Effect of adding dexmedetomidine as an adjuvant to 0.5% ropivacaine in supraclavicular brachial plexus block- a Randomized controlled study

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Abstract

Introduction- Dexmedetomidine has been demonstrated to be safe and effective in various neuraxial and regional anesthetic procedures in humans, with fewer adverse effects in several studies.

Methodology- This study aimed to study and compare the efficacy of Dexmedetomidine 1µg/kg plus 0.5% Ropivacaine versus 0.5% Ropivacaine alone in brachial plexus block by supraclavicular approach. After obtaining institutional ethics committee approval this prospective, randomized, comparative study was conducted on 60 patients, 18-60 years, either sex scheduled for elective upper limb surgery under supraclavicular brachial plexus block. The primary objective was to study the effects of 0.5% Ropivacaine with Dexmedetomidine 1µg/kg in brachial plexus block in the form of onset and duration of sensory and motor blockade. Secondary objectives included grading the quality of motor block, Sedation Score, Duration of analgesia, Hemodynamic changes, and Side effects, if any.

Observations- Group D showed a faster onset and a longer duration of sensory and motor blockage. Rescue analgesia was given with Injection Diclofenac Sodium 75 mg intravenous when patient Numeric Rating Score> 4. The mean sedation score was comparable at baseline, 5th and 10th minutes ($P>0.05$), significantly higher in Group D from 15^{th} to 480^{th} minutes ($P<0.05$), and subsequently comparable from 600^{th} to 1440^{th} minutes ($P>0.05$).

Conclusion-When given as an adjuvant to Ropivacaine 0.5% in supraclavicular brachial plexus block, Dexmedetomidine significantly reduces the onset time and increases the duration of sensory and motor block. It also provides excellent sedation during surgery, improves the quality of block, extends the duration of analgesia, and does not cause significant respiratory depression

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INTRODUCTION

A peripheral nerve block is an excellent alternative to general anesthesia and central nerve block during surgery. Peripheral nerve blocks are less risky than general anesthesia and have specific advantages. They give intraoperative anesthesia and post-operative

analgesia with no systemic adverse effects. [1-4] Peripheral nerve blocks minimize post-anesthesia nausea, vomiting, atelectasis, hypotension, ileus, dehydration, and deep vein thrombosis. It eliminates the hemodynamic effects associated with laryngoscopy and tracheal intubation. As a result of their high success rate and the capacity to give sustained post-operative analgesia, brachial plexus blocks are among the most well-researched peripheral nerve blocks available today Many medicines, including opioids, clonidine, hyaluronidase, dexamethasone, and midazolam, have been studied previously as an adjunct to regional anaesthesia to lower the overall dose and enhance the blockade effects. [2,3] Dexmedetomidine is an alpha two receptor agonist, and its α2/α1 selectivity is eight times more than clonidine. [4] Dexmedetomidine has been shown in several animal experiments to augment sensory and motor block and prolong the duration of analgesia, among other things. [3] Dexmedetomidine has been demonstrated to be safe and effective in various neuraxial and regional anesthetic procedures in humans, with fewer adverse effects in several studies. This study aimed to study and compare the efficacy of Dexmedetomidine 1mcg/kg plus 0.5% Ropivacaine versus 0.5% Ropivacaine alone in brachial plexus block by supraclavicular approach. The primary objective was to study the effects of 0.5% Ropivacaine with Dexmedetomidine 1mcg/kg in brachial plexus block in the form of onset and duration of sensory and motor blockade. The secondary objectives encompassed the assessment of various outcome variables, such as grading the quality of motor block, evaluating the Sedation Score, determining the Duration of analgesia, monitoring Hemodynamic changes, and noting any potential side effects.

MATERIAL AND METHODS

After obtaining institutional ethics committee approval (IEC/NOV/16/13, dated 2nd Nov 2016) and informed written consent from each patient, this prospective, randomized, comparative study was conducted on 60 American Society of Anesthesiologists (ASA) grade I-II patients, 18-60 years of age, of either sex scheduled for elective upper limb surgery under supraclavicular brachial plexus block. Patients who refused consent, with known hypersensitivity to local anesthetics, on adreno-receptor agonist and antagonist therapy, with respiratory, renal, hepatic or cardiac disease, uncontrolled diabetes mellitus, bleeding disorder, preexisting peripheral neuropathy and pregnant woman were excluded from the study.

Sample size estimation

As per the study by Nema et al. [4], an average time of onset of sensory blockade was 14.20±5.229 minutes for patients who received Ropivacaine and 7.20±2.483 minutes for patients who received Ropivacaine with Dexmedetomidine.

Effect Size = Difference per SD (DSD) = (M1-M2)/σ =1.71

Where Mean of group 1= M1=14.20, Mean of group 2= M2=7.20 and Common standard deviation (SD) =σ =40.9. From Cohen Power Tables for effect size at 80% power and 5% level of significance, it has been found that there was a need of 6 patients per group. The number of patients in each group was in the ratio of 1:1. Thus the required sample size for the study was

12. But to increase the accuracy of the data, we included 30 patients in each group.

METHODOLOGY

After a detailed pre-anaesthetic check-up, all patients were randomly allocated using a computer-generated random number table to one of two groups (group C or D), each consisting of 30 patients.

Group C- Patients received 30 ml of 0.5% Ropivacaine with 1 ml 0.9% Normal saline.

Group D- Patients received 30 ml of 0.5% Ropivacaine with 1µg/Kg Dexmedetomidine.

In the operating room, intravenous access and standard monitoring (electrocardiogram, pulse oximeter and non-invasive blood pressure) were attached. The patient was made to lie supine with the head turned away 45^0 from the side to be blocked and the ipsilateral arm adducted; painting was done with antiseptic solution, and draping was done. Subclavian artery was palpated 1 cm above the midpoint of the clavicle. Local Anesthesia was given with 1 ml Inj. Lignocaine 2% sufficient to raise the skin wheal at the needle entry site. All the patients received PNS guided brachial plexus block through the supraclavicular approach by an experienced anesthesiologist using a nerve stimulator (SenStimTM). An insulated 1.5 inch 25 G needle was introduced just lateral to the subclavian pulsation in a backward, downward, and medial direction. The needle was connected to nerve locator, and 1.5 mA current at 1 Hz was applied for stimulation. Once the contraction of deltoid was observed, the intensity of current was decreased to 0.5 mA with the contractions of deltoid intact but ensuring no muscle contraction on a current of 0.3 mA to prevent intraneural injection. At this point, after confirming negative aspiration, the solution containing local anesthetic combined with dexmedetomidine or normal saline (depending on the group to be studied was injected. The end of the injection was considered time 0. Sensory and motor blocks were evaluated every 1 minute until 30 minutes after injection till complete recovery of sensory and motor blocks. Sedation score was recorded every 1 minute for the first 30 minutes and after that every 30 minutes till complete recovery from the motor and sensory blocks. Onset time of sensory block was defined as the time interval between the end of total local anesthetic administration and decreased sensation (Grade 1). Duration of sensory block was defined as the time interval between end of local anesthetic administration and complete resolution of anesthesia on all nerves.

Sensory block was assessed by pinprick test using a 3-point scale: [5]

0	Normal sensation(sharp pinprick)
1	Decreased sensation
2	Complete loss of sensation

The onset of motor block was defined as the time interval between the end of total local anesthetic administration and Grade 1 motor block. Duration of motor block was defined as time interval between the end of local anesthetic administration and complete resolution of motor block.

Motor block was assessed using Modified Bromage Score: [6]

0	Normal motor function
1	Ability to flex & extend wrist & fingers
2	Ability to flex & extend fingers only
3	Complete motor block with the inability to move elbow, wrist & fingers

The following numeric scale assessed quality of block:

Grade (Excellent)	4	No complaints from the patient
Grade 3 (Good)		Minor complaints with no need for supplemental analgesia
Grade (Moderate)	2	Complaint that required supplemental analgesia
Grade (Unsuccessful)	1	Patient given general anesthesia

The Ramsay Sedation Score assessed sedation score: [7]

1. Patient anxious, agitated, or restless
2. Patient cooperative, oriented and tranquil
3. Patient responds to commands
4. Patient exhibits brisk response to light glabellar tap or loud auditory stimulus
5. Patient exhibits sluggish response to light glabellar tap or loud auditory stimulus
6. Patient exhibits no response

Pain score (Numerical Rating Scale Score - NRS) was used to assess pain intensity. The scale consists of a line, 10 cm long depicting: [8]

0 - No pain and 10 - worst possible pain

Duration of analgesia was defined as the time interval between complete sensory blockade till patient's first request for rescue analgesia. A numerical rating scale for pain was recorded every 1 min for the first 30 min followed by every 30 min till the score of 4. Rescue analgesia was given at the score of >4 and the time of administration was noted. Rescue analgesia was given with Injection Diclofenac Sodium 75 mg intravenous when patient NRS> 4.

Block was considered incomplete when any segment supplied by median, radial, ulnar or musculocutaneous nerve was not having analgesia even after 30 min of drug injection. These patients were supplemented with intravenous fentanyl (1µg/kg). It was considered a failed block when more than one nerve remained unaffected. In this case, general anesthesia was administered and those cases were excluded from the analysis.

Hemodynamic parameters were recorded every 1 minute for first 30 minutes and thereafter every 30 minutes till complete recovery from motor and sensory blocks. Adverse events included **a**naphylaxis, dryness of mouth, thirst, circum-oral numbness, convulsion, hematoma, phrenic

nerve palsy, diaphragmatic palsy, hypotension (20% decrease from baseline), bradycardia (heart rate <50 beats per minute), hypoxia (SpO_2<90%) were noted and treated according to standard protocol.

Statistical analysis

The data were analyzed by using SPSS software, version 25.00. Quantitative variables were expressed as mean+/-SD, and unpaired t-test was applied. Proportional comparisons were done using the Z test for two sample proportions $P \leq 0.05$ was taken as level of statistical significance.

Observations

Both groups' demographic characteristics were comparable and summarised in (Table 1). Most of the patients (94%) underwent surgery for radius and ulna fractures.

Table 1 Demographic distribution of patients

	Group C (n=30)	**Group D (n=30)**	**P value**
Age (years)	40.26±15.54	41.97±14.74	0.665
Sex (M/F)	23/7	18/12	0.164
Weight (kg)	64.86±11.85	64.23±10.40	0.826
Height (cm)	166.80±07.34	165.77±07.18	0.583
BMI (kg/m^2)	23.24±03.79	23.33±03.21	0.929
ASA physical status:			
I	18	20	
II	12	10	
Duration of surgery (min)	77.33±32.92	87±34.93	0.275

Unpaired 't' test applied. P value < 0.05 was taken as statistically significant

Z test for two sample proportion.

Group D showed a faster onset and a longer duration of sensory and motor blockage (Table 2). The sensory and motor block onset time was considerably shorter in Group D than in Group C (P<0.05). The sensory and motor block length was

considerably longer in Group D than in Group C (P<0.05). The duration of analgesia in Group D was substantially longer than in Group C (P<0.05), Group D had higher block quality than Group C, which was statistically significant (P<0.05) [table 3]. The mean sedation score was comparable at baseline, 5th and 10th minutes (P>0.05), significantly higher in Group D from 15th to 480th minutes (P<0.05), and subsequently comparable from 600th to 1440th minutes (P>0.05).[fig 1]

Table 2 Sensory and motor block onset time, block and analgesia duration in both groups

	Group C (Mean±SD)	**Group D (Mean±SD)**	**P value**
Onset time of sensory block (min)	14.33±5.313	7.40±2.400	< 0.001
Onset time of motor block (min)	21.03±8.105	11.50±3.569	< 0.001
Duration of sensory block (min)	311.67±66.169	437.33±99.960	< 0.001
Duration of motor block (min)	279.50±66.119	391.53±106.930	< 0.001
Duration of analgesia (min)	381.00±82.269	972.57±235.370	< 0.001

Unpaired 't' test applied. *P value < 0.05 was taken as statistically significant

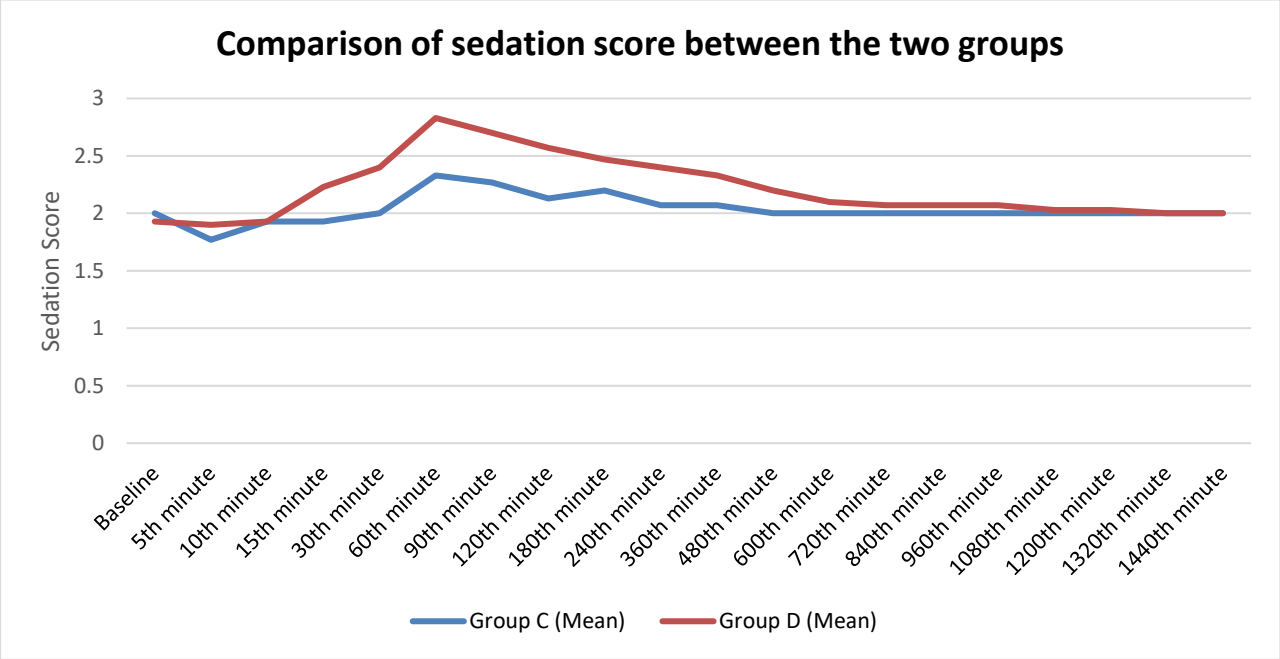

Fig 1: Line diagram showing comparison of sedation score between the two groups

Table 3 Comparison of Quality of Block between the two groups

Block grade	Group C		Group (D)		P value
	No.	**%**	**No.**	**%**	
1	0	0.0	0	0.0	-
2	9	30.0	7	23.3	0.26
3	13	43.3	8	26.7	0.017*
4	8	26.7	15	50.0	0.0008*

Z test for two sample proportion applied. P value < 0.05 was taken as statistically significant

Group D had superior hemodynamic stability (supplementary table). Mean heart rate was comparable (P>0.05) at baseline, however, it was considerably lower in Group D compared to Group C from the 5th to the 480th minute (P<0.05). Group D had substantially lower systolic blood pressure than Group C (P<0.05). The mean diastolic blood pressure was comparable at baseline, 5th and 10th minutes (P>0.05), but considerably lower in Group D from 15th to 360th minutes (P<0.05). However, the diastolic blood pressure was comparable from 480th to 1440th minutes (P>0.05). Mean arterial pressure was comparable at baseline, 5th and 10th minutes (P>0.05), but mean arterial pressure was considerably lower in Group D from 15th to 360th minutes (P0.05), and again from 480th to 1440th minutes (P>0.05).

DISCUSSION

In our study, we found a significant decrease in onset time and increase in duration of sensory and motor block and increased duration of analgesia without any adverse effects in the dexmedetomidine group compared to those found in the control group. Kathuria et al. (2015) [9] found that the onset of sensory and motor block was earlier in Dexmedetomidine group D than in control group C. The duration of sensory and motor block and the duration of analgesia was also prolonged in Dexmedetomidine group D when compared with control group C. Zhang et al. (2014)[10] and Marhofer et al. (2013)[11] found that

Dexmedetomidine added to Ropivacaine prolongs the duration of the block. The dose selection of dexmedetomidine was based on previous studies where dexmedetomidine 1 µg/kg and clonidine 1 µg/kg were used in Bier's block as an adjuvant to lignocaine and in the supraclavicular block as an adjuvant to 0.5% ropivacaine. [12]

The mean time taken for the onset of the sensory block was 14.33±5.313 minutes in ropivacaine group C and 7.40±2.40 mins in ropivacaine + dexmedetomidine group D (P<0.001) and the onset of motor block was 21.03±8.105 mins in group C and 11.50±3.569 mins in group D (P<0.001). Esmaoglu et al[2], Nema et al[4] and Kathuria et al. (2015)[9] also found that the sensory and motor block onset time was significantly shorter in the dexmedetomidine group than in the control group with (P<0.05).

The mean duration of sensory and motor block was 437.33±99.96 mins and 391.53±106.93 mins in the dexmedetomidine group and 311.67±66.169 mins and 279.50±66.119 mins in the control group (P<0.05). Nema et al. (2014)[4], Marhofer et al[11] and Das et al 2016[12] also reported that the average duration of the sensory and motor blockade in the dexmedetomidine group was longer than the longer than the control group.

In our study, a significantly increased duration of analgesia was found in the dexmedetomidine group (972.57±235.37) compared to a control group (381±82.269) (P<0.001). A similar result was obtained in the previous study done by Nema et al[4] and Das et al[12], who observed that the average duration of analgesia in the dexmedetomidine group was longer as compared to the control group.

The mean Ramsay sedation scores were statistically insignificant until 10 minutes (P>0.05). At 15 minutes, the mean Ramsay sedation score was (2.23±0.57) in the dexmedetomidine group and in the control group (1.93±0.52) (P<0.05) and it was statistically significant. We observed that from 15 minutes onwards till 480 mins of the intraoperative period sedation score was significantly higher in the dexmedetomidine group than in the control group (P<0.05), with a maximum mean sedation score of 2.83 at 60 minutes. In the post-operative period, the sedation score was on the higher side in the dexmedetomidine group as compared to the control group. Keplinger et al[13], Rastogi et al[14], Patki et al[15], Das et al[12] and Rancourt et al[16] concluded that the sedation was enhanced in a dose-dependent manner in the dexmedetomidine group. Most volunteers in the dexmedetomidine

group lost at least 1 point on the sedation score, mostly between 60 and 120 minutes after the injection. In our study, we observed that after giving SCB, initially, heart rate started falling in dexmedetomidine group compared to the control group. After 5 mins, throughout intraoperative and postoperative periods, heart rate remained significantly low in the dexmedetomidine group as compared to the control group. Although the heart rate was on the lower side in dexmedetomidine group as compared to the control group, but no active intervention was required in the dexmedetomidine group to increase heart rate. Abdallah et al[17] found that dexmedetomidine produced reversible bradycardia in 7% of Brachial plexus block patients. Patki et al[15] and Esmaoglu et al[2] also observed lower heart rates in the dexmedetomidine group.

Systolic, diastolic and mean blood pressure remained significantly lower in the dexmedetomidine group. However, no active intervention was required in the dexmedetomidine group. Sudani et al[18] and Rancourt et al[16] also found the intra-operative hemodynamics to be on the lower side in group Ropivacaine + Dexmedetomidine, without any appreciable side-effects.

The baseline mean respiratory rate per minute and percentage of peripheral saturation were 17.03±2.36 and 98.70±0.70 in Ropivacaine alone group C and 17.50±2.43 and 98.36±0.99 in ropivacaine + dexmedetomidine group D. So baseline respiratory rate and saturation were comparable in both the groups (*P*=0.453 and 0.140). After giving block, the mean respiratory rate remained significantly lower in the dexmedetomidine group compared to the control group till 360 min, with the lowest mean rate 17.47±2.64 at 90 mins. After 360 mins, there was no significant difference in respiratory rate between both groups. At 30, 60, 90 and 120 minutes, SpO_2 was found to be lower (98.37%, 97.90%, 98.53% and 98.60%) in group D compared to group C (*P*<0.05). But no patient required oxygen supplementation for oxygen desaturation in dexmedetomidine group.

In group D, 50% of the patients who achieved block didn't require any form of sedation, analgesia or counselling (grade 4 quality of block) as opposed to 26.7% in group C, which was statistically significant (P<0.05). Harshavardhana et al[19] found that the dexmedetomidine enhances the quality of block as compared with clonidine.

No side effects (nausea, vomiting, dry mouth, etc.) were reported during the

intraoperative and post-operative period in both the groups in our study and also in the study by Arun et al[20], Sudani et al[18] and Esmaoglu et al[2]. Whereas, Abdallah et al[17] found reversible bradycardia in 7% of patients.

CONCLUSION:

When given as an adjuvant to Ropivacaine 0.5 per cent in Supraclavicular brachial plexus block, Dexmedetomidine significantly reduces the onset time and increases the duration of sensory and motor block. It causes a significant but transient decrease in heart rate, systolic, diastolic, and mean blood pressure, as well as respiration rate, although they do not require any treatment. It also provides excellent sedation during surgery, improves the quality of block, extends the duration of analgesia, and does not cause significant respiratory depression; no other significant intra-operative or post-operative effects were observed in either group, providing a wider safety margin.

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22.

Supplementary Table Hemodynamic parameters at different time points in two groups

Time interval	Group C		Group D		*P* value
	Mean	**SD**	**Mean**	**SD**	
Heart rate(beats/minute)					
Baseline	86.43	16.72	78.60	15.89	0.068
5th minute	90.86	17.17	76.00	17.02	0.001*
10th minute	89.06	16.15	74.87	17.55	0.001*
15th minute	89.90	15.73	71.07	19.97	<0.001*
30th minute	88.90	15.27	68.77	17.38	<0.001*
60th minute	84.50	12.60	68.50	16.45	<0.001*
90th minute	82.80	11.66	69.00	16.97	<0.001*
120th minute	82.27	12.56	70.30	16.50	0.002*
180th minute	84.13	12.83	70.87	16.72	0.001*
240th minute	85.73	12.52	72.40	16.12	<0.001*
360th minute	89.03	14.26	73.27	14.71	0.001*
480th minute	84.97	15.52	74.83	16.65	0.018*
600th minute	84.07	13.61	76.83	14.59	0.052
720th minute	82.57	13.13	81.33	15.72	0.743
840th minute	81.20	12.47	80.33	13.89	0.800
960th minute	78.97	11.19	81.93	14.61	0.381

1080th minute	76.87	11.22	79.57	16.02	0.453
1200th minute	77.90	11.22	77.47	13.34	0.892
1320th minute	78.70	11.37	76.47	14.73	0.514
1440th minute	78.73	10.33	77.23	14.12	0.641
Systolic blood pressure (mmHg)					
Baseline	125.13	7.93	124.53	8.72	0.781
5th minute	126.46	8.31	123.60	8.80	0.199
10th minute	125.73	7.55	122.80	8.49	0.163
15th minute	122.90	8.60	118.73	6.96	0.044*
30th minute	122.33	7.86	118.20	6.56	0.031*
60th minute	121.53	6.64	115.73	8.31	0.004*
90th minute	121.57	6.58	117.23	7.97	0.025*
120th minute	121.53	6.63	115.73	8.31	0.004*
180th minute	123.20	7.81	116.23	9.52	0.003*
240th minute	122.87	12.52	115.20	8.58	<0.001*
360th minute	125.40	10.40	117.97	8.94	0.004*
480th minute	122.50	5.49	121.33	9.35	0.558
600th minute	122.57	5.93	121.47	8.36	0.559
720th minute	122.40	6.67	123.20	7.68	0.668
840th minute	120.97	7.48	123.87	7.50	0.139
960th minute	120.83	6.33	122.73	10.91	0.413

1080th minute	122.57	5.93	121.47	8.36	0.559
1200th minute	118.87	6.79	121.87	7.01	0.097
1320th minute	119.76	6.47	121.20	7.24	0.422
1440th minute	120.80	6.64	122.10	7.26	0.472
Diastolic BP(mmHg)					
Baseline	79.46	7.24	80.93	12.60	0.582
5th minute	82.00	6.91	79.53	9.57	0.257
10th minute	80.46	6.79	78.90	9.70	0.472
15th minute	78.80	7.39	74.53	8.46	0.042*
30th minute	79.20	7.49	73.20	9.12	0.007*
60th minute	79.27	5.15	72.27	9.68	<0.001*
90th minute	79.60	5.26	73.20	10.36	0.003*
120th minute	79.27	5.14	72.27	9.67	<0.001*
180th minute	81.10	6.19	73.77	11.34	0.003*
240th minute	81.53	5.88	72.23	10.69	<0.001*
360th minute	83.13	5.61	73.50	9.77	<0.001*
480th minute	79.40	5.06	78.33	10.86	0.627
600th minute	80.00	5.90	77.37	9.37	0.198
720th minute	77.80	6.04	79.33	9.28	0.451
840th minute	77.73	5.47	81.10	9.79	0.106
960th minute	76.37	4.91	80.43	11.45	0.094

1080th minute	76.60	4.56	80.97	11.55	0.059
1200th minute	76.10	6.25	77.87	9.84	0.410
1320th minute	77.63	6.81	77.47	9.64	0.938
1440th minute	79.77	7.11	76.70	9.02	0.149
Mean arterial pressure(mmHg)					
Baseline	94.68	6.65	95.47	10.21	0.728
5th minute	96.80	6.51	94.27	8.33	1.195
10th minute	95.53	6.27	93.50	8.23	0.286
15th minute	93.57	7.12	89.37	7.11	0.026*
30th minute	93.47	7.19	88.17	7.68	0.008*
60th minute	93.40	5.11	86.73	8.73	<0.001*
90th minute	93.63	5.24	87.83	8.84	0.003*
120th minute	93.35	5.09	86.76	8.76	<0.001*
180th minute	95.13	6.12	87.92	10.37	0.001*
240th minute	95.31	6.29	86.56	9.62	<0.001*
360th minute	97.22	6.75	88.32	8.89	<0.001*
480th minute	93.77	4.80	92.67	9.91	0.586
600th minute	94.19	5.42	92.07	8.50	0.254
720th minute	95.02	7.91	93.96	8.24	0.611
840th minute	94.52	8.21	95.36	8.45	0.700
960th minute	91.30	4.50	94.47	10.11	0.122

1080th minute	91.80	4.39	94.47	9.96	0.185
1200th minute	90.36	5.83	92.53	8.23	0.242
1320th minute	91.68	6.15	92.04	8.41	0.847
1440th minute	93.44	6.51	91.84	7.88	0.395

P value < 0.05 was taken as statistically significant