Original Article

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A Comparative Study between Intrathecal Clonidine and Buprenorphine with Intrathecal Bupivacaine for Lower Abdominal Surgeries

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Abstract

Purpose: Subarachnoid (spinal) block is a safe and effective alternative to general anesthesia when the surgical site is located on the lower extremities, perineum (eg, surgery on the genitalia or anus), or lower body wall (eg, inguinal herniorrhaphy). In no other way, can an anaesthesiologist obtain so much of an effect for the introduction of a small quantity of the drug. Likewise a properly chosen adjuvant to local anaesthetic agent produces the best way to achieve a good quality regional block.

Aim of Study: To compare the effect of intrathecal Clonidine 75 micrograms (µg) and Buprenorphine 150 µg with 2.5ml (12.5mg) of intrathecal 0.5% hyperbaric Bupivacaine. With regards to: 1) Sensory characteristics, 2) Motor characteristics, 3) Hemodynamic stability and 4) Side effects.

Methodology: A prospective randomized experimental study were performed on 50 patients posted for lower abdominal surgery belonging to ASA I and aged between18-60 years after obtaining an informed consent and ethical clearance.

Result: Addition of 150 µg Buprenorphine significantly enhances the onset of sensory block (90±15 secs) and motor block (150±15 secs) than compared to Clonidine onset of sensory block(150±20 secs) and motor block(210±20 secs) (p<0.05). Hemodynamic was well maintained with buprenorphine group. And addition of Buprenorphine 150µg to intrathecal Bupivacaine(0.5%) produces prolonged analgesia (526±96) than compared to the Clonidine group of 362±36mins (p<0.05) with no serious adverse effect noted perioperatively in either groups.

Conclusion: The addition of Buprenorphine to intrathecal Bupivacaine (0.5%) prolongs the duration of post operative analgesia than compare to clonidine. Buprenorphine has faster onset of sensory and motor blockade than compare to clonidine.

Keywords: Clonidine; Buprenorphine; Hyperbaric; Lower Abdominal Surgery Analgesia; Bromage Scale [1].

Introduction

Spinal anaesthesia may be defined as the temporary interruption of transmission of the nerve impulses across the nerve fibers by injecting drug into the sub arachnoid space. It is safe and satisfactory if performed with the knowledge of its physiological consequences and in many instances, it is the method of choice in view of patient's condition and produces an ideal operating condition and post operative pain relief.

Bupivacaine has been used since 1963; Bupivacaine is more potent than Lignocaine and has longer duration of action. Its disadvantage is a slow onset of action and decreased motor block [2]. Hyperbaric Bupivacaine 0.5% is extensively and the only local anaesthetic used intrathecally in India. Peri--operative hemodynamic status and post operative pain relief are important issues with bupivacaine. Many adjuvants are commonly used to overcome these demerits. So our concern is to choose an ideal adjuvant with Bupivacaine which provides a stable intraoperative condition, prolonging the post operative analgesia with minimal side effects.

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Clonidine is a selective alpha (α) 2 agonist agent, routinely used as a premedicant for general anaesthesia. Its use decreases the requirement of analgesics and anaesthetic drugs intraoperatively. Intrathecally clonidine produces analgesia by indirectly inhibiting the activity of wide dynamic range (WDR) neurons [2,3].

Buprenorphine is a semi synthetic, highly lipophilic opioid which was originally derived from thebaine, one of the most chemically reactive opioid alkaloids. Buprenorphine, a partial opiate agonists which posses high analgesic potency, long duration and low acute toxicity [4,16]. Buprenorphine binds to substantia gelatinosa of the dorsal horn of the spinal cord and produces presynaptic and (post synaptic) inhibition of neuronal cell excitation [5].

Keeping the pharmacological and economical profile of both clonidine and buprenorphine, we performed a double blind randomized study in our institute for comparing the effects of clonidine and buprenorphine with intrathecal bupivacaine. The chief aims of this pharmacological comparison were to observe the effects on duration of analgesia, hemodynamic parameters with addition of these adjuncts.

Materials & Methods

Over a period of 5 months duration, a double blinded prospective randomized study was performed in our institute. Ethical committee clearance was obtained for our study. All patients belonging to the following inclusion criteria were randomly divided into two groups (Group BB and Group BC): sample size: 50.

Inclusion Criteria

All patients aged between a) 18-60 years, b) ASA Grade I and II c) Patients posted for lower abdominal surgeries.

Exclusion Criteria

a) Patients with local sepsis, b) Patients with bleeding diathesis, c) Patients with raised intracranial pressure(ICP), d) Patients with any co-morbid diseases like ischemic heart disease (IHD), hypertension, bronchial asthma, diabetes mellitus and morbidly obese patients.

Group BB (n=25) received 2.5 ml of 0.5% hyperbaric Bupivacaine along with 0.5 ml of Buprenorphine (150 µg). And Group BC (n=25) received 2.5 ml of 0.5% hyperbaric Bupivacaine + (75µg) 0.5 ml of Clonidine. The study was double blinded, spinal anesthesia was given by the anesthesiologist with the study drug, who was not involved in the patients monitoring. The patients and the monitoring anesthesiologist were blinded to the study solutions. Ethical committee clearance and patients consent were obtained. All the patients were evaluated on the previous day of surgery; the procedure was explained to each patient and informed consent was taken. All the patients were premedicated with ranitidine 150 mg, Alprazolam 0.5 mg orally on previous night. On the day of surgery, patient's basal pulse and basal blood pressure were recorded. A peripheral intravenous line with 18 gauge cannula was secured in one of the upper limbs. Patients were preloaded with 500 ml of Ringer lactate solution. Lumbar puncture was performed with 23 gauge spinal needle (Quincke's) using a midline approach with the patients in the left or right lateral decubitus position. The lumbar 3-4 inter space was chosen for all the patients and when a free flow of clear cerebrospinal fluid was obtained, the study drug was administered at a rate of not more than 0.3ml per second.

Immediately after the injection the needle was withdrawn, the patient turned supine, supplemented with oxygen through simple face mask and allowed to remain so until the maximum level of sensory blockade was achieved and the change in position if required was then allowed. Assessment of the sensory and the motor blockade were done at the end of each minute till the maximum level achieved. Measurements of blood pressure, pulse rate, respiratory rate, and arterial oxygen saturation were obtained at regular intervals of 2 mins for initial 20 mins and 5 mins thereafter.

Sensory block was assessed using a short beveled 22 gauge needle and was tested in the midclavicular line on chest, trunk and legs on either side. Analgesia was defined as loss of the sensation to pinprick and, Anaesthesia as loss of sensation of touch. The following were observed: 1) Time of onset of analgesia: defined as time taken from the injection of the drug to onset of analgesia at T10 level, 2) Maximum level of analgesia achieved. 3) Time taken for achieving maximum level of analgesia, 4) Total duration of analgesia: defined as the time taken from the onset of analgesia to the point where the patient complained of pain in the operated site requiring rescue analgesics, if VAS [visual analogue scale]>5.

Motor blockade: Was assessed using (Bromage 1965) Bromage scale :

0: full movement of leg.

1: inability to raise the extended leg (just able to move knees)

2: inability to flex the knee (able to move feet only)

3: inability to flex the ankle joint (unable to move feet or knees)

During recovery, motor blockade was assessed as follows:

0: No movement, complete paralysis.

1: Flickering movement

2: Movement with gravity

3: Movement against gravity

4: Movement against resistance

5: Normal power.

The following parameters were noted : a)Time taken for onset of motor blockade: defined as the time taken for complete inability to flex both the lower limbs at hip joint, b) Quality of motor blockade assessed by Bromage scale [1] c) Total duration of surgery.

Intra operative complications like fall in blood pressure, variation in pulse rate, complaints like nausea, vomiting, pruritus, sweating were noted at 2^{nd},5^{th},10^{th} and every 15 mins till surgery. Similarly in post operatively complaints like nausea, vomiting, pruritus, and any other side effects associated with study drug were noted, treated and tabulated.

Incremental titrated doses of Mephentermine (i.v) 3 mg were given to patients whose systolic blood pressure fell below 30% of basal systolic blood pressure or below 90mmHg of systolic blood pressure-hypotension [6]. Bradycardia (<60 beats/min) was treated with injection Atropine 0.6mg. Nausea and vomiting were treated with injection Ondensetron (i.v).

Post operatively, the patients were observed for the duration of analgesia by using visual analogue scale scoring system of 0 to 10, with no pain being 0 and most severe pain being 10 and post operative complications if any were noted. Patients were given rescue analgesia once the visual analogue scores was more than 5, time taken for complete recovery of motor power was also noted.

At the end of the study, the data was complied systematically and was subjected to statistical analysis using student 't' test and SPSS version 10.0 for windows. Value of $p<0.05$ was considered significant.

Results

The groups were comparable with respect to age, weight, sex and duration of surgery. There was no statistically significant difference in either of the groups, ($p>0.05$) (Table 1).

Sensory characteristics are tabulated (Table 2). Group BB shows early onset of sensory loss (90±15 secs) with same segment higher block (T4) than the Group BC. Block regression was significantly slower with addition of intrathecal Buprenorphine and the mean total duration of analgesia was prolonged to nearly 9 hours in Group BB than compared to nearly 7 hours in Group BC (Graph 1).

Motor characteristics are tabulated (Table 3). Group BB shows early onset of motor block (150±15 secs) and early regain of motor power (170±40mins) than compared to Clonidine group motor block onset (210±20 secs) and duration of motor blockade (210±50 mins). With the dosage used of 150µg of Buprenorphine and 75µg of Clonidine there was no sedation, sweating or other serious complications like respiratory depression were observed in either groups.

In our study (Graph 2), intra operative blood pressure was well maintained in either of the groups. Intraoperative need of vasopressor was more with Group BC compared to Group BB. In Group BC ten patients exhibited hypotension with SBP< 80 mmHg. It occurred 15- 30 min after SAB four patients required intravenous Mephentermine to maintain SBP at or above 100 mmHg. In Group BB, eight patients manifested hypotension, out of eight three patients required additional vasopressor mephentermine to balance the sympathetic tone. Hypotension was associated with bradycardia was also noticed in 3 patients in group BC and 2 patients in group BB. It

Table 1: Demography

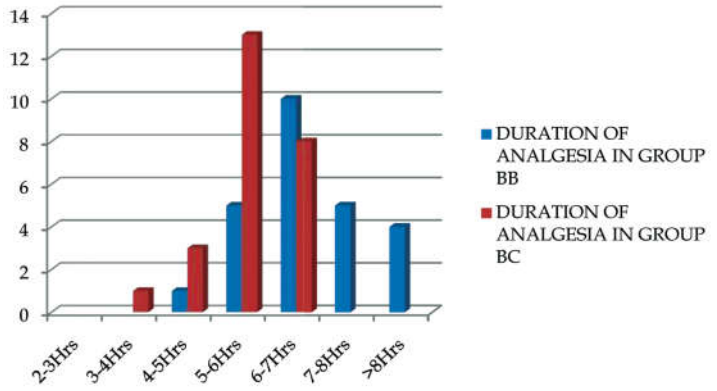
	Group BB	Group BC	*P* Value
Mean Age	28.72	37.6	>0.05
Mean Weight	56.36Kg	52.3Kg	>0.05
Male:Female Ratio	18:07	11:14	0.1
Duration of Surgery FOR 45-60mins	20	20	>0.05
Duration of Surgery FOR 60-120mins	5	5	>0.05

Table 2: Sensory charateristics

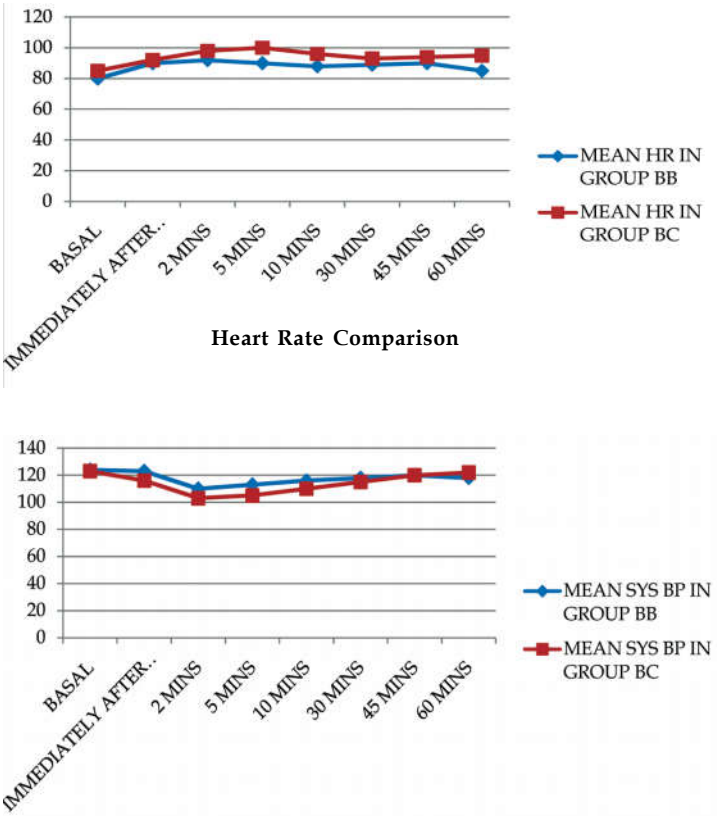
	Group BB	Group BC	*P* value
Mean Onset Time	1mins 38secs	2mins 40secs	<0.05
Mean Max Level Obtained	T4	T4	
Mean Time For Achieving Mean Max Level	5.28±2.2mins	6.12±3.2mins	<0.05
Mean Total Duration Of Analgesia	526.8±25 mins	362±36 mins	<0.05

Table 3: Motor characteristics

	Group BB	Group BC	*P* value
Mean Time Required To Attain Max Motor Blk	150±15secs	220±40secs	<0.05
Quality Of Motor Blockade	Bromge grade III→ 100%	Bromage grade III→100%	
Duration Of Motor Blockade	170±40mins	210±50mins	<0.05



Graph 1: Duration of post operative analgesia



Graph 2: Hemodynamic changes – group bb and group bc

responded to i.v. Atropine 0.6mg.

Subsequently in all these patients there were no further changes in SBP or HR. No patients of either group had sedation, nausea and vomiting post dural puncture headache or transient neurological symptoms at the post operative follow up.

Discussion

Clonidine, a partial α_2 adrenergic agonist, has antinociceptive properties. Clonidine produces spinal cholinergic activation: Cholinergic interaction in spinal α_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 Aδ and C- fibers at lamina V, thereby producing analgesia [2,7,8]. Clonidine has been used orally, epidurally and intrathecally to prolong the analgesia provided by local anaesthetics when given intrathecally or epidurally [3]. Clonidine has been used in varying doses from 15µg to 300µg intrathecally by various authors. Recently it has been established that with local anaesthetics, the maximum dose of intrathecal Clonidine to be 1-2µg/kg [3]. Higher doses of sole Clonidine is said to produce marked sedation as well as hemodynamic disturbances. Plateau effect of analgesic effect of Clonidine is seen around a dose of 150µg [9,10]. In view of this, in the present study we selected a dose of 75µg of Clonidine.

Our hospital protocol includes routine use of Buprenorphine as intrathecal

additive to produce post operative analgesia. Buprenorphine being a lipid soluble and non ionized drug passes rapidly via the arachanoid granulation into the venous and lymphatic vessels which allow minimal increase of CSF concentration with minimal risk of respiratory depression [11]. In addition Buprenorphine, because of its high affinity for opiate receptors is likely to produce greater duration of analgesia than other lipophilic agents [5].

In the present study, we noticed that in Group- BB onset time for sensory blockade was earlier compared to Group- BC, showing that Buprenorphine enhances action of spinally administered local anaesthetics. However, there was no clinically significant difference in the maximum level of sensory blockade achieved in both the groups.

Clonidine is believed to prolong the motor blockade produced by local anaesthetic agents [2]. Clonidine produces local vasoconstriction by acting on vascular smooth muscle (α-receptors), which decreases absorption of local anaesthetics from sub arachanoid space thereby prolonging the duration of action [12,13,14]. The motor blockade of Buprenorphine is by potential direct inhibition of motor activity by administration of Buprenorphine through by opioid receptor activity at substantia gelatinosa[5]. Buprenorphine enhanced motor block from spinal bupivacaine may be useful in the clinical setting. Many lower abdominal surgical procedures require muscle relaxation, and spinal bupivacaine with other adjuncts provides only modest motor block [11]. In our study the mean time for motor block onset was significantly faster in Buprenorphine group than compared to Group BC, similarly the mean time taken for maximum motor blockade was clinically and significantly faster in Buprenorphine group than compared to Group BC. This concurs with the study result conducted by Manika Sen [15].

Clonidine after neuraxial administration affects arterial blood pressure in a complex manner because of opposing actions at different sites. The α_2 adrenergic agonism produces sympathicolysis and reduces the blood pressure through effects on brainstem nuclei and on sympathetic pre-ganglionic neurons. However, these effects are counteracted by direct vasoconstriction resulting from the effect of α_1 and α_2 adrenergic agonistic actions on the peripheral vasculature [2,13].

On other hand, in group BB also the variation in hemodynamic parameter mimics that of group BC which was uneventful. The peripheral vasodilatation leading to noticeable hypotension caused by intrathecal local anaesthetics was counter balanced by addition of opioid adjuncts like fentanyl, Buprenorphine etc acting on mu receptor at substantia gelatinosa[5,16].

Pruritus was observed in 4 patients of Buprenorphine group, which was observed near the tip of the nose and the area around it. However, none of the patients described it as a disturbing complaint. Capogna G, Celleno D, Tagariello V [17] observed increased incidence of nausea, vomiting and pruritus with increase dose of Buprenorphine (300 micrograms)

In the present study, in Group-BB the total duration of analgesia was significantly higher compared to Group-BC. This ability of intrathecal Buprenorphine to prolong analgesia without any side effects has many fold advantages. It provides adequate post-operative analgesia. In unexpected prolongation of superficial surgical procedures, maintenance of analgesia provides additional time for the surgeon to complete the surgery without resorting to alternative anaesthesia [2,17].

Conclusion

The use of intrathecal Buprenorphine significantly hastens the onset of sensory and motor block along with a good quality of surgical relaxation. And Intrathecal Buprenorphine significantly produces prolongation of analgesia. Both the adjuncts manifests with no significant side effects.

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