kept in covered syringes was injected during the procedure. Premedication consists of Glycopyrrolate 5 ug/kg intramuscularly and Ondansetron 0.08 mg/kg intravenously. Preloading was done with Ringer Lactate (RL) solution (10ml/kg).Lumbar puncture was done with No. 25 G spinal needle and free, clear flow of CSF obtained. Intrathecal drug was injected into subarachnoid space according to the group allotted to them by double

blind technique. Supine position was given immediately. Motor and Sensory block was assessed every minute. Sensory block was assessed by a pin prick test performed with 22 G short bore needle. Motor block was assessed by asking the subject to lift his lower limbs. Complete motor block is when no voluntary movement is possible. During surgery, patient did not receive any sedation. IV fluids administered preoperatively dictated by blood loss and hemodynamic instability. Baseline observation was started before intrathecal drug injection. Heart rate, NIBP, ECG and peripheral Oxygen saturation (SPO2) was monitored intraoperatively. After intrathecal drug injection, data was recorded during 1st hr at 15, 30, 45, 60 minutes and there after every hour up to l2 hrs followed by 4 hrly interval up to 24 hours. Assessment of pain was done using "Visual Analogue Scale" between 0-10 (Grade 0- 0-1=Good analgesia, Grade 1- 1-4=Moderate analgesia, Grade 2- 4-7=Mild analgesia, Grade 3- 7-10=No analgesia). Supplemented analgesia used was Diclofenac 75mg intramuscular when VAS >3. Motor block was assessed according to "Modified Bromage Scale" between 0 to 3.Sedation was judged by "Ramsay Sedation Scale" between 1 to 6 (Score 1= Anxious or agitated or restless or both, Score 2= Co-operative, oriented and tranquil, Score 3= Responding to commands only, Score 4=Brisk response to light Glabellar tap, Score 5=Sluggish response to light Glabellar tap, Score 6=No response to light Glabellar tap). Post-operatively, patient vitals monitored and looked for any complications half hourly for 3 hrs and hourly for the next 24 hours. Patients were monitored for post-operative pain by using VAS and were supplemented with analgesics if VAS > 4 and monitored for the time to first analgesic usage and total 24 hours consumption of analgesic drug will be noted.

Statistical Analysis: The detailed data was entered into well tabulated Microsoft Excel sheet and subsequently analyzed statistically 'One-way ANOVA with post-hoc Bonferroni test' test was used depending upon the nature of data. Graphical display was done for visual inspection.

RESULTS

In total, distribution of males and females were statistically similar. Majority of patients in each group were above 40 years. There was no significant difference in mean age of patients in each study group. In total, 76.7% patients were of ASA grade I in each group and 23.3% in ASA grade II in all the three group. Distribution of ASA grading was similar (Table 1).

Table 1: Demographic characteristics of study population

Demographic characteristics	Group A	Group B	Group C
Age groups			
<30	05 (16.7%)	06 (20%)	04(13.3%)
31-40	11 (36.7%)	10 (33.3%)	12 (40%)
>40	14 (46.7%)	14 (46.7%)	14 (46.7%)
Mean±SD	39.23±7.0	38.60±8.5	39.97±7.3
Sex			
Male	16 (53.3%)	16 (53.3%)	14 (46.7%)
Female	14 (46.7%)	14 (46.7%)	16 (53.3%)
ASA grade			
I	23 (76.7%)	23 (76.7%)	23 (76.7%)
II	07 (23.3%)	07 (23.3%)	07 (23.3%)

Intraoperatively, at 5 minutes,15 minutes,30 minutes,45 minutes,60 minutes,90 minutes, 120 minutes,150 minutes,180 minutes,210 minutes and 240 minutes pulse rate, systolic and diastolic blood pressures in each group did not vary significantly ($p>0.05$ for all intergroup comparisons) suggesting no difference vitals parameters in three groups.

Table 2: Sedation score in three study groups

Groups	Mean	SD	95% CI		Min	Max
A	1.93	0.25	1.84	2.03	1	2
B	2.10	0.30	1.99	2.21	2	3
C	2.20	0.40	2.05	2.35	2	3

($p=0.007$, significant compared to group A, one-way ANOVA with post-hoc Bonferroni test). Mean sedation score in group C (2.20±0.4) was significantly higher than group A (1.93±0.25) ($p=0.007$). There was no significant difference in group B and group C. Sensory onset was significantly early in group B compared to group A ($p<0.0001$) and group C ($p<0.0001$). Also there was significant difference in group C and group A ($p<0.0001$). Similarly, motor onset was significantly early in group B compared to group A ($p<0.0001$) and group C ($p<0.0001$). Also there was significant difference in group C and group A ($p<0.0001$).

Table 3: Duration of sensory and motor blockade in study groups

Parameter	Group	Mean	SD	95% CI		Min	Max
Duration of Sensory Block	A	114.43	5.82	112.26	116.61	104	122
	B	149.20	6.96	146.60	151.80	138	161
	C	130.63	7.21	127.94	133.33	116	140
Duration of Motor Block	A	167.33	9.23	163.89	170.78	150	182
	B	225.83	8.03	222.83	228.84	210	240
	C	183.37	5.26	181.40	185.33	170	191

Duration of sensory block was significantly longer in group B compared to group A (p<0.0001) and group C (p<0.0001). Also it was significantly longer in group C than group A (p<0.0001). Duration of motor block was significantly longer in group B compared to group A (p<0.0001) and group C (p<0.0001). Also it was significantly longer in group C than group A (p<0.0001).

Table 4: Duration of surgery and duration analgesia in three study groups

Parameter	Group	Mean	SD	95% CI		Min	Max
Duration of Surgery	A	103.33	12.69	98.60	108.07	84	130
	B	110.17	15.45	104.40	115.94	70	130
	C	105.50	14.76	99.99	111.01	70	130
Duration of Analgesia	A	201.60	11.67	197.24	205.96	182	217
	B	296.30	12.13	291.77	300.83	267	310
	C	240.73	9.40	237.22	244.24	220	250

For surgery: p>0.05; For analgesia: p<0.0001 Vs Group A, p<0.0001 Vs Group A, p<0.0001 Vs Group B, significant. Duration of surgery was not significantly different in all the three groups. Duration of analgesia in group B (269.30±12.13) was significantly higher (p<0.0001) than group A (201.6±11.67) and group C (240.73±9.4). Also it was significantly higher in group C compared to group A (p<0.0001). Occurrence of adverse events in our study was low. Bradycardia was noted in one patient from group A and B and atropine was required in similar number of patients. Hypotension was found in 2 patients from group A and one patient each in group B and C and Mephenteramine was required in similar number of patients in each group. There were no respiratory depression and itching in any patient in any of the groups. Incidence of side effects was not significant.

DISCUSSION

Pain is still a challenge for the entire medical field. Pain in the post-operative period is associated with various systemic side effects including respiratory, cardiovascular and other systems, which increases the morbidity and mortality. Anesthesiologists are leaders in the development of acute postoperative pain services, application of evidence-based practice to acute postoperative pain, and creation of innovative approaches to acute pain management. Provision of effective analgesia for surgical and other medical patients is an important component of this multidimensional role. In present study, duration of analgesia was measured as time interval between intrathecal injection to patients 1st request of analgesic. Mean duration of analgesia with intrathecal injection of bupivacaine+normal saline was 201.60±11.67mins, while it was 296.30±12.13mins with intrathecal injection of bupivacaine+clonidine and 240.73±9.40minutes with patients received bupivacaine (15mg)+Fentanyl. Duration of analgesia in group B (269.30±12.13 mins) was significantly higher (p<0.0001) than group A (201.6±11.67 mins) and group C (240.73±9.4 mins). Also it was significantly higher in group C compared to group A (p<0.0001). Therefore, there is significant difference between duration of motor blockade in group A, group B and group C (p< 0.001). Intraoperatively,pulse rate, systolic and diastolic blood pressures in each group did not vary significantly (p>0.05 for all intergroup comparisons) suggesting no difference vitals parameters in three groups. Sedation was assessed by Ramsay's sedation score graded from 1 to 6 depending upon whether patient is awake or in deep sleep. Mean sedation score in group B and C (2.20±0.4) was significantly higher than group A (1.93±0.25) (p=0.007). There was no significant difference in group B and group C. Kanazi *et al* found that Dexmedetomidine (3 mcg) or clonidine (30 mcg), when added to intrathecal bupivacaine, produces a similar prolongation in the duration of the motor and sensory block with preserved hemodynamic stability and lack of sedation[8]. Chopra P *et al* studied the effect of low- dose clonidine when added to a bupivacaine-fentanyl mixture increased the duration of effective analgesia and the duration of sensory and motor block in gynecological surgery. The incidence of intraoperative pain and requirement of postoperative analgesics was significantly less when clonidine was added to intrathecal bupivacaine with or without fentanyl[9]. Van Tuijl *et al* studied effect of Intrathecal low-dose hyperbaric bupivacaine-clonidine combination in outpatient knee arthroscopy. They found that the addition of 15 mcg clonidine to 5 mg of intrathecal hyperbaric bupivacaine prolongs the duration of motor block and improves the quality of the block[10]. Florio P *et al*studied effect of low-dose spinal anesthesia with hyperbaric bupivacaine with intrathecal fentanyl for operative hysteroscopy. They found that low-dose spinal anesthesia is a feasible technique in the inpatient setting for operative hysteroscopy in women with high surgical risks[11]. Idowu OA *et al* studied the effects of intrathecally administered fentanyl on duration of analgesia in patients undergoing spinal anaesthesia for elective caesarean section. They found that the addition of 25 mcg of fentanyl to bupivacaine intrathecally for elective

caesarean section increases the duration of complete and effective analgesia thereby reducing the need for early postoperative use of analgesics[12]. There was significant difference in onset and duration of sensory and motor blockade when clonidine and fentanyl added to bupivacaine. It produces prolonged sensory and motor blockade. It may be more suitable for major surgeries on abdomen and lower extremities. Duration of analgesia significantly more when clonidine and fentanyl were added to bupivacaine. Mild sedation is observed with clonidine and fentanyl. Sedation score was not more than 3 in any of these patients, none of these patients were deeply sedated or associated with respiratory depression in our dose. Thus clonidine and fentanyl are good adjuvant drug and their use intrathecally as an additive to bupivacaine does extend the duration of spinal anesthesia significantly, lowering the need to administer general anesthesia if duration of surgery is prolonged. Further they also provide excellent post-operative analgesia. The drawback of intrathecal clonidine and fentanyl is increase in duration of motor blockade which may not be suitable for short duration of surgeries. But for surgeries which extend longer than usual expected time clonidine and fentanyl are good additives intrathecally with bupivacaine than bupivacaine alone and in addition when these additives are used less analgesics are consumed post-operatively. So, less chances of adverse effects of NSAIDS. Clonidine is better than fentanyl in these surgeries which extend longer than usual expected time as clonidine is having early onset of sensory and motor actions than fentanyl and longer duration of sensory and motor blockade and also longer duration of post-operative analgesia with comparitively same side effects as fentanyl in our dose. In conclusion, 0.5µg/kg clonidine and 0.5µg/kg fentanyl seems to be an attractive alternative as an adjuvant to spinal bupivacaine in surgical procedures of prolonged duration with minimal side effects and excellent quality of spinal analgesia.Clonidine when compared with Fentanyl, offers a better additive with Bupivecaine owing to earlier onset and prolonged duration of sensory and motor blockade as well as longer duration of analgesia.

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Source of Support: None Declared
Conflict of Interest: None Declared