ORIGINAL ARTICLE

Intrathecal Administration of Bupivacaine and Bupivacaine With Different Doses of Clonidine For Post-operative Analgesia in Lower Abdominal and Lower Limb Surgeries – A Comparative Study

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Abstract

Local anesthetic agent like bupivacaine used for spinal anaesthesia in surgeries of lower half of the body provides short-term analgesic effect in initial postoperative period. Adjuvant intrathecal clonidine is recommended for additional analgesic effect. This study was conducted to find out efficacy of clonidine in 50 microg and 75 microg doses in combination with bupivacaine for postoperative analgesia in lower abdominal and lower limb surgeries when administered intrathecally. The present prospective, randomized study was conducted on 90 patients of ASA grade I and II, aged 18-60 years of either sex scheduled for lower abdominal and lower limb surgeries in ASCOMS, Sidhra, Jammu.Patients were equally distributed in three groups - A, B and C. Group A patients received 15 mg bupivacaine alone, Group B patients received 15 mg bupivacaine and 50 ?g clonidine and Group C patients received 15 mg bupivacaine and 75 ?g clonidine. Postoperatively after the conclusion of surgery, analgesia and sedation scores were recorded at 1, 2, 3, 4, 6, 12, 24 and 48 hours. At the end of 48 hours, the patients were evaluated for the quality of analgesia, sedation, amnesia and the side effects. The requirement of the rescue analgesic during the period was calculated, recorded and compared at the end of surgery. Data regarding the various parameters was statistically analysed using Anova test. A p value of <0.05 was considered as statistically significant. Female patients dominated all the three groups. The groups were comparable with respect to gender, age and weight. Mean number of rescue analgesics required were significantly less in Group C (0.6) when compared to Group B (1.8) and Group A (2). Moreover, intraoperative mean heart rate in Group A was significantly more when compared to Group B and Group C. Moreover, intraoperative mean systolic, diastolic and arterial blood pressure respectively were significantly more in Group A and Group B as compared to Group C. VAS score was significantly lower in Group C as compared to Groups A and B. Sedation and amnesia were significantly more in Groups B and C as compared to Group A. Rescue analgesia was required in a significantly higher number of patients in Groups A and B as compared to Group C. Addition of clonidine 75 mg to 3 ml of 0.5% bupivacaine provided significantly better pain relief in lower limb and lower abdominal surgeries, less consumption of analgesics, minimal sedation and amnesia without any major side effects.

Key words

Spinal anaesthesia, intrathecal clonidine, bupivacaine, lower abdominal surgeries.

Introduction

Spinal anaesthesia is a preferred method for surgeries on lower half of the body as it uses small dose of anaesthetic, is easy to perform, offers a rapid onset, has minimal side effects on mental status, blood loss is less and offers protection against thromboembolic episodes. However, advantages are at times offset by relatively short duration of action and complaints of post-operative pain when it wears off (1,2).

Bupivacaine is the most commonly employed local anaesthetic for subarachanoid block, but has limited duration of action. Perioperative haemodynamic status is also a concern (3). By adding adjuvant drugs to

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intrathecal local anesthetics, quality and duration of spinal blockade can be improved, along with prolonging postoperative analgesia. Other advantages include reducing dose of local anesthetics, as well as total amount of systemic postoperative analgesics (4).

Intrathecally injected drugs include opioids, benzodiazepines, anti-cholinestreas, baclofen, vasoconstrictors, alpha 2 agonists, etc (5). Clonidine, an alpha 2 receptor agonist is being promoted as an alternative to neuraxial opioids for control of pain. It has proven to be a potent analgesic, free of some of the opioid related side effects (6). It produces antinociceptive effects without any neurotoxicity and can be used in the treatment of somatic pain. It has the ability to potentiate the effects of local anesthetics (7). It does not produce pruritus or respiratory depression and prolongs the sensory blockade and reduces the amount or concentration of local anesthetic required to produce postoperative analgesia (7, 8). Intrathecal administration of clonidine produces a high drug concentration in the vicinity of ?-2 adrenoreceptors in the spinal cord and it blocks the conduction of C and A? fibres, while increasing potassium conductance in isolated neurons in vitro and intensifies conduction block of local anaesthetics (6). Clonidine is now an acceptable adjuvant to local anaesthetics for epidural route; nevertheless clinical trials provide evidence that less clonidine is needed intrathecally than epidurally to produce nearly same analgesic effect with fewer side effects (1).

Considering the effectiveness of spinal administration of local anesthetics and clonidine for postoperative analgesia, this study was undertaken to access of effect of combination of local anesthetics bupivacaine and adjuvant clonidine in terms of quality and duration of post operative analgesia.

Materials and Methods

The current study was conducted in the Department of Anaesthesiology and Intensive care, Acharya Shri Chander College of Medical Sciences and Hospital, Sidhra, Jammu. After obtaining approval of the Institutional Ethics Committee and written informed consent, 90 patients of ASA grade I and II, aged 18-60 years, of either sex, scheduled for lower abdominal and lower limb surgeries were enrolled in this prospective study.

Patients excluded were those with ASA grade >II, having cardiovascular disease, any neurological disease, with history of allergy to the studied drugs and those with uncontrolled hypertension.Patients were randomly distributed in three groups of 30 each. Group A patients received 15 mg bupivacaine in 8% glucose, Group B patients received 15 mg bupivacaine in 8% glucose and 50 ?g clonidine and Group C patients received 15 mg bupivacaine in 8% glucose and 75 microg clonidine. All solutions were diluted with saline to a total volume of 4 ml. After taking a detailed history, a thorough general and systemic examination of the patient was carried out. All the patients were kept fasting overnight prior to surgery and given a premedication of diazepam 5 mg night before surgery and again on the morning of surgery. A good intravenous line with 16 or 18 G cannula with Ringer's lactate solution was established. Vital parameters like blood pressure (systolic, diastolic and mean arterial pressures), heart rate, electrocardiogram (ECG) and oxygen saturation (SpO2) were recorded before the subarachnoid block as the baseline values, then every 2 minutes after the administration of spinal anaesthesia for 20 minutes and thereafter at every 5 minutes interval till the completion of surgery. During surgery if there was any complication like bradycardia/ tachycardia, hypotension/hypertension, fall of SpO2, nausea/vomiting, it was recorded and treated accordingly.

Under all aseptic precautions and with the patient in a sitting position, drug according to the group was administered in the subarachnoid space through a 25 G Quincke's needle at L 3-4 intervertebral space, after confirming dural puncture with free flow of CSF. Immediately after administration of the local anaesthetic solution subarachnoidally, the patients were placed in the supine position. All the patients received supplemental oxygen at the rate of 3 litres per minute via a ventimask. The level of sensory analgesia, defined as loss of sensation to pinprick, was recorded bilaterally at two minutes interval till the level stabilizes, when there was complete loss of sensation and surgeon was asked to proceed with the surgery.

Postoperatively after the conclusion of surgery, analgesia and sedation scores were recorded at 1, 2, 3, 4, 6, 12, 24 and 48 hours. Pain intensity at rest and on movement (to raise head and attempt to sit up), and on coughing was assessed with a 10 cm visual analog scale (VAS; 0=no pain and 10=worst imaginable pain). Sedation scores were recorded using SOCA scoring system. Vital parameters like heart rate, blood pressure, arterial oxygen saturation and any complications or side effects were recorded at the same time.

In case of patient complaint of pain the rescue analgesic was provided to the patient in form of injection diclofenac sodium, 1.5 mg per kg body weight, deep intramuscular into the gluteal region. Only a score of 3 or more on the VAS qualified a patient for receiving the rescue analgesic.

At the end of 48 hours, the patients were evaluated for the quality of analgesia, sedation, amnesia and the side effects. The requirement of the rescue analgesic during the period was calculated, recorded and compared at the end of surgery.

Data regarding the various parameters was statistically analysed using Anova test. A p value of <0.05 was considered as statistically significant.

Results

Female gender dominated all the three groups. In Group A, Group B and Group C, there were 19 (63.33%), 21 (70%) and 20 (66.67%) female patients. However, gender distribution of patients were comparable in all the three groups (p=0.66). The mean age ± standard deviation of patients in Group A was 46.10 ± 13.03 years (range 24-78), in Group B was 46.13 ± 11.19 years (range 28-75) and in Group C was 48.60 ± 13.25 years (range 23-75). The mean age was comparable in all the three groups (p=0.68). Similarly, mean weight of patients in all the three groups were also comparable.

Type of surgeries performed included gynaecology (57.78%), orthopaedics (31.11%), general surgery (7.78%) and urology (3.33%). Duration of surgery for male patients ranged from 42 to 177 minutes, while those for female patients ranged from 62 to 147 minutes. Mean duration of surgery for Group A was 98.23 minutes, for Group B 97.67 minutes and for Group C was 91.30 minutes. There was no significant difference in the studied groups (p=0.56).

Mean number of rescue analgesics required were significantly less in Group C (0.6) when compared to Group B (1.8) and Group A (2). Moreover, intraoperative mean heart rate in Group A was 84.44 bpm, in Group B was 76.67 bpm and in Group C was 76.3 bpm, the difference being statistically significant (p=0.02). Similarly, intraoperative mean systolic, diastolic and arterial blood pressure respectively were significantly more in Group A and Group B as compared to Group C (p=0.01, p=0.00, p=0.01). However, the difference in the intraoperative mean oxygen saturation amongst the three groups was statistically not significant (p=0.29).

Visual analogue scale (VAS) scores among the three groups 'at rest', 'on movement' and 'on coughing' are given in Tables 1, 2 and 3. In all the three tables, VAS

Table 1. VAS Scores (in cms) Among the Three Groups 'at rest'

Time in hrs	Mean VAS scores ± Standard deviation			p-value	F-value	Remarks
	Group A (±0.30)	Group B (± 0.48)	Group C (±0.18)			
1	3.11	3.16	2.67			
2	3.37	3.36	2.77			
3	3.61	3.68	2.92			
6	4.05	4.26	3.13			
12	3.94	4.18	2.75	1.56E-21	87.36	HS
18	3.50	3.09	2.49			
24	3.29	2.98	2.75			
36	3.82	3.06	5.69			
48	3.32	2.91	2.51			
Group Mean	**3.56**	**3.42**	**2.75**			

HS=Highly significant

Table 2. VAS Scores (in cms) Among the Three Groups 'on Movement'

Time in hrs	Mean VAS scores ± Standard deviation			p-value	F-value	Remarks
	Group A (±0.34)	Group B (±0.49)	Group C (±0.21)			
1	3.39	3.37	2.82			
2	3.73	3.57	2.97			
3	4.05	3.96	3.15			
6	4.47	4.60	3.54			
12	4.46	4.61	3.11	1.42E-.23	102.29	HS
18	3.99	3.54	2.79			
24	3.79	3.39	3.04			
36	4.24	3.41	3.06			
48	3.80	3.31	2.89			
Group Mean	**3.99**	**3.76**	**3.04**			

HS= Highly significant

Table 3. VAS Scores (in cms) 'on coughing' between the three groups

Time in hrs	Mean VAS scores ± Standard deviation			p-value	F-value	Remarks
	Group A (±0.29)	Group B (±0.54)	Group C (±0.25)			
1	3.91	3.44	2.91			
2	4.18	3.73	3.11			
3	4.50	4.07	3.32			
6	4.82	4.89	3.82			
12	4.85	4.96	3.37			
18	4.43	3.69	2.99	9.16E-29	148.38	HS
24	4.29	3.67	3.33			
36	4.65	3.79	3.34			
48	4.25	3.47	3.14			
Group Mean	**4.43**	**3.99**	**3.26**			

HS= Highly significant

Table 4. Number of Patients Requiring Rescue Analgesia in the Three Groups

Rescue Analgesic needed	Group A-Number (%)	Group B-Number (%)	Group C-Number (%)	p-Value	F - Value	Remarks
Yes	30 (100.00)	26 (86.67)	17 (56.67)	0.013326	3.4621	S
No	0	4 (13.33)	13 (43.33)			

S = Significant

score is significantly lower in Group C as compared to Group A and Group B. Mean computed sedation score in the three groups as recorded by the sedation, orientation, comprehension, amnesia (SOCA) scale for Group A was 10.38, for Group B was 9.24 and for Group C was 9.20. Sedation and amnesia were more in Groups B and C as compared to Group A. The difference among the three groups was significant though it did not warrant any treatment in any of the groups.

Mean pulse rate revealed significantly higher rates in Group A and Group B compared to Group C though it did not warrant any treatment in any of the groups. Mean respiratory rate in Group A was higher than in other two groups. The difference was statistically significant though clinically not significant.

Rescue analgesia was required in a significantly higher number of patients in Groups A and B as compared to Group C. Almost half of the number of patients in Group C (13 out of 30) did not require any rescue analgesic (Table 4). Mean requirement of rescue analgesic in Group As was 2, in Group B was 1.8 and in Group C was 0.6 injection per patient. Thus, rescue analgesic requirement in Group C was less than in the other two groups the difference was statistically significant.

Discussion

Postoperative pain is a major concern after almost all major surgeries. Pain may hinder early intense physical therapy, the most important factor for good rehabilitation. Despite advances in the treatment of postoperative pain in lower limb surgeries, many patients still suffer from pain after surgery probably due to difficulties in balancing an effective postoperative treatment regimen with acceptable side-effects.

Various techniques have been used to provide effective post-operative pain relief after lower abdominal and lower limb surgeries including supplemental intravenous opioids, intravenous and epidural patient controlled analgesia and nerve blocks. Regional nerve block techniques are usually performed at the end of surgery producing additional discomfort to the patient, especially when the effect of spinal analgesia has already dissipated. Also the block may not be properly applied since they require experience to be performed correctly resulting in the need of alternative mode of pain management.

Intrathecal opioids are frequently used for prolonging the duration of postoperative analgesia. Although intrathecal morphine provides prolonged pain relief of up to 24 hours its routine use has been limited because of the risk of delayed respiratory depression (9).

Clonidine produces spinal cholinergic activation. Cholinergic interaction in spinal alpha 2 adrenergic receptors which are located on descending nor?adrenergic pathways produces nor?adrenaline release that causes analgesia directly and also it releases acetylcholine (Ach) to produce analgesia. Clonidine also blocks A and C fibers at lamina V, thereby producing analgesia (10). The current study was undertaken to study the effectiveness with different doses of clonidine combined with bupivacaine for postoperative analgesia in 90 patients undergoing infraumblical and lower limb surgeries. The purpose of this study was to provide safe and effective analgesia for the postoperative period. In our study, clonidine 50 micrograms and 75 micrograms were used as adjuvant to bupivacaine (0.5%) in a bid to provide a pain-free post-operative period to our patients.

Mean visual analog scores at rest in the three groups were 3.56 (Group A), 3.42 (Group B) and 2.75 (Group C) and the difference was statistically significant. The VAS scores in Group A were persistently greater than or equal to 3 throughout the study period. This was reflected in the rescue analgesia requirements which were higher in Group A. These findings support those of Saxena et al. wherein they found the VAS scores to be greater than or equal to 3 throughout 1 to 3 days postoperatively while using bupivacaine alone (11). That scores of more than 3 were regularly recorded in Group A even at rest suggests inadequate analgesia and the need for additional analgesics. Our findings are in consonance with those of Grandhe *et al.*, who used 1.5 ml of 0.5% bupivacaine with two doses of clonidine 1 microg/kg and 1.5 microg/kg and found that VAS scores were lower in the higher dosage group (12).

However the results of Sethi et al. (6) were at variance to our study, who found that even lower dose of clonidine i.e.1 microg/kg combined with 12.5 mg of 0.5% bupivacaine significantly increased the duration of spinal analgesia. On the contrary to our study, Dobrydnjov *et al.* (8) compared two doses of clonidine 15 microg and 30 microg with hyperbaric bupivacaine 6 mg for inguinal herniorrhaphy and recommended that the dose of 15 microg of clonidine provides good analgesia for the postoperative pain.

Mean sedation scores in the three groups were 10.38, 9.24 and 9.20 in Group A , Group B and Group C respectively, lower scores were recorded in Group B and Group C denoting sedation and amnesia of a desired level. These findings were in accordance with those of kothari *et al.* (13) and Baker *et al.* (14), who documented that more sedation and amnesia with the use of a combination of bupivacaine and clonidine as compared

to bupivacaine alone. Our study recorded a lower respiratory rates in Group B (16.51) and Group C (16.20) than in Group A (19.58). However no incidences of respiratory depression were reported in any group. This is in accordance with the work of Baker *et al.* (14) who reported lower respiratory rates with the combination of bupivacaine and clonidine 150 microg given intrathecally. The higher respiratory rate in Group A could possibly reflect pain as evidenced by the higher VAS scores.

Regarding the need for additional analgesia in patients in various groups, we found that the need for rescue analgesia was less in Group C (56.67%) as compared to Group A (100%) and Group B (86.67%) and mean doses of rescue analgesic given in Group A, Group B and Group C were 2, 1.8 and 0.6 respectively. These findings are in consonance with the findings of Neimi (15) in which 3 microg/kg of clonidine was added to 15 mg of 0.5% bupivacaine administered intrathecally in patients undergoing knee arthroscopy.

In Group C, we found the least consumption of rescue analgesics probably reflecting a longer duration of analgesia. The analgesic effect following its intrathecal administration is mediated spinally through activation of post synaptic alpha-2 receptors in substantia gelatinosa of spinal cord. This is in accordance with the findings of Grandhe *et al.* (12). In their study one group received clonidine 1 microg/kg and other group received clonidine in the dosage of 1.5 microg/kg body weight and requirement of rescue analgesia given was less in clonidine group in the dosage of 1.5 microg/kg.

Side effects like nausea, vomiting, shivering, pruritis seizures, urinary retention and respiratory depression usually seen with intrathecal administration of drugs especially if opioids are used. But, in our study, we did not get any major side effects. This is in consonance with the work of Grandhe *et al.* (12), who concluded that clonidine in the dose of 1-1.5 microg/kg when added to bupivacaine, results in minimal side effects.

Conclusion

In conclusion it can be said that the addition of clonidine 75 ?g to 3 ml of 0.5% bupivacaine (heavy) provides significantly better pain relief in lower limb and lower abdominal surgeries leading to reduction in pain (VAS) scores, less consumption of additional analgesics, minimal sedation and amnesia without any major side effects.

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