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RESEARCH ARTICLE

COMPARATIVE EVALUATION OF SPINAL BLOCK CHARACTERSTICS AFTER INTRATHECAL CLONIDINE-BUPIVACAINE AND BUPIVACAINE ALONE IN LOWER LIMB SURGERIES

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ABSTRACT

Context: Various adjuvants are being used with local anesthetics for prolongation of intraoperative and postoperative analgesia. The α2-adrenergic agonist clonidine has the ability to potentiate the effects of local anesthetics.

Aims: The purpose of this prospective, double blind study study was to compare onset, duration of sensory and motor block, effect on hemodynamics, level of sedation, duration of post operative analgesia and any adverse effects of clonidine

Settings and Design 50 American Society of Anesthesiology (ASA) class I and II patients undergoing lower limb surgery under spinal anesthesia were randomly allocated into two groups.

Methods and Material: Control Group received Inj. Bupivacaine 0.5% (heavy) 2.5ml + saline 0.5ml & Study Group received Inj. Bupivacaine 0.5% (heavy) 2.5ml + preservative free Inj. Clonidine 50µg intrathecally..

Statistical analysis used: Unpaired students t-test and Z-test was used for comparing data.
Results: We found statistically highly significant differences in mean time of sensory regression to L – 1, mean time to attain the Bromage Score of 1 & mean time of first rescue analgesic request.The patients did not suffer any serious side effects, apart from nausea & vomiting & dryness of mouth.

Conclusion: Administration of clonidine intrathecally does potentiate the duration of analgesia, sensory and motor block.

INTRODUCTION

Spinal anesthesia was introduced into clinical practice by Karl August Bier in 1898.More than a century has passed and even today, it is one of the most popular techniques for both elective and emergency surgical procedures particularly caesarean section, lower abdominal surgeries, orthopedic and urological surgeries just to name a few. Despite the proliferation of drugs, devices and techniques, pain management remains a compelling issue in health care.

The prime emphasis of acute pain treatment must be to decrease the pain as much as possible (ideally, to zero). This must be achieved, however, with reasonable cost, safety for the patient, and exclusive of drug and treatment-related side effects.

This is true even in patients undergoing spinal anesthesia which is a well known technique for operations on the lower extremities. Although it is easy to perform and provides fast onset and effective sensory and motor block, it has a limited duration of action.

The need for using additives in local anaesthetics was, in former times, due to a desire to prolong the anaesthetic action which could allow surgery for several hours. The duration of tetracaine could be prolonged up to 6 h by the addition of adrenaline. Today, bupivacaine is the most commonly used local anaesthetic for spinal anaesthesia. The duration of bupivacaine spinal anaesthesia after a single-shot injection is adequate for hip and knee arthroplasties. Spinal anaesthesia can be extended with the use of continuous catheter techniques. Therefore, the purpose of the development of new additives has been related mainly to the prevention and relief of postoperative pain, together with the aim of reducing the dose

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of local anaesthetics and allowing early ambulation after surgery.

The α2-adrenergic agonist clonidine has a variety of different actions, including the ability to potentiate the effects of local anesthetics[1]. However, unlike spinal opioids, clonidine does not produce pruritus or respiratory depression. It also prolongs the sensory blockade[2,3,4]. It also reduces the amount or concentration of local anesthetic required to produce postoperative analgesia[5]. It has been used as a sole agent as well as admixed with opioids and local anesthetics in labour analgesia and orthopedic surgery[6].

This study is a comparative evaluation of spinal block characterstics after intrathecal clonidine-bupivacaine and bupivacaine alone in lower limb surgeries. Spinal block characterstics to be observed are in terms of onset of spinal block, duration of sensory block, effect on heart rate and blood pressure, level of sedation, duration of post operative analgesia and any adverse effects encountered.

Subject and Methods

This study was conducted on 50 ASA 1 and 2 patients posted for routine lower limb surgeries who were divided into two groups. Control Group received Inj. Bupivacaine 0.5% (heavy) 2.5ml + saline 0.5ml. Study Group received Inj. Bupivacaine 0.5% (heavy) 2.5ml + preservative free Inj. Clonidine 50µg (in 0.5 ml of NS). Patients with hypertension / hypotension, diabetes, peripheral neuropathy, cardiac dysrythmias, conduction defects, any other contraindication to spinal anesthesia were excluded..

All the patients underwent pre-anaesthetic evaluation as per the protocol in PAC clinic . The anaesthetic & surgical plan was explained to the patients in a simple language & informed consent obtained. The patients were divided into two groups of 25 each using chit in a box technique. On the day of surgery, inside the operation theatre, basal pulse rate and blood pressure were obtained. A wide bore intravenous line was established and the patients were connected to monitors such as ECG, SpO2, a non invasive blood pressure recording device. The patients received Ringer's lactate infusion 10 ml/kg, prior to intrathecal anesthesia. All the patients received Inj. Ondansetron 4 mg i/v. The patients were positioned sitting for spinal puncture. Under strict aseptic precautions, lumbar puncture was done at L3–L4 interspace using 26 G Quinke Spinal Needle by midline approach. After ensuring a free flow of CSF, Control Group received Inj. Bupivacaine 0.5% (heavy) 2.5ml + saline 0.5ml & Study Group received Inj. Bupivacaine 0.5% (heavy) 2.5ml + preservative free Inj. Clonidine 50µg (in 0.5 ml of NS). The observer was blinded to the drug administered intrathecally.

Time of onset of block i.e. from completion of spinal injection to achieving T10 block (in minutes) was recorded. Maximum height of block (sensory) by using pinprick (toothprick) was recorded every 30 seconds. Hemodynamic parameters were recorded every 5 min. during surgery and every 30 min. during post operative period.

Time to attain highest motor blockade was recorded by using modified Bromage Scale as:

Grade	Criteria
I	Free movement of legs and feet
II	Just able to flex knees with free movement of feet
III	Unable to flex knees, but with free movement of feet
IV	Unable to move legs or feet

Duration of sensory block was recorded as regression of block to L1, using pinprick method.

Duration of motor blockade was recorded as time required to attain a Bromage Score of 1.

Duration of post operative analgesia was recorded by using Visual Analogue Scale (VAS) during post operation period every 30 min using the following scale:. 0 - no pain, 1 – 3 mild pain , 4 – 6 moderate pain & > 6 severe pain.

Inj. Tramadol 2.0 mg/kg i/v was given as rescue analgesic for pain relief.

Bradycardia (HR < 50/min) was treated with inj. Atropine 0.6mg i/v., if accompanied with hypotension. If the fall in Mean Arterial Pressure was > 20% from baseline, it was treated with i/v bolus of 200 ml Ringer Lactate and Inj. Mephentermine 6 mg i/v, if required.
Level of sedation was recorded as:

0	No sedation
1	Drowsiness
2	Asleep but arousable
3	Unarousable with loss of verbal contact

Post operative monitoring for regression of sensory block to L1, Bromage Score & post operative pain using VAS, along with heamodynamic parameters were noted every 30 min till the VAS scores were > 5.

Any adverse effect such as nausea & vomiting, shivering, dryness of mouth, bradycardia etc. that occurred during the observation period was noted down.

Unpaired students t-test was used for intergroup comparison of various data obtained such as time to sensory regression of the block to L1, duration of motor blockade, duration of post operative analgesia etc. Z-test was used for comparing intra-group data such as various heights of block attained & various degrees of motor block attained within the group.

RESULTS

There was no statistical difference between the mean age of the patients in the two groups ($p > 0.05$). Also, the mean weights of the patients was 53.2 kg in the control group & 56.24 kg in the study group.The types of surgery in the two groups were almost similar in the two groups. The mean duration of operations between the two groups was comparable & not found to be statistically significant ($p > 0.05$). The mean length of operation in the control group was 85.4 min & in the study group was 93.8 min.

The mean time of onset of action of the drugs in the two groups (6.4 ± 3.0 min in the control group & 7.3 ± 3.2 min in the study group) was not found to be statistically significant ($p > 0.05$). Similarly, the mean time to attain highest Bromage Score in the control group was 10.9 ± 1.9 min & in the study group was 10.2 ± 3.7 min ($p > 0.05$).

On comparing the various heights of block attained in the two groups, we found that significantly more patients in the study group reached T9 level as compared to the patients in control group & significantly more patients in the control group reached T10 level as compared to the patients in study group.
Only one patient in the control group & 3 patients in the study group out of 25 in the each group reached a Bromage Score (BS) of 3 while the rest of them reached a score of 4. The result was not found to be statistically significant.

The mean pulse rate varied from 74 – 83 beats/min in control group & from 76 – 87 beats/min in the study group.(**FIG. 1**) Both the groups showed a steady downward trend of pulse rate after injection of the drug to the end of the operation. No episode of bradycardia occured in any group at any point of time.

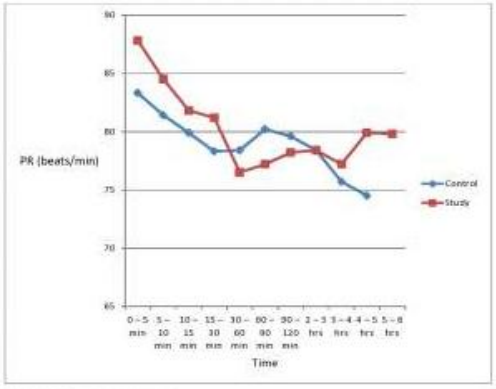

FIGURE – 1, Trends of Pulse Rate

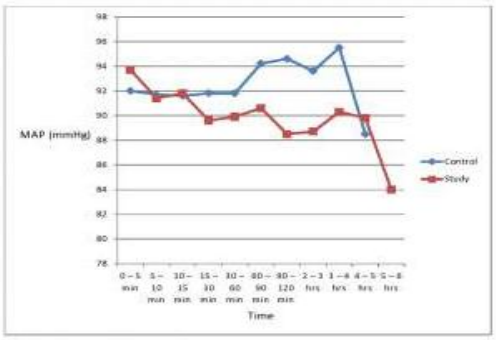

FIGURE – 2, Trends of Mean Arterial Pressure

Mean Arterial Pressure (MAP) varied from 88 – 96 mmHg in the control group & from 84 – 93 mmHg in the study group **(FIG. 2)**. As shown graphically, the MAP values in the study group were lower than that in the control group. The maximum fall in the MAP (10%) that occured in the control group was after 4 hrs of the intrathecal injection. In the study group, the maximum fall (15%) occured after 5 hrs of the intrathecal drug.

We found statistically highly significant differences in mean time of sensory regression to L – 1, mean time to attain the Bromage Score of 1 & mean time of first rescue analgesic request as shown in the **Table 1, Fig,3, Fig.4, Fig. 5.**

Table 1 Parameters of regression of block.

Groups	Control	Study	p value
Mean time of sensory regression to L – 1 (min)	129.6 ± 16.3	183.2 ± 46.8	< 0.001
Mean time to attain the Bromage Score of 1 (min)	153.8 ± 19.3	228.6 ± 46.7	< 0.001
Mean time of first rescue analgesic request (min)	175.6 ± 26.1	278.2 ± 56.4	< 0.001

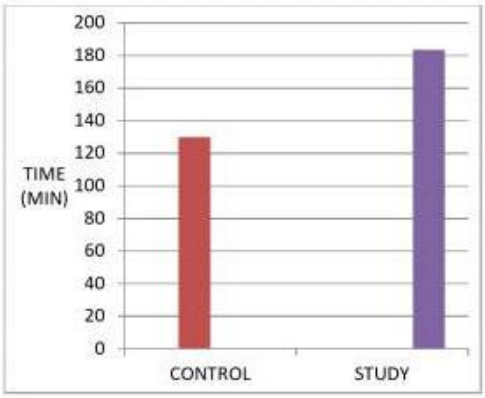

FIGURE – 3, showing mean time of sensory regression to L – 1 (min)

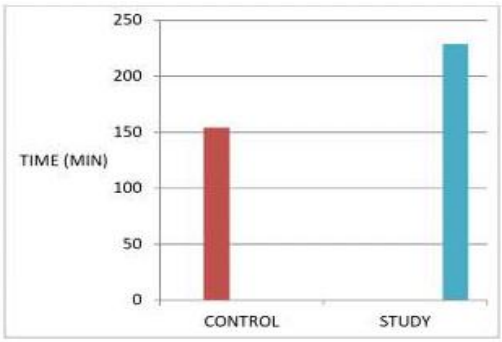

FIGURE – 4, showing mean time to attain the Bromage Score of 1 (min)

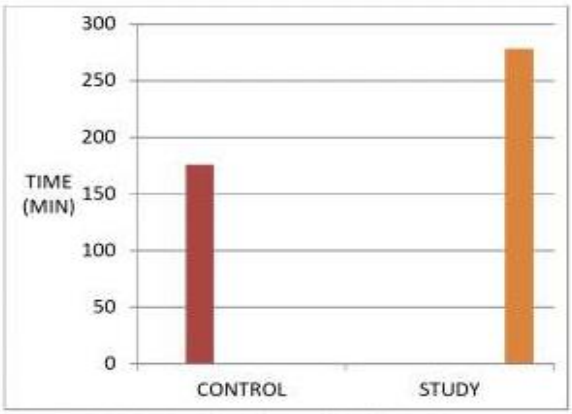

FIGURE – 5, showing mean time of first rescue analgesic request (min.)

The patients did not suffer any serious side effects, apart from nausea & vomiting & dryness of mouth. Only one patient in the control group & 2 patients in the study group suffered nausea & vomiting. Only 2 patients in the study group & none in the control group complained of dryness of mouth. Six patients out of total 25 patients, were sedated in the control group and 16 patients in the study group were sedated. Unpaired t- test was

used to evaluate the significance of the result & the result was found to be statistically significant ($p < 0.05$). **(Table 2)**

Table – 2 Comparison of various adverse effects in the two groups.

Adverse effects		Control	Study	p value
Sedation	Nausea & Vomiting	1	2	
	Dryness of mouth	-	2	
	Grade 0	19	9	
	Grade 1	6	9	
	Grade 2	-	7	
	Total no. of patients found sedated	6	16	$p < 0.05$
	Total no. of patients	25	25	
	Any other	-	-	

DISCUSSION

The difference of mean time of onset of action of the drugs & the mean time to attain highest Bromage Score was not statistically significant between the two groups. Similar results were also shown by Racle J P . *et. al.*[1].

Patients who received intrathecal Clonidine with Bupivacaine attained a higher dermatomal block level than the patients who received Normal Saline with Bupivacaine intrathecally. Benhamou Dan, *et al.*[7] also demonstrated that clonidine increased the spread of the sensory block, intraoperatively. Nicol ME, *et al,*[8] tried to explain this in their study on parturients postulating that because clonidine becomes slightly hypobaric at body temperature, rostral spread might have occurred with the patient in the sitting position for several minutes after the intrathecal injection.

In the present study, a total of 4 patients (1 in control group & 3 in Clonidine group) out of total 50 patients studied, attained a Bromage Score of 3. All other patients in both the groups attained the BS of 4. Although the result was not found to be statistically significant ($p > 0.05$), other investigators observed a complete motor blockade of the lower extremities in all patients[9]. This difference could be due to the difference in the amount of drug delivered intrathecally. They used a total drug volume of 4.6 ml with 18 mg of Bupivacine, while in our study the total 3 ml of drug & 12.5 mg of Bupivacaine was used.

The hemodynamic parameters were stable in both the groups. Both Pulse Rate & Mean Arterial Pressure were lower in the clonidine group than that of control group. Blood Pressure was responsive to I/V fluid administration as is evident from the fact that there was significant difference in the I/V fluid requirement in the clonidine group than in the control group. Clonidine, after neuraxial or systemic administration, affects arterial BP in a complex manner because of opposing actions at multiple sites. The α-2-adrenergic agonists produce sympatholysis and reduce arterial BP through effects at specific brainstem nuclei and on sympathetic preganglionic neurons in the spinal cord, effects that are counteracted by direct vasoconstriction resulting from the α-2-adrenergic agonists on the peripheral vasculature. As a result, the dose response for neuraxial clonidine on arterial BP in humans is generally considered to be U-shaped[10, 11]. Furthermore, combining α-2-adrenergic receptor agonists with local anesthetics can potentially increase the degree of sympatholysis and resulting hypotension.

The difference in the mean time of sensory regression to L1 in our study was found to be statistically highly significant ($p < 0.001$), with regression occurring more slowly in clonidine group. Sethi B.S., *et al.*[12] , in a similar study in gynaecological patients found that the mean time from injection to regression of the level of sensory analgesia by two segments was longer in the Clonidine group than in Control group ($p<0.001$). The mechanism of clonidine-induced potentiation of sensory block in spinal anesthesia is reported to be mediated by presynaptic (inhibition of transmitter release) and postsynaptic (enhancing hyperpolarization)[13, 14] effects. Although clonidine might have a vasoconstrictive effect in large concentrations, the role of vasoconstriction in prolonging sensory block seems to be minor, even in usual clinical doses (1–2 µg/kg) [15].

The duration of motor block was prolonged ($p<0.001$) with addition of Clonidine to a Local Anesthetic solution for intrathecal block. Similar result was demonstrated by Bonnet F. *et. al.*[16] who studied the effect of different concentrations of clonidine, an α2 agonist, on sensory and motor blockade during spinal anesthesia. Racle JP *et al*[1] & Bonnet F *et al*[3] also demonstrated that intrathecal clonidine combined with local anesthetic significantly potentiates the intensity and duration of motor blockade. The explanation for this could be that the α 2-adrenoceptor agonists induce cellular modification in the ventral horn of the spinal cord (motor neuron hyperpolarization) and facilitate the local anesthetic action.
There was a statistically significant difference ($p < 0.001$) between the mean time of first rescue analgesic request between the clonidine (278.2+56.4) & the study groups(175.6+26.1). Similar results were also demonstrated by Strebel, S. *et al.*[9] while studying the effect of varying doses of intrathecal Clonidine (37.5 µg, 75 µg, 150 µg) along with Bupivacaine (in 8% glucose). Tuijl *et al.*[17], have also demonstrated that addition of 75 µg clonidine to hyperbaric bupivacaine prolongs spinal analgesia and the motor block after Caesarean section and improves early analgesia. In their study, immediate postoperative analgesia was better with the combination of bupivacaine and clonidine as demonstrated by a significantly later first request for analgesia, less need for morphine top-ups in the recovery period and lower VAS scores in the Bupivacaine - Clonidine group. The analgesic effect following its intrathecal administration is mediated spinally through activation of post synaptic α-2 receptors in substantia gelatinosa of spinal cord. The rationale behind intrathecal administration of clonidine is to achieve a high drug concentration in the vicinity of α-2 adrenoreceptors in the spinal cord and it works by blocking the conduction of C and Aδ fibres, increases potassium conductance in isolated neurons in vitro and intensifies conduction block of local anaesthetics.
Some of the adverse effects noted in our study were nausea & vomiting, dryness of mouth, sedation. However, none of the adverse effects noted were found to be statistically significant in either groups, except for sedation. Clonidine caused sedation in significantly higher number of patients than in control group. The nausea & vomiting was not very marked & was settled after one dose of an antiemetic.

Administration of clonidine intrathecally does potentiate the duration of analgesia, sensory and motor block. It maintains the heamodynamic stability & is associated with sedation in significant no. of the patients, but is devoid of any other major side effect such as nausea and vomiting, respiratory depression etc.

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