

Comparative Evaluation of the Efficacy of Intrathecal Fentanyl, Clonidine and Fentanyl-Clonidine Combination as an Adjuvant to Bupivacaine for Infra-Umbilical Surgery

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Received : January 10, 2018
Accepted : February 18, 2018
Published : March 15, 2018

Abstract

Background: The aim of this study was to evaluate the level of sensory block, onset and duration of motor block, post-operative analgesia, and adverse effects of combination of clonidine and fentanyl given intra-theccally with hyperbaric bupivacaine. **Material and Methods:** Ninety patients were randomized into three groups of group BC (n=30): hyperbaric 0.5% bupivacaine, clonidine, and 0.9% NaCl intra-theccally; group BF (n=30): hyperbaric 0.5% bupivacaine, fentanyl, and 0.9% NaCl intra-theccally; group BFC (n=30): hyperbaric 0.5% bupivacaine, 0.3 ml of clonidine, and fentanyl intra-theccally. **Results:** Either adjuvant, fentanyl or clonidine when added to intra-theccal bupivacaine prolongs the motor block and decreases the requirement of rescue analgesic in 24 hours but time to first rescue analgesic request is more prolonged in clonidine as compared to fentanyl. Clonidine is superior to fentanyl in prolonging the sensory block. Combination of intra-theccal fentanyl and clonidine as compared to fentanyl alone, as adjuvant to bupivacaine, is superior in prolonging the sensory block, motor block and time to first rescue analgesic request. Combination of intra-theccal fentanyl and clonidine as compared to clonidine alone, as adjuvant to bupivacaine, produces similar sensory block but is superior in prolonging the motor block and time to first rescue analgesic request. **Conclusion:** The combination of fentanyl and clonidine, as adjuvant to intra-theccal bupivacaine, is superior for surgical procedures of long duration and those procedures which mandate muscle relaxation.

Keywords: Analgesics, Adjuvants, Bupivacaine, Fentanyl, Clonidine, Muscle Relaxation.

Introduction

Spinal anaesthesia is one of the most commonly used techniques for infra-umbilical surgeries as it is very economical, easy to administer, produces rapid onset of anaesthesia and complete muscle relaxation [1]. Hyperbaric bupivacaine is the most commonly used intra-theccal local anaesthetic [2]. However, post-operative pain control is a major problem because spinal anaesthesia using local anaesthetics alone is associated with relatively short duration of action and thus early analgesic intervention is needed in post-operative period [3].

To overcome bupivacaine shortcoming various adjuvants like opioid, neostigmine, clonidine, midazolam etc. have been used along with local anaesthetic agents to avoid intra-operative visceral and somatic pain and to prolong post-operative analgesia. Adjuvants also reduce the dose of local anaesthetics and thus their side effects [4]. Fentanyl is associated with dose dependent side effects like respiratory depression, pruritus, urinary retention etc [5]. Clonidine, a selective partial agonist for α_2 -adrenoreceptors may cause hypotension, bradycardia and sedation but is not associated with the significant side effects of spinal opioids [6].

Material and Methods

Our study was conducted on patients admitted to different surgical departments at Muzaffarnagar Medical College & Hospital, Muzaffarnagar. It was a randomised prospective double blinded study. Patients were randomly by computer generated random number table and evenly assigned into three groups: BC, BF and BFC with 30 patients each. Patients with age 18 – 60 years, American Society of Anaesthesiologist (ASA) category I/II and expected surgical duration \leq 2 hours were included in the study. Patients with co-morbidities like cardiovascular disease, diabetes mellitus, allergic to any of the test drugs, alcoholic or with history of substance abuse or chronic pain and contraindication to spinal anaesthesia were excluded.

All patients were explained the study protocol and familiarized with Visual Analog Scale (VAS). An informed and written consent was taken to participate in the study. All patients received a dose of 0.25 mg alprazolam a night before the surgery. In the operation theatre, baseline recordings of ECG, pulse oximeter and non-invasive blood pressure (NIBP) were recorded. An intravenous access with 18 gauge intravenous (IV) cannula was made on right dorsum of hand and patients were preloaded with 10 ml/kg ringer lactate. The patients were divided into three groups: (i) Group BC (n=30): 2.6 ml of hyperbaric 0.5% bupivacaine (13 mg), 0.3 ml of clonidine 45 μ g, and 0.3 ml of 0.9% NaCl intra-theccally (total volume = 3.2 ml). (ii) Group BF (n=30): 2.6 ml of hyperbaric 0.5% bupivacaine (13 mg), 0.3 ml of fentanyl 15 μ g, and 0.3 ml of 0.9% NaCl intra-theccally (total volume = 3.2 ml). (iii) Group BFC (n=30): 2.6 ml of hyperbaric 0.5% bupivacaine (13 mg), 0.3 ml of clonidine 45 μ g, and 0.3 ml of fentanyl 15 μ g intra-theccally (total volume = 3.2 ml).

Heart rate and NIBP were recorded before and immediately after intra-theccal injection i.e. 0 minutes and thereafter at 2 and 5 minutes and every 5 minutes during the surgery and every

15 minutes in the post-operative period until the discharge criteria from post-anaesthesia care unit (PACU) were met. A decrease in systolic BP of more than 20% (as compared to the baseline) or $<$ 90 mm Hg systolic, whichever is low, was treated with incremental doses of 5 mg intravenous ephedrine and fluid at 2 ml/kg. A heart rate less than 50 beats/min was treated using increments of 0.5 mg intravenous atropine. Level of sensory block was assessed by temperature appreciation to a spirit soaked cotton on both the sides in mid-clavicular line at 2 and 5 minutes and then every 5 minutes until 2 consecutive readings were similar (maximum sensory block height). During the intra-operative period the sensory level was assessed every 30 minutes. The degree of motor block was assessed by the modified Bromage scale at 2, 5, 10, 15, 20 minutes after the intra-theccal injection or till the maximum block is achieved, whichever is earlier. In case of inadequate sensory block (as per the surgical requirement) or inadequate motor block (Modified Bromage scale $<$ 2) at 20 minutes or the patient required addition supplementation during surgery, the case was considered as a failure. Sedation was assessed using Ramsey sedation scale 30 minutes after intra-theccal injection [7].

In PACU, the patients was assessed every 15 minutes for heart rate, NIBP and every 30 minutes for sensory block (until 2 segment regression) and motor block (until normal motor function returned i.e. modified Bromage scale is 0). Pain and sedation were assessed at 3 hours, 4 hours, 6 hours, 12 hours and 24 hours after the intra-theccal injection. Pain was assessed by VAS. Rescue analgesia was given by 75 mg diclofenac intramuscularly, if VAS $>$ 3 or analgesia demanded by the patient. It was not repeated within 6 hours of the earlier dose and not more than 3 doses in 24 hours. Time from intra-theccal injection to voluntary voiding of urine was noted. In case any patient was not able to void urine, if required, Foley's catheterization was placed. Any other adverse effect in the post-operative period (till 24 hours) like nausea, vomiting, respiratory depression, dryness of mouth, skin rash, itching,

headache or any other neurological symptom were recorded.

Besides hemodynamics, the following parameters were also observed i.e. sensory block [maximum sensory block height achieved, time to achieve maximum sensory block (tS1), time for 2 segment regression of sensory block (tS2), duration of sensory block i.e. (tS1-tS2)], motor block [maximum motor block achieved, time to achieve maximum motor block (tM1), time for complete regression of motor block (tM2), duration of motor block i.e. tM1-tM2], time to first rescue analgesia

request, number of times rescue analgesia request in 24 hours, sedation score using Ramsey sedation scale, side effects, if any.

Results

90 subjects who were scheduled for surgery were enrolled with 30 children in each group. Various demographic parameters are summarized in **Table 1**. Outcome variables and statistical comparison among groups for sensory block, motor block and analgesia are summarized in **Table 2** and **3**.

Table 1: Demographic parameters.

Group	Age (years) (mean ± SD)	Sex n (%)		ASA physical status n (%)		BMI (kg/m ²) (mean ± SD)
		Male	Female	1	2	
BC (n=30)	39.33 ± 11.62	20 (66.6%)	10 (33.3%)	24 (80%)	6 (20%)	21.93 ± 3.18
BF (n=30)	40.30 ± 11.167	21 (70%)	9 (30%)	22 (73.33%)	8 (26.66%)	21.53 ± 2.95
BFC (n=30)	42.00 ± 11.72	22 (73.33%)	8 (26.66%)	25 (83.33%)	5 (16.66%)	21.67 ± 3.06

Table 2: Sensory block, motor block, analgesia and side effects in the three groups.

	BC (n=30)	BF (n=30)	BFC (n=30)
Sensory Block			
Maximum sensory block height (dermatome) [median]	T6	T6	T5
Time to achieve maximum sensory block (min) (mean ± SD)	8.67 ± 3.46	8.50 ± 3.26	8.50 ± 3.26
Time for segment regression of sensory block (min) (mean ± SD)	201 ± 37.10	133.17 ± 29.23	203.67 ± 33.80
Duration of sensory block (min) (mean ± SD)	192.33 ± 36.55	124.66 ± 29.48	195.33 ± 34.11
Motor Block			
Maximum motor block achieved (modified Bromage scale) (mean ± SD)	2.87 ± 0.34	2.90 ± 0.30	2.93 ± 0.25
Time to achieve maximum motor block (min) (mean ± SD)	8.167 ± 3.43	7.00 ± 2.82	6.50 ± 2.33
Time for complete regression of motor block (min) (mean ± SD)	215.33 ± 33.01	167.87 ± 24.88	284.17 ± 26.88
Duration of motor block (min) (mean ± SD)	207.17 ± 32.61	160.83 ± 25.63	277.67 ± 26.90
Analgesia			
Time to first rescue analgesic request (min) (mean ± SD)	323 ± 57.98	240.83 ± 31.62	424.50 ± 45.95
Number of times rescue analgesic required in 24 hrs (mean ± SD)	1.53 ± 0.57	1.53 ± 0.62	1.57 ± 0.57
Side Effects			
Headache	0	2	4
Backache	0	6	8
Nausea/vomiting	0	2	0
Itching	0	6	2
Respiratory depression	0	0	0
Dryness of mouth	2	0	0
Others	0	0	0

Discussion

Either adjuvant, fentanyl or clonidine when added to intra-theat bupivacaine is similar in prolonging the motor block and decreasing the requirement of rescue analgesic in 24 hours but time to first rescue analgesic request is more prolonged in clonidine as compared to fentanyl. Also, clonidine is superior to fentanyl in prolonging the sensory block. Combination of intra-theat fentanyl and clonidine as compared to fentanyl alone, as adjuvant to bupivacaine, is superior in prolonging the sensory block, motor block and time to first rescue analgesic request. Combination of intra-theat fentanyl and clonidine as compared to clonidine alone, as adjuvant to bupivacaine, produces similar sensory block but is superior in prolonging the motor block and time to first rescue analgesic request. There is no difference in the 24 hour rescue analgesic requirement and clinically significant side effects among the three groups.

Our study obtained similar results to study performed by Hamid *et al.* in sixty adult patients scheduled for anal surgery under spinal anaesthesia which were divided into 4 groups: control group, received only bupivacaine 0.5%. Clonidine group, received 30 µg clonidine added to bupivacaine 0.5%; fentanyl group, received 50 µg fentanyl added to bupivacaine 0.5% and fentanyl/clonidine group, received 15 µg clonidine combined with 25 µg fentanyl added to bupivacaine 0.5%. They concluded that the addition of low dose clonidine to fentanyl as adjuvant to spinal bupivacaine significantly increased the duration of sensory block [8].

Our results are similar with a study done by Routrey *et al.* who did a prospective randomized study in which eighty patients posted for lower limb orthopaedic surgery and divided into two groups of forty each. One group (group C) received intra-theat hyperbaric bupivacaine (2.5 ml) and 50 µg clonidine (diluted to 0.5 ml) while other group (group F) received intra-theat hyperbaric bupivacaine (2.5 ml) and fentanyl 25 µg (diluted

Table 3: Statistical comparison among groups for sensory block, motor block and analgesia (Data expressed as *P* value).

	BF vs BC	BC vs BFC	BF vs BFC
Sensory Block			
Maximum sensory block height	<0.509	<0.152	0.036*
Time to achieve maximum sensory block	<0.375	<0.845	<1.002
Time for segment regression of sensory block	<0.0001*	<0.771	<0.0001*
Duration of sensory block	<0.0001*	<0.743	<0.0001*
Motor Block			
Maximum motor block	<0.718	<0.439	<0.675
Time to achieve maximum motor block	<0.155	<0.031*	<0.45
Time for complete regression of motor block	<0.066	<0.001*	<0.01*
Duration of motor block	<0.100	<0.001*	<0.001*
Analgesia			
Time to first rescue analgesic request (min)	<0.008	<0.001*	<0.024*
Number of times rescue analgesic required in 24 hrs	<1.002	<0.783	<0.795

**P*<0.05

to 0.5 ml). They found out that duration of sensory and motor block was significantly prolonged in Group C compared to Group F [9].

Juliao *et al.* showed that addition of clonidine (30 µg) and combination of sufentanil (5 µg) and clonidine (15 µg) caused a significant prolongation of motor block compared to groups receiving only sufentanil or no adjuvant to bupivacaine (15 mg). Though our results were mostly similar, we didn't find a significant difference between groups BC and BF [10].

Bograet *et al.* found addition of fentanyl to intra-theat bupivacaine increases the post-

operative analgesic effect but less than combination of clonidine with bupivacaine [11]. Our results are also consistent with those of Bhure *et al.* who found better post-operative analgesia by adding clonidine (75 µg) to 2.2 ml of 0.5% bupivacaine as observed by a significant delay in the first request for analgesia. They also found the time to first rescue analgesic request to be significantly longer on adding of clonidine (75 µg) to bupivacaine as compared to fentanyl (25 µg) [12].

We found that the combination of fentanyl and clonidine, as adjuvant to intra-theatrical bupivacaine is better, for surgical procedures of long duration and those procedures which mandate muscle relaxation. Optimal dose of adjuvants to be used is a matter of further evaluation. However, for surgical procedures of short duration and for procedures not requiring muscle relaxation, the use of combination of fentanyl and clonidine, as adjuvant to bupivacaine, would be inappropriate since it delays motor recovery.

Contributors: SR: manuscript writing, patient management; SPS, MA: manuscript editing, patient management; VB: critical inputs into the manuscript. SR will act as guarantor. All authors approved the final version of this manuscript.

Funding: None; *Competing interests:* None stated.

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