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"TWO DIFFERENT DOSES OF INTRATHECAL CLONIDINE FOR POST - OPERATIVE ANALGESIA IN LOWER LIMB SURGERIES - A COMPARISON"

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ABSTRACT **Background and Aim :** Clonidine is added to intrathecal bupivacaine to increase the duration of block and provide post-operative analgesia. The study aimed to compare two different doses of clonidine with bupivacaine in lower limb surgery, and to know the optimal analgesic dose of clonidine. **Methods:** In this single blind randomized, prospective comparative study, forty patients of the ASA grade I or II, posted for lower limb surgery, were randomly allocated into two groups. Group C-30 received 3 mL of 0.5% hyperbaric bupivacaine with 30 µg of clonidine and Group C-15 received 3 mL of 0.5% hyperbaric bupivacaine with 15 µg of clonidine. The mean onset of block, regression by two segments, duration of analgesia , hemodynamic parameters and adverse effects were assessed. Data analysis was done with statistical software SPSS Ver. 20 with Unpaired T test and Chi-square test. **Results:** Onset of block was significantly faster ($p < 0.01$) with Group C30 than Group C15 (0.98 ± 0.07 min vs 1.34 ± 0.19 min) , whereas regression by two segments(192.45 ± 10.69 min vs 168.20 ± 7.89 min) and duration of analgesia (233.25 ± 23.23 mins vs 179.75 ± 9.06min) was significantly prolonged in Group C30 than Group C15. Incidence of adverse events was comparable and not statistically significant ($p > 0.05$) in Group C15 (40%) than in Group C30 (60%). **Conclusion:** Both doses of clonidine provide equally safe, effective and excellent quality of post-operative analgesia. 30mcg of Clonidine is the optimal analgesic dose for lower limb surgeries due to faster onset , longer time for regression by two segments and prolonged duration of post-operative analgesia without any significant adverse effects.

KEYWORDS : Clonidine, Lower limb surgeries , Postoperative analgesia, Haemodynamic stability.

INTRODUCTION

Neuraxial anaesthesia is nowadays becoming popular for lower limb surgeries because of its ease of practice with minimal complications. The most common local anaesthetic used for this technique is 0.5% hyperbaric bupivacaine. However, the duration anaesthesia of bupivacaine alone may be short for prolonged surgeries.1 The uncontrolled pain in trauma patients can affect overall recovery of patient. Thus, attenuation of the post-operative pain is important to so as to decrease the complications and facilitate healthy recovery.

Addition of small doses of adjuvants, like opioids2, clonidine3, dexmedetomidine4, etc. to local anesthetics to fasten the time of onset, improve the quality of intraoperative anesthesia, prolong analgesia, and reduce the complications associated with high-dose intrathecal administration of hyperbaric bupivacaine. Clonidine is widely preferred as it increases the duration and intensity of pain relief, and decreases the systemic and local inflammatory stress response. It produces analgesia by depressing the release of C-fiber transmitters and by hyperpolarization of post synaptic dorsal horn neurons.[5,6]

It has been used in high (>150 mcg)7, low(<150 mcg) and small (<75 mcg) doses. However the optimal dose remains unknown.

This study has been tailored to compare two different doses of clonidine 15mcg and 30mcg as an adjuvant to intrathecal hyperbaric bupivacaine aiming to find out adequate effective dose for postoperative analgesia.

MATERIALS & METHODS

After approval from the ethical committee, single blind randomized, prospective comparative study was performed.40 patients undergoing lower limb surgeries with BMI<35 kg/m2, age between 18-50 years, accepted as ASA grade I & II, and were divided into two groups :- Group C15 and Group C30.

Group C15 – 0.5% Bupivacaine + Inj. Clonidine 15µg ; total volume 3.2 ml Group C30 – 0.5 % Bupivacaine + Inj. Clonidine 30µg ; total volume 3.2 ml A detail history and thorough general & systemic examination was done. All routine investigations like Hb, CBC, LFT, KFT, RBSL, ECG & urine examination were performed day prior to surgery.

The patients were familiarized with the 10 cm visual analogue scale (VAS) for pain during the pre- anaesthetic visit .After confirming the informed valid consent ,vitals like ECG, blood pressure and SpO2, were recorded and preloading was done with 10 ml/kg ringer lactate over 30 min. Under all aseptic precautions, with the help of 25-gauge Quincke needle, spinal puncture was done in L3-L4 space in sitting position. All patients received a coded intrathecal drug volume of 3.2 ml of 0.5% hyperbaric Bupivacaine with clonidine.

After administration of the drug, the vital parameters like pulse rate, blood pressure, respiratory rate, oxygen saturation, ECG were monitored continuously during the procedure. Time of onset of block was subjectively assessed by patient complaining of a feeling of warmth, heaviness of limbs, or a tingling sensation, objectively confirmed by decreased VAS scores to pinprick to 5 or less at the calf level. Level of sensory block was assessed by pinprick test, and motor block was assessed using Bromage scale. Level of sedation was assesed : No sedation – 0 , Drowsiness – 1, Asleep but arousable – 2, Unarousable with loss of verbal contact - 3 . PAIN SCORE was assessed using 10 cm Visual analog scale (VAS) and recorded before the injection, every min for 5 min, every 5 minutes until surgery lasted, every 15 min till 3 hrs and later at hourly intervals until 6 hours after the injection. The maximum ascent of sensory block , time to achieve sensory block up to T10, regression of block by two segments and the duration of analgesia were also noted.

Haemodynamic parameters were assessed. Hypotension was defined as a more than 30% fall from basal value or < 90 mmHg of systolic blood pressure and was treated with Leg raise, IV fluids and Inj. Mephenteramine 6mg i.v. and bradycardia was defined as heart rate less than 60/ min and was treated with Inj. Glycopyrollate 0.2mg i.v.

STATISTICAL ANALYSIS DETAILS

Data analysis was done with statistical software SPSS Ver. 20. Quantitative data was presented with Unpaired T test and Qualitative data was presented using Chi-square test. P value less than 0.05 was taken as significant.

RESULTS

Demographic data like age , height , weight , sex , ASA grades , was compared between the two groups and was statistically not significant, p > 0.05.

Table No.1 : Hemodynamic parameters

Variables	Group C15	Group C30	P value
Pulse /min	77.90 ± 7.17	79.10 ± 6.83	0.591
RR /min	15.50 ± 1.36	14.30 ± 1.84	0.024
SpO2 %	98.95 ± 0.89	98.80 ± 0.83	0.585
SBP mmHg	127.70 ± 8.52	131.45 ± 9.10	0.187
DBP mmHg	78.65 ± 6.22	77.85 ± 6.74	0.699
MAP mmHg	95.00 ± 6.09	95.72 ± 6.97	0.731

Both groups were comparable in all hemodynamic parameters, without any statistical significance. Bradycardia was observed in first 10 to 30 min, in 20% of total patients , but mean pulse rate was not statistically significant in both the groups throughout. (p > 0.05) . We saw that 12.5% of patients in both groups had hypotension, during first 10-45 min but fall in systolic blood pressure was not significant. (p > 0.05).

Table No.2 : Characteristics of block - 1

Variables	Group C15	Group C30	P value
Level of sensory block (T10/T8/T6)	3/8/9	1/11/8	P = 0.46
Grade of motor block (3/4)	10/10	12/8	P = 0.52
Level of sedation (0/1)	18/2	15/5	P = 0.21
Maximum ascent of sensory block (T10/T8/T6)	3/8/9	1/9/10	P = 0.57

We have compared characteristics of block (Table 2 and 3). The level of sensory block , grade of motor block, Level of sedation and maximum ascent of sensory block, between both the groups were comparable and not statistically significant, p > 0.05.

Table No.3 : Characteristics of block - 2

Variables	Group C15	Group C30	P value
Time of onset of block	1.34 ± 0.19	0.98 ± 0.07	P < 0.01
Time required to reach T10	2.47 ± 0.23	2.56 ± 0.23	P = 0.202
Regression by two segments (in min)	168.2 ± 7.89	192.45 ± 10.69	P <0.01
Duration of Analgesia (in min)	179.75 ± 9.06	233.25 ± 23.23	P <0.01

Time of onset of block in group C15 was 1.34 ± 0.19 min and in group C30 was 0.98 ± 0.07 min. And when compared to each other, difference between time of onset of block in group C15 and group C30 was statistically highly significant ; P value < 0.01.

Also, Time required to reach T10 level was comparable between the two groups : 2.47 ± 0.23 min in group C15 and 2.56 ± 0.23 min in group C30 , was not statistically significant with p value > 0.05 .

Regression by two segments was found prolonged in group C30 (192.45 ± 10.69 min) as compared to group C15 (168.20 ± 7.89 min) , and this difference was found statistically highly significant , P < 0.01 . Duration of analgesia ranged between 170 - 188 min and 210 – 256 min in group C15 and group C30 respectively. (179.75 ± 9.06 min in Group C15 and 233.25 ± 23.23 min in Group C30). Thus, duration of analgesia was longer in Group C30 than Group C15 and the difference between the groups was statistically highly significant (P value □0.01) We observed that , 8 (40%) patients from Group C30 and 12 (60%) patients from Group C15 had adverse events like hypotension, bradycardia and sedation,but they were not seen significant between the two groups (p = 0.6997)

DISCUSSION

Many patients experience pain following surgery despite advancements in the treatment of postoperative pain in lower limb procedures. The most crucial element for successful rehabilitation is early, rigorous physical treatment, which might be hampered by pain. And thus it is important to alleviate this pain.

Lower limb surgeries are safely & popularly being performed under spinal anaesthesia, as it is a simple, effective, and affordable procedure with advantages of giving surgical anaesthesia an prolonged postoperative pain relief [8] . The preferred local anaesthetic for spinal anaesthesia for many years is hyperbaric bupivacaine 0.5%. Bupivacaine injections are known not to result in a prolonged period of postoperative analgesia [9]. So, it is necessary to add adjuvants like clonidine to bupivacaine to prolong spinal anaesthesia and postoperative analgesia.[8-10]

The need to determine the optimal effective dose of clonidine led us to the current study where we compared 15 and 30 mcg of intrathecal clonidine with 0.5% hyperbaric bupivacaine.

Roh et al. [9] (2008) found that ability of clonidine to modulate spinal cord NMDAR activation via suppression of NR1 phosphorylation, is a possible mechanism of potency of intrathecal clonidine administration in a rat model of neuropathic pain. Intrathecally ,clonidine activates the post synaptic alpha-2 receptor in the substantia gelatinosa of spinal cord, producing analgesia. [10,11]

For postoperative analgesia, many researchers have added 75 mcg of intrathecal clonidine to local anaesthetics [1,6,7] . We considered ways to further reduce the dosage of clonidine without sacrificing its effectiveness.

In our study, demographic characteristics of the two groups including the age, gender,weight, height and ASA grades were not significant. There was no significant difference regarding the sensory block levels, motor block grade, sedation level, and distribution according to maximum ascent of sensory block between the two groups.

The haemodynamic stability of our patients was maintained in both 15 mcg and 30mcg clonidine groups, & was similar to the findings of Dobrydnjov et al. [12] . 20% of patients developed bradycardia,but none of them needed any active bradycardia treatment. This was in line with past studies , Sethi et al. [6] found relatively few instances of hypotension and bradycardia requiring treatment when 1 mcg/kg of intrathecal clonidine was used for spinal anaesthesia. Study of Kothari N et al.[13] showed that the addition of clonidine did not change the incidence of bradycardia.

We observed that 12.5% of patients in both groups had hypotension, but no statistically significant hypotension in any clonidine group at any point of time was found compared to the control which was in accordance with the findings of Strebel et al., [14] and in contrast to the findings of some other authors, like Neimi et al. [1] and Grandhe et al. [15] who used higher doses of clonidine (3 µg/kg and 1-1.5 µg/kg , respectively.

Higher doses of clonidine resulted in noticeably higher sedation scores, like in the study of Filos et al. [10]. We found that with administration of clonidine (15 and 30 µg), 17.5% patients were sedated, but sedation in both groups was statistically insignificant.. In addition, Kothari et al.[13] also discovered that adding 50 mcg of clonidine to bupivacaine made 35%–45% of patients drowsy.

We observed faster onset of action in 30mcg clonidine group like in the study of Saxena et al. [6] . who observed faster onset in all clonidine groups as compared to control, whereas Agarwal D et al. [16] studied same doses of clonidine with 9mg bupivacaine and observed no such significant difference.

The maximum sensory level achieved in both groups was higher in our study (T6), similar to the study of Kakunje et al. [17] as clonidine compared to the study by Sagiroglu et al. (T8). [18]

Regression by two segments was prolonged with 30mcg clonidine. Few studies support our findings, Manish Patil et al. [19] also reported prolonged time for two segment regression in clonidine group (204 min) as compared to control group (126min).

Our research can be compared with those of Saxena et al [6], and Agarwal D. et al.[16] who also discovered a statistically significant analgesia prolonging in the clonidine groups. Contrary to this , Thakur A. et al. [20] observed no such significant prolongation in duration of analgesia with clonidine 15mcg and 30mcg. Adding intrathecal clonidine 30 mcg to bupivacaine prolonged intraoperative anaesthesia and the time until the first analgesic request after lower limb surgeries. These results agree with those of earlier research of Bharat et al. [21]

CONCLUSION

From the present study it can be summarized that both doses of clonidine (15mcg and 30mcg) as an adjuvant to 0.5% hyperbaric bupivacaine provide equally safe, effective and excellent quality of post-operative analgesia. However, 30mcg clonidine provides faster onset , longer time for regression by two segments and prolonged duration of post-operative analgesia without any significant adverse effects.

Hence, we concluded that 30mcg is the optimal analgesic dose of clonidine for post-operative analgesia with to 0.5% hyperbaric bupivacaine for lower limb surgeries with minimal side effects.

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