Research Article

Comparison of Bupivacaine 0.5% and Bupivacaine + Clonidine Intrathecally for intraoperative and Postoperative analgesia in Lower Limb Orthopaedic Surgeries

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Abstract

Background: A randomized controlled study was designed to investigate the effects of addition of clonidine to hyperbaric bupivacaine 0.5% for spinal anaesthesia in patients undergoing lower limb orthopaedic surgeries, in terms of vital parameters, onset and duration of sensory and motor block, intra and post operative pain and adverse effects. **Methods:** Sixty adult ASA Grade I and II patients of either sex posted for lower limb orthopedic surgeries were randomly divided equally in to clonidine or control group. Control group received intrathecal 3.0 ml of 0.5% hyperbaric bupivacaine with 0.5 ml of normal saline and Clonidine group received identical volume of intrathecal clonidine with hyperbaric bupivacaine. **Results:** Mean time for post operative analgesia was significantly longer in clonidine group (9.6 hours) than in the control group (3.55 hours). (p-value<0.01). Heart rate and blood pressure compared at 30 minute and 45 minute intervals were significantly less in clonidine group. (p-value < 0.05). Bradycardia and hypotension did not require any therapeutic intervention. Clonidine group patients were found to be more sedated than control group. **Conclusion:** Adding clonidine 75 µg to intrathecal bupivacaine prolongs the duration of spinal anaesthesia and analgesia. It is safe and is likely to be as effective as higher doses of bupivacaine without severe adverse effects.

Key words: Intrathecal Clonidine, Bupivacaine, Postoperative pain, Spinal anaesthesia

Introduction

Spinal anaesthesia has increasingly become the technique of choice for lower limb orthopedic surgeries due to quick onset of action and reliability in producing uniform sensory and motor blockade and ease of administration. Its main disadvantage relates to its limited duration of action and hence lack of long-lasting postoperative analgesia. Spinal anesthesia and postoperative analgesia can be prolonged by using adjuvant to local anesthetic like adrenaline [1], midazolam [2], opioids [3], neostigmine [4], clonidine [4-7] etc. In our study the α2-adrenergic agonist clonidine which has the ability to potentiate the effects of local anaesthetics [4-9] has been used as an adjuvant. Unlike spinal opioids, clonidine does not produce pruritus or respiratory depression [3, 9] but prolongs the sensory blockade [6, 10, 11] and motor blockade [10, 11] reduces the amount or concentration of local anaesthetic required to produce postoperative analgesia [6, 12]. The aim of this randomized double blinded controlled study was to investigate the effect of addition of clonidine to hyperbaric bupivacaine 0.5%, for spinal anaesthesia in patients undergoing lower limb orthopaedic surgeries, on analgesic efficacy, quality of block, duration of motor blockade, duration of analgesia and adverse effects.

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Materials and Methods

After approval from the hospital ethical committee, this study was carried out in 60 adult ASA Grade I and II patients of either sex posted for lower limb orthopaedic surgeries. Excluding criteria were systemic disorders like diabetes mellitus, hypertension, heart disease, allergy to bupivacaine or clonidine and all known contraindications for spinal anaesthesia, such as spine deformity, increased intracranial pressure, neurological disorders, hemorrhagic diathesis, or infection at the puncture site.

A double-blind, randomized, placebo-controlled study design with two parallel groups was used. After informed written consent selected patients were randomly allocated into two groups.

Clonidine group: 3.0ml Bupivacaine (0.5%) + Inj Clonidine 75mcg (preservative free) + normal saline to make the volume 3.5ml intrathecally

Control group: 3.0 ml Bupivacaine (0.5%) + 0.5 ml normal saline intrathecally.

Both the patient and anaesthesiologist were unaware of the study solutions. Syringes were prepared immediately before the spinal injection ensuring the volumes at 3.5 ml by a third person other than the anaesthesiologist who administered the drugs intrathecally and later on did the parameter assessment. This third person only did the random allocation and he knew the status of experiment/control of the patient to unblind the status in case of an emergency. Sedatives and hypnotics were avoided during the pre operative and intra operative period. Intravenous line was secured with a wide bore cannula and all patients were preloaded with ringer lactate solution at 10ml/kg. Lumbar puncture was done in the sitting position under aseptic conditions in the L3-L4 space with a 25G Quincke needle. Intrathecal study drug was injected as per the group and patient was placed in the supine position. The time at which the intrathecal injection was completed was considered as zero. Noninvasive arterial blood pressure, heart rate, and oxygen saturation assessed at zero time and then every 5 minutes during the surgery. The level of sensory blockade was tested by pinprick method in midline and the motor blockade was tested with the modified Bromage scale used by Breen et al [13]. The time of onset sensory and motor block, time to full recovery of motor block, level of intraoperative sedation and time to first rescue analgesic were recorded. Hypotension, defined as a decrease of systolic blood pressure of more than 20% from baseline, was treated with mephentermine and bradycardia, defined as a heart rate decrease of more than 20% from baseline was treated with atropine. For rescue analgesia inj tramadol 100 mg or inj diclofenac sodium 75 mg was given. A note was also made of blood loss, urine output, IV fluid input. Patients were observed for any discomfort, nausea, vomiting, shivering, pain, bradycardia and any other side effect and the need for additional medications was recorded. Statistical analysis was carried out with Stata 10. Demographic characteristics, hemodynamic parameters, onset, peak and duration of sensory and motor block and duration of postoperative analgesia, level of sedation were compared between groups using unpaired t test. Pulse rate at different time intervals within the same group were compared using paired t test. For categorical data chi-square test was applied. $P < 0.05$ was considered significant.

Results

Both groups were comparable regarding their demographic characteristics as shown in Table I.

Table I: Demographic characteristics

Parameter	**Clonidine group (n=30) Mean ± SD**	**Control group (n=30) Mean ± SD**
Age (yrs)	34.4±7.56	35.33 ±7.4*
Weight (kg)	53.5±8.91	55.3±7.41*
Sex (M:F)	15:15	17:13 *
ASA I : II	24:6	25:5 *

*** p-value> 0.05 ** p-value significant at 0.05 *** p-value significant at 0.01**

Table II compares the time for onset of sensory and motor blockade in both groups.

Table II: Analysis of Sensory, Motor blockade and Duration of analgesia

Parameter	**Clonidine group (n=30) Mean ± SD**	**Control group (n=30) Mean ± SD**
Time in seconds for onset of sensory blockade	172.33±37.17	181 ±37.35*
Time in seconds for onset of motor blockade	302±57.97	288.3±53.848*
Duration of motor blockade	244±32.55***	167.5±23.44
Time for first rescue analgesia in hours	574±63.17 ***	219±38.4

*** p-value> 0.05 ** p-value significant at 0.05 *** p-value significant at 0.01**

Time required for onset of sensory and motor blockade was similar in both groups. Duration of motor block was significantly more in clonidine group. (244 ± 32.55). The difference in the mean duration of motor blockade among both the groups was significant (P< 0.00l). Mean time for post-operative analgesia was significantly longer in clonidine group than control group (9.6 hours and 3.55 hour respectively)(p-value < 0.01)

Table III has compared hemodynamic parameters (heart rate and systolic blood pressure) in both groups at different time intervals.

Table III: Analysis of heart rate, systolic and diastolic blood pressure

Measured at different interval from start of intrathecal block		**0 min Mean±S.D**	**5 min Mean±S.D**	**10 min Mean±S.D**	**15 min Mean±S.D**	**30 min Mean±S.D**	**45 min Mean±S.D**	**60 min Mean±S.D**	**120 min Mean±S.D**
Heart rate/min	Clonidine group	83.86 ±9.4*	82.53 ±7.8**	79.13 ± 6.8**	74.4 ± 6.46***	69.73 ± 8.08***	70.13 ± 7.2***	71.93 ± 7.5***	79.2 ± 8.82**
	Control group	82.33 ± 17.71	86.8 ± 8.3	90.9 ± 6.4	93.3 ±5.84	83.4 ±10.3	84.06 ±7.76	84.86 ±7.64	83.66 ±6.62
Systolic B.P mm Hg	Clonidine group	125 ±12.52*	123.66 ± 11.59*	119.33± 10.1 **	112.66 ± 7.68*	107.4 ± 10.7**	107.66 ± 9.85***	109.66 ± 10.21***	110.33 ± 9.44***
	Control group	126.66 ± 12.12	124.3 ± 9.98	113.66 ±8.07	110.8 ± 7.38	114.4 ±11.8	116 ±10.56	117.33 ± 11.42	120.33 ±9.99

*** p-value> 0.05 ** p-value significant at 0.05 *** p-value significant at 0.01**

Pulse rate and blood pressure was higher in control group at all time intervals as compared to clonidine group. Heart rate progressively reduced from 82.53±7.8 at 5 minutes interval to 69.73±8.08 at 30 minutes interval in clonidine group (p-value < 0.05**)**. Mean heart rate was significantly higher at all time intervals in control group than in clonidine group **(**p-value< 0.01**).** In clonidine group we observed sedation score 0 in 9 patients, sedation score 1 in 16 patients and sedation score 2 in 5 patients while all patients from control group showed sedation score 0. Though patients from clonidine group were found to be more sedated, respiratory depression was not observed. Respiratory rate and oxygen saturation (SpO2) were similar in both groups.

Table IV: Complications

Complications	**Clonidine Group (n = 30)**	**Control Group (n = 30)**
Bradycardia	3	2
Hypotension	3	2
Urinary Retention	0	0
Dryness of mouth	9	4
Respiratory depression	0	0
shivering	2	2
Position-dependent headache	0	0

There was no significant difference between the groups. (p-value> 0.05).

There was no significant difference between the groups (p-value > 0.05). Complications in both groups were not serious enough to warrant any intervention. There was no morbidity.

Discussion

In recent years, clonidine which is a selective partial agonist for α-2 adrenoreceptor, has been used to prolong spinal anaesthesia. It is known to increase both sensory and motor block of local anaesthetics [5, 6, 10, 11]. Clonidine is now an acceptable adjuvant to local anaesthetics for epidural route [14]. Clinical trials provide evidence that less clonidine is needed intrathecally than epidurally to produce the same analgesic effect with fewer side effects [7].

Hypotension was less pronounced after intrathecal than oral clonidine [8]. Intrathecal clonidine has been used to enhance postoperative analgesia in cesarean deliveries, repair of femoral fractures, and ambulatory knee arthroscopy etc.[6,7,8,12]. According to Niemi L [14] marked haemodynamic changes and sedation was seen, which limits the usefulness of intrathecal clonidine when used in very high doses (3µg/kg) . VanTuijl I et al [15] used low doses of intrathecal Clonidine (15 µg) with satisfactory outcome. Their patients were for inguinal herniorrhaphy and knee arthroscopy. We included lower limb orthopaedic surgeries.

Time required for onset of sensory and motor blockade was found to be similar in both groups in our study. Similar to many other studies [6, 17, 18, 19] we also found that addition of 75 µg of clonidine to 0.5% bupivacaine significantly prolongs the block and postoperative analgesia (8 to 10 hrs) and thus reduces the postoperative analgesic requirement. De Negri P et al [20] observed minimal influence on haemodynamic parameters even with 105 micrograms of intrathecal clonidine as reflected in our study.

A statistically significant decrease in arterial pressure and heart rate was noted in the Clonidine group compared to the Control group, none of the patients required any therapeutic intervention for either. Heart rates started dropping in Clonidine group after 15 minutes, maximum being after 30 minutes, bradycardia was never severe enough to be a cause for concern. We observed more sedation in clonidine group which is well known side effect of clonidine [11, 14, 21] but no respiratory depression was seen in our study. Dryness of mouth, a typical side effect of clonidine [11, 22] was also reported by more patients in the clonidine group but was not worrisome. In conclusion, the present study indicates that adding clonidine 75 µg to intrathecal bupivacaine prolongs spinal anaesthesia and the duration of analgesia. It is safe and is as effective as bupivacaine in higher dosage without severe adverse effects.

Conclusion

Present study indicates that adding clonidine 75 µg to intrathecal bupivacaine prolongs spinal anaesthesia and the duration of analgesia. It is safe and is as effective as bupivacaine in higher dosage without severe adverse effects.

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