e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2023; 15(7); 275-279

Original Research Article

To Evaluate the Effects of Adjuvant Clonidine in Combination with Bupivacaine, As Compared to Solo Bupivacaine for Axillary Brachial Plexus Block: A Comparative Assessment

Alok Kumar Sahoo[1], Chittaranjan Panigrahi[2], Soumyakanta Sethi[3]

[1]Assistant Professor, Department of Anaesthesiology, SCB Medical College, Cuttack, Odisha, India
[2]Associate Professor, Department of Anaesthesiology, DD Medical College, Keonjhar, Odisha, India
[3]Assistant Professor, Department of Anaesthesiology, SCB Medical College, Cuttack, Odisha, India

Received: 14-04-2023 / Revised: 24-05-2023 / Accepted: 21-06-2023
Corresponding author: Alok Kumar Sahoo
Conflict of interest: Nil

Abstract:

Background: The extension of axillary block is advantageous in numerous cases as it permits a more protracted or comprehensive surgical procedure while reducing the need for additional analgesic medications. In this study, we conducted a comparative analysis of the efficacy of Clonidine as an adjuvant to Bupivacaine (0.5%) and Bupivacaine plain in the context of axillary brachial plexus block. The Visual Analogue Scale (VAS) score and other block characteristics were systematically assessed at regular intervals and in the postoperative period.

Methods: A cohort comprising 110 adult patients classified under ASA 1, 2, and 3 were systematically assigned to two distinct groups using an alternate allocation method. In this study, Group A was administered a solution containing 0.25% Bupivacaine (40 mL) along with 1 mL of clonidine at a concentration of 150µg. On the other hand, Group B received a solution consisting of 0.25% Bupivacaine (40 mL) along with 1 mL of 0.9% saline. These solutions were administered via perivascular Axillary block.

Results: The patient cohorts exhibited similarities in regards to age, gender, presence of concurrent medical conditions, and American Society of Anesthesiologists (ASA) classification. In the bupivacaine clonidine cohort, the duration of analgesia was extended by an average of 208 minutes in comparison to the administration of bupivacaine alone. The initiation of sensory and motor blockade was reduced by an average of 2.7 minutes and 3 minutes, respectively, in the clonidine treatment cohort. The average duration of sensory block in the bupivacaine-clonidine group was 503.3 ± 125.9 minutes, whereas in the bupivacaine only group, it was 287.1 ± 82.9 minutes. The results indicate a notable extension in the clonidine cohort, amounting to approximately 216.2 minutes. The average duration of motor block in the bupivacaine-clonidine group was found to be 409.8 minutes, whereas in the bupivacaine only group, it was observed to be 259.6 ± 74.8 minutes. This indicates a statistically significant increase in duration of 150.2 minutes in the clonidine treatment group. The study observed several side effects, namely hypotension, bradycardia, and sedation. The incidence rates of these side effects were 7.3%, 9.1%, and 36.3%, respectively, in the bupivacaine-clonidine group. In comparison, the bupivacaine only group had incidence rates of 1.8%, 3.6%, and 9.1%, respectively.

Conclusion: Clonidine serves as a valuable adjunct to bupivacaine in the context of Axillary block. It greatly extends the period of pain relief, as well as the duration of sensory and motor blockade. Additionally, it expedites the initiation of sensory and motor blockade, albeit to a lesser extent.

Keywords: Bupivacaine, Clonidine, Dexmedetomidine, Axillary brachial plexus block

Introduction

The perception of pain is a multifaceted phenomenon that is subject to the influence of an individual's emotional state and prior experiences. By the conclusion of the 19th century, it was widely acknowledged within medical academia that acute pain constituted a distinct sensory modality, which could be effectively mitigated through the implementation of conduction blockade using local anaesthetics [1]. Regional nerve blocks not only effectively alleviate pain, but also serve to enhance surgical procedures and mitigate subsequent pain. Since the inception of brachial plexus block in medical practise, various local anaesthetic drugs have been employed, with lignocaine and Bupivacaine being the primary agents utilised [1, 2]. However, it is worth noting that the duration of action of these drugs is somewhat restricted. Numerous pharmaceutical substances have been employed as adjuvants to local anaesthetic agents with the aim of extending the duration of peripheral

nerve blocks. Clonidine, a partial α- adrenoceptor agonist, and Dexmedetomidine, an α2 agonist, have been documented to extend the duration of anaesthesia and analgesia in the context of these blocks [3, 4]. The α2:α1 selectivity of Dexmedetomidine is found to be eight times greater than that of clonidine, indicating its strong preference for the α2 subtype. This characteristic renders Dexmedetomidine a significantly more potent sedative and analgesic agent [4-7].

Several scholarly investigations have explored the impact of clonidine as an adjunct to local anaesthetic agents in peripheral nerve and plexus blocks [8-13]. The majority of these studies indicate that clonidine exhibits a protracted duration of block and confers a favourable analgesic effect [8-11]. However, the majority of these studies employed intermediate-acting local anaesthetic agents, namely mepivacaine, prilocaine, and lidocaine [12, 13]. There is a limited number of studies that have investigated the use of clonidine as an adjuvant to Bupivacaine in plexus blocks [7, 9]. Several academic studies have reported a noteworthy extension of block duration, whereas other studies have indicated no statistically significant

prolongation [14-19]. Furthermore, there is a paucity of data concerning the effects observed within the Asian population.

The objective of the current investigation is to examine the impact of incorporating clonidine as a supplementary agent to Bupivacaine, in comparison to the use of Bupivacaine alone, for the purpose of Axillary Brachial Plexus Block in individuals undergoing Orthopaedic surgery specifically targeting the forearm or hand. The primary focus is to assess whether this combination can effectively extend the duration of analgesic effects.

Materials and methods

Study design

The study protocol was done in SCB Medical College, Cuttack. A total of 110 patients of ASA I, II, III classes undergoing orthopaedic surgery of forearm or hand were enrolled in the study (55 patients in each group) after obtaining informed consent.

Sample population

The sample size was determined utilising a significance level of 5% and was informed by the results documented in prior scholarly investigations. The minimum necessary sample size to identify a statistically significant distinction between the groups was determined to be 108 (54 participants in each group). The sample size was determined based on a significance level (alpha) of 5% and a statistical power (beta) of 80%. In the current investigation, the minimum required sample size was determined to be 54 individuals per group, resulting in a total of 108 patients. The study consisted of a total of 110 participants, with an equal distribution of 55 individuals in each group.

Exclusion criteria

Individuals presenting with Mallampati class 4 airway configuration, contraindication to the administration of an axillary brachial plexus block or patient taking the study medications is

present. Hemodynamic instability refers to a medical condition characterised by an abnormality in the stability of the cardiovascular system. This condition History of significant neurological, psychiatric, neuromuscular, cardiovascular, pulmonary, renal, or hepatic pathology. Substance abuse involving alcohol or illicit drugs, Women who are currently pregnant or breastfeeding, Individuals undergoing pharmacotherapy with psychotropic or adrenergic agents, Patients receiving long-term analgesic treatment, excluding those prescribed simple analgesics such as nonsteroidal anti-inflammatory drugs (NSAIDs), were not included in the scope of this research investigation.

The enrolled participants were assigned to either group A or group B in an alternating manner. No preoperative medication was administered. No supplementary sedative medication was administered. The axillary block was administered using the perivascular technique to administer medications in the following manner: In this study, Group A was administered a solution consisting of 0.25% Bupivacaine at a volume of 40 mL, along with an additional 1 mL containing 150µg of clonidine. The total volume of the solution is 41 millilitres. In the study, Group B was administered a solution consisting of 0.25% Bupivacaine at a volume of 40 mL, along with an additional 1 mL of 0.9% saline. The total volume of the solution is 41 millilitres. The analgesic duration, sensory block onset and duration, motor block onset and duration, heart rate, blood pressure, and sedation levels were documented at the initial minute and at 5, 10, 30, 60, 120, 180, 240, 360, and 480 minutes following the conclusion of the injection.

Statistical Analysis

Data was entered in a personal computer and analyzed using computer software, Statistical Package for Social Sciences (SPSS) version 10. Data is expressed in its frequency and percentage as well as mean and standard deviation. Following statistical analysis was employed to analyze the data: Chi square Analysis, Mann Whitney U test and Student's T test.

Results

Table 1: Patient characteristics

Variables	*Group A*	*Group B*
No of patients, n	55	55
Age	43.13 ± 12.64	40.24 ± 12.41
Duration of Analgesia (min)	519.64 ± 02.38	310.73 ± 84.74
Gender	Male- 36 Female- 19	Male- 40 Female- 15
ASA	ASA 1- 37 ASA 2- 16 ASA 3 - 2	ASA 1- 39 ASA 2- 14 ASA 3 - 2
Sedation Score	Score 1 - 35 Score 2 -19 Score 3 - 1	Score 1- 50 Score 2- 5 Score 3 - 0
Hypotension , n	4	1
Bradycardia, n	5	2

In this study, participants assigned to Group A were administered a solution containing 0.25% Bupivacaine at a volume of 40 mL, along with an additional 1 mL of clonidine at a concentration of 150µg. In the study, Group B was administered a solution consisting of 0.25%
Bupivacaine in a volume of 40 mL, along with an additional 1 mL of 0.9% saline. The total volume of the solution is 41 millilitres. The comparative analysis of the American Society of Anesthesiologists physical status scores (ASA scores) between the two cohorts. A majority of the patients in both groups exhibited ASA class 1, with 67.3% in group A and 70.9% in group B. The percentage of patients classified as ASA 2 was 29.1% in group A and 25.5% in group B. In both cohorts, there were two patients (3.6% each) classified as class 3. The chi-square analysis conducted on the provided data indicates that there is no statistically significant disparity observed between the two groups. The aforementioned data and statistical analysis demonstrate that the two cohorts (A&B) exhibit similar patient characteristics, including age, gender, comorbidities, and ASA status.

Table 2: Outcome measures

	Group A	*Group B*	*t value*	*p value*
Sensory Block- Onset (min)	9.04 ± 4.99	11.73 ± 6.06	-2.543	< 0.05
Sensory Block Duration (min)	503.27 ± 125.99	287.09 ± 82.95	10.628	< 0.001
Motor Block - Onset (min)	13.33 ± 4.41	15.36 ± 5.92	-2.046	< 0.05
Motor Block - Duration (min)	409.82 ± 89.29	259.64 ± 74.76	9.564	< 0.001
Duration of Analgesia (min)	519.64 ± 102.38	310.73 ± 84.74		< 0.001

Discussion

This research investigation explored the impact of incorporating clonidine into bupivacaine for Axillary block in individuals undergoing orthopaedic surgery of the forearm or hand, with the objective of extending the duration of analgesia. The study exclusively enrolled patients classified under ASA class 1, 2, and 3. Class 4 was excluded in order to mitigate potential morbidity resulting from the reported adverse effects of clonidine, such as hypotension and bradycardia. The majority of research studies presented findings based on the American Society of Anesthesiologists (ASA) classification system, specifically encompassing ASA classes 1, 2, and 3. In our research, the majority (96.48%) of the patients exhibited ASA class 1 and 2, as per the American Society of Anesthesiologists classification system.

The average age of group A was 43.1 years, while the mean age of group B was 40.24 years. The majority of the patients in both group A (65.5%) and group B (72.7%) were male. The observed age and sex distribution pattern can be comprehended in light of the fact that all individuals included in the study underwent orthopaedic surgery due to fractures resulting from road traffic accidents. Individuals seeking medical care at the hospital as a result of road traffic accidents exhibit comparable demographic characteristics in terms of age and gender. The investigation conducted by Duma et al. [14] exhibits a comparable demographic distribution, with 60% of the participants being males. The average age was reported as 43.3 years for the bupivacaine-clonidine group and 36.7 years for the bupivacaine only group. The patients in both groups exhibited comorbidities including diabetes, hypertension, and bronchial asthma. These medical conditions were evenly distributed among the groups, and there was no

statistically significant difference observed between the groups, as determined through the application of a chi-square test.

The duration of postoperative analgesia, which refers to the time elapsed until the initial request for pain relief, exhibited a statistically significant increase in the bupivacaine clonidine group (519.6 ± 102.4 minutes) compared to the bupivacaine group (310.7 ± 84.7 minutes), resulting in a mean extension of 208 minutes. Popping et al [19] conducted a comprehensive analysis of thirteen clinical trials, encompassing a total of 17 comparisons. Thirteen comparative analyses

revealed that the administration of clonidine resulted in a significant extension of the analgesic effect. Fang et al [15] reported a mean prolongation of 188 minutes in the clonidine group, as per their study findings.

Research findings indicate that the administration of clonidine via perineural injection exhibits analgesic properties by means of systemic absorption. Only two studies have conducted a comparative analysis of clonidine administration via different routes. In a clinical study, participants were administered a dosage of 150 micrograms of clonidine via subcutaneous injection or combined with mepivacaine for the purpose of conducting a brachial plexus block [6]. The duration of postoperative analgesia was found to be significantly extended in patients who received clonidine administered into the plexus sheath. In the second instance, a dosage of 140 micrograms of clonidine was administered alongside ropivacaine for the purpose of conducting a sciatic-femoral nerve block or alternatively, it was injected intramuscularly [7]. In the aforementioned clinical trial, it was observed that the administration of clonidine did not exhibit any discernible influence on the quality or duration of postoperative analgesia, regardless of the route of administration. In our research, the administration of clonidine demonstrated a significant extension in the duration of analgesia and the need for supplementary analgesic medication, with an average increase of approximately three and a

half hours. This may result in a favourable outcome, potentially resulting in a reduction in the overall dosage of analgesics required following a surgical procedure.

The inclusion of clonidine resulted in a reduction of the average time for the initiation of sensory and motor block by 2.7 minutes and 3 minutes, respectively. This finding demonstrates statistical significance as determined through the utilisation of a t-test for data analysis. Nevertheless, the clinical significance of a disparity of 2.7 minutes and 3 minutes is questionable, as indicated in Table 2. In their study, Fang et al. [15] observed a reduction in the onset time of sensory block and motor block by 1.3 minutes in the clonidine group. Popping et al. (2019) conducted a meta-analysis of randomised trials, wherein they observed that clonidine exhibited a shortened onset time for sensory block in 5 out of 11 comparisons. The present discovery derived from our research study stands in opposition to the majority of previously documented series. In the study conducted by Duma et al. [14], no statistically significant difference was observed between the two groups in terms of the onset of block. Indeed, the onset of median motor block in the group administered with bupivacaine and clonidine exhibited a longer duration of 30 minutes, in contrast to the group solely administered with bupivacaine, which demonstrated an onset duration of 10 minutes. The median time for the onset of sensory block was observed to be 10 minutes in both study groups. Erlacher et al [7] also documented an elongation in the onset time of the block within the cohort receiving bupivacaine clonidine.

The average duration of sensory block in the group receiving a combination of bupivacaine and clonidine was found to be 503.3 ± 125.9 minutes, whereas in the group receiving only bupivacaine, the average duration was 287.1 ± 82.9 minutes. This study demonstrates a notable extension in the duration of the sensory block among participants in the clonidine group, with an average increase of approximately 216.2 minutes. Popping et al [19] conducted a meta- analysis wherein they observed a significant prolongation of the duration of sensory block in

10 out of 13 comparisons. The researchers discovered that the administration of clonidine had a substantial impact on the length of time in question, as evidenced by a statistically significant result ($p<0.001$). Fang et al [15] documented an extension of the sensory block by an average span of 68 minutes within the bupivacaine clonidine cohort.

The average duration of motor block in group A was found to be 409.8 minutes, whereas in group B, it was observed to be 259.6 ± 74.8 minutes. This indicates a mean difference of 150.2 minutes. Fang et al [15] documented an extension of motor block with an average duration of 242 minutes in the bupivacaine- clonidine cohort. Erlacher et al. [7] documented a significant increase in the duration of action in the clonidine intervention group, with a mean extension of 244 minutes. The meta-analysis conducted by Popping et al. [19] examined a collection of randomised trials that investigated the duration of motor block. In total, seven trials were included in the analysis, which evaluated eleven different comparisons. Out of these nine, there was a notable increase in length observed within the clonidine group.

Conclusion

Clonidine demonstrates efficacy as a beneficial adjunct to bupivacaine for the administration of Axillary block. The administration of this treatment greatly extends the relief from pain, as well as the length of time that the sensory and motor functions remain blocked. Additionally, it expedites the initiation of sensory and motor blockade, albeit to a lesser extent. The potential benefits of sedation as a side effect can be advantageous for a patient undergoing surgery while under regional anaesthesia. Additionally, other side effects such as hypotension and bradycardia, although present, do

not possess significant limitations to the clinical utility of this approach.

References

1. Eisenach JC, De Kock M, Klimscha W. a2-Adrenergic agonists for regional anesthesia. Anesthesiology 1996; 85: 655–74
2. Murphy DB, McCartney CJ, Chan VW: Novel analgesic adjuncts for brachial plexus block: A systematic review. Anesth Analg. 2000; 90: 1122–8
3. Elia N, Culebras X, Mazza C, Schiffer E, Trame`r MR: Clonidine as an adjuvant to intrathecal local anesthetics for surgery: Systematic review of randomized trials. Reg Anesth Pain Med. 2008; 33:159–67
4. Eledjam JJ, Deschodt J, Viel E, et al. Brachial plexus block with bupivacaine: effects of added alpha adrenergic agonists: comparison between clonidine and epinephrine. Can J Anesth. 1991; 38:870–75
5. Bernard JM, Macaire P. Dose-range effects of clonidine added to lidocaine for brachial plexus block. Anesthesiology. 1997; 87:277–84
6. Singelyn FJ, Gouverneur JM, Robert A. A minimum dose of clonidine added to mepivacaine prolongs the duration of anesthesia and analgesia after axillary brachial plexus block. Anesth Analg. 1996; 83: 1046–50
7. Erlacher W, Schuschnig C, Orlicek F, et al. The effects of clonidine on ropivacaine 0.75% in axillary perivascular brachial plexus block.Acta Anaesthesiol Scand. 2000; 44: 53–7
8. Gaumann DM, Forster A, Griessen M, et al. Comparison between clonidine and epinephrine admixture to lidocaine in brachial plexus block. Anesth Analg 1992; 75: 69–74
9. Culebras X, Van Gessel E, Hoffmeyer P, Gamulin Z. Clonidine combined with a long-acting local anesthetic does not prolong postoperative analgesia after brachial plexus block but does induce hemodynamic changes. Anesth Analg. 2001; 92: 199–204
10. Sia S, Lepri A. Clonidine administered as an axillary block does not affect postoperative pain when given as the sole analgesic. Anesth Analg 1999; 88: 1109–12
11. Iohom G, Machmachi A, Diarra DP et al. The effects of clonidine added to mepivacaine for paronychia surgery under axillary brachial plexus block. Anesth Analg.2005 Apr;100(4):1179-83
12. Broch O, Breucking E: Comparison of clonidine and tramadol added to prilocaine brachial plexus block-analgesia, sensory and motor block. Anasthesiol Intensivmed Notfallmed Schmerzther. 2005 Sep;40(9): 526-31
13. Contreras-Dominguez, Carbonnel-Bellolio, Sanzana Salamanca E et al: Addition of sodium bicarbonate and/or clonidine to mepivacaine: influence on axillary brachial plexus block characteristics. Rev Esp Anestesio; Reanim. 2006 Nov;53(9):532-7
14. Duma A, Urbanek B, Sitzwohl C, Kreiger A, Zimpfer M, Kapral S: Clonidine as an adjuvant to local anaesthetic axillary brachial plexus block: A randomized, controlled study. Br J Anaesth. 2005; 94:112–6
15. Fang L, Liu F, Li L, Wang TJ, Yang LS, Sun XX: Effects of clonidine combined with various local anesthetics in brachial plexus block. Zhonghua Yi Xue Za Zhi. 2004; 84:1712–3
16. CucchiaroG, Ganesh A. The effects of clonidine on postoperative analgesia after peripheral nerve blockade in children. Anesth analg. 2007 Mar;104(3):532-7
17. Winnie AP. Brachial Plexus Block. In: Winnie AP, ed.Plexus Anesthesia Vol 1. Philadelphia: W.B. Saunders, 1993;117–88
18. Vester-Andersen T, Eriksen C, Christiansen C. Perivascular axillary block III: blockade following 40 ml of 0.5%, 1% or 1.5% mepivacaine with adrenaline. Acta Anaesthesiol Scand. 1984; 28:95–8
19. Popping, M.D, Nadia Elia, M.D, Emmanuel Marret, M.D. et al: Clonidine as an Adjuvant to Local Anesthetics for Peripheral Nerve and Plexus Blocks: A Meta-analysis of Randomized Trials Anesthesiology. 2009; 111:406–15