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COMPARISION OF CLONIDINE AND DEXMEDETOMIDINE AS ADJUVANTS TO INTRAVENOUS REGIONAL ANAESTHESIA – A PROSPECTIVE RANDOMISED CONTROL STUDY

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ABSTRACT **Background and Aims:** Intravenous regional anaesthesia (IVRA) provides reliable and rapid analgesia with good muscular relaxation of the extremity distal to the tourniquet, but tourniquet pain and absence of post-operative analgesia are major drawbacks. α2 agonists, clonidine and dexmedetomidine are known to potentiate peripheral nerve blocks. The aim of this study was to compare clonidine and dexmedetomidine as adjuvants to IVRA with respect to block characteristics, tourniquet pain and post-operative analgesia. Methods: A prospective, randomised, double-blind study was conducted on 60 adult patients of American Society of Anesthesiologists physical status grades I and II, in two groups of 30 eac, to receive either clonidine 1 µg/kg or dexmedetomidine 1 µg/kg added to 40 ml 0.5% preservative-free lignocaine. Independent samples t-test was used for analysing demographic data, haemodynamic data and block characteristics and Mann– Whitney U-test for skewed data. Results: Sensorimotor block onset was significantly faster and recovery delayed with dexmedetomidine as compared to clonidine. Intra-operative visual analogue scale (VAS) at 10 min, 15 min and 40 min and post-operative VAS at 30 min and 2 h were significantly higher with clonidine. Fentanyl consumption and sedation were comparable. Duration of analgesia was significantly longer with dexmedetomidine. Haemodynamic parameters were comparable. **Conclusions:** Dexmedetomidine significantly facilitates onset, prolongs recovery of sensory as well as motor block and also prolongs duration of analgesia as compared to clonidine. Both decrease tourniquet pain satisfactorily and have comparable intra-operative fentanyl requirement. Patient satisfaction is better with dexmedetomidine

KEYWORDS : Clonidine, dexmedetomidine, fentanyl, intravenous regional anesthesia

INTRODUCTION

Intravenous regional anaesthesia (IVRA) or bier's block is an ideal technique for short operative procedures on extremities, performed on day care basis. The advantages of IVRA are high indices of reliability, rapid onset of analgesia and good muscle relaxation. The disadvantage is application of tourniquet throughout the procedure. The duration of surgery is limited by the time during which the tourniquet is safely inflated.another drawback is the absence of post operative analgesia. Advancements in this field have been primarily aimed at increasing the tourniquet tolerance, improving the overall quality of intra operative and post operative analgesia and reducing drug related adverse effects. In an attempt to improve peri operative analgesia, various methods have been used, which include supplementation by narcotics and NSAIDS, either systemically or as adjuvants to IVRA. However none of them has been proven as ideal. Clonidine enhances peripheral nerve blocks of local anaesthetics by selectively blocking Ad and C fibers. Where as Dexmedetomidine, a potent α2 receptor agonist, is approximately 8 times more selective towards α2 receptors than clonidine. 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.

MATERIAL AND METHODS:

A comparative prospective double blinded study study was conducted in government general hospital, Rangaraya medical college ,Kakinada over a period of July 2022 to December 2022. After attaining ethical committee approval 60 subjects were taken for the study with ASA grade I and II aged between 25-55 years belonging to both the genders.

INCLUSION CRITERIA:

- Patients of either sex
- Patients belonging to ASA grade l and ll
- Age between 18 and 60 years
- Patients scheduled for forearm and hand surgeries in the distal region of upper limb

EXCLUSION CRITERIA:

- Patients belonging to ASA grade lll and lV
- Patients who are allergic to study drugs
- Patients with peripheral vascular disease, sickle cell anaemia, significant cardiovascular disease, psychiatric disease
- Patients with crush injury or open wound

At pre-operative visit, the visual analogue scale scoring system was explained along with nature and safety of procedure. Written, valid, informed consent was taken.

Sample size calculation was done on the basis of previous study. The primary outcome was taken as pain free period and assuming 85% of study power and 5% α error, the minimum sample size was calculated to be 27 patients per group. Therefore 30 patients in each group were planned.

Patients were assigned randomly into each group in a double blind manner.

1) Group C received lignocaine with clonidine (1 µg/kg)
2) Group D received lignocaine with Dexmedetomidine (1 µg/kg)

The lignocaine used in this study was 0.5%(10ml of 2% lignocaine was added to 30ml of normal saline) preservative free and constant(200mg) in both the groups. To make the total volume of test solution 40ml, 0.9% normal saline was added.

On arrival to operating room, starvation was confirmed. No premedication was given. Patient's baseline pulse rate, ECG and non invasive blood pressure were recorded. A wide bore intravenous line was established on unaffected limb and infusion was started with lactated Ringer's solution.

A 22 gauge IV cannula was inserted into the distal vein of extremity to be operated. cotton pad was applied to the arm. Two torniquets were placed over the cotton pad. The arm was exsanguinated using Esmarch bandage. The proximal torniquet was inflated to 100 mm hg above the patient's systolic blood pressure. The absence of the radial artery pulsations and failure of the pulse oximetry tracing in ipsilateral index finger was confirmed. 40 ml of test solution was injected over 10 seconds by an anesthesiologist who was blinded to the study drug.

The sensory block was assessed by pinprick with a 22 gauge short bevelled needle every 30 sec. patients response was evaluated in dermatomal sensory distribution of medial and lateral cutaneous, median, ulnar, radial nerves.

Motor function was assessed by asking the patient 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.Motor block onset time was noted as the time

elapsed from injection of study drug to complete motor block.
After sensory and motor block were achieved, distal cuff was inflated to 250 mm hg, followed by release of proximal tourniquet and the surgery was started.

Mean arterial pressure (MAP), heart rate(HR) and arterial oxygen saturation were monitored before torniquet application and at 5, 10, 15, 20, 40min and 60min after the injection of study drugs.

Assessment of tourniquet pain scores was made by VAS between 0 and 10 (0 – " no pain " and 10 – " worst pain imaginable ") and sedation was assessed by RAMSAY sedation score before tourniquet application and at 5, 10, 15, 20, 40min and 60min after the injection of anaesthetic. Intra operatively, intravenous boluses of fentanyl (1 mcg/kg) were given for tourniquet pain when required (VAS > 3), and total fentanyl consumption was recorded.

The tourniquet was not deflated before 30min and was not inflated for more than 1 hr and 30min. At the end of surgery tourniquet was deflated by a cyclic deflation technique.

Sensory recovery time (time elapsed after tourniquet deflation up to recovery of sensation in all dermatomes) was determined by pin prick test. Complete motor recovery was recorded when all the voluntary movements were shown at the end of surgery and after the removal of tourniquet.

MAP, HR, VAS and the degree of sedation values were recorded 30 min after tourniquet removal and 2, 4, 6, 12 and 24 hrs after tourniquet deflation.

Post operatively patients received diclofenac 75mg IM if VAS was > 5. the duration of analgesia was the time elapsed between tourniquet release and the first IM intake of diclofenac.

QUALITY OF ANAESTHESIA

At post operative period , the anaesthesiologist was asked to qualify the operative conditions according to the following numeric scale
4 = excellent (no complaint from patient)
3 = good (minor complaint with no need for supplemental analgesic)
2 = moderate (complaint that required supplemental analgesic)
1 = unsuccessful (patient was given general anaesthesia)

Patient satisfaction score was recorded post operatively after 24 hrs as
5 – very satisfied
4 – satisfied
3 – neutral
2 – dissatisfied
1 – very dissatisfied

It was based on the patient's subjective assessment of quality of anaesthesia.

STATISTICAL ANALYSIS

The sample size was chosen after reviewing many randomized control studies on the same subject. The statistical evaluation was performed using SPSS version 20.0 (IBM). Independent sample t-test was used for evaluation of demographic data, hemodynamic data, block characteristics, duration of surgery and tourniquet, duration of anlgesiaand intra operative analgesic requirement.

Mann – whitney U-test was used for VAS, sedation scores and patient satisfaction scores. $P < 0.05$ was considered statistically significant.

RESULTS AND OBSERVATION:

Both groups were comparable with respect to age, sex, weight, base line heamodynamic vitals, duration of surgery, duration of tourniquet inflation and intra operative and post operative hemodynamic variables.

TABLE 1 : Comparison of Demographic variables HR - heart rate ; MAP - mean arterial pressure ; SD – standard deviation

Data /parameter	Clonidine(n=30)	Dexmedetomidine (n=30)	P value
Age (years)	42.63±11.51	37.47±11.41	0.086
Sex (male:female)	18:12	19:11	0.999
Weight (kg)	60.10±9.67	61.06±9.81	0.702
Baseline HR(/min)	80.37±7.95	76.7±8.46	0.089
Baseline MAP(mmhg)	92.13±5.62	90.40±5.59	0.236
Surgical duration(min)	68.67±6.222	67.37±6.886	0.446
Tourniquet duration(min)	73.97±6.228	72.07±6.523	0.253

There was a significant difference in both groups with respect to mean onset and recovery of sensory and motor block. Sensory block onset and recovery were 6.18 ± 1.07 min and 5.1 ± 1.12 min, respectively in Group C and 4.28 ± 1.23 min and 7.3 ± 1.49 min, respectively in Group D. Motor block onset and recovery were 11.27 ± 1.66 min and 6.9 ± 0.84 min, respectively in Group C and 8.63 ± 1.86 min and 9.53 ± 1.07 min, respectively in Group D.

Table 2 : Onset regression of sensory and motor blockade

	Group C	Group D	P value
Sensory block onset	6.18±1.07	4.28±1.23	0.004
Motor block onset	11.27±1.66	8.63±1.87	0.001
Sensory block recovery	5.1±1.12	7.3±1.49	0.003
Motor block recovery	6.9±0.84	9.53±1.07	0.005

Figure 1 : Comparison of onset of sensory and motor block

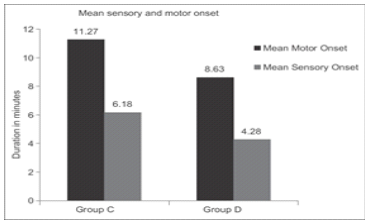
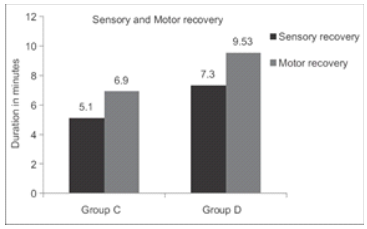


Figure 2: Comparison of recovery of sensory and motor block



The intra-operative VAS score was significantly higher in Group C at 10 min, 15 min and 40 min than in Group D (P = 0.001). During post-operative period, VAS score was significantly higher at 30 min and at 2 h in Group C . However, the fentanyl consumption in both groups was comparable. There was no statistically significant difference in the two groups with respect to intra-operative and post-operative sedation as assessed by Ramsay sedation score. The maximum sedation score achieved was 2, that is, awake but drowsy at around 15-20 min in both groups.

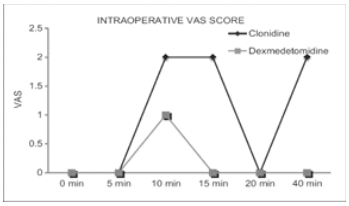
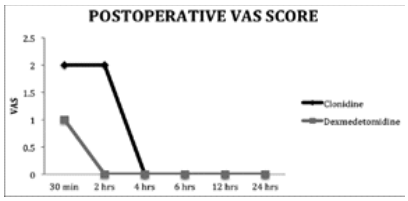
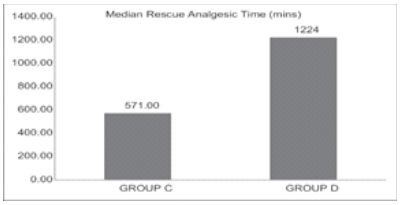


Figure 3: Comparison of postoperative VAS score



The mean duration of analgesia, based on time for request of first dose of supplemental analgesic, was significantly longer in Group D ($P < 0.001$) . The patient satisfaction was significantly higher in Group D ($P = 0.003$).



None of the patients had significant bradycardia or hypotension so as to require any intervention

DISCUSSION

IVRA provides analgesia in the distal part of a limb by intravenous injection of a local anaesthetic solution into the vein of the same limb, while 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 safely inflated. Tourniquet pain, described as a dull and aching pain sensation, is a well-known limitation. Another drawback with this technique is the absence of post-operative analgesia. Different agents are used as additives to local anaesthetic for IVRA, including phencyclidines, non-steroidal anti-inflammatory drugs, opioids, muscle relaxants, neostigmine and magnesium; however, none of them have demonstrated a clear advantage.

The pharmacological properties of α2 agonists, which include sedation, analgesia, anxiolysis, peri-operative sympatholysis, cardiovascular stabilising effects, reduced anaesthetic requirements and preservation of respiratory function, have been extensively studied and clinically employed in regional anaesthesia. Dexmedetomidine is 8-10 times more selective toward 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 anaesthetics, irrespective of the route of administration.

Gupta et al. conducted a study with two different doses of dexmedetomidine as an adjunct in IVRA and concluded that addition of dexmedetomidine 1 μg/kg to lignocaine improves quality of anaesthesia and post-operative analgesia in comparison to 0.5 μg/kg. We used 1 μg/kg dexmedetomidine and compared it with 1 μg/kg clonidine in our study.

Kol et al. suggested that addition of 0.5 μg/kg dexmedetomidine had more potent effect, shortening sensory block onset time and prolonging sensory block recovery time more than lornoxicam in IVRA.

In our study, the onset of sensory as well as motor block was significantly shortened and recovery was prolonged by addition of dexmedetomidine to lignocaine as compared to clonidine. The duration of analgesia was significantly longer in the dexmedetomidine group. This could be attributed to more selective action of dexmedetomidine on α2 adrenergic receptors and its lipophilic nature as compared to clonidine. Clonidine is a partial agonist and dexmedetomidine is a complete agonist at the α2 adrenergic receptors. Addition of dexmedetomidine to lignocaine for IVRA has been shown to improve quality of anaesthesia in previous studies. Dexmedetomidine enhances the local anaesthetic action of lignocaine via α2A adrenoceptors. Peri-operative dexmedetomidine administration decreases the requirements for opioid or non-opioid analgesics both intra- and post-operatively. 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. Memis et al. concluded that addition of dexmedetomidine to lignocaine attenuated tourniquet pain and reduced the fentanyl consumption. In our study, the intra-operative and post-operative differences in VAS scores in the two groups could be attributed to the pharmacokinetic differences between clonidine and dexmedetomidine. Dexmedetomidine is 3.5 times more lipophilic and has 8 times more specificity for α2 receptors as compared to clonidine. Moreover, there was no significant difference in the fentanyl consumption in the two groups.

In the present study, we recorded the time for demand of rescue analgesic as a measure of post-operative analgesia. The duration of post-operative analgesia was significantly higher with dexmedetomidine as an adjuvant as compared to clonidine. Most of the patients who received dexmedetomidine did not demand analgesic or complain of pain for 24 h post-operatively. α2 adrenergic receptors located at nerve endings may have a role in the analgesic effect of the drugs by preventing norepinephrine release. The effect is more pronounced with dexmedetomidine as it is more selective and a complete agonist at these receptors. Swami et al. concluded that dexmedetomidine prolongs duration and enhances quality of sensorimotor block as compared with clonidine as an adjuvant to bupivacaine in peripheral nerve block.

Both the adjuvants did not cause significant sedation in the present study. This is in accordance with study conducted by Memis et al. Other studies have shown significant sedation with dexmedetomidine. Also, we did not observe any side effects in both the study groups. In our study, no haemodynamic changes were observed with the use of dexmedetomidine or clonidine in IVRA. This could be explained by the cyclical deflation of tourniquet done in our study, which prevented sudden release of drugs in the systemic circulation.

The limitation of our study is a small sample size, but it had significantly important results.

CONCLUSION

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

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