Original Article

Indian Journal of Emergency Medicine
Volume 9 Number 2, April - June 2022
DOI: http://dx.doi.org/10.21088/ijem.2395.311X.9223.4

Comparative Evaluation of efficacies of Clonidine & Dexmedetomidine as an adjuvant to Intrathecal Hyperbaric 0.5% Bupivacaine in patients scheduled for Elective Lower Limb Surgeries

Rikhav Shah[1], Madhav Navlekar[2]

How to cite this article:
Rikhav Shah, Madhav Navlekar/Comparative Evaluation of efficacies of Clonidine & Dexmedetomidine as an adjuvant to Intrathecal Hyperbaric 0.5% Bupivacaine in patients scheduled for Elective Lower Limb Surgeries/Indian J Emerg Med 2023;9(2):77–82.

Abstract

Background and Aim: Several adjuvants have been utilized to enhance the standard of analgesia over the time of post- surgery. We have undertaken this study to evaluate and compare the efficacies of clonidine and dexmedetomidine as an adjuvant to intrathecal hyperbaric 0.5% bupivacaine in patients scheduled for elective lower limb surgeries.

Material and Methods: The present study is blinded randomized case control done in the department of the Emergency Medicine in the medical college and associated hospital. All patients undergoing elective lower limb surgery were included for the study. After obtaining the consent letter signed from the patients; total of 180 patients were included in the study. Patients were divided into 3 groups: Group A (control group): received 15mg of 0.5% hyperbaric bupivacaine with 0.5ml normal saline. Group B (clonidine group): received 15mg of 0.5% hyperbaric bupivacaine with 50µg clonidine. Group C (dexmedetomidine group): received 15mg of 0.5% hyperbaricbupivacaine with 5µg dexmedetomidine. Various parameters were examined were: Onset of sensory blockade and motor blockade, Maximum level of sensory blockade and time taken for the same, Maximum level of motor blockade and time taken for the same.

Results: There is no clinical significance between group B and group C regarding mean time taken for onset of sensory blockade. The mean duration of analgesia is 194 ± 26.98 mins in group A (controlgroup), 346.37 ± 32.16 mins in group B (clonidine group) 373.37 ± 38.17 mins in group C (dexmedetomidine group). There is a statistically highly significant difference between group A and group B.

Conclusion: The supplementation of bupivacaine with dexmedetomidine 5 µg or clonidine 50 µgin spinal anaesthesia produces significant shorter onset of motor and sensory block with longer duration of sensory and motor block when compared to bupivacaine alone.

Keywords: bupivacaine; clonidine; dexmedetomidine; lower limb surgeries.

Author's Affiliation: [1]Assistant Professor, 2Associate Professor, Department of Emergency Medicine, Gujarat Adani Institute of Medical Science, Bhuj, Kutch-370001, Gujarat, India.

Corresponding Author: Madhav Navlekar, Associate Professor, Department of Emergency Medicine, Gujarat Adani Institute of Medical Science, Bhuj, Kutch-370001, Gujarat, India.

E-mail: researchguide86@gmail.com

Received on: 24-01-2023

Accepted on: 22-02-2023

INTRODUCTION

Surgeries in lower abdominal region may be performed with the use of general or regional anesthetics. Spinal block has extensive popularity, as well as sufficient post-surgery pain control is necessary to avoid unfavorable outcome of surgical abuse. The perfect spinal anesthetic would offer quick and sufficient surgical anesthetic, facilitating early movements in body and the capability to permit quick discharge.[1,2] It allows the patient to remain awake, minimize or completely avoid the problem associated with airway management. With spinal anaesthesia, the technique is simple to perform; the onset of anaesthesia is more rapid, avoids poly pharmacy and also provides post-operative analgesia.[3,4]

Bupivacaine is three to four times more potent than lignocaine and has longer duration of action. Its disadvantages are slow onset of action and decreased motor block. Hyperbaric bupivacaine 0.5% is extensively used in India for spinal anaesthesia. Though the duration of action of bupivacaine is prolonged, it does not produce prolonged post-operative analgesia. Hence an adjuvant is required for producing prolonged post-operative analgesia. The discovery of opioid receptors and endorphins in spinal and supra spinal regions soon led to the use of spinal opiates. Morphine was the first opioid administered intrathecally to augment neuraxial blocks.[5,6]

Most of the clinical studies about the intrathecal α2 adrenergic agonist are related to clonidine. Dexmedetomidine, a highly selective α2 adrenergic agonist has evolved as a panacea for various applications and procedures in the perioperative and critical care settings.[7] It is also emerging as a valuable adjunct to regional anesthesia and analgesia, where gradually evolving studies can build the evidence for its safe use in central neuraxial blocks. They have been found to prolong the duration of spinal block following intrathecal administration.[8,9]

Dexmedetomidine is a highly specific and selective alpha-2 adrenoceptor agonist with 8 times more affinity for alpha-2 adrenoceptor than clonidine. The ratio of alpha-1: alpha-2 receptor binding selectivity for dexmedetomidine is 1:1620 compared to 1:220 for clonidine.[10,11] While clonidine has been used as an adjuvant to local anaesthetic agents for intrathecal purposes with successful results, there are only a few studies available for dexmedetomidine for such studies. Hence, we have undertaken this study to evaluate and compare the efficacies of clonidine and dexmedetomidine as an adjuvant to intrathecal hyperbaric 0.5% bupivacaine in patients scheduled for elective lower limb surgeries.

MATERIALS AND METHODS

The present study is blinded randomized case control done in the department of the Emergency Medicine in the medical college and associated hospital. All patients undergoing elective lower limb surgery were included for the study. After obtaining the consent letter signed from the patients; total of 180 patients were included in the study. The ethical clearance was obtained from the ethical committee of the institute. All patients were explained about the procedures and an informed written consent was obtained.

Inclusion Criteria

1. Patients aged between 18 and 60 years
2. ASA III
3. Scheduled for elective lower limb surgeries.

Exclusion Criteria

1. Any contraindication of regional anaesthesia, or patient refusal.
2. Body weight more than 120 kg
3. Height Post spinal surgeries,
4. Spinal deformity
5. History of allergy to study drugs
6. Pregnancy
7. Coagulopathy
8. Cardiac, liver, or kidney diseases.
9. Neurological disorder.

A total of 180 patients in the age group between 20 years and 60 years of either sex belonging to ASA physical status I and II posted for elective lower limb surgeries were grouped randomly into three groups (n=60). Randomization was done using sealed envelope technique. Group A (control group): received 15mg of 0.5% hyperbaric bupivacaine with 0.5ml normal saline. Group B (clonidine group): received 15mg of 0.5% hyperbaric bupivacaine with 50µg clonidine. Group C (dexmedetomidine group): received 15mg of 0.5% hyperbaricbupivacaine with 5µg dexmedetomidine.

Total volume of the injected solution was 3.5ml in all three groups. Preoperative assessment was done for each patient and informed written consent

was taken. Patients were kept NPO for solids 6 hours and clear fluids 2 hours before surgery. All patients were premedicated on the night before surgery with Tablet Ranitidine 150mg and Tablet Alprazolam 0.5mg. Intravenous line was secured with 18 gauge cannula and preloaded with 500 ml of Ringer lactate solution half an hour before anaesthesia.

In the operating room, appropriate equipment for airway management and emergency drugs were kept ready. The horizontal position of the operating table was checked. Patients were shifted to the operating room and positioned. Non-invasive blood pressure monitor, pulseoximeter and ECG leads were connected to the patient. Preoperative baseline systolic and diastolic blood pressure, mean arterial pressure, pulse rate, respiratory rate and oxygen saturation were recorded.

Intraoperative monitoring On sitting position, the skin over the back was prepared with antiseptic solution and draped with sterile towel. Under aseptic precautions subarachanoid block was performed at level of L3-L4 through a midline approach using 25G Quincke spinal needle and study drug was injected with operative table kept flat. The patients were made to lie supine immediately and the time of injection of study drug was noted.

In the perioperative period the following parameters were studied.

- Onset of sensory blockade and motor blockade
- Maximum level of sensory blockade and time taken for the same
- Maximum level of motor blockade and time taken for the same
- Two segments sensory regression time
- Total duration of analgesia
- Total duration of sensory blockade and motor blockade.

Sensory blockade was tested using pinprick method with a blunt tipped 27G needle at every minute for first 5 mins and every 5 mins for next 15 mins and every 10 mins for next 30 mins and every 15 mins till the end of surgery and there after every 30 mins until sensory block was resolved.

Quality of motor blockade was assessed by Bromage scale.

- Level of sedation was noted.
- Side effects if any were noted.

Haemodynamic monitoring was done during the block every 5 mins for first 15 mins and every 10 mins for next 30 mins and once in 15 mins till the end of surgery and post operatively every hourly employing multi parameter monitor which displays heart rate (HR), 53 systolic blood pressure (SBP) diastolic blood pressure (DBP), mean arterial pressure (MAP), ECG and SpO_2.

Onset of sensory blockade: was defined as time taken from theinjection of study drug till loss of pin prick sensation at T10 level. Time taken for maximum sensory blockade: was defined as the time taken from the injection of study drug to the maximum sensory blockade attained. Onset of motor blockade: was defined as the time taken from theinjection of study drug till the patient was unable to move hip but was able to move knee and ankle.

Quality of motor blockade was assessed by Bromage scale

Bromage 0 - able to move hip, knee and ankle.

Bromage 1- unable to move hip but able to move knee and ankle.

Bromage 2 - unable to move hip and knee but able to move ankle.

Bromage 3- unable to move hip, knee and ankle.

Time taken for maximum motor blockade: was defined as the time taken from the injection of study drug to maximum motor blockade attained (Bromage 3). Duration of two segment sensory regression: was defined as the time taken fromthe maximum level of sensory block attained till the 54 sensation has regressed by 2 segments. Duration of analgesia: was defined as the time taken frominjection of study drug till the patient requests for rescue analgesic in the postoperative period. Duration of sensory blockade: was defined as the time taken from time of injection of study drug till the patient feels the sensation at S1 dermatome.

Duration of motor blockade: was defined as the time taken from time of injection of study drug tillthe patient attains complete motor recovery (Bromage 0). Level of sedation: was assessed using subjective sedation score. 0 awake, conscious, no sedation to slightly restless 1 calm and composed 2 awakens on verbal commands 3 awakens on gentle tactile stimulation 4 awakens only on vigorous shaking 5 unarousable Hypotension was defined as reduction of systolic blood pressure more than 30%below baseline value and was treated with increased rate of intravenous fluids and incremental doses of injection ephedrine. Adverse effects: Any discomfort like nausea, vomiting, shivering, pruritus and adverse events such as hypotension, bradycardia, respiratory depression and ECG changes were noted.

Statistical Analysis:

60 patients were selected for each group in our study. The data collected was subjected to statistical analysis using Statistical Package for Social Sciences (SPSS). Results were expressed as range, mean, and standard deviations. The comparison of normally distributed continuous variables between the groups was performed using oneway analysis of variance (ANOVA). Nominal categorical data between study groups were compared using the chi-square test or Fisher's exact test. Ordinal categorical variables and non-normal distribution continuous variables were compared using the Mann-Whitney U-test. 'P' value < 0.05 was considered to be significant.

RESULTS

All 180 patients who satisfied the inclusion and exclusion criteria completed the study without any exclusion. Inter group analysis was done and the collected data was analyzed by chi square test. Results were obtained in the form of range, mean and standard deviation. The probability value 'p' of less than 0.05 considered statistically significant.

The minimum age in group A (control group), group B (clonidine group) and group C (dexmedetomidine group) were 20 years. The maximum age in group A is 50 years, in group B is 59 years and in group C is 55 years. The mean age in group A is 34.21 ± 13.79 years, group B is 40.10 ± 15.12 years and group C is 37.11 ± 15.62 years. There is no significant difference in the age of patients between the groups. All the three groups were similar with respect to age distribution (p>0.05). The sex distribution of the patients in all the three groups showed that there is no significant difference in the sex distribution of the patients between the groups.

The mean time of onset of sensory blockade in group A (control group) is 6.12 ± 4.70 mins, in group B (clonidine group) is 4.8 ± 4.9mins and in group C (dexmedetomidine group) is 5.21 ± 4.41 mins. There is a statistically highly significant difference when group A was compared with group B and with group C (p=0.000) and there is statistically significant difference between group B and group C (p=0.028). However there is no clinical significance between group B and group C regarding mean time taken for onset of sensory blockade.

Four out of 60 patients in group A (control group), 16 out of 60 patients in group B (clonidine group) and 24 out of 60 patients in group C (dexmedetomidinegroup) had T4 level of sensory blockade. Eight out of 60 patients in group A, 10 out of 60 patients in group B and 4 out of 60 patients in group C had T5 level of sensory blockade. Forty eight out of 60 patients in group A, 34 out of 60 patients in group B and 32 out of 60 patients in group C had T6 level of sensory blockade. There is no statistically significant difference between the groups (p=0.28).

The mean time taken for attaining the maximum sensory blockade is 11.8 ± 5.14mins in group A (control group), 9.94 ± 4.84 mins in group B (clonidinegroup) and in group C (dexmedetomidine group) is 9.24 ± 0.11mins. There is a statistically highly significant difference when group A compared with group B and with group C (p=0.000) and there is a statistically significant difference between group B and group C (p=0.001). However there is no clinical significant difference between group B and group C regarding the mean time taken for attaining the maximum sensory blockade.

The mean duration of analgesia is 194 ± 26.98 mins in group A (controlgroup), 346.37 ± 32.16 mins in group B (clonidine group) 373.37 ± 38.17 mins in group C (dexmedetomidine group). There is a statistically highly significant difference between group A and group B (p=0.000) and between group C and group C (p=0.000) and between group B and group C (p=0.001). However there is no clinical significant difference between group C and group D.

DISCUSSION

Dexmedetomidine is a highly specific and selective alpha-2 adrenoceptor agonist with8 times more affinity for alpha-2 adrenoceptor than clonidine. The ratio of alpha- 1:alpha- 2 receptor binding selectivity for dexmedetomidine is 1:1620 compared to 1:220 for clonidine. with respiratory depression, nausea, vomiting, itching, and urinary retention. Hence, attempts were made to increase duration of analgesia produced by subarachnoid block by adding various agents intrathecally.[10,11]

For intrathecal blockade, starting from 15 µg to 300 µg along with local anesthetics, and different doses of dexmedetomidine for intrathecal blockade starting from 3 µg to 15 µg along with local anesthetics.[12] In most of these studies, 5 µg of dexmedetomidine was used. Hence, we selected a 5 µg dose of preservative free dexmedetomidine for our study. Asano et al. showed that binding affinity to spinal α2 receptors of dexmedetomidine when

compared with clonidine is approximately 1:10.

Intrathecal alpha 2 agonists are found to have antinociceptive action for both somatic and visceral pain.[9] So in this context alpha 2 agonists may be a very useful drug along with the local anesthetic 0.5% hyperbaricbupivacaine for spinal anaesthesia. One hundered and eighty patients of ASA Grade-I and Grade-II posted for elective lower limb surgeries were selected randomly into 3 groups (n=60). Randomization was done using simple sealed envelope technique.[10,13]

In a study conducted by Sarma et al the doses of dexmedetomidine and clonidine used was 5µg and 50µg respectively. The doses of dexmedetomidine and clonidine were found to be equipotent in the ratio of 1:10 and would produce similar effects on the characteristics of bupivacaine spinal anaesthesia. Hence in our study we selected 10 times the dose of dexmedetomidine as clonidine that is 50 µg.

In our study the mean time taken for onset of sensory block is 6.12 ± 4.10 mins in the control group, 5.47 ± 4.9 mins in the clonidine group and 5.21 ± 4.41 mins in the dexmedetomidine group. There is a statistically significant decrease in the onset of sensory blockade in clonidine group and in the dexmedetomidine group compared to the control group.[10]

In a study conducted by Saxena H et al. authors observed the onset of sensory blockade to be 10.61 ± 4.53 mins in control group and 6.62 ± 4.37 mins, 6.58 ± 4.38 mins and 6.13 ± 4.93 mins in clonidine group (15 µg, 30 µg and 37.5 µg respectively) and in this study there was a significant reduction in the onset time which concurs with our study. But compared to our study the onset time of sensory block is higher and this could be possibly due to the dose of clonidine used being less than compared to our study.

The mean time taken for maximum sensory blockade in the present study is 11.8 ± 5.5 mins in the control group, 9.13 ± 4.12 mins in the clonidine group and 9.6 ± 4.75 mins in dexmedetomidine group. There is a statistically significant decrease in the mean time taken for the maximum sensory blockade in the clonidine group and dexmedetomidine group compared to the control group. Our study is comparable with the study conducted by Shukla D et al who also observed a significant decrease in the meantime taken for the maximum sensory blockade in the dexmedetomidine group.

The mean duration of analgesia in our study is 195 ± 26.13 mins in control group, 346.37 ± 32.16 mins in clonidine group and 373.34 ± 38.17 mins in dexmedetomidine group. There is a statistically highly significant increase in the duration of analgesia in dexmedetomidine and clonidine group compared to the control group.

Our study concurs with the study conducted by Grandhe RP et al., where authors observed the mean duration of analgesia of 7.12 ± 4.11 hours in the control group and 10.7 ± 4.12 hours when using clonidine of 1µg/kg with a mean weight of 64.10 ± 23.8 kg. In our study the mean duration of motor blockade was 170.20 ± 24.99 mins in control group, 283 ± 28.72 mins in clonidine group and 307.70 ± 39.99 mins in dexmedetomidine group. There is a statistically highly significant increase in the duration of motor blockade in dexmedetomidine group and clonidine group compared to the control group. Our study almost concurs with the study conducted by Kaabachi O et al. who observed the mean duration of motor blockade to be 256 ± 83 mins when using clonidine of 1µg/kg.

CONCLUSION

From the present study it can be concluded that the supplementation of bupivacaine with dexmedetomidine 5 µg or clonidine 50 µgin spinal anaesthesia produces significant shorter onset of motor and sensory block with longer duration of sensory and motor block when compared to bupivacaine alone.

REFERENCES

1. Sinha, R.; Gurwara, A.; Gupta, S. J. J. J. o. t. S. o. L. S. Laparoscopic surgery using spinal anesthesia. 2008, 12, 133.
2. Olawin, A. M. Spinal anesthesia. 2019.
3. Shatri, G.; Singh, A. Thoracic segmental spinal anesthesia. 2021.
4. Apfelbaum, J. L.; Hawkins, J. L.; Agarkar, M.; Bucklin, B. A.; Connis, R. T.; Gambling, D. R.; Mhyre, J.; Nickinovich, D. G.; Sherman, H.; Tsen, L. C. J. A. Practice guidelines for obstetric anesthesia: an updated report by the American Society of Anesthesiologists Task Force on obstetric anesthesia and the Society for Obstetric Anesthesia and Perinatology. 2016, 124, 270-300.
5. Gantasala, B. V.; Singam, A.; Taksande, K. J. J. o. C.; Research, D. Bupivacaine (0.5%) Versus (0.5%) Bupivacaine with Ketamine (50 mg) for Subarachnoid Block in Lower Abdominal Surgeries: A Randomised Comparative Study. 2019, 13.
6. Vasantha, N. S. K.; Madhusudhana, R. J. A.,

Essays; Researches. Intrathecal bupivacaine with neostigmine and bupivacaine with normal saline for postoperative analgesia: A cost-effective additive. 2018, 12, 328.

7. Vaibhaw, V.; Singh, N. N.; Rohit, K.; Kumar, N. Intrathecal Dexmedetomidine and Fentanyl as an Adjuvant to Isobaric Levobupivacaine for Lower Limb Orthopaedic Surgery: A Comparative Study.
8. Mahendru, V.; Tewari, A.; Katyal, S.; Grewal, A.; Singh, M. R.; Katyal, R. J. J. o. a., clinical pharmacology. A comparison of intrathecal dexmedetomidine, clonidine, and fentanyl as adjuvants to hyperbaric bupivacaine for lower limb surgery: A double blind controlled study. 2013, 29, 496.
9. Munnoli, B.; Singh, G.; Mohammad, B.; Gupta, I.; Attar, J.; Naveen, N. K. J. J. o. E. o. M.; Sciences, D. A randomised, double-blind, placebo-controlled trial comparing dexmedetomidine and clonidine as an adjuvant to intrathecal ropivacaine in lower limb surgery. 2016, 5, 6680-6684.
10. Sankara Ganapathy, V. A Comparative Study of Intrathecal Dexmedetomidine and Clonidine as an Adjuvant to Intrathecal Bupivacaine in Elective Lower Limb Surgeries. Thanjavur Medical College, Thanjavur, 2017.
11. Manjunath, H.; Treja, C. J. J. o. E. o. M.; Sciences, D. A comparative clinical study of effect of adding 5 [micro] g dexmedetomidine versus 50 [micro] g clonidine to intrathecal 12.5 mg of 0.5% hyperbaric bupivacaine on spinal block characteristics in patients undergoing elective lower abdominal surgeries. 2015, 4, 14792-14800.
12. Solanki, S.; Bharti, N.; Batra, Y.; Jain, A.; Kumar, P.; Nikhar, S. J. A.; care, i. The analgesic effect of intrathecal dexmedetomidine or clonidine, with bupivacaine, in trauma patients undergoing lower limb surgery: a randomised, double-blind study. 2013, 41, 51-56.
13. Saiyad, J. H.; Patel, S. K.; Patel, U. S. J. N. J. o. M. R. A Comparison of Dexmedetomidine and Fentanyl as an Adjuvant to Intrathecal Hyperbaric Bupivacaine in Elective Lower Limb Surgeries. 2021, 11, 125-130.