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A comparative study on sedative and cardiorespiratory effects of clonidine and dexmedetomidine added to ropivacaine in supraclavicular brachial plexus block in upper extremity surgery

Anamitra Mandal[1], Sourav Naiya[2], Sarbari Swaika[3], Swarup Dutta[4], Swapnadeep Sengupta[5]

[1]Assistant Professor, Department of Anesthesiology, [2]Assistant Professor, Department of Community Medicine, Deben Mahata Government Medical College and Hospital, Purulia, [3]Professor, Department of Anesthesiology, IPGME&R, Kolkata, [4]Associate Professor, Department of Anesthesiology, Bankura Sammilani Medical College and Hospital, Bankura, [5]Assistant Professor, Department of Anesthesiology, Calcutta National Medical College and Hospital, Kolkata, West Bengal, India

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ABSTRACT

Background: Supraclavicular brachial plexus block is widely used peripheral nerve block technique used for surgery of the upper extremity. Several drugs have been used with local anesthetic as adjuvants for rapid, dense, and prolonged analgesia. **Aims and Objectives:** The aims and objectives of the study are to compare the degree of sedation and cardiorespiratory effects of clonidine and dexmedetomidine added to ropivacaine in supraclavicular brachial plexus block. **Materials and Methods:** A double-blinded comparative study was done on eighty patients who were randomly allocated equally into two groups and received clonidine and dexmedetomidine added to ropivacaine 0.5%. Intraoperative degree of sedation and cardiorespiratory parameters were monitored in regular intervals and compared to find difference. **Results:** Heart rate was consistently lower with dexmedetomidine. Systolic, diastolic, and mean arterial pressures (MAPs) were comparable in both groups at all time points except at 45 min when diastolic and MAP were lower with dexmedetomidine and it was statistically significant. Sedation score in Group D was higher except at 5 min and difference was statistically significant. All patients in both groups were sedated and easily arousable. There was statistically significant difference in peroperative oxygen saturation between the groups although it was clinically not significant. **Conclusion:** There was more hemodynamic effect of dexmedetomidine than clonidine but these effects can be managed by medication easily. In addition to this, it was found that dexmedetomidine provides conscious sedation without any respiratory depression. Comparing the risk and benefit dexmedetomidine can be used with local anesthetic in supraclavicular brachial plexus block in upper extremity surgery.

Key words: Anesthetics; Blood pressure; Brachial plexus block; Clonidine dexmedetomidine; Heart rate; Oxygen saturation; Ropivacaine

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INTRODUCTION

Regional nerve block can provide effective surgical anesthesia as well as post-operative analgesia. Moreover, regional nerve block avoids the unwanted effect of the anesthetic drugs used during general anesthesia and the stress of laryngoscopy and tracheal intubation. Supraclavicular brachial plexus block is a popular and widely

Address for Correspondence:
Dr. Anamitra Mandal, Department of Anesthesiology, Deben Mahata Government Medical College and Hospital, Purulia, West Bengal, India. **Mobile:** +91-9046141980. **E-mail:** anamitra84@gmail.com

employed regional nerve block technique for perioperative anesthesia and analgesia for surgery of the upper extremity. Local anesthetics alone for supraclavicular brachial plexus block provide good operative condition but have shorter duration of post-operative analgesia. Hence, various drugs, such as adjuvants (epinephrine, buprenorphine, fentanyl, tramadol, midazolam, dexamethasone, neostigmine, clonidine, and dexmedetomidine) were used with local anesthetics in brachial plexus block to achieve quick, dense, and prolonged block. Recent data suggest that, with the complexity of neurotransmitters responsible for nociception both at the peripheral and central level, it may be necessary to use combinations of adjuncts to achieve maximal benefit with minimal adverse effects.[1]

Regarding effect on hemodynamic variable, it was found lower heart rate (HR)[2-4] and blood pressure (BP)[4] with dexmedetomidine in peripheral nerve block. Various study shows arousable sedative effects with dexmedetomidine in peripheral nerve block[2,3] and more sedative effect with clonidine.[5] No significant difference in peroperative oxygen saturation (SpO_2) with dexmedetomidine or clonidine in peripheral nerve block in compare to other drug was found in different studies.[5,6]

Dexmedetomidine and clonidine both have been used in peripheral nerve blocks as adjuvant with local anesthetic. Dexmedetomidine and clonidine which are alpha-2 adrenoceptor agonist have sedative and analgesic effects, cause rapid onset of sensory and motor block, and increase duration of analgesia. Although these drugs are potential adjuvant, there are limited number of studies concluding safety profile of these drugs. Our study was designed to evaluate sedation and cardiorespiratory effects of these drugs when used as adjuncts to ropivacaine.

Aims and objectives

The aims and objectives of the study are to compare the degree of sedation and cardiorespiratory effects of clonidine and dexmedetomidine added to ropivacaine in supraclavicular brachial plexus block.

MATERIALS AND METHODS

A comparative study was adopted to find the sedation and cardiorespiratory effects between two groups managed with different combination of drugs (combination of ropivacaine with dexmedetomidine and a combination of ropivacaine with clonidine) during supraclavicular brachial plexus block in upper extremity surgery. The study was done on total of 80 patients, equally divided in both groups, in a teaching institute and tertiary care hospital West Bengal, India, during 2012–2013.

Due to the scarcity of previous published data, a pilot study was done on 10 similar patients (5 in each group in a different setting) to determine the estimated effect size required for sample size calculation.[7] Sample size calculation was done for comparative study for equal allocation using the formula of$N=2\times \sigma^2 \times((Z_{1-\alpha}+Z_{1-\beta})/(\delta-\delta_0))^2$, Where N is sample size in each group, $(\delta-\delta_0)$ is clinically acceptable margin that is difference of mean, σ is common standard deviation and considering desired power of study 80%, α error 5%, and 10% to account for contingency. An estimated sample size of 80 had been equally allocated in two groups randomly. Patients aged 20–50 years and of American Society of Anesthesiologists (ASA) physical status class I and II were included in the study and pregnant or lactating mothers and those had known allergies to any of the drugs, infection at the site of the block, co-morbid conditions, psychiatric disorder, coagulopathy, or any bleeding disorder were excluded from the study. All the patient fulfilled the inclusion, exclusion criteria and given informed consent were line listed and randomly allocated in two groups named "C" and "D" using simple randomization of flipping a coin (Head=Group C, Tail=Group D). It was a double-blinded study design where patients and researchers were unaware of the drugs, administered to the patients. An independent anesthesiologist not involved in the study had done the randomization, group allocation, and drug preparation before the procedure. Continuous monitoring of the patients was done by the researchers according to the standards of basic anesthesia monitoring as per ASA guidelines. Patients allotted in "Group C" received ropivacaine (0.5%) 30 mL with clonidine (1 μg/kg body weight) and in "Group D" received ropivacaine (0.5%) 30 mL with dexmedetomidine (1 μg/kg body weight) after pre-anesthetic evaluation during upper extremity surgery.

Calculated dose of dexmedetomidine or clonidine according to patients' body weight was diluted with normal saline to make 1 mL of solution. Patients were monitored using standard monitoring guideline. After aseptic preparation of the area, supraclavicular brachial plexus block was performed using nerve stimulator (Plexygon, 7501.31; Vygon, Italia S.r.l., Italy). Correct needle placement within the fascia was confirmed by the distal responses of the hand or wrist flexion or extension[8] and elbow flexion.

The degree of sedation was assessed using Ramsay Sedation Scale[9] (awake, excited, or agitated - Grade 1; awake, quiet, responds - Grade 2; quiet, responds to commands - Grade 3; asleep, response strongly to verbal or tactile stimulation - Grade 4; asleep, response lazily to verbal or tactile stimulation - Grade 5; asleep, no responds to stimulation - Grade 6) and cardiorespiratory variables (i.e., SpO_2, systolic BP [SBP], diastolic BP [DBP], mean

arterial pressure [MAP], HR, electrocardiogram [ECG]) were assessed by pulse oximeter, NIBP, and ECG monitoring. Hypotension was defined as <80% of the pre-anesthetic level. Bradycardia was defined as HR<60 beats/min. These parameters were assessed continuously and data were collected at every 5 min up to 15 min then every 15 min up to 1 h. After that, at 30-min interval, these variables were monitored up to 2 h. In the post-operative period, these variables were assessed at 2, 6, 12, and 24 h.

Ethics

Institutional Ethical Committee clearance as per national laws and regulations and Helsinki Declaration was obtained before the study. Study participants were explained the purpose of the study, risk-benefit of the procedure and informed consent was obtained.

Statistics

Data were collected, compiled, and presented using tables and diagram using Microsoft office© and appropriate statistical test was done using Epi Info© software. Descriptive parts of the results were represented with mean (standard deviation) or number (percentage) and statistical analysis was done using independent samples t-test, Chi-square test where applicable.

RESULTS

Randomly allocated 40 patients in the group named "Group D" received ropivacaine with dexmedetomidine for supraclavicular brachial plexus block and 40 patients in the group named "Group C" received ropivacaine with clonidine. The clinical profile of both groups was comparable with regard to baseline cardiovascular or clinical parameters and mean duration of surgery and was statistically non-significant (Table 1). Most of the patients had ORIF (#both bone forearm) surgery and no statistically significant difference was found regarding the types of surgery performed between the groups.

In this study, it was found that there was statistically significant lower HR in ropivacaine with dexmedetomidine group at 15, 30, 45, and 60 min, but not <60 beats/min in compare to ropivacaine with clonidine group (Table 2). It was also found that there was significantly lower DBP and MAP in ropivacaine with dexmedetomidine group at 45 min (Figure 1). The hemodynamic parameters were comparable at the end of 120 min (Table 3). This study found that there was statistically significant difference in per operative sedation score between the two groups at 0, 10, 15, 30, 45,

Table 1: Comparison of baseline cardiovascular and clinical parameters between two groups (n=80)

Cardiovascular and clinical parameters	Mean±SD		Statistics (P-value)*
	Group D* (n=40)	Group C* (n=40)	
Pulse	84.32±7.74	81.45±8.84	0.126
SBP/mmHg	126.95±6.73	126.50±5.85	0.751
DBP/mmHg	79.42±6.74	78.85±7.10	0.712
Hb (%)	11.64±1.54	11.85±1.34	0.522
Platelet count (lakh/mm^3)	1.60±0.12	1.62±0.11	0.578
FBS (mg/dL)	87.47±8.13	89.45±9.97	0.335
PPBS (mg/dL)	118.4±5.64	117.85±7.80	0.719
Urea	23.57±3.55	22.90±3.433	0.39
Creatinine	0.88±0.15	0.83±0.13	0.119
BT	3.81±0.48	3.64±0.42	0.1
CT	5.27±0.49	5.17±0.35	0.327
Duration of surgery in minutes	88.37±22.74	86.50±19.22	0.692

*Group D: Ropivacaine with dexmedetomidine, Group C: Ropivacaine with clonidine. Statistical test used independent samples t-test (Significance level of 0.05). SD: Standard deviation, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, Hb: Hemoglobin, FBS: Fasting blood sugar, PPBS: Postprandial blood sugar, BT: Bleeding time, CT: Clotting time

Table 2: Comparison of per operative heart rate in different times between two groups (n=80)

Per operative heart rate in different times (min)	Group D*		Group C*		Statistics (P-value)*
	n	Mean±SD	n	Mean±SD	
0	40	81.8±8.43	40	81.3±7.06	0.775
5	40	78.62±7.54	40	80.05±7.24	0.391
10	40	73.97±7.3	40	75.2±7.81	0.471
15	40	69.62±6.8	40	72.95±6.43	**0.028**
30	40	65.57±7.29	40	71±7.35	**0.001**
45	40	64.3±7.66	40	69.9±9.17	**0.004**
60	40	64.7±9.17	40	69.4±7.89	**0.016**
90	33	65.81±9.71	28	69.85±6.82	0.07
120	14	70.57±6.5	6	73±7.64	0.476

*Group D: Ropivacaine with dexmedetomidine, Group C: Ropivacaine with clonidine. Statistical test used independent samples t-test (Significance level of 0.05). SD: Standard deviation

Table 3: Comparison of per operative blood pressure in different times between two groups (n=80)

Per operative blood pressure in different times		Group D*		Group C*		Statistics (P-value)*
Time (min)	Blood pressure	n	Mean ± SD	n	Mean ± SD	
0	SBP	40	124.45 ± 7.28	40	125.1 ± 7.47	0.695
	DBP	40	77.42 ± 8.81	40	76.92 ± 9.26	0.805
	MAP	40	93.10 ± 7.42	40	92.98 ± 7.52	0.945
5	SBP	40	122.17 ± 9.57	40	120.95 ± 8.1	0.539
	DBP	40	74.65 ± 9.23	40	72.82 ± 8.26	0.355
	MAP	40	90.49 ± 8.65	40	88.87 ± 6.77	0.352
10	SBP	40	120.25 ± 9.54	40	119.02 ± 8.84	0.553
	DBP	40	73.15 ± 7.62	40	74.7 ± 7.65	0.367
	MAP	40	88.85 ± 7.63	40	89.4 ± 7.07	0.705
15	SBP	40	118.45 ± 9.56	40	118.42 ± 8.47	0.990
	DBP	40	73.85 ± 8.79	40	73.25 ± 7.14	0.739
	MAP	40	88.72 ± 8.16	40	88.31 ± 6.34	0.803
30	SBP	40	115.17 ± 9.67	40	116.4 ± 7.41	0.527
	DBP	40	72.42 ± 8.78	40	70.75 ± 11.54	0.467
	MAP	40	86.67 ± 7.88	40	85.97 ± 8.62	0.702
45	SBP	40	114 ± 8.9	40	117 ± 8.04	0.118
	DBP	40	68.72 ± 7.09	40	72.55 ± 8.15	**0.028**
	MAP	40	83.82 ± 6.91	40	87.37 ± 7.42	**0.030**
60	SBP	40	108.7 ± 24.34	40	116.85 ± 8.63	0.05
	DBP	40	71.37 ± 8.18	40	72.37 ± 9.85	0.623
	MAP	40	83.82 ± 9.58	40	87.2 ± 8.82	0.105
90	SBP	33	117.3 ± 8.16	28	116.28 ± 8.05	0.627
	DBP	33	70.9 ± 9.23	28	70.14 ± 9.72	0.754
	MAP	33	86.37 ± 8.06	28	85.52 ± 8.39	0.689
120	SBP	14	117.78 ± 6.41	6	118.66 ± 4.92	0.768
	DBP	14	71.07 ± 8.46	6	69.33 ± 9.89	0.693
	MAP	14	86.64 ± 6.47	6	85.78 ± 7.61	0.797

*Group D: Ropivacaine with dexmedetomidine, Group C: Ropivacaine with clonidine. Statistical test used independent samples t-test (Significance level of 0.05). SD: Standard deviation, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MAP: Mean arterial pressure

Table 4: Comparison of per operative sedation score between two groups (n=80)

Per operative sedation score in different time (min)	Group D*		Group C*		Statistics (P-value)*
	n	Mean±SD	n	Mean±SD	
0	40	2	40	2.15±0.36	**0.01**
5	40	2.75±0.43	40	2.65±0.48	0.335
10	40	3.22±0.42	40	2.6±0.49	**0.001**
15	40	3.5±0.5	40	2.65±0.48	**0.001**
30	40	3.75±0.43	40	2.65±0.48	**0.001**
45	40	3.77±0.42	40	2.65±0.48	**0.001**
60	38	3.71±0.56	40	2.6±0.49	**0.001**
90	33	3.72±0.45	28	2.64±0.48	**0.001**
120	14	3.64±0.63	6	2.33±0.51	**0.001**

*Group D: Ropivacaine with dexmedetomidine, Group C: Ropivacaine with clonidine. Statistical test used independent samples t-test (Significance level of 0.05). SD: Standard deviation

60, 90, and 120 min and all the patients in both groups were easily arousable (Table 4). The statistically significant difference at 0 min may be due to intraobserver variation during data collection as six patients with clonidine had Grade 3 sedation score (responds to commands).

We found statistically significant difference in per operative SpO_2 between the groups (10, 15, and 30 min) though this difference has no clinical significance as all the patients in both groups maintained SpO_2>97% (Table 5). None of the patients required additional oxygen at post-anesthesia care unit. None of the patients developed respiratory depression.

DISCUSSION

Lin et al.[2] reported that dexmedetomidine has a double effect, playing an anti-central sympathetic role and activating the vagus nerve to lower plasma catecholamine levels which can lower BP and HR, providing stable hemodynamics. Swami

Table 5: Comparison of peroperative SpO_2 between two groups (n=80)

Per operative SpO_2 (min)	Group D*		Group C*		Statistics (P-value)*
	n	Mean±SD	n	Mean±SD	
0	40	98.57±0.93	40	98.8±1.01	0.305
5	40	98.55±0.81	40	98.62±0.89	0.697
10	40	97.62±1.29	40	98.22±0.73	**0.013**
15	40	97.37±1.07	40	98.25±0.98	**0.001**
30	40	97.77±0.91	40	98.5±0.84	**0.001**
45	40	98.32±0.65	40	98.55±0.55	0.101
60	38	98.6±0.54	40	98.82±0.67	0.120
90	33	98.63±0.6	28	98.71±0.59	0.616
120	14	99.14±0.66	6	99.33±0.51	0.541

*Group D: Ropivacaine with dexmedetomidine, Group C: Ropivacaine with clonidine. Statistical test used independent samples t-test (Significance level of 0.05). SD: Standard deviation, SpO_2: Oxygen saturation

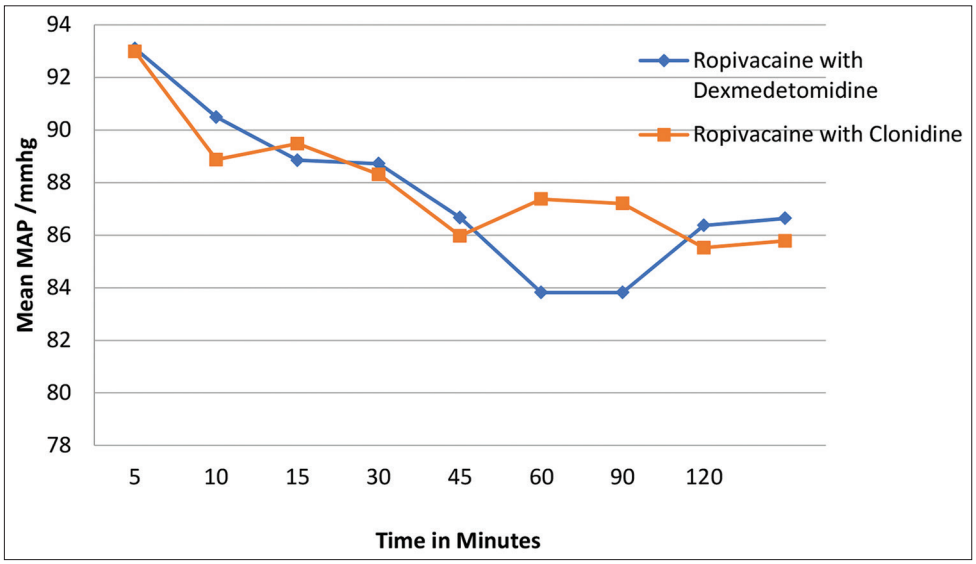

Figure 1: Comparison of per operative mean arterial blood pressure between two groups. (n=80). *Group D-ropivacaine with dexmedetomidine, Group C-ropivacaine with clonidine

et al.[3] reported stable hemodynamics in both groups with dexmedetomidine and clonidine except for significant lower pulse rate in dexmedetomidine group at 60, 90, and 120 min as compared with clonidine group, but not <60 beats/min which is consistent with our study. Esmaoglu et al.[4] found that SBP levels in levobupivacaine-dexmedetomidine group at 10, 15, 30, 45, 60, 90, and 120 min were significantly lower than those in levobupivacaine group. Diastolic pressure levels in levobupivacaine-dexmedetomidine group at 60, 90, and 120 min were significantly lower than those in levobupivacaine group. HR levels in levobupivacaine-dexmedetomidine group, except basal measurements, were significantly lower than those in levobupivacaine group. Singh and Aggarwal[6] in their study found that perioperative and post-operative HR was variable at each time interval and was also lower in the clonidine group in comparison with the control group but the difference was not significant. Chakraborty et al.[5] observed no statistically significant difference in HR, BP between the two groups (bupivacaine with clonidine vs. bupivacaine with normal saline) at any time point.

Our study results related to sedation were consistent with other studies.[2,3,5] Swami et al.[3] in their study found that patients in dexmedetomidine group did not require any sedation intraoperatively and they were comfortable throughout the surgery with arousable sedative effects. Lin et al.[2] also found that the patients who received dexmedetomidine in cervical plexus block were sedated and arousable. According to them, it is due to slight intravenous effect that is caused by tissue capillary reabsorption and its direct effect on the peripheral nerves. El Saied et al.[10] found no difference in sedation score between clonidine and control group. However, Chakraborty et al.[5] found that the patients who received clonidine were more sedated. Singh et al.[6] reported that sedation, which is often associated with clonidine, was not apparent in their study.

Chakraboty et al.[5] found no statistically significant difference in per operative SpO_2 between the two groups (bupivacaine with clonidine vs. bupivacaine with normal saline) at any time point. Singh et al.[6] observed that

SpO_2 between the clonidine and the control group was comparable throughout the study period and all the patients had saturation of oxygen >99% in both groups at all times of the observation.

Limitations of the study

The major limitations of our study were that we could not use ultrasound-guided blocks because it was not available at the time of our study; this could have helped us to lower dosages and volumes of local anesthetic. Interobserver variation may also induce bias in the study.

CONCLUSION

From the results of our study, it can be concluded that in peripheral nerve blocks, dexmedetomidine can be used with local anesthetic safely though there was more hemodynamic effect than clonidine as these effects can be managed by medication easily. In addition to this, it was found that dexmedetomidine provides conscious sedation without any respiratory depression. Comparing the risk and benefit dexmedetomidine can be used with local anesthetic in supraclavicular brachial plexus block in upper extremity surgery, but further studies are needed to evaluate its safety, efficacy, and effectiveness over clonidine.

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Authors Contribution:
AM- Definition of intellectual content, literature survey, preparation of first draft of manuscript, implementation of study protocol, data collection, data analysis, manuscript preparation and submission of article; **SN**- Design, data analysis, manuscript preparation, editing, manuscript revision, statistical analysis and interpretation; **SS**- Design of study and review manuscript; **SD**- Review manuscript; **SS**- Editing and manuscript revision.

Work attributed to:
Bankura Sammilani Medical College and Hospital, Bankura, West Bengal, India.

Orcid ID:
Anamitra Mandal - https://orcid.org/0009-0001-7701-2056
Sourav Naiya - https://orcid.org/0009-0001-7559-024X
Swapnadeep Sengupta - https://orcid.org/0000-0001-8594-4315
Sarbari Swaika – https://orcid.org/0000-0002-0525-8460
Swarup Dutta - https://orcid.org/0000-0002-1493-7270

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