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Comparative Evaluation of Adjuncts, Clonidine versus Dexmedetomidine to Lignocaine In Intravenous Regional Anesthesia (IVRA) For Upper Limb Orthopedic Surgeries.

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Abstract:
Background*: Intravenous Regional Anesthesia (IVRA) provides reliable and rapid anesthesia of the extremities distal to the tourniquet, but tourniquet pain and absence of post-operative analgesia are major disadvantages. Hence the present study, to compare the α2 agonists, clonidine and Dexmedetomidine as adjuncts to IVRA with respect to block characteristics, tourniquet pain and post-operative analgesia was conducted as these (α2 agonists) are known to potentiate peripheral nerve blocks.*
Patients and Methods*: In this prospective randomized, double-blind study, 60 patients of ASA-I and ASA-II, undergoing upper limb orthopedic surgeries were randomly allocated into two groups, each of 30 patients. Group-I received Clonidine1µg/kg and Group-II received Dexmedetomidine 1µg/kg dissolved in 40ml of 0.5% of preservative-free lignocaine. Statistical analysis of data i.e. demographic, hemodynamic and block characteristics was done by using various analytical tests and p- value of< 0.005 was considered statistically significant.*
Results: *Intra-operative Visual-Analogue Scale (VAS) at 5min, 10 min, 15min, 20min and 40min and post-operative VAS at 2hrs and 4hrs and 12hrs were significantly higher in group-I (clonidine group). Sensorimotor block onset was significantly faster and recovery delayed with group-II (Dexmedetomidine group) as compared to group-I (clonidine group). Duration of analgesia was significantly longer with group-II (Dexmedetomidine group). Demographic data, hemodynamic parameters, fentanyl consumption and sedation were comparable among the two groups.*
Conclusion: *Dexmedetomidine significantly facilitates onset, prolongs recovery of sensory and motor block as well as duration of post-operative analgesia as compared to clonidine. Patient satisfaction was better in Dexmedetomidine group; however, patients of both groups have comparable intra-operative fentanyl requirement and both decrease tourniquet pain satisfactorily.*
Keywords: *Clonidine, Dexmedetomidine, Fentanyl, Intravenous regional anesthesia (IVRA),Visual Analogue Scale (VAS)*

I. Introduction

Intravenous regional anesthesia (IVRA) or Bier′s block is an ideal technique for short operative procedures on extremities, performed on day-care basis. The advantages of the IVRA are high indices of reliability, rapid onset of analgesia and good muscular relaxation. However, the disadvantage of IVRA is application of a tourniquet throughout procedure and duration of surgery is limited by the time during which the tourniquet could be safely inflated. Another disadvantage is the absence of post operative analgesia[1].

Advancements in the field have been primarily aimed at increasing tourniquet tolerance, improving overall quality of intra-operative, post-operative analgesia and minimizing the drug-related adverse effects. In an attempt to improve peri-operative analgesia, various methods have been used, which include supplementation by narcotics and non-steroidal anti-inflammatory drugs, either systemically or as adjuvant to IVRA. However, none of these methods have been proven as ideal[1,2].

Clonidine enhances peripheral nerve blocks of local anesthetics by selectively blocking Aδ and C-fibres. Dexmedetomidine, a potent α2 adrenoceptor agonist, is approximately 8 times more selective towards α2 adrenoceptors than clonidine[2].

In the present study, we have evaluated and compared the effects of adding clonidine or dexmedetomidine to lignocaine for IVRA in upper limb orthopedic surgeries.

II. Patients And Methods

After obtaining approval from the institutional ethical committee and informed consent for incorporating into the study from each patient, 60 patients of either sex and belonging to ASA-I and ASA-II,

who were scheduled to undergo elective upper limb orthopedic surgeries, were randomly allocated to one of the two groups (each having 30 patients).

GROUP-I received 0.5% lignocaine 40ml with 1µg/kg of clonidine. 0.5% lignocaine was constituted by adding 30 ml of NS with clonidine 1µg/kg to 10 ml of preservative-free 2% lignocaine.

GROUP-II received 0.5% lignocaine 40ml with 1µg/kg of dexmedetomidine. 0.5% lignocaine was constituted by adding 30ml of NS with dexmedetomidine 1µg/kg to 10ml of preservative-free 2% lignocaine.

Patients with coagulation disorders, peripheral vascular diseases, sickle cell anemia, allergy to any study drug and patients on adrenoceptor agonist or antagonist therapy were excluded. At the time of pre-operative visit, Visual Analogue Scale (VAS) scoring system was explained to all patients.

On arrival to the holding up area of operating room, monitoring was attached (ECG, NIBP, SPO2, HR) and baseline parameters recorded. Wide-bore intravenous (IV) cannula was established on the unaffected limb and IV fluid started with crystalloid solution. No premedication given.

A 22-gauge IV cannula was inserted into the distal vein of the extremity to be operated. Cotton pad was applied to the affected arm and two tourniquets were applied over the cotton pad. The arm was exsanguinated using Esmarch bandage. Proximal tourniquet was inflated to 100mmHg above the patient´s systolic blood pressure. The absence of radial pulse and failure of the pulse-oximetry tracing in ipsilateral index finger was confirmed. 40ml of the 0.5% lignocaine with adjuvant was injected over 15 seconds by an anesthesiologist who was blinded to the study drug. The sensory block was assessed by pinprick with a 22-gauge short- beveled needle every 30 seconds. Patient´s response was evaluated in dermatomal sensory distribution of medial and lateral cutaneous, ulnar, median and radial nerves. Motor function was assessed by asking the patients to flex and extend the wrist and fingers and complete motor block was noted when no voluntary movement was possible. Sensory block onset time was noted as time elapsed from injection of study drug to sensory block achieved in all dermatomes and motor block onset time was noted as time elapsed from injection of study drug to complete motor block.

Once sensory and motor block confirmed, distal cuff was inflated to 250mmHg, followed by deflation of proximal tourniquet and surgery started. Vital parameters like, HR, NIBP, ECG and SPO2 were recorded before tourniquet inflation and every 5 minutes till the procedure was finished. Assessment of tourniquet pain score was made by VAS scoring between 0 to 10 (0- no pain and 10- worst pain) and sedation was assessed by Ramsay sedation score before tourniquet inflation and at 5min, 10min, 15min, 20min and 40min after the injection of anesthetic agent. Intra-operatively IV boluses of fentanyl 1µg/kg were given for tourniquet pain when required (VAS>3) and total fentanyl consumption was recorded.

At the end of procedure, tourniquet deflation was performed by cyclical deflation technique; however, tourniquet was not deflated before 30 min and was not inflated for more than 1hr and 30 min. Sensory recovery time (time elapsed after tourniquet deflation up to recovery of sensation in all dermatomes) was determined by pinprick test. Complete recovery of motor power was assessed by asking the patients to flex and extend wrist and fingers at 30s intervals. Complete motor recovery was recorded when all voluntary movements were shown at the end of surgery and after removal of tourniquet.

Vital parameters (HR, NIBP), sedation score and VAS were recorded at 30 min after deflation of tourniquet and at 2hr, 4hr, 6hr, 12hr and 24 hr after tourniquet deflation. Patients were given Ketorolac 30 mg IM once they complained of pain in PACU (Post-anesthesia Care Unit). Duration of analgesia was the time elapsed between tourniquet deflation and the first time patient complaining of pain necessitating Ketorolac IM injection. If no analgesic was necessary within 24hrs, the duration of analgesia was considered 1440 min.

Patients satisfaction score was recorded post-operatively after 24hrs as; 5-very satisfied, 4-satisfied, 3-neutral, 2- dissatisfied and 1-very dissatisfied. It was based on patient´s subjective assessment of the quality of anesthesia. During the study period, any local or systemic complications were recorded.

Statistical analysis of data was performed, using various statistical tests. Independent samples t-test was used for evaluation of demographic data, hemodynamic parameters, block characteristics, duration of surgery and tourniquet, onset of tourniquet pain, duration of analgesia and intra-operative analgesic requirements. Mann-Whiteney U-test was used for VAS, sedation scores and patient satisfaction score. $p<0.005$ was considered as statistically significant.

III. Results

The demographic profile, baseline hemodynamic parameters, duration of surgery, duration of tourniquet inflation, intra-operative and post-operative hemodynamic parameters among both the groups were more or less comparable and were statistically insignificant. [Table 1]

Table 1: Demographic profile, Baseline vital signs and Surgical characteristics among the two groups.

Data/ Parameters	Group-I(Clonidine) (n=30)	Group-II(Dexmedetomidine) (n=30)
Age(yrs) Mean ±SD	41.75±10.62	39.42±11.21
Sex(M:F)	19:11	18:12
Weight(kg) Mean ±SD	65.21±8.81	63.92±9.24
ASA (I:II)	25:5	23:7
Baseline HR(beats per minute) Mean ±SD	76.36±9.38	75.61±10.11
Baseline MAP(mmHg) Mean ±SD	96.29±7.32	97.42±6.82
Surgical Duration(minute) Mean ±SD	52.84±8.52	54.69±7.92
Tourniquet Duration(minute) Mean ±SD	58.63±7.91	59.13±8.10

Abbreviations: HR-Heart Rate, MAP- Mean Arterial Pressure, SD- Standard Deviation.

There was a significant difference in both groups with respects to mean onset and recovery of sensory and motor block. Sensory block onset and recovery were 7.52±2.01min and 5.90±1.91min respectively in Group-I (Clonidine group) and 4.93 ±1.57min and 7.81 ±1.72min respectively in Group-II (Dexmedetomidine group) p<0.001. Motor block onset and recovery were 12.31 ±2.15min and 6.81 ±1.12 respectively in Group-I and 7.91 ±1.92min and 10.41 ±1.51min respectively in Group-II (p<0.001). [Figure I&II]

Intra-operative VAS score was significantly higher in Group-I (Clonidine) at 5min, 10 min, 15 min, 20min and 40 min than in Group-II (Dexmedetomidine) p<0.001. [Figure-III]

During post-operative period, VAS score was significantly higher at 2hrs and 4hrs and 12hrs in Group-I than in Group-II [Figure-IV]. However, the rescue analgesia, fentanyl consumption was more or less comparable in both groups, with 70.15 ±15.5µg in group-I and 66.25±18.30µg in group-II.

There was statistically insignificant difference among two groups with respect to intra-operative and post-operative sedation, as assessed by Ramsay sedation score.

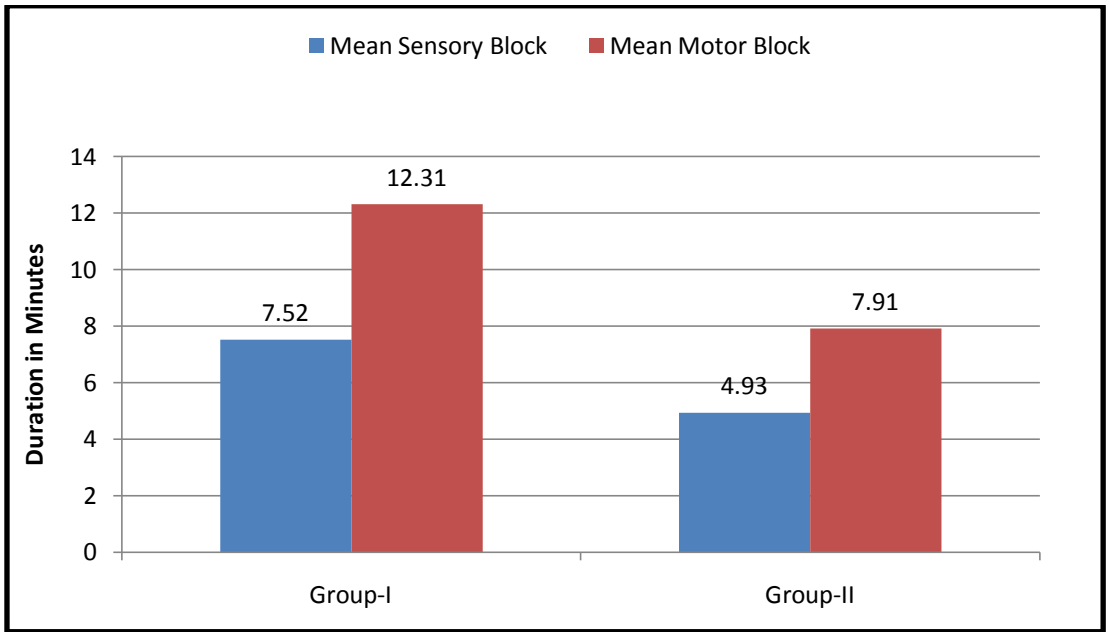

Figure-I: Comparison of Onset of Sensory and Motor Blocks.

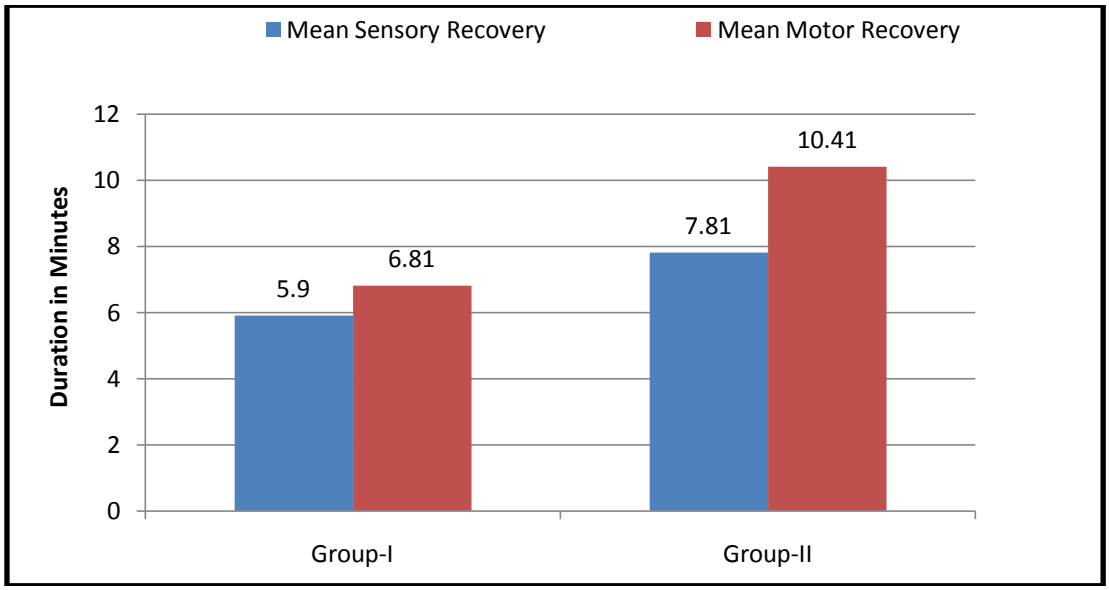

Figure-II: Comparison of Recovery of Sensory and Motor Blocks.

The mean duration of analgesia, based on the time of request for first dose of rescue supplemental analgesia (VAS≥3) in Group-I (Clonidine) was 601.20 ±599.55min, while in Group-II (Dexmedetomidine) it was 1208 ±560.11min, which was significantly longer in Group-II ($p<0.001$). [Figure-V]

IV. Discussion

IVRA provides analgesia in the distal part of a limb by intravenous injection of a local anesthetic solution into the vein of the same limb, while the circulation to the limb is occluded by application of tourniquet. The duration of surgery is limited by the time during which the arterial tourniquet could be kept inflated safely. Tourniquet pain, described as a dull and aching pain sensation, is a well-known limitation. Skin compression, tourniquet size and inflation pressure have been implicated, but the exact mechanism remains unclear. Another disadvantage with this technique is the absence of post-operative analgesia. Different agents have been used as adjuncts to local anesthetics for IVRA, including NSAID´s, opioids, muscle relaxants, phencyclidines, neostigmine and magnesium [3,4]. However, none of these agents have been demonstrated as an ideal adjuvant.

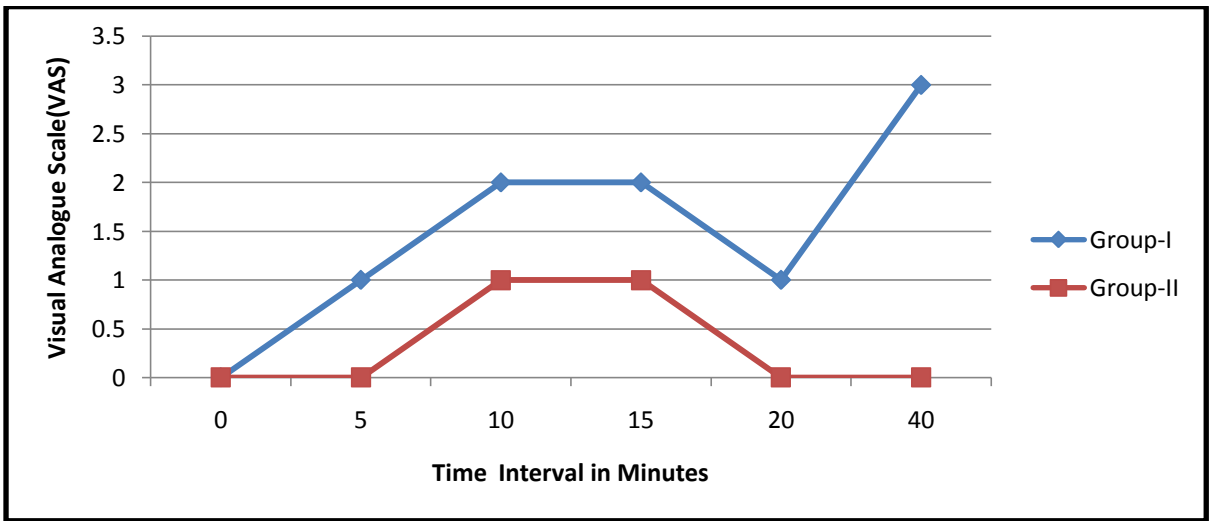

Figure-III: Comparison of intra-operative VAS score at different time intervals.

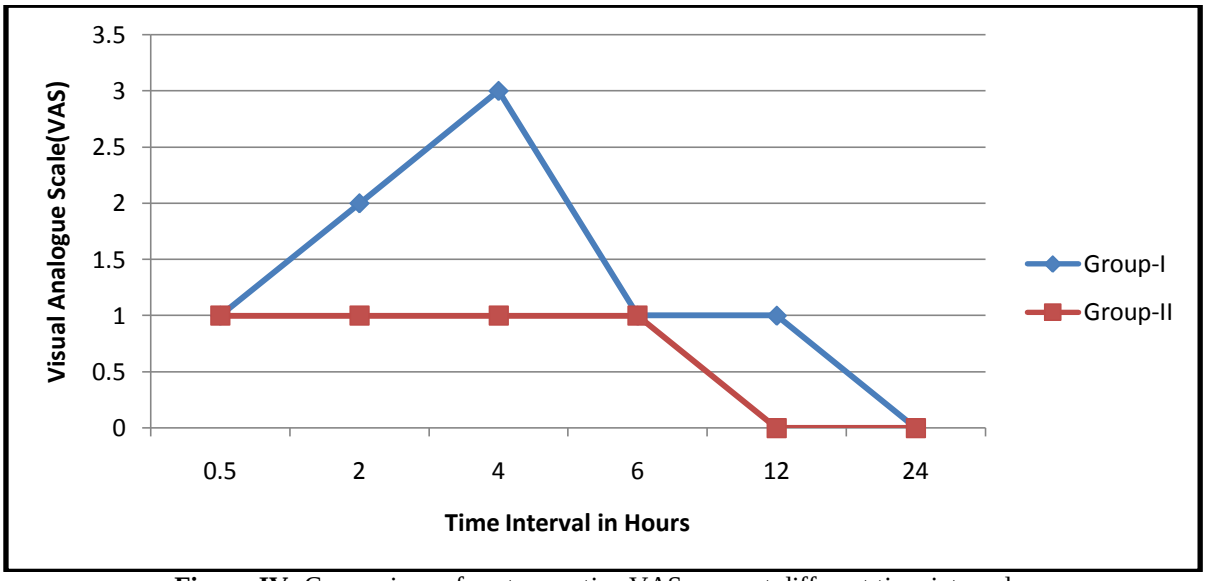

Figure-IV: Comparison of post-operative VAS score at different time intervals.

The pharmacological properties of α2 agonists (which we have used in our present study) include sedation, analgesia, anxiolysis, peri-operative sympatholysis, cardiovascular stabilising effects, decreased anesthetic requirements and preservation of respiratory functions, have been extensively studied and clinically employed in regional anesthesia[5,6]. Dexmedetomidine is 8-10 times more selective towards α2 adrenergic receptors and is 3.5 times more lipophilic than clonidine. It thus prolongs the duration of both sensory and motor blockade induced by local anesthetics, irrespective of the route of administration[7,8,9].

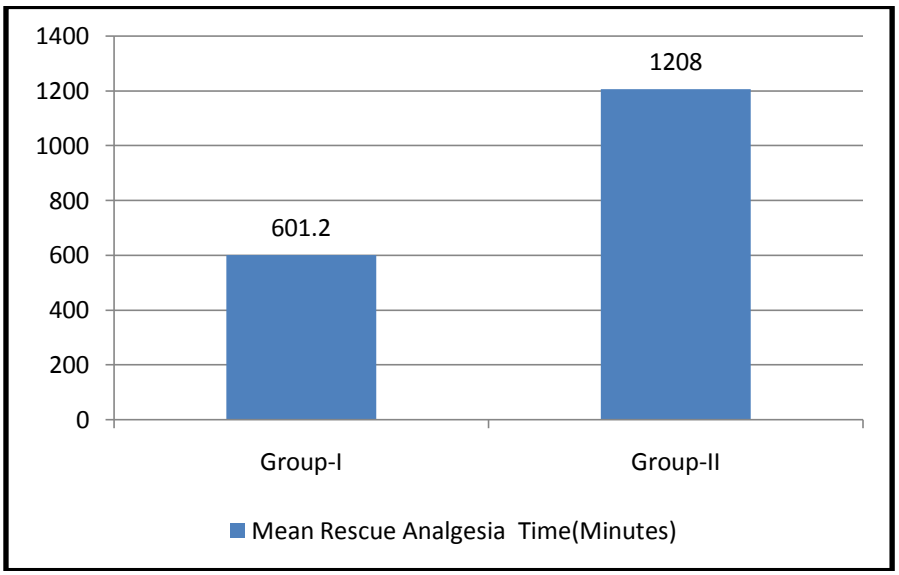

Figure-V: Comparison of Mean Rescue Analgesia Time (Minutes) among two groups.

Gupta et al, in their study with two different doses of dexmedetomidine as an adjuvant to IVRA have concluded that addition of 1µg/kg of dexmedetomidine to lignocaine improves quality of anesthesia and post-operative analgesia as compared to 0.5µg/kg of dexmedetomidine[10]. So we used 1µg/kg of dexmedetomidine and compared it with 1µg/kg of clonidine in our study.

In our study, the onset of sensory and motor block was significantly shortened and recovery was prolonged by addition of dexmedetomidine to lignocaine as compared to clonidine. The duration of analgesia was longer in Group-II (Dexmedetomidine group). This could be attributed to more selective action of dexmedetomidine on α2 adrenergic receptors and its more lipophilic nature as compared to clonidine[7].

Addition of dexmedetomidine to lignocaine for IVRA has been shown to improve quality of anesthesia by various previous studies [1-11]. Dexmedetomidine enhances the local anesthetic action of lignocaine via α2 adrenoceptors[12]. Peri-operative dexmedetomidine administration decreases the analgesic requirements, both intra-operative and post-operative[13]. Intravenous dexmedetomidine, as a premedication, was effective because it

reduces patient anxiety, sympatho-adrenal responses and opioids analgesic requirements, but it did not reduce tourniquet pain [14, 15]. In our study, the patient satisfaction score was significantly better with dexmedetomidine than with clonidine.

Tourniquet pain and lack of post-operative analgesia are major drawbacks of IVRA. Various studies have shown that addition of clonidine to lignocaine in IVRA decreases tourniquet pain and improves post-operative analgesia [16-17]. Clonidine has also been reported to depress nerve action potentials especially in C-fibres by a mechanism independent of the stimulation of α2 adrenergic receptors [18]. *Momis et al*, in their study have concluded that addition of dexmedetomidine to lignocaine in IVRA attenuates tourniquet pain and reduces the fentanyl requirements [11].

In our study, the intra-operative and post-operative differences in VAS scores in the two groups could be attributed to the pharmaco-kinetic differences between clonidine and dexmedetomidine. The duration of post-operative analgesia was significantly higher with Group-II (Dexmedetomidine) as compared to Group-I (Clonidine). Most of the patients in Group-II (Dexmedetomidine) did not demand analgesia or complain of pain for 24hrs post-operatively. Alpha-2 adrenergic receptors located at nerve endings may have a role in the analgesic effect of the drugs by preventing norepinepherine release. The effect is more pronounced with dexmedetomidine as it is more selective and a complete agonist at these receptors [7]. Clonidine and dexmedetomidine have been compared in various studies as adjuncts to local anesthetics [19, 20]. *Swami et al*, concluded that dexmedetomidine prolongs duration and enhances quality of sensorimotor block as compared to clonidine as an adjuvant to bupivacaine in peripheral nerve blocks [21].

Both the adjuncts did not cause significant sedation in the present study. This is in accordance with study conducted by *Momis et al*[11]. Other studies have shown significant sedation with dexmedetomidine [1, 22]. Also, we in our study did not observe any side effect in both study groups. Dexmedetomidine administration produces abrupt hypertension and bradycardia till the central sympatholytic effects dominates, resulting in moderate decrease in both MAP and HR from baseline [19]. In our study, no such hemodynamic changes were observed with the use of clonidine or dexmedetomidine in IVRA. This could be explained by the cyclical deflation of tourniquet, done in our study, which prevents sudden release of drugs in the systemic circulation.

V. Conclusions

Dexmedetomidine when added to lignocaine for IVRA significantly facilitates onset and prolongs the recovery of sensory and motor block as compared to clonidine. Both α2 adrenoceptor agonists decrease tourniquet pain without any associated hemodynamic instability or other significant side-effects. Block quality, duration of post-operative analgesia and patient satisfaction were better with dexmedetomidine group.

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