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Original Article

Competence of Oral Clonidine in Bupivacaine and Dexamethasone Induced Supraclavicular Brachial Plexus Block

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ABSTRACT

Introduction: *The brachial plexus is a web of nerves in the shoulder that suggests drive and sensory signals from the spinal cord to the arms and hands. The motive of the count of adjuvants to local anesthetics for a peripheral nerve block is to have the former onset of sensory and motor block.****Methods& Materials:*** *A comparative randomized double-blinded placebo-controlled study was carried out in the Department of Anesthesia, Analgesia, Palliative & Intensive Care Medicine, Dhaka Medical College Hospital, Dhaka from October 2018 to June 2019. A total of 60 patients were fulfilling the criteria. Then informed written consent was taken and data analysis by performed using Statistical Package for the Social Sciences (SPSS) Version 23.0* ***Results:*** *Among the study population (N=60), a tablet of Clonidine100 mcg was given in group A and a Placebo drug was given in group B equally. Around 76.7% were found ASA class I in group A and 83.3% in group B .The mean onset of sensory block & motor block was found 7.6±0.8 &18.3±1.1 minutes in group A respectively and 13.0±1.4 & 18.7±1.8 minutes in group B respectively. After 9 hours, the mean visual analog scale (VAS) score was found 0.03±0.21 in group A and 3.6±1.3 in group B.****Conclusion:*** *The use of oral clonidine in supraclavicular brachial plexus block provides quick onset of sensory block. In this outcome, oral clonidine expands the quality of anesthesia and analgesia when it was used as the administration of medication before a treatment or procedure.*

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Keywords: *Clonidine, Brachial Plexus, Analgesics*

INTRODUCTION

The brachial plexus is a network of nerves in the shoulder that implies movement and sensory signals from the spinal cord to the arms and hands [1]. The brachial plexus injuries usually stem from trauma to the neck and can cause pain, weakness, and numbness in the arm and hand. Most people with minimal brachial plexus injuries recover 90 to 100% of their normal function [2,3]. Brachial plexus block commonly rises through interscalene, supraclavicular, infraclavicular, or axillary methods. The supraclavicular level is the ultimate site to achieve anesthesia of the entire upper extremity just distal to the shoulder as the plexus remains relatively tightly packed at this level, resulting in a rapid and high-quality block [4]. Brachial plexus can be seen in between scalene muscle as hypoechoic round nodules (honeycombs or bunch of grapes) at 1-2 cm depth. The motive for the addition of adjuvants to local anesthetics for a peripheral nerve block is to have prior onset of sensory and motor block and to prolong the duration of postoperative analgesia with lesser adverse effects. Numerous lessons in adults suggest that dexamethasone increases the duration of action of local anesthetics when used as an adjunct [5]. The guidance of ultrasound for regional anesthesia has become renowned to identify anatomical variants and easy and precise needle placement. It also helps to screen the extent of local anesthetic solution in the suitable tissue planes to the reduction of the occurrence of pneumothorax, arterial puncture, and direct nerve impairment [6]. Dexamethasone is a long-acting glucocorticoid with effective anti-inflammatory and analgesic consequences. It also benefits by lessening the release of inflammatory mediators, reducing ectopic neuronal discharge, and constraining potassium channel-mediated discharge of nociceptive C-fibers [7]. Bupivacaine is the most commonly administered drug in brachial plexus blocks, however, the onset of action and duration of anesthesia are the limiting factors. To decrease these drawbacks, many drugs including clonidine, tramadol, morphine fentanyl, and dexamethasone have been co-administered with a local anesthetic to achieve rapid onset, advance the analgesic intensity and prolong the duration of action [8,9,10,11]. Clonidine is an alpha-2 receptor agonist that provides analgesia by acting at peripheral and central receptors. Clonidine not only enhances the rapidity of onset but also extends the duration of sensory & motor blockade & extends the duration of analgesia post-operatively without major haemodynamic variations. Also, clonidine is more sedative potential, lessening anxiety & improved patient relaxation in intra-operative & post-operative periods [12]. Clonidine reduces the intubation response during laryngoscopy, controls intra-operative blood pressure and heart rate, reduces plasma catecholamine level resulting in reduced surgical stress response, and also decreases the threshold to cold stimuli by acting on the central thermoregulatory centre [13]. This study intends to understand the competence of oral clonidine as an adjuvant in bupivacaine and dexamethasone-induced supraclavicular brachial plexus block.

OBJECTIVES

- To understand the competence of oral clonidine as an adjuvant in bupivacaine and dexamethasone-induced supraclavicular brachial plexus block.

Specific objectives:

- To measure the onset time of sensory and motor block.
- To measure the duration of sensory and motor block.
- To measure the duration of analgesia according to the VAS score.
- To compare the postoperative requirement of analgesics between two groups up to 12 hours.

METHODS & MATERIALS

A comparative randomized double-blinded placebo-controlled study was carried out in the Department of Anesthesia, Analgesia, Palliative & Intensive Care Medicine, Dhaka Medical College Hospital, Dhaka from October 2018 to June 2019. A total of 60 patients fulfilling the inclusion and exclusion criteria were selected for the study who were going for upper limb surgery distal to the mid-arm (elbow, forearm, and hand) in the Dhaka Medical College Hospital. Selected patients were enrolled with unique IDs. Subjects were briefed about the objectives of the study, risks and benefits, freedom for participating in the study and confidentiality. Then informed written consent was taken. The patients were divided into two groups by random sampling method and were fixed with 30 patients in each group. In Group-A patients received 100(mcg) Tab. clonidine, while in GroupB patients received Tab. Vitamin B-complex as placebo orally with sips of water 45 minutes before supraclavicular brachial block. All patients of both groups were blocked with 15 ml of 0.5% bupivacaine + 1 ml dexamethasone + 4 ml distilled water under ultrasound guidance. The thesis protocol was approved by the Ethical Review Committee, DMCH.

Inclusion criteria:

- Patients undergoing upper limb surgery at the level of the elbow, forearm, and hand
- Age between 18 to 60 years of both genders.
- Informed consent for inclusion in the study
- Weight between 40 to 70 kg.

Exclusion criteria:

- Patient with severe renal, respiratory, hepatic or cardiac disease, chronic diseases i.e. psychological or neurological or neuromuscular disorder&contralateral phrenic nerve injury.
- Drug abusers& patients who have allergies to local anesthetics
- Family history of HTN, DM, systemic infection, neuropathy, and brachial plexus injury
- Inability to perform the pinprick test because of a dressing or cast
- Morbidly obese patient

Operational definition

Sensory block duration:

The time interval between administration of the study drug to complete sensory recovery of all nerves.

Motor block duration:

The time interval between the administration of the study drug to complete recovery of motor function of hand & forearm.

Duration of analgesia:

The time interval between the onset of complete sensory block to the time when the patient was beginning to experience pain according to VAS. (VAS score > 3)

Data analysis:

Statistical analyses were carried out by using the Statistical Package for Social Sciences version 23.0 for Windows (SPSS Inc., Chicago, Illinois, USA). The mean values were calculated for continuous variables. The quantitative observations were indicated by frequencies and percentages. The chi-Square test with Yates correction was used to analyze the categorical variables, shown with cross-tabulation. Student t-test was used for continuous variables. P values <0.05 was considered statistically significant.

RESULTS

Among the study population (N=60), a tablet of Clonidine100 mcg was given to 30 patients classified as group A (n=30) and the Placebo drug was administered to the rest of the patients classified as group B (n=30). Eight patients 26.7% belonged to age 21-30 years in group A and seven patients 23.3% in group B. The mean age was found 34.8±13.2 years in group A and 38.1±15.0 years in group B. The difference was not statistically significant (p=0.374ns) between the two groups. Around three-fifths of the patients 56.7% were male in group A and around half 53.3% in group B. The difference was not statistically significant (p=0.795ns) between the two groups. The mean weight was found 53.7±8.9 kg in group A and 52.1±7.7 kg in group B. The difference was not statistically significant (p=0.579 ns) between the two groups **(Table I).**

Table I: Distribution of the study population based on Characteristics (N=60)

Characteristics	**Group A**	**Group B**	***p-value***
Age	**(n,%)**	**(n,%)**	
≤20	6,20.0%	5,16.7.%	
21-30	8,26.6%	7,23.3%	
31-40	7,23.3%	7,23.3%	0.374^{ns}
41-50	5,16.7.%	3,10.0%	
>50	4,13.3%	8,26.7%	
Mean±SD:	34.8±13.2	38.1±15.0	
Gender			
Male	17,56.7%	16,53.3%	0.795^{ns}
Female	13,43.3%	14,46.7%	
Weight	53.7±8.9	52.1±7.7	0.579^{ns}
Range	40-70	40-66	

***p- value* reached from unpaired t-test**

Around three-fourths of the patients (23,76.7%) were found ASA class I in group A and twenty-five 83.3%. The difference was not statistically significant (p=0.519ns) between the two groups **(Table II).**

Table II: Distribution of the study population based on ASA class (N=60)

ASA class	**Group A (n,%)**	**Group B (n,%)**	***p-value***
I	23,76.7%	25,83.3%	0.519^{ns}
II	7,23.3%	5,16.7%	

**p- value* reached from chi square test
*ASA=American Society of Anesthesiologist.

The mean onset of sensory block was found at 7.6±0.8 minutes in group A and 13.0±1.4 minutes in group B. The difference was statistically significant (p=0.001s) between the two groups. The mean duration of sensory block was found 652.9±35.6 minutes in group A and 454.2±30.8 minutes in group B. The difference was statistically significant (p=0.001s) between the two groups. The mean onset of motor block was found 18.3±1.1 minutes in group A and 18.7±1.8 minutes in group B. The difference was not statistically significant (p=0.30ns) between the two groups. The mean duration of the motor block was found 574.5±34.3 minutes in group A and 366.1±51.2 minutes in group B and the difference was statistically significant (p=0.001s) between the two groups. The mean duration of analgesia was found 731.8±41.8 minutes in group C and 528.8±47.7 minutes in group B. The difference was statistically significant (p=0.001s) between the two groups **(Table III).**

Table III: Distribution of the study population based on onset & duration of sensory and motor block and Duration of analgesia (min)(N=60)

Sensory block	**Group A**	**Group B**	***p-value***
Onset of sensory block (minute)	7.6±0.8	13.0±1.4	0.001^{s}
Range	6-9	10-15	
Duration of sensory block (minute)	652.9±35.6	454.2±30.8	0.001^{s}
Range	590-710	390-496	
Motor block			
Onset of motor block (minute)	18.3±1.1	18.7±1.8	0.30^{ns}
Range	14-18	16-21	
Duration of motor block (minute)	574.5±34.3	366.1±51.2	0.001^{s}
Range	510-640	248-540	
Analgesics			
Duration of analgesia (min)	731.8±41.8	528.8±47.7	0.001^{s}
Range (min-max)	660-810	453-640	

The mean pulse rate- after 0 min, after 5 min, after 10 min, after 15 min, after 30 min, after 45 min, after 60 min, after 120 min, and after 180 min were significantly

(p<0.05) higher in group B than group A. The mean arterial pressure- after 5 min, after 10 min, after 15 min, after 30 min, after 45 min, after 1 hour, after 2 hours, after 3 hours, and after 4 hours were significantly (p<0.05) higher in group B than group A **(Table IV).**

Table IV: Distribution of the study population based on Pulse rateand MAP (mmHg)(N=60)

Pulse rate (b/min)	**Group A (n,%)**	**Group B (n,%)**	**P value**
	Mean ±SD	**Mean ±SD**	
Before given study drug	85.07±4.09	84.57±7.66	0.754^{ns}
After 0 min	89.03±4.34	94.50±8.77	0.003^{s}
After 5 min	86.50±4.27	96.20±6.93	0.001^{s}
After 10 min	83.37±4.60	89.40±7.83	0.001^{s}
After 15 min	79.93±5.26	87.73±7.82	0.001^{s}
After 30 min	77.10±5.95	85.77±9.53	0.001^{s}
After 45 min	72.97±7.67	86.47±6.47	0.001^{s}
After 60 min	70.00±7.65	85.70±7.13	0.001^{s}
After 120 min	75.73±8.04	88.90±6.61	0.001^{s}
After 180 min	78.47±7.29	87.83±5.00	0.001^{s}
MAP (mmHg)	**Group C (n=30)**	**Group B (n=30)**	**P value**
	Mean ±SD	**Mean ±SD**	
Before given study drug	93.22±9.36	91.17±9.86	0.412^{ns}
After 0 min	93.77±9.46	96.64±8.13	0.213^{ns}
After 5 min	93.07±10.03	98.40±7.46	0.023^{s}
After 10 min	89.99±7.26	94.04±6.24	0.024^{s}
After 15 min	88.67±7.81	92.59±7.08	0.046^{s}
After 30 min	84.45±6.96	91.76±7.42	0.001^{s}
After 45 min	80.22±8.43	92.31±6.87	0.001^{s}
After 1 hour	76.96±8.08	92.60±6.59	0.001^{s}
After 2 hour	81.61±7.84	91.96±7.39	0.001^{s}
After 3 hour	85.17±7.39	91.39±5.89	0.001^{s}
After 4 hour	87.67±6.85	93.16±5.58	0.001^{s}
After 8 hour	88.22±7.56	91.61±5.42	0.051^{ns}
After 12 hour	88.05±7.41	91.62±6.59	0.054^{ns}

**P* value reached from unpaired t-test

*MAP=Mean arterial pressure.

After 9 hours, the mean visual analog scale (VAS) score was found 0.03±0.21 in group A and 3.6±1.3 in group B, which was statistically significant, and an analgesic drug was given in group B patients for the first time, so later on VAS

score gradually declined in this group. After 12 hours, the mean VAS score was found 3.6±1.38 in group A and an analgesic drug was given in this group of patients for the first time, so later on VAS score was gradually decline in this group. The difference was statistically significant ($p<0.05$) between the two groups **(Table V).**

Table V: Distribution of the study population based on VAS score in different follow up (N=60)

VAS score	Group C (n=30)	Group B (n=30)	P value
	Mean ±SD	Mean ±SD	
After 2 hour	0.0±0.0	0.0±0.0	-
After 3 hour	0.0±0.0	0.0±0.0	-
After 4 hour	0.0±0.0	0.0±0.0	-
After 5 hour	0.0±0.0	0.0±0.0	-
After 6 hour	0.0±0.0	0.03±0.18	-
After 7 hour	0.0±0.0	0.53±0.77	-
After 8 hour	0.0±0.0	2.17±1.4	-
After 9 hour	0.03±0.21	3.6±1.3	0.001[s]
After 10 hour	0.07±0.37	2.8±1.21	0.001[s]
After 11 hour	1.3±1.14	1.73±1.51	0.215[ns]
After 12 hour	3.13±1.13	0.53±1.04	0.001[s]
After 13 hour	3.6±1.38	0.17±0.53	0.001[s]
After 14 hour	1.8±1.58	0.03±0.18	0.001[s]

*_p value_ reached from unpaired t-test
VAS= Visual Analogue Scale

Two patients 6.7% in group A and most of the patients (29,96.7%) in group B were found one-time requirement of analgesic drugs within 12 hours of the postoperative period according to VAS. The difference was significant ($p<0.05$) between the two groups **(Table VI).**

Table VI: Distribution of the study population based on Requirement of analgesic drugs (N=60)

Analgesic drugs	Group A (n,%)	Group B (n,%)	*p value*
One time	2,6.7%	29,96.7%	0.001[s]

Around two-fifths of the patients 43.3% had a dry mouth in group A and 2(6.7%) in group B, which was significant ($p<0.05$) but other complaints were not significant ($p>0.05$) between the two groups **(Table VII).**

Table VII: Distribution of the study population based on Complaints (N=60)

Complaints	**Group A (n,%)**	**Group B (n,%)**	***pvalue***
Dry mouth	13,43.3%	2,6.7%	0.001^{s}
Nausea or vomiting	1,3.3%	4,13.3%	0.350^{ns}
Bradycardia	3,10.0%	1,3.3%	0.605^{ns}
Hypotension	4,13.3%	1,3.3%	0.350^{ns}

**p-value* reached from chi square test

DISCUSSION

Supraclavicular brachial plexus block was performed under ultrasound guidance in this current analysis. The actual time ultrasound imaging presented improved visualization of the brachial plexus, exactness of the needle placement, and spreading of local anaesthetics around the brachial plexus. Identification of the adjacent structures like blood vessels (subclavian artery and vein), first rib, and pleura was helpful to avoid procedure-related complications. Adjuvant (neostigmine, opioids, dexamethasone) improves analgesia and reduces systemic side effects and total dose of local anaesthetics. This comparative study was shown to evaluate the competence of oral Clonidine in supraclavicular brachial plexus block under ultrasound guidance with bupivacaine and dexamethasone. In this current study, among the study population (N=60), a tablet of Clonidine100 mcg was given to 30 patients classified as group A (n=30) and a Placebo drug was administered to the rest of the patients classified as group B (n=30). The mean age was found 34.8±13.2 years in group A and 38.1±15.0 years in group B. Another related article found that the mean age was 36.04±10.4 in group 1 (Clonidine) & 33.68±7.83 (others)[14]. In this present analysis, in the case of the patient's weight, the difference was not statistically significant (p=0.579 ns) between the two groups. Another similar published article revealed that the difference was also not statistically significant [15]. The current analysis depicted that around three-fourths of the patients 76.7% were found ASA class I in group A and twenty-five 83.3% in group B. The difference was not statistically significant (p=0.519ns) between the two groups. A related journal found that 46.9% were found in ASA class I in group R & 56.2% in group RC [16]. The mean onset of sensory block was found at 7.6±0.8 minutes in group A and 13.0±1.4 minutes in group B. The difference was statistically significant (p=0.001s) between the two groups depicted in this present study. A relevant study carried out in India found that the onset of sensory block was earlier in group II (4.36±0.81 min for sensory block & 9.83±1.12 min for motor block) than in group 1 (4.84±0.65 min for sensory block & 10.85±0.79 min for motor block). The duration of both the sensory block & motor block was significantly prolonged by clonidine (p<0.001) [17].A contradictory study based on Dexamethasone described that the onset of the upper extremely sensory block in the intervention group was lesser than in the control group and the difference was significant (p=0.026)

[18]. Another article pointed out that the mean onset of sensory block was found 293.6±19.1 minute in group A (Tramadol 1mg/kg) and 259.0±39 minute in group B (Clonidine 1µg/kg) and the difference was statistically significant (p=0.001s) between two groups [19]. A similar analysis found that the onset of sensory and motor block was considerably faster (p<0.05) in group C (20 ml of bupivacaine, 7 ml of 2% lignocaine & 100 µg of clonidine) in contrast with group B (20 ml of bupivacaine, 7 ml of 2% lignocaine) [20].A study demonstrated in West Bengal, India found that the onset of sensory and motor block was found to be statistically significant in group C (Ropivacaine& Clonidine) and group D (Ropivacaine&Dexmedetomidine) [21]. A contrasting article found that the duration of sensory block and motor block was not statistically significant (p>0.05) between the two groups [22]. In this study, the mean duration of sensory block was found 652.9±35.6 minutes in group A and 454.2±30.8 minutes in group B. The mean duration of the motor block was found 574.5±34.3 minutes in group A and 366.1±51.2 minutes in group B. The difference was statistically significant (p<0.05) between the two groups. Another contradictory analysis showed that the mean duration of sensory block was found 247.2±25.2 minutes in group A (Tramadol 1mg/kg) and 301.3±34 minutes in group B (Clonidine 1µg/kg) and the difference was statistically significant (p=0.001s) between two groups [19]. A related article found that the duration of sensory block in group C (Clonidine) was 9.7+/-1.6 hours, 13.3+/-1.9 hours in group D (Dexmedetomidine), and the duration of motor block was found 9.1+/-1.7 in group C, 12.1+/-2.0 in Group D. The duration of sensory & motor block was longer in Dexmedetomidine than the Clonidine group [23]. In our study, the mean duration of analgesia was found 731.8±41.8 minutes in group C and 528.8±47.7 minutes in group B. The difference was statistically significant (p=0.001s) between the two groups. In another article, the author showed that the mean duration of analgesia was found 313±21.4 in group A (Tramadol 1mg/kg) and 470.7±38.6 minute in group B (Clonidine 1µg/kg) and the difference was statistically significant (p=0.001s) between two groups [19]. Another published article found that the mean duration of analgesia was 268.27±12.18 min in patients of Group C (Clonidine) and 223.15 ±14.31 min in patients of Group T (Tramadol) with a statistically significant difference (p=0.000) [22]. This study observed that the mean arterial pressure- after 5 min, after 10 min, after 15 min, after 30 min, after 45 min, after 1 hour, after 2 hours, after 3 hours, and after 4 hours were significant (p<0.05) higher in group B than group A. another article revealed that the mean MAP was 91.57±10.663 mmHg in group C and 92.80±8.023 mmHg in group CL group. The difference was not statistically significant (p>0.05) between the two groups [24]. Another randomized study depicted that reported baseline values of MAP were comparable in both groups. B and A groups, there was a significant reduction of intraoperative MAP and heart rate in both groups compared to that of baseline. There was a significantly lower (p<0.05) MAP in Group A (Clonidine) than that of Group B (Dexmedetomidine) when the MAP was measured at 10 min intervals intraoperative and thereafter at half-an-

hour intervals till 4 hours postoperatively [25]. These observations were close to this study. The present study observed that after 9 hours, the mean VAS score was found 0.03±0.21 in group A and 3.6±1.3 in group B, which was statistically significant, and an analgesic drug was given in group B patients for the first time. After 12 hours, the mean VAS score was found 3.6±1.38 in group A and an analgesic drug was given to this group of patients for the first time. The difference was statistically significant ($p<0.05$) between the two groups. A relevant article reported that VAS score in the postoperative period up to 6hrs was comparable in both groups. RC (Ropivacaine& Clonidine) group reached the maximum VAS score at 10hrs and R (Ropivacaine) group at 8hrs, showing an extended duration of analgesia in the RC group, which was similar to this study results [12]. This current study observed that two patients 6.7% in group A and twenty-nine 96.7% patients in group B were found one-time requirement of rescue analgesic within 12 hours of the postoperative period according to VAS. The difference was significant ($p<0.05$) between the two groups. Others authors reported in another article that 1st dose of analgesia was not required in the case of any patient of the Clonidine group [26]. This observation was similar to the present study. So, preoperative use of oral clonidine reduces the requirement for analgesic drugs. This study reported that thirteen 43.3% patients had a dry mouth in group A and two 6.7% in group B, which was significant ($p<0.05$) but other complaints were not significant ($p>0.05$) between the two groups. The incidence of shivering was significantly lower in the patients of Group C (Clonidine) (4 patients) when compared to Group T (Tramadol) (7 patients) at 30 min. Mild pruritus was observed in 5 patients of Group T which was resolved by assurance. 3 patients of Group T suffered from nausea and vomiting while no such episode occurred in patients of Group C [22]. In this study 3 patients had bradycardia and 4 patients had hypotension also in the Clonidine group. The present study revealed that clonidine had some effect in terms of anti-sialagogue as a premedication. Another study found that bradycardia was noted in the Clonidine group [14].

CONCLUSION

The use of oral clonidine in supraclavicular brachial plexus block with bupivacaine and dexamethasone under ultrasound direction provides rapid onset of sensory block. However, it does not affect the onset of motor block. Additionally, clonidine extends the duration of analgesia with adequate sedation and less adversative things. In this finding, oral clonidine expands the quality of anaesthesia and analgesia when it was used as the administration of medication before a treatment or procedure.

RECOMMENDATIONS

According to all above the observations, it was recommended that clonidine as premedication with local anesthetics ensures the improved quality of anesthesia and analgesia with moderate sedation and fewer side effects in supraclavicular brachial plexus block.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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