Addition of Dexmedetomidine to Low Dose Solution of Lidocaine for Intravenous Regional Anesthesia A Randomized Study

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ABSTRACT

Background and Aims: Intravenous Regional Anesthesia (IVRA) provides analgesia of distal part of limb by intravenous injection of local anesthesia in to the vein of the same limb, while the circulation to the limb is occluded by application of tourniquet. However, IVRA is limited by local anesthesia toxicity, tourniquet pain and absence of postoperative analgesia. Various additives to local anesthetics such as ketamine, clonidine, opioids, NSAIDs are used to address these issues. The aim of our study was to evaluate the effectiveness of Dexmedetomidine to low dose Lidocaine solution for IVRA.

Patients and Methods: A prospective, randomized double blind study was conducted on 60 patients divided in to two groups of thirty each; Group I patients received 40 ml of Lidocaine 0.25% while Group II patients received 40 ml of 0.25% of lidocaine mixed with 1 mcg/kg of dexmedetomidine. The motor and sensory block onset and recovery times were assessed. Tourniquet pain and sedation score were assessed intraoperatively and postoperatively.

Results: Sensory and motor block onset times were shorter and recovery times were prolonged in Dexmedetomidine group. The quality of anesthesia was better in the Dexmedetomidine group and the fentanyl dose required was also lower in the dexmedetomidine group. There was a significant difference in the postoperative analgesia time which was demonstrated by less use of intramuscular diclofenac in dexmedetomidine group.

Conclusions: A safe intravenous dose of lidocaine can be used for IVRA for superficial hand surgery, and the addition of 1 mcg /kg dexmedetomidine shortened the onset times for both sensory and motor blockade and improved the quality of anesthesia, with prolonged postoperative analgesia time. By adding dexmedetomidine we were able to reduce the dose of lidocaine to 0.25% concentration without compromising analgesia. JMS 2016; 19(1):21-25

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INTRODUCTION

Intravenous regional anesthesia (IVRA) or Bier's block was first introduced by August Bier, a German surgeon, in 1902.¹ IVRA is technically simple and reliable, with success rates between 94% and 98%.¹ IVRA is a type of regional anesthesia that is executed by using pressure to the proximal extremity with the use of a pneumatic tourniquet isolating the limb from systemic circulation. This anesthesia technique is considered easy with fast anesthesia induction, fast recovery, fast muscle relaxation, and with better ability to control anesthesia region. All these characteristics have made the technique an appropriate choice for open surgeries

with short duration (60-90 min) as well as for reduction of closed fractures.

No specific anatomic knowledge is required; intravenous regional anesthesia requires the anesthesiologists to only insert a needle or cannula into a suitable vein. The onset of analgesia is rapid so that surgery or manipulation may begin within 510 minutes and muscular relaxation is good. However, it has some limitations such as tourniquet pain, lack of postoperative analgesia, and local anesthetic toxicity in case of tourniquet malfunction.² Various additives to local anesthetics, such as opioids, non-steroidal anti-inflammatory drugs (NSAID), ketamine, atracurium, dexamethasone and clonidine are used.

Alpha-2-adrenergic receptor (adrenoceptor) agonists have been the focus of interest for their sedative, analgesic, and perioperative sympatholytic and cardiovascular stabilizing

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effects with reduced anesthetic requirements.³ Dexmedetomidine, a potent α -2- adrenoceptor agonist, is approximately 8 to 10 times more selective toward the α -2- adrenoceptors than clonidine. Dexmedetomidine has been shown to decrease anesthetic requirements by up to 90% and to induce analgesia in rats, volunteers, and patients.^{3,4} Use of high dose solutions can induce systemic toxicity in case of tourniquet malfunction or early deflation.

We designed this study to evaluate the effect of dexmedetomidine when added to low dose lidocaine solution in IVRA. We planned to investigate the sensory and motor block onset and recovery time, the quality of anesthesia, intraoperative and postoperative hemodynamic variables, intra-operative and postoperative pain, sedation, and the other side effects of dexmedetomidine.

Patients and Methods

This study was conducted after approval of hospital ethical and research committee. The procedure was explained to the patients and informed consent was obtained. Sixty ASA physical status grades I and II patients scheduled for surgery of the hand or the forearm (i.e., carpal tunnel release and tendon release) at King Abdullah Medical City Associated Hospital, Madina Munawara, were included in this study. Patients with Raynaud's disease, sickle cell anemia, or a history of allergy to any drug used were excluded from the study. Patients were divided into two groups of thirty each. Group I patients received 40 ml of Lidocaine 0.25%; group II patients received 40 ml lidocaine 0.25% with dexmedetomidine 1 mcg/kg. The study design was randomized and double-blinded. A randomization list was generated and identical syringes containing each drug were prepared by personnel blinded to the study, according to the list. After the patients had been taken to the surgery room, mean arterial blood pressure (MAP), peripheral oxygen saturation (SpO₂), and heart rate (HR) were monitored.

Before establishing the anesthetic block, two cannulas were placed: one 22-G cannula in a vein on the dorsum of the operative hand and the other 18-G cannula in the other hand for crystalloid infusion (Ringer lactate). The operative arm was elevated, then exsanguinated with an Esmarch bandage, and a pneumatic tourniquet was placed around the upper arm, and the proximal cuff was inflated to 250 mmHg. Circulatory isolation of the operative arm was verified by absence of radial pulse, and loss of pulse oximetry tracing of the ipsilateral index finger. IVRA solution was injected over

90 seconds by an anesthesiologist blinded to the drugs.

The sensory block was assessed by a pinprick performed with a 22-gauge short-beveled needle taken out continuously every 30 seconds after 6 minutes of injection. Patient response was evaluated in the dermatomal sensory distribution of the medial and lateral antebrachial cutaneous, ulnar, median, and radial nerves. Motor function was assessed by asking the subject to flex and extend his/her wrist and fingers, and complete motor block was noted when no voluntary movement was possible. Sensory block onset time was noted as the time elapsed from injection of study drug to sensory block achieved in all dermatomes, and motor block onset time was the time elapsed from injection of study drug to complete motor block.

After sensory block was achieved, the distal cuff was inflated followed by the release of the proximal tourniquet and the operative procedure was then started. MAP, HR, and SpO₂ were recorded before and after tourniquet application and then every 5 minutes after the injection of anesthetic. Hypotension (20% decrease from baseline blood pressure value) was treated with intravenous ephedrine (5 mg/ml bolus), and the total dose of ephedrine was calculated. Bradycardia (20% decrease from baseline value heart rate or <50 bpm) was treated with intravenous atropine 0.5 mg, and arterial oxygen desaturation (<94%) was treated with Oxygen supplementation through a nasal cannula.

Assessment of tourniquet pain scores was made on the basis of the visual analog scale (VAS) [0 = 'no pain' and 10 = 'worst pain imaginable'] and the degree of sedation (the Ramsay sedation scale 1- 6: 1 = patient is anxious and agitated or restless, or both; 2 = patient is cooperative, oriented, and tranquil; 3 = patient responds to commands only; 4 = patient exhibits brisk response to light glabellar tap or loud auditory stimulus; 5 = patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus; and 6 = patient exhibits no response) measured before and after tourniquet application, and 5, 10, 15, 20, 30, and 40 minutes after the injection of the anesthetic.⁽⁵⁾ Intraoperatively, boluses of 1 µg/kg fentanyl were provided for tourniquet pain treatment when required (when VAS was >3), and total fentanyl consumption was recorded. The tourniquet was not deflated before 30 minutes and was not inflated for more than 1 hour 30 minutes. At the end of surgery, tourniquet deflation was performed by cyclic deflation technique. Patients were instructed to receive 75 mg IM diclofenac once a day when VAS was >3, and total amounts of

diclofenac administered to each group were recorded. The duration of analgesia was the time that elapsed between tourniquet release and the first intramuscular intake of diclofenac.

Patient satisfaction score was recorded post-operatively after 24 hours as: 5 - very satisfied, 4 - satisfied, 3 - neutral, 2 - dissatisfied and 1 - very dissatisfied. It was based on patients' subjective assessment of the quality of anesthesia. During the study period, any local or systemic complications were recorded. All the measurements were performed by an anesthesiologist who was blinded to the medication administered.

Statistical Package for Social Sciences version 20.0 (IBM Corp., Armonk, NY, USA) software was used for data analysis. Independent samples t- test was used for evaluation of demographic data, hemodynamic data, block characteristics, duration of surgery and tourniquet, onset of tourniquet pain, duration of analgesia and intra-operative analgesic requirement. Mann-Whitney U-test was used for VAS, sedation scores and patient satisfaction score. $P < 0.05$ was considered statistically significant.

RESULTS

There were no significant differences concerning gender, age and the duration of operation between the two study groups (table 1). None of the patients was excluded from the study because of technical failure. No treatment was needed for hypotension or bradycardia in any patient.

Sensory and motor block onset time were statistically shorter ($p < 0.05$) in group II patients (table 2). The intra-operative VAS score for tourniquet pain after inflation at 5, 10, 15, 20, and 40 minutes was significantly higher in group I patients. The patient satisfaction score was higher in dexmedetomidine group (table 3).

Quality of anesthesia was significantly better in group II patients and the amount of fentanyl required during the procedure was significantly lower in group II patients ($p < 0.01$). The duration of postoperative analgesia was significantly longer in group II patients, the total amount of diclofenac required for post-operative analgesia was lower in group II patients (table 4).

There was statistically significant difference between groups in postoperative analgesic consumption (diclofenac), and duration of analgesia time in postoperative period (table 4). All the patients in group I

received additional analgesia, while only 8 patients in group II received additional analgesic in the postoperative period which was statistically significant ($p < 0.05$). There was no statistical difference between groups for sedation values at any intraoperative and postoperative period.

DISCUSSION

The pharmacological properties of α -2 agonists, which include sedation, analgesia, anxiolysis, peri-operative sympatholysis, cardiovascular stabilizing effects, reduced anesthetic requirements and preservation of respiratory function, have been extensively studied and clinically employed in regional anesthesia.^{9,10} Dexmedetomidine is 8-10 times more selective toward α -2 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.¹¹⁻¹³

Systemic toxicity of local anesthetics may be a life-threatening situation. It typically manifests as central nervous system (CNS) toxicity (tinnitus, disorientation, and ultimately, seizures) or cardiovascular toxicity (hypotension, dysrhythmias, and cardiac arrest). The dose capable of causing CNS symptoms is typically lower than the dose and concentration that results in cardiovascular toxicity. This is because the CNS is more susceptible to local anesthetic toxicity compared with the cardiovascular system.¹⁴

Our study demonstrated that the addition of 1 mcg/kg dexmedetomidine to lidocaine for IVRA allowed the use of a low-lidocaine dose to the safe intravenous dosage limit, as a consequence decreasing the likely risk of local anesthetic toxicity in case of malfunction or early release of the tourniquet. It also improved the quality of anesthesia, provided satisfactory intraoperative analgesia, and extended postoperative analgesia, with no side effects reported.

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 lidocaine only group. The duration of analgesia, assessed by time for requirement of rescue analgesic, was significantly longer in the dexmedetomidine group. This could be attributed to more selective action of dexmedetomidine on α -2 adrenergic receptors and its lipophilic nature and the

fact that dexmedetomidine is a full agonist at the α -2 adrenergic receptors.¹¹

Addition of dexmedetomidine to lignocaine for IVRA has been shown to improve quality of anesthesia in previous studies.^{15,16} Dexmedetomidine enhances the local anesthetic action of lignocaine via α -2A adrenoceptors.¹⁷ Peri-operative dexmedetomidine administration decreases the requirements for opioid or non-opioid analgesics both intra- and post-operatively.¹⁸ Intravenous dexmedetomidine as a premedication was effective because it reduced patient anxiety, sympathoadrenal responses and opioid analgesic requirements, but it did not reduce tourniquet pain.^{19,20} Even in our study, the patient satisfaction score was significantly better in dexmedetomidine group.

Acute dexmedetomidine IV administration produces abrupt hypertension and bradycardia until the central sympatholytic effect dominates, resulting in moderate decreases in both MAP and HR from baseline and it also has a sedative effect.²¹ The sedative, proanesthetic, and proanalgesic effects of dexmedetomidine at 0.52 μ g/kg given intravenously stem mainly from its ability to blunt the central sympathetic response. It also minimizes opioid-induced muscle rigidity, lessens postoperative shivering, causes minimal respiratory depression, and has hemodynamic stabilizing effect.²²

In previous clinical studies, clonidine has been used as an adjuvant for IVRA. Gentili et al,²³ were the first to report the efficacy of IVRA clonidine in decreasing tourniquet pain. Lurie et al,²⁴ evaluated the efficacy of clonidine at a dose of 1 mg/kg added to IVRA-lidocaine in decreasing the onset of severe tourniquet pain and found that it delayed the onset time. Gorgias et al,²⁵ found that the addition of clonidine to lidocaine for IVRA delayed the onset of unbearable tourniquet pain and decreased analgesic consumption for tourniquet pain relief. Atracurium and ketamine has been added to low dose lidocaine solutions for intravenous regional anesthesia by the author,²⁶ previously and demonstrated effectiveness of these additives to reduce the dose of lidocaine.

In our study, we observed that dexmedetomidine improved the quality of the anesthesia and decreased the postoperative analgesic requirements. This improvement in quality may be due to the peripheral action of the dexmedetomidine on the α -2-adrenergic receptor subtype, whereas less analgesic requirements and occurrence of sedation after release of the

tourniquet may be due to the central action of dexmedetomidine. Memis *et al*,²⁷ and Esmaoglu *et al*,²⁸ drew similar conclusions in their studies however Esmaoglu et al, did not show any differences in the sensory and motor block onset and regression times

between the two groups, although they also used 1 mcg/kg of dexmedetomidine. We demonstrated that the addition of 1 mcg/kg dexmedetomidine to lidocaine 0.25% for IVRA leads to a significant decrease in the sensory and motor block onset times. It was also found that sensory and motor block recovery times were significantly prolonged in this group. The results of our study are in agreement with those of Memis et al.²⁷

CONCLUSIONS

The addition of 1 mcg /kg dexmedetomidine to low dose lidocaine solution for IVRA shortens the onset times for both sensory and motor blockade, improves the quality of the anesthesia and extends postoperative analgesia time, and allows reduction of the lidocaine dose used for IVRA to the safe dose. It also allows early tourniquet deflation without causing adverse effects regardless of the tourniquet time.

REFERENCES

1. Brown EM, McGriff, Malinowski RW. Intravenous regional anaesthesia (Bier block): review of 20 years' experience. *Can J Anaesth* 1989; 36:307-10.
2. Johnson CN. Intravenous regional anesthesia: new approaches to an old technique. *CRNA* 2000; 11:57-61.
3. Kamibayashi T, Maze M. Clinical uses of alpha2-adrenergic agonists. *Anesthesiology* 2000; 93:1345-1349.
4. Aho M, Erkola O, Kallio A, Scheinin H, Korttila K. Dexmedetomidine infusion for maintenance of anesthesia in patients undergoing hysterectomy. *Anesth Analg* 1992; 75:940-946.
5. Ramsay MA, Savege TM, Simpson BR, Goodwin R. Controlled sedation with alphaxalone-alphadolone. *BMJ*. 1974;2:656659.
6. Turan A, Memis D, Karamanlioglu B, Guler T, Pamukcu Z. Intravenous regional anesthesia using lidocaine and magnesium. *Anesth Analg* 2002; 100:1189-92.
7. Turan A, Karamanlioglu B, Memis D, Kaya G,

- Pamukcu Z. Intravenous regional anesthesia using prilocaine and neostigmine. *Anesth Analg* 2002;95:1419-22.
8. Bigat Z, Boztug N, Hadimioglu N, Cete N, Coskunfirat N, Ertok E. Does dexamethasone improve the quality of intravenous regional anesthesia and analgesia? A randomized, controlled clinical study. *Anesth Analg* 2006; 102:605-9.
9. Bajwa SJ, Bajwa SK, Kaur J, Singh G, Arora V, Gupta S, et al. Dexmedetomidine and clonidine in epidural anaesthesia: A comparative evaluation. *Indian J Anaesth.* 2011; 55:11621.
10. Mahendru V, Tewari A, Katyal S, Grewal A, Singh MR, Katyal R. A comparison of intrathecal dexmedetomidine, clonidine.