

## Addition of Dexmedetomidine as an Adjuvant to Local Anesthetic Agent in Intravenous Regional Anesthesia

Vishwas Sathe<sup>1</sup>, Deepika Sathe<sup>2</sup>, Robin Gupta<sup>3</sup>, Kanha Agrawal<sup>4</sup>

<sup>1</sup>Professor, <sup>2</sup>Assistant Professor, <sup>3</sup>Senior Resident, <sup>4</sup>Senior Resident, Department of Anesthesia, MGM Medical College, Kamothe, Navi Mumbai, Maharashtra 410206, India.

### Abstract

*Aims and objectives:* To compare addition of dexmedetomidine as an adjuvant to local anesthetic agent in intravenous regional anesthesia. *Materials and Methods:* We conducted a prospective, randomized, double blind study, in which 50 patients undergoing posted for hand and forearm surgeries were enrolled for the study. Patients were randomly distributed in two Groups (25 in each Group). Group I - 25 patients were administered lignocaine (3 mg/kg) to total volume without adjuvant in IVRA. Group II - 25 patients were administered (1 mcg/kg) dexmedetomidine as an adjuvant to lignocaine (3 mg/kg) to total volume in IVRA. *Results:* Onset of sensory and motor block was hastened by the addition of Dexmedetomidine to local anesthetic agent. The mean time taken to achieve complete sensory block and motor block was maximum in control group as compared to Study Group. All patients in both the groups had excellent quality of surgical anesthesia, and duration of sensory and motor block was prolonged with the addition of Dexmedetomidine (1 mcg/kg) as compared to Control Group. The total duration of post-operative analgesia was highly significant with addition of Dexmedetomidine as compared to control group. *Conclusion:* All patients in both the Groups had excellent quality of surgical anesthesia, and duration of sensory and motor block was prolonged with the addition of Dexmedetomidine (1 mcg/kg) as compared to control group. The total duration of post-operative analgesia was highly significant with addition of Dexmedetomidine as compared to control group. Addition of Dexmedetomidine (1 mcg/kg) to lidocaine (3 mg/kg) as an adjuvant can be used safely.

**Keywords:** Dexmedetomidine; Lignocaine; Hemodynamic responses.

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### Introduction

Intravenous Regional Anesthesia (IVRA) is a simple and reliable method of providing anesthesia for hand and forearm surgeries. The administration of IVRA only requires the skill necessary to perform a venipuncture but IVRA does not provide effective anesthesia and post-operative analgesia.<sup>1</sup> To improve the quality of IVRA and post-operative

analgesia, addition of various drugs to local anesthetics has been investigated.<sup>2-5</sup> Recently, *alpha*<sub>2</sub>-adrenergic receptor (adrenoceptors) agonists have been the focus of interest for their sedative, and analgesic and peri-operative sympatholytic and cardiovascular stabilizing effects.<sup>6</sup>

Studies investigating the addition of clonidine to local anesthetic solution in IVRA have demonstrated reduced tourniquet pain and improved post-

**Corresponding Author:** Deepika Sathe, Assistant Professor, Department of Anesthesia, MGM Medical College, Kamothe, Navi Mumbai, Maharashtra 410206, India.

**E-mail:** manishkkn1120@gmail.com

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operative pain relief without adverse effects but did not influence the speed or quality of Bier's Block.<sup>7</sup> Dexmedetomidine, an imidazole compound, is the pharmacologically active dextroisomer of medetomidine. It is a potent *alpha*<sub>2</sub>-adrenoceptor agonist with eight times higher affinity for *alpha*<sub>2</sub>-adrenoceptor than clonidine, shown to improve the quality of anesthesia, tourniquet pain and reduce post-operative analgesic requirement.<sup>8,9</sup>

Various studies have shown that small doses of intravenous dexmedetomidine can enhance sensory and motor anesthesia with few side effects.<sup>10</sup> The present study is designed to evaluate and compare safety, efficacy and feasibility of addition of dexmedetomidine (1 mcg/kg) with lignocaine (3 mg/kg) (up to volume of 40 ml solution diluted with normal saline) and to find out prolongation of analgesia and side effects, if any.<sup>11-13</sup>

### Aims and Objectives

The aim of this study was to compare addition of dexmedetomidine (1 mcg/kg) as an adjuvant to lignocaine (3 mg/kg) with control group for Intravenous Regional Anesthesia (IVRA) in terms of efficacy, time of onset of sensory block, motor block and regression of sensory and motor block and total duration of sensory and motor block, quality of anesthesia, hemodynamic effects, side effects and complications, duration of post-operative analgesia and need for rescue analgesia.

### Materials and Methods

After approval by hospital research ethics committee, informed, written consent for anesthesia was taken. 50 patients posted for hand and forearm surgeries with ASA Grade I or II in age group (20 yr-60 yr) were included for the study. Patients with ASA Grade III and above, allergy to study drugs, patients taking other sedative drugs, pregnant patient, patients with history of any cardiac, pulmonary, liver, neuro-psychiatric diseases, patients with history of any coagulation disorders, Raynaud's disease, Sickle cell anemia were excluded from the study. The study was carried out from January 2012 to November 2013, at Mahatma Gandhi Mission Medical College and Hospital, Kamothe, Navi Mumbai.

Group I - 25 patients were administered lignocaine (3 mg/kg) to total volume of 40 ml without adjuvant in IVRA. Group II - 25 patients were administered (1 mcg/kg) dexmedetomidine as an adjuvant to lignocaine (3 mg/kg) to total volume

of 40 ml in IVRA. The patients were randomly divided into two Groups as designated above and demographic data were noted. Baseline vital parameters were noted. Two Intravenous (I.V.) cannula were inserted, one (22G) in the operative hand as distal as possible and the other (20G) in the non-operative hand for infusion and drug administration. A double tourniquet was positioned on the operative arm. The operative extremity was exsanguinated by elevation and wrapping it with a 10 cm Esmarch bandage. The proximal tourniquet was inflated by 100 mm Hg more than systolic BP to a minimum of 250 mm Hg and the Esmarch bandage was removed. Circulatory isolation of the operative arm was confirmed by inspection of the hand and by the absence of the radial pulse. The Bier's block was achieved by using (3 mg/kg) lignocaine diluted with saline to a total volume of 40 ml in the control group (Group I) and (1 mcg/kg) of dexmedetomidine + (3 mg/kg) lignocaine diluted with saline to a volume of 40 ml in Group II. IVRA solution were administered slowly through I.V. cannula over 3 mins. After sensory and motor blocks was achieved, the distal tourniquet was inflated to 250 mm Hg, the proximal tourniquet was released I.V. cannula if operative hand removed and patient was handed over to surgeons. At the end of operation, the tourniquet was deflated by cyclic deflation technique, and tourniquet deflation time should not be less than 1 hr after injecting IVRA. Failure of block was managed by supplemental I.V. opioids. If total failure of block occurs, general anesthesia was given. Majority of complications occur due to leaking tourniquet which can be prevented by confirming adequate tourniquet pressure and deflation of the tourniquet at the end of surgery was done by cyclic deflation technique. Complications due to local anesthetic toxicity were watched for and treated accordingly.

### Statistical Analysis

All the collected data was entered in Microsoft Excel sheet and then transferred to SPSS software ver. 17 for analysis. Qualitative data was presented as frequency and percentages and analysed using Chi-square test. Quantitative data was presented as mean and SD and compared by *t*-test. *p*-value < 0.05 was taken as level of significance.

### Results

G1 = Group 1

G2 = Group 2

**Table 1:** Demographic profile

Age group	Groups		Total
	G1	G2	
20 to 30 years	10 (40%)	16 (64%)	26 (52%)
30 to 40 years	5 (20%)	4 (16%)	9 (18%)
40 to 50 years	6 (24%)	2 (8%)	8 (16%)
50 to 60 years	4 (16%)	3 (12%)	7 (14%)
<b>Total</b>	25 (100%)	25 (100%)	50 (100%)
Male	18 (72%)	22 (88%)	40 (80%)
Female	7 (28%)	3 (12%)	10 (20%)
<b>Total</b>	25 (100%)	25 (100%)	50 (100%)

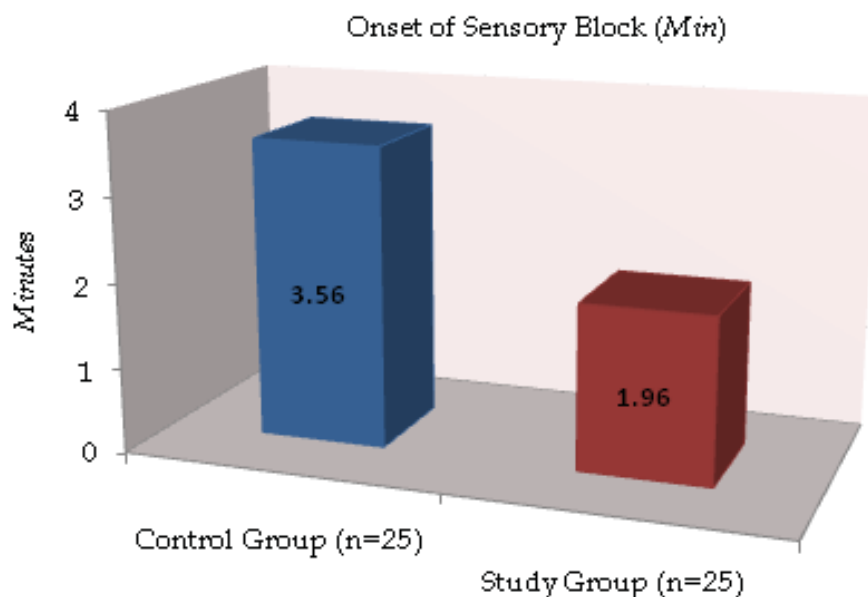
Majority of the patients were in age groups of 20–30 years. Majority of patients were males (80%). Males under 30 years formed majority of the study group, shown in Table 1. Table 2 shows as in Efficacy, time of onset of sensory block, motor block and regression of sensory and motor block and total duration of sensory and motor block, quality of anesthesia.

**Table 2:**

	Groups				p value
	G1		G2		
	Mean	SD	Mean	SD	
Onset of sensory block (minutes)	3.56	0.92	1.96	1.1	0.001
Onset of motor block (in minutes)	5.76	1.27	3.82	1.44	0.001
Regression of Sensory block (minutes)	4.04	0.72	6.44	1.43	0.001
Regression of Motor block (minutes)	6.36	0.8	9.56	1.8	0.001
Post-operative analgesia (in minutes)	25	6.61	234	40.62	0.001

Mean onset of sensory analgesia in G1 Group was at 3.56 mins, and in G2 Group it was 1.96 minutes. On application of (unpaired 't' test) for (p value < 0.05) for comparing G1 & G2, the difference was found to be statistically significant. Onset of sensory analgesia was faster in G2 than G1. Addition of dexmedetomidine as an adjuvant to IVRA hastens onset of sensory block, displays in Fig. 1. Mean onset of motor block in G1 was at 5.76 mins whereas in G2 was 3.82 mins. On application of (unpaired 't' test) for comparing G1 & G2 (p < 0.05), the difference was found to be statistically significant. Onset of motor block was faster in G2 than G1. Addition of dexmedetomidine as an adjuvant to IVRA hastens onset of motor block, displays in Fig. 2.

Mean time taken for regression of analgesia in G1 was 4.04 mins, and in G2 was 6.44 minutes. On application of (unpaired 't' test) (p < 0.05%) for comparing G1 & G2, the difference was found to be statistically significant. Time taken for regression of sensory analgesia was slower in G2 than by G1. Addition of dexmedetomidine as an adjuvant to IVRA delays regression of sensory block, displays in (Fig. 3). Mean regression time taken for recovery of motor block in G1 was 6.36 mins, and G2 was 9.56 minutes. On application of unpaired t-test (p < 0.05%) for comparing G1 & G2, and the difference was found to be statistically significant. Regression of motor block was slower in G2 than G1. Addition of dexmedetomidine as an adjuvant to IVRA delays regression of motor block, displays in Fig. 4.



**Fig. 1:** Onset of Sensory Block (Min) amongst different study population

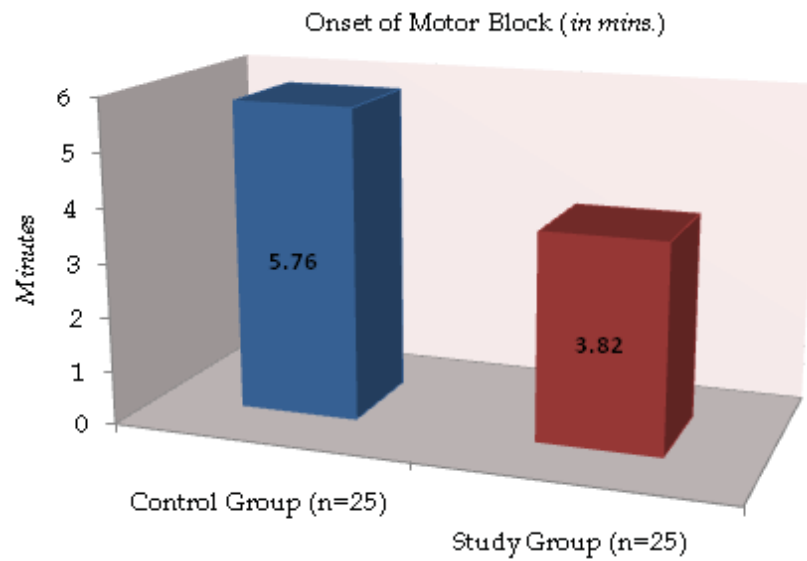


Fig. 2: Onset of Motor Block (Min) amongst different study population

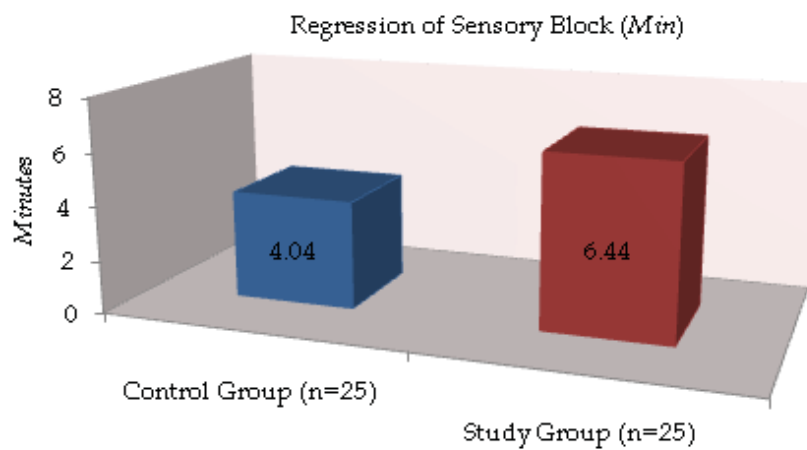


Fig. 3: Regression of Sensory Block (Min) amongst different study population

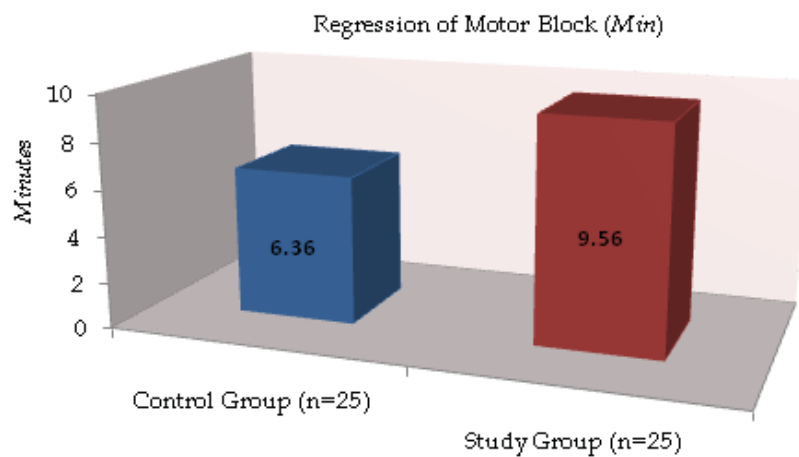


Fig.4: Regression of Motor Block (Min) amongst different study population

Mean duration of post-operative analgesia in G1 Group was 25 mins, and in G2 Group was 234 minutes. On application of (unpaired 't' test) ( $p < 0.05\%$ ) for comparing G1 & G2, the difference was found to be statistically significant. Total duration of post-operative analgesia in G2 is significantly longer than G1. Addition of dexmedetomidine as an adjuvant to IVRA prolongs the duration of post-operative analgesia significantly, displays in Fig. 5.

Pressure compared to the pre-operative values was regarded as hypotension. Mean fall in BP in both Groups was  $< 20\%$  of baseline value. On application of (unpaired 't' test) for comparing G1 & G2 the difference was found to be statistically insignificant. Addition of Dexmedetomidine in IVRA does not cause any significant alteration in Systolic Blood Pressure. Addition of Dexmedetomidine in IVRA does not cause any significant alteration in heart rate, displays in Fig. 7. Mean drop in heart rate was  $< 20\%$  of baseline line value. On application of (unpaired 't' test) for comparing G1 & G2 the difference was found to be statistically insignificant.

**Comparative study of intra-operative mean Systolic Blood Pressure and Heart rate**

Displays as in Fig. 6, A 20% decrease of Blood

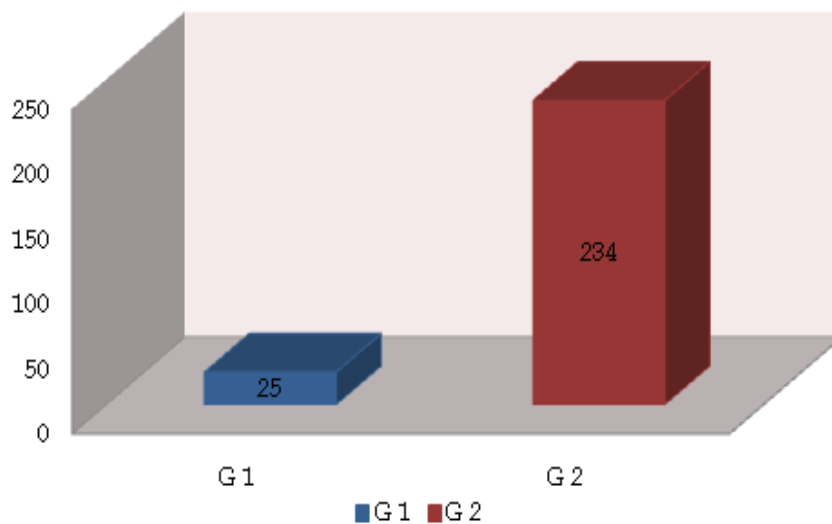


Fig. 5: Post-operative analgesia (Min) amongst different study population

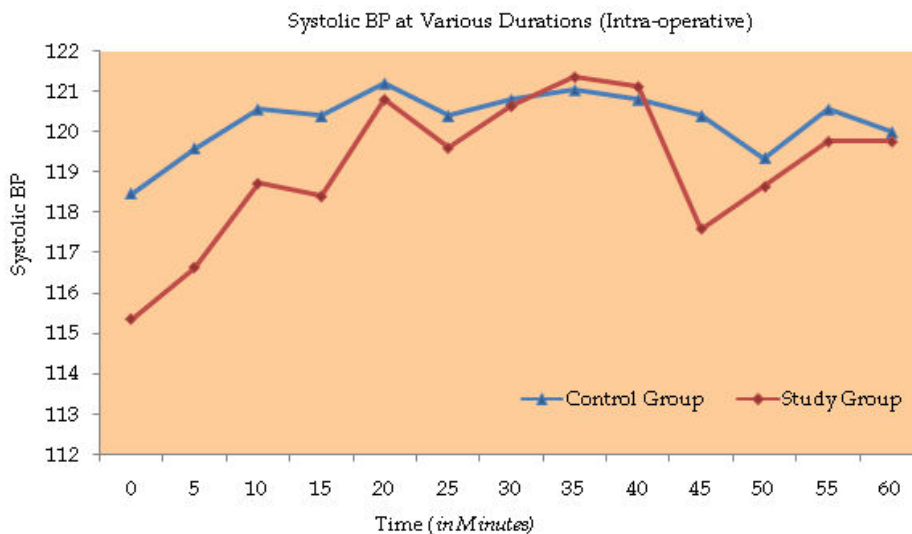


Fig. 6: Intra-operative Systolic BP amongst different study population at various time intervals

**Comparative Study of Post-operative mean Systolic Blood Pressure and Heart rate**

Mean drop in post-operative systolic BP was < 0% of baseline value, displays in Fig. 8. On application of (unpaired 't' test) for comparing G1 & G2 the difference was found to be statistically insignificant. We conclude that addition of Dexmedetomidine in IVRA does not cause any significant alteration

in blood pressure in post-operative period up to 24 hrs. Mean drop in heart rate in post-operative period was < 20% of baseline value, displays in Fig. 9. On application of (unpaired 't' test) for comparing G1 & G2 the difference was found to be statistically insignificant. We conclude that addition of Dexmedetomidine in IVRA does not cause any significant alteration in heart rate in post-operative period.

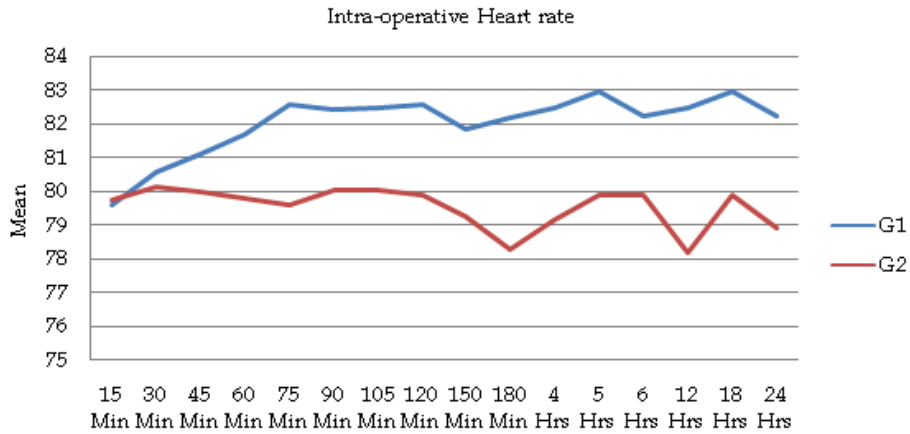


Fig. 7: Intra-operative heart rate amongst different study population at various time intervals

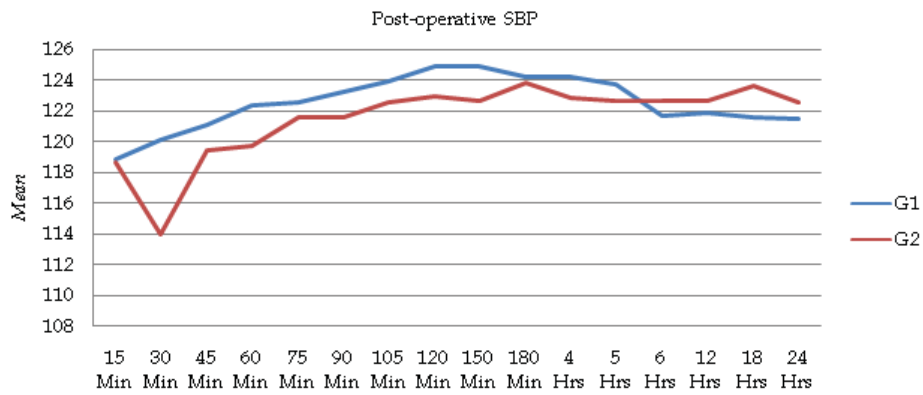


Fig. 8: Post-operative Systolic BP amongst different study population at various time intervals

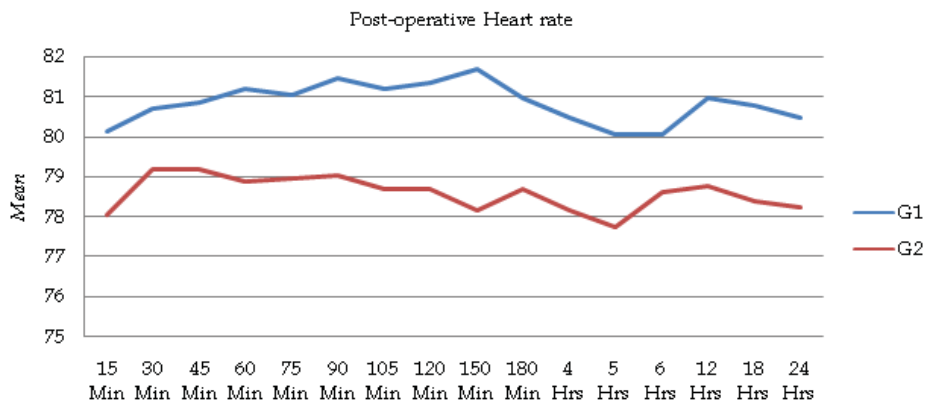


Fig. 9: Post-operative Heart rate amongst different study population at various time intervals



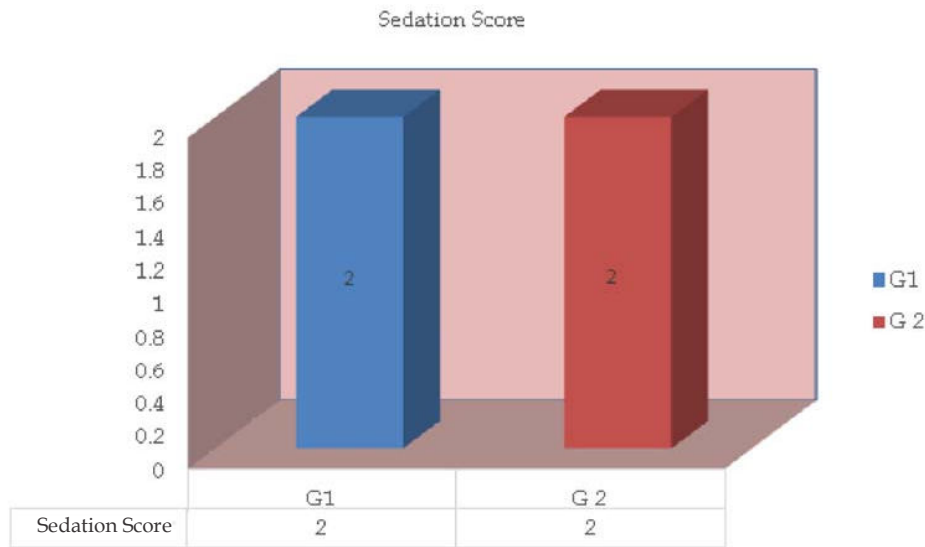


Fig. 10: Sedation score amongst different study population at various time intervals

**Intra-operative and Post-Operative sedation score**

Sedation score was monitored intra-operatively at interval of 5 mins and post-operatively at interval of 15 mins. for first 2 hrs. and thereafter, up to 24 hrs according to Ramsey Sedation Scale, displays in (Fig. 10).

In our study, the post-operative sedation score according to Ramsey scale was comparable in both the control and study groups. In post-operative period, all the patients in both the groups were cooperative, alert, oriented and tranquil with sedation score of 2/6. Addition of dexmedetomidine in IVRA does not cause any intra operative and post-operative sedation after deflation of tourniquet, shown as in (Table 3).

Table 3: Intra-operative and Post-operative Complications

Complications	Groups		Total
	G1	G2	
None	25 (100%)	22 (88%)	47 (94%)
Bradycardia	0 (0%)	1 (4%)	1 (2%)
Hypotension	0 (0%)	2 (8%)	2 (4%)
Total	25 (100%)	25 (100%)	50 (100%)

In our study, we came across a few complications. 2 out of 25 patients in G2 had hypotension and 1 out of 25 patients in G2 had bradycardia after release of tourniquet. Treatment of complications among the patients, none was excluded from the study because of technical failure or inadequate block. None of the patients had CNS or respiratory depression after tourniquet deflation. None of the patients required rescue analgesics intra-operatively in either of

the Groups. The incidence of Complications in both Group are not significant. Addition of Dexmedetomidine as an adjuvant to IVRA does not give rise to any significant complications.

**Discussion**

Modern surgical procedures require fast and effective regional anesthesia techniques, such as intravenous regional anesthesia. Intravenous regional anesthesia provides safe and effective care for patients undergoing upper extremity surgery when the surgical procedure last for less than 1 hr. However, use of this technique is limited by the development of tourniquet pain and by the absence of analgesia after tourniquet release. Pre-operative Dexmedetomidine administration decreases the requirements for opioids or non opioids analgesic both intra- and post-operatively.<sup>14</sup>

Our study demonstrated that the addition of Dexmedetomidine, in dose of 1 mcg/kg of body weight, to lignocaine for IVRA not only improved quality of anesthesia and post-operative analgesia without causing significant side effects but also shortened the onset of sensory and motor block as compared to placebo.

**Onset of sensory block**

In our study mean, time for onset of sensory block in G1 was 3.56 + 0.92 mins as compared to study Group G2 which was 1.98 + 1.1 mins. Comparison between G1 & G2 was statistically significant by

(unpaired 't' test), showing that the addition of Dexmedetomidine (1 mcg/kg) hastens the onset of sensory block. Similar results were observed in a study conducted by A Esmoğlu *et al.*<sup>15</sup> who added dexmedetomidine (1 mcg/kg) as adjuvant to lignocaine in study group and compared it with plain lignocaine for IVRA. They observed that onset of sensory block was significantly faster in group receiving dexmedetomidine as adjuvant in comparison with control group. Another study conducted by Dilek Memis *et al.*<sup>16</sup> found similar results. They compared two groups, with study group receiving 0.5 mcg/kg of dexmedetomidine as an adjuvant to IVRA. They observed that the onset of sensory block was faster in group receiving dexmedetomidine as an adjuvant.

Alok Kumar *et al.*<sup>17</sup> in his study compared 72 patients undergoing hand surgery who were randomly assigned to three groups to receive IVRA. They received 20 ml of 1% lignocaine with either 1 ml of isotonic saline or (0.5 mg/kg) ketamine or (1 mcg/kg) dexmedetomidine. He observed that onset of sensory block was shortened in the Ketamine Group followed by Dexmedetomidine Group.

#### **Onset of motor block**

In our study mean, time for achieving motor block in G1 was  $5.76 + 1.27$  min. as compared to  $3.82 + 1.44$  mins. in G2 Group. Comparison between G1 & G2 was statistically significant by using (unpaired 't' test) showing that addition of dexmedetomidine (1 mcg/kg) to lignocaine (3 mg/kg) as adjuvant hastens the onset of motor block. Similar results were observed in a study conducted by Dilek Memis *et al.*<sup>16</sup> who added dexmedetomidine (0.5 mcg/kg) as adjuvant to lignocaine in study group and compared it with plain lignocaine for IVRA. They observed that onset of motor block was significantly faster in group receiving dexmedetomidine as adjuvant in comparison with control group. Another study conducted by A Esmoğlu *et al.*<sup>15</sup> found different results. They compared study group receiving (1 mcg/kg) of dexmedetomidine as an adjuvant with control group of lignocaine (3 mg/kg). They observed that the onset of motor block was slower in group receiving dexmedetomidine as an adjuvant. Alok Kumar *et al.*<sup>17</sup> in his study compared 72 patients undergoing hand surgery who were randomly assigned to three groups to receive IVRA. They received 20 ml of 1% lignocaine with either 1 ml of isotonic saline or (0.5 mg/kg) ketamine or (1 mcg/kg) dexmedetomidine as an adjuvant. He observed that onset of motor block was faster in the Ketamine Group than Dexmedetomidine Group followed by control Group.

#### **Regression of sensory block**

Sensory regression time was noted by pin prick method at every 30 sec interval and was defined as time interval between tourniquet deflation to recovery of pinprick sensation in all dermatomes. In our study, in the Control Group G1 mean time for regression of sensory block was  $4.04 + 0.72$  mins. as compared to Study Group G2 which was  $6.44 + 1.43$  mins. This comparison was statistically significant by using (unpaired 't' test) showing that the addition of dexmedetomidine (1 mcg/kg) to (3 mg/kg) lignocaine delays the time to regression of sensory block. Similar results were observed in a study conducted by A. Esmoğlu *et al.*<sup>15</sup> who added dexmedetomidine (1 mcg/kg) as adjuvant to lignocaine in study group and compared it to plain lignocaine for IVRA. They observed that regression of sensory block was slower in group receiving dexmedetomidine as adjuvant in comparison with control group. Another study conducted by Dilek Memis *et al.*<sup>16</sup> found similar results. They compared two groups with study group receiving (0.5 mcg/kg) of dexmedetomidine. They observed that the regression of sensory block was faster in study group than control group.

#### **Regression of motor block**

In our study, in the Control Group (G1) mean time for regression of motor block was  $6.36 + 0.8$  mins. as compared to Study Group (G2) which was  $9.56 + 1.8$  mins. These comparison were statistically significant by using (unpaired 't' test) showing that the addition of dexmedetomidine (1 mcg/kg) to (3 mg/kg) lignocaine delays the time to regression of motor block. Similar results were observed in a study conducted by A. Esmoğlu *et al.*<sup>15</sup> who added dexmedetomidine 1 mcg/kg as adjuvant to lignocaine in study group and compared it to plain lignocaine for IVRA. They observed that regression of motor block was significantly slower in group receiving dexmedetomidine as adjuvant in comparison with control group. Another study conducted by Dilek Memis *et al.*<sup>16</sup> found similar results. They compared two groups with study group receiving (0.5 mcg/kg) of dexmedetomidine. They observed that the regression of motor block was slower in group receiving dexmedetomidine as an adjuvant.

#### **Post-operative analgesia**

Assessment of post-operative analgesia was done by using Visual Analogue Scale (VAS) score. Total duration of analgesia was monitored up to 4 hrs post using Visual Analogue Scale. It is the



standard tool for rating of pain using a 0–10 scale (0 = no pain, 10 = worst possible pain) and time of 1<sup>st</sup> rescue analgesia was noted. In our study, in the Control Group (G1) mean time for post-operative analgesia was 25 + 6.61 mins. Compared to Study Group (G2) receiving 1 mcg/kg dexmedetomidine as an adjuvant mean time for post-operative analgesia was 234 + 40.62 mins.

On comparison between G1 & G2 this difference in post-operative analgesia time was statically significant by using One-way Anova and showed that addition of dexmedetomidine 1 mcg/kg delays the time taken for 1<sup>st</sup> rescue analgesia. Study conducted by Dilek Memis *et al.*<sup>16</sup> found similar results. They compared two groups with study group receiving (0.5 mcg/kg) of dexmedetomidine. They observed that the need for post-operative analgesia was prolonged in group receiving dexmedetomidine as an adjuvant. Alok Kumar *et al.*<sup>17</sup> in his study observed that time to first analgesic requirement was significantly longer in dexmedetomidine group after tourniquet release as compared to ketamine/control group.

### Cardiovascular changes

The common cardiovascular changes noted intra-operatively and after release of tourniquet were hypotension and bradycardia. Systolic Blood Pressure and Heart Rate (HR) were recorded every 5 mins intra-operatively and post-operatively at intervals of 15 mins up to 4 hrs and at every 1 hr thereafter. till 24 hrs. A 20% decrease of Blood Pressure compared to the pre-operative values was regarded as hypotension. HR lower than 55 beats/min was regarded as bradycardia. In our study, a fall in systolic blood pressure was observed in 2 pts. in study group (G2) after release of tourniquet. This can be explained probably by entry of blood into operative limb in 2 patients after release of tourniquet leading to fall in blood pressure. A fall in heart rate was also observed in 1 patient in study group (G2) after release of tourniquet but comparison between both groups were statistically insignificant.

Acute dexmedetomidine I.V. administration produces abrupt hypertension and bradycardia until the central sympatholytic effects dominate resulting in moderate decrease in both MAP and HR from baseline, and it also has a sedative effect. Studies conducted by Alok Kumar *et al.*<sup>17</sup> found that there were no hemodynamic changes observed with use of dexmedetomidine in IVRA. Similar studies were conducted by A Esmoğlu *et al.*<sup>15</sup> and they also did not find any changes in hemodynamic status of patients.

### Respiratory rate

Respiratory depression was defined as respiratory rate less than 10 breaths per minute. No incidence of respiratory depression was noted in our study, oxygen saturation was maintained around 97%–100% in both the groups.

### Post-operative sedation score

In our study, the post-operative sedation score according to Ramsey scale was comparable in both the control and study groups. In post-operative period, patients in both the groups were co-operative, alert, oriented and tranquil with sedation score of 2/6. Similar results were found in the study conducted by D Memis *et al.*<sup>16</sup> Whereas studies conducted by Alok Kumar *et al.*<sup>17</sup> and A. Esmoğlu *et al.*<sup>15</sup> found sedation score values higher in study group than control group. This was explained by central effect of dexmedetomidine after tourniquet deflation.

### Complications

In our study, we came across few complications, out of three patients who received (1 mcg /kg) dexmedetomidine as an adjuvant in intravenous regional anesthesia two of them had hypotension and one patient had bradycardia after deflating tourniquet. Two patients in G2 group who had received dexmedetomidine (1 mcg/kg) as an adjuvant to lignocaine had met with hypotension after deflating tourniquet which was treated with Inj Mephentramine (6 mg) I.V. and crystalloid infusion. One patient in G2 group who had received dexmedetomidine (1 mcg/kg) as an adjuvant to lignocaine had met with bradycardia after deflating tourniquet and required atropine (0.6 mg). None of the patients had respiratory depression, oral tingling, dizziness or any other complications. On the whole frequency of complications was very less. All the patients were satisfied with this type of anesthesia.

### Conclusion

Our study demonstrated that onset of sensory and motor block was hastened by the addition of Dexmedetomidine to local anesthetic agent. The mean time taken to achieve complete sensory block, motor block was maximum in control group as compared to study group. All patients in both the groups had excellent quality of surgical anesthesia, and duration of sensory and motor block was prolonged with the addition of Dexmedetomidine

(1 mcg/kg) as compared to control group. The total duration of post-operative analgesia was highly significant with addition of Dexmedetomidine as compared to control group. No incidence of any accidental deflation of tourniquet occurred and in two patients we observed bradycardia, and in one patient we observed hypotension after deflating tourniquet with Dexmedetomidine. Addition of Dexmedetomidine (1 mcg/kg) as an adjuvant to lidocaine (3 mg/kg) can be used safely for early onset and delayed regression of motor and sensory block with prolonged post-operative analgesic effect with minimal side effect. Since, total duration of post-operative analgesia is 234 mins in study group and 25 mins in control group with minimal side effects. We conclude that addition of Dexmedetomidine (1 mcg/kg) to lidocaine (3 mg/kg) as an adjuvant can be used safely.

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