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Original Article

Comparison of Analgesic effect of Dexmeditomidine and Paracetamol as Adjuvant with Lignocaine Hydrochloride for Intravenous Regional Anesthesia

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ABSTRACT

Objective: To compare and evaluate the analgesic effect of Dexmeditomidine and Paracetamol as adjuvant with lignocaine hydrochloride following upper limb surgeries.

Study Design: Quasi-experimental study

Place and Duration of Study: Combined Military Hospital, Rawalpindi, Allied Hospital, Faisalabad, Fauji Foundation Hospital, Rawalpindi Pakistan

Methodology: Sixty ASA physical status I and II patients undergoing upper limb surgery were included in this study. Patients were divided into three groups (n=20) in each group. Regional anesthesia was achieved with 3mg/kg of Lignocaine hydrochloride(L) (02%) in Group A (n=20). Group B received 3 mg/kg of Lignocaine hydrochloride plus Dexmedetomidine (D/L) 0.5 µg/kg. Group C (n=20) received 3 mg/kg of lignocaine hydrochloride plus 300 mg of paracetamol (P/L). Onset and recovery time of Sensory and motor blocks and post-operative pain using visual analogue score was evaluated.

Results: Group B showed significantly less sensory block onset time and motor block onset time as compared with Group A and Group C. Similarly, sensory block recovery time and motor block recovery time were significantly more in Group B compared to other groups. visual analogue score was significantly less in Group B in comparison with Group A and C. First postoperative analgesic request time was significantly longer in the Group B than in Group C.

Conclusion: It was concluded that Dexmedetomidine/Lignocaine hydrochloride provides better analgesia compared to paracetamol/Lignocaine hydrochloride in intravenous regional anesthesia.

Keywords: Dexmeditomidine, Intravenous regional anesthesia, Paracetamol, Postoperative analgesia.

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INTRODUCTION

In the current scenario of clinical practice, anesthetists prefer regional anesthesia upon general anesthesia to minimize recovery and post anesthesia complications.[1] Despite of advancement in the general anesthesia techniques and their safety profile, intravenous regional anesthesia (IVRA) is still preferable on general anesthesia for many surgical procedures.[2] IVRA is one of the oldest anesthesia technique still in use today. Its safety and utilization in many surgical procedures attest from more the 100 years of experience. Intravenous regional anesthesia (IVRA) is safe, technically simple, and cost-effective technique and can be a suitable alternative to brachial plexus block for upper limb surgeries of short duration as compared to general anesthesia with 94-98% success rates in limb surgeries.[3] Many local anesthetic agents for regional anesthesia have been reported in literature.[4] among these local anesthetic agents, lignocaine hydrochloride is an agent of choice due to its rapid onset of action and minimum complications.[5] The main problem with Intravenous regional anesthesia is its less duration of anesthesia, short postoperative analgesia, and tourniquet pain. To overwhelmed this problem, various adjuvants to lignocaine hydrochloride have been studied previously.[6] The greatest drawback of IVRA is its inability to provide postoperative analgesia when compared to peripheral nerve blocks. To overcome this situation, adjuvants such as opioids (fentanyl, sufentanil, morphine, pethidine, and tramadol) and nonsteroidal anti-inflammatory drugs (paracetamol, tenoxicam, and aspirin) have been used along with local anesthetic to prolong post-tourniquet deflation analgesia as well as to accelerate the onset of analgesia.[7] Addition of clonidine, the α2 adrenergic agonist, has shown to improve tourniquet pain tolerance, but has no effect on the onset or quality of analgesia. In addition, its effect of prolonging postoperative analgesia is controversial. Dexmedetomidine being more potent and selective adrenergic α2 agonist than clonidine may provide a better quality and longer

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duration of analgesia when used as an adjuvant for IVRA.[8] The primary outcome of the present study is to compare the quality of block, sensory and motor block characteristics, and duration of postoperative analgesia following IVRA with paracetamol anddexmedetomidine. The rationale of this study was to collate the efficacy of paracetamol and dexmeditomidine with lignocaine hydrochloride in Intravenous regional anesthesia as adjuvant and its adequacy of sensory and motor block and also compared the intra-operative and Post-operative analgesia and any other complications were also studied.

METHODOLOGY

After ethical committee acceptance the quasi-experimental study was conducted at Combined Military Hospital, Rawalpindi, Allied Hospital, Faisalabad, Fauji Foundation Hospital, Rawalpindi.

Inclusion Criteria: ASA physical status I–II patients planned for upper limb operation were included in the study.

Exclusion Criteria: Patients with debilitating illness, mentally incapacitated, or pregnant ladies, those allergic to the drugs and non-consenting individuals were also excluded from the study.

Patients were randomly allocated in three groups {A,b,C} with 20 patients (n=20) in each group. A list was generated randomly, and anesthetic drug was prepared in identical syringes by an anesthesia resident who is blind to this study. Patients were premeditated with intravenous midazolam (0.05 mg/kg) and atropine (0.01mg/kg) 45 minutes before the operation. within the operation theatre , vital signs (MAP, Spo2, Pulse) of the patients were monitored. Two IV. lines were placed, one was on the dorsal side of the operative hand and also the other within the opposite limb for IV Fluids. The operative arm was uplifted for two min so exsanguinated with an Esmarch bandage. A pneumatic double tourniquet was then fixed round the upper arm, and also the upper cuff was puffed up to 250mmHg. Circulatory isolation of the arm was jugged by inspection, absence of a pulse, and a loss of the pulse oximetry tracing within the same sided fore finger. IVRA was done with 3mg/kg of lignocaine hydrochloride (02% Lignocaine hydrochloride) mixed with saline to a complete of 40 mL in Group-1 (n_20), 3mg/kg of lignocaine hydrochloride plus dexmedetomidine 0.5µg/kg mixed with normal saline to a complete of 40 mL in Group-2 (n_20), and three mg/kg of lignocaine hydrochloride plus 300mg of paracetamol mixed with saline to a complete of 40mL in Group 3 (n_20). The solutions were prepared by an anesthesiology residentwho is blind to the current study. The solutions were injected over ninety seconds by an anesthesiologist blinded to the study drugs. After injection, sensory block was assessed with pinprick test every twenty seconds till the beginning of surgery with a 24-gauge pin within the different nerve-innervated territories of the hand and forearm.

Motor function was jugged by flexion and extension of the wrist and fingers of the hands of the patients; complete motor block was done when voluntary movement was not made by the patients. Sensory block onset time was the time from infusion of anesthetic drug to sensory block in innervated areas, and motor block onset time was the time from infusion of anesthetic agent to complete motor block After the complete sensory and motor blocks achievement the upper tourniquet was puffed up to 2.5 times the blood pressure, the lower tourniquet was released, and surgery was initiated. Mean arterial blood pressure, Heart Rate(pulse), Spo2(oxygen saturation) levels were noted pre and post tourniquet application and throughout the operation at different intervals (5,10, 15,20,30,40, and 50 min) and after deflation of the tourniquet by a post graduate resident, who was not involved in this research. Tourniquet Pain was evaluated by using a10-cm VAS). Sedation levels were evaluated by using Ramsey sedation scale as follows: (1) patient as anxious and agitated or restless, or both, (2) patient was 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. Both visual analogue score and sedation levels was noted pre and post tourniquet application and throughout the operation at different intervals (5, 10, 15, 20, 30, 40, and 50 min). If the patient reported visual analogue score more than 4, 0.1mg/kg of tramadol was given and requirement for analgesics (dose and time) was noted. During operation, 5mg intravenous ephedrine was given for hypotension (systolic blood pressure _90 torr or 50 torr not up to the conventional value), 0.5 mg intravenous atropine was given for bradycardia (HR_50/min), and 4mg intravenous ondansetron for nausea and vomiting. Oxygen was given with the help of face mask if Spo^2 (oxygen saturation) will not up to 92%. All these complications were also noted with regard to time. At the end of the surgery, the anesthesia standard was categorized by the anesthetist who was blinded to the

study drug as follows: (4) excellent(no complaint from the patient) (3); good, minor complaint with no need for supplemental analgesics (2); moderate, complaint that required a supplemental analgesic(1); unsuccessful, patient was given anaesthesia. Patient satisfaction was categorized as follows: (4) excellent, (3) good, (2) moderate, (1) poor. Surgical conditions and field dryness view was categorized by the surgeon who was blind to the study as follows: (3) perfect, (2) acceptable, (1) poor, (0) unsuccessful. The tourniquet wasn't deflated before 30 minutes and wasn't puffed up over two hours. At the end of operation,the tourniquet deflation was done by the cyclic deflation technique. Sensory recovery time was recorded (time lapsed after tourniquet deflation till the recovery of pain all the innervated areas determined by pinprick test performed every 30 seconds). Motor block recovery time was recorded (the time lapsed after tourniquet deflation up to finger's movement). First analgesic requirement time was also recorded (the time lapsed after tourniquet deflated to first patient request of analgesic). During the first two hours in the post anesthesia care unit and after that in the ward, patients were inquired by an anesthetist not involved in study for nausea and vomiting, skin rash, tachycardia, bradycardia, drop in blod pressure, hypertension, dizziness, tinnitus, hypoxia, and other complications were recorded if happened during the post-operative 24 hours within the ward.

Data were extracted using Mean±SD for quantitative variables and frequency and percentage for qualitative ones. Comparison between groups was made using analysis of variance (ANOVA) using prism graph pad software (version. 7). *p*-value below 0.05 was considered statistically significant.

RESULTS

The mean age of group A, B and C were 28.55± 9.22, 30.2±10.07 and 29.7±9.61 years, respectively (*p*= <0.0001). Average weight of group A, B and C patients were 67.35±8.08 kg, 69.8±8.14 kg and 70.2±8.37 kg, respectively (*p*=0.86). Group A consist of 29 males and 26 females; while group B consist of 22 males and 33 females (*p*=0.181). Total operation time was 48.5±8.15 minutes in A, 50.9±9.07 minutes in group A and 50.15± 9.20 minutes in group C (*p*=0.85). Mean sensory block onset time (SBOT) and mean sensory block recovery time (SBRT) in each group were shown in Table-I. Group B (Dexmeditomidine adjuvant with lignocaine hydrochloride) showed significantly less SBOT and MBOT (*p*=0.0045 and <0.0001) compared with group A (Lignocaine hydrochloride alone) and group C (Paracetamol adjuvant with lignocaine hydrochloride). Similarly, sensory block recovery time (SBRT) and motor block recovery time (MBRT) were significantly high in group B compared to other groups (*p*=< 0.0001, Sensory block onset time(SBOT), Sensory block recovery time(SBRT), Motor block onset time(MBOT), Motor block recovery time(MBRT), First postoperative analgesia required time(FPOART)

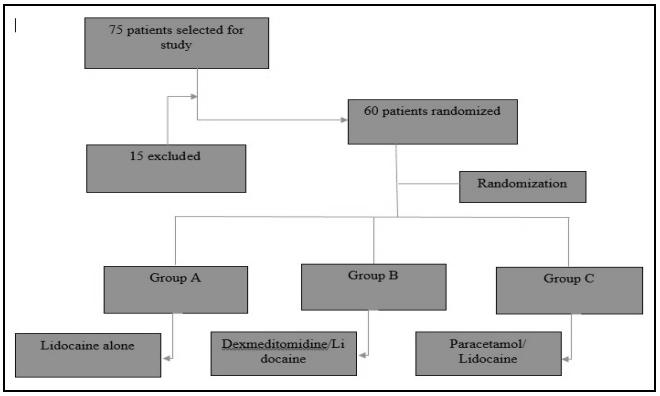

Figure: Flowchart of patients randomization in the study (n=60)

Table-I: Demographic data and clinical variable (n=60)

Parameters	Group-A (n=20)	Group-B (n=20)	Group-C (n=20)	*p*-value
Age (Mean±SD)	28.55±9.22	30.2±10.07	29.7±9.61	<0.0001
Weight (Mean±SD)	67.35±8.08	69.8±8.14	70.2±8.37	0.8577
Height (Mean±SD)	65.95±8.98	69.05±9.11	68±8.68	0.5396
Sex (male/female)	17/3	16/4	17/3	0.65
Operation Time (Mean±SD)	48.5±8.15	50.9±9.07	50.15±9.20	0.8555
Tourniquet Time	52.5±8.15	54.8±8.95	54.15±9.20	0.6961
SBOT	7.65±2.73	5±1.45	5.85±1.98	0.0045
SBRT	6±1.45	7.85±1.98	5±1.45	<0.0001
MBOT	12.55±3.03	6.65±2.73	9.95±3.63	<0.0001
MBRT	5.85±1.98	7.55±3.03	6±1.45	<0.0001
FPOART	94.11±3.03	114.69±3.35	96.56±2.55	<0.0001

All patients showed no serious adverse effects in 24 hours of IVRA. There was no any postoperative sedation, hallucination, nausea, vomiting or allergy and no significant mean arterial pressure and vital sign changes recorded during the study. Post-operative pain was significantly less in L/D group as compared to L/P group after first hour and in next time lapsed pain scores were significantly lower in L/D group than control (Group A) as compared with L/P group till the 3th hour reading so it had been statistically insignificant there after (Table-II).

The time to postoperative analgesic demand was significantly longer in L/D group (114.69±3.35min) compared to L/P group (96.56±2.55min) and group A (94.11±3.03min). (*p*< 0.0001).

Table II: Visual analogue pain score with different time intervals (Mean±SD) (n=60)

Parameters	Group-A (n=20) (Mean±SD)	Group-B (n=20) (Mean±SD)	Group-C (n=20) (Mean±SD)
Before tourniquet	1.3±0.5	1.2±0.7	1.7±0.5
After tourniquet	0.1±0.3	0.3±1	0.2±0.2
5 min	0.2±0.3	0.1±0.2	0.5±0.2
10 min	0.5±2	0.5±2	0.4±1.3
15 min	0.3±2	0.3±1	0.14±0.2
20 min	1.9±3	0.3±1	1.8±2
30 min	1.9±3	0.3±1	1.8±0.7
50 min	3±3	0.5±2	1.9±2.1
1 hr	0.4±2	0.2±1	0.3±2.5
3 hr	3.7±4	3.4±2	3.7±1.2
6 hr	2.8±2	2.4±2	2.5±2
9 hr	2.9±4	2.3±1.5	2.4±3
12 hr	3±3	2±4	1±3
24 hr	1.6±2	1.8±0.9	1.7±0.8

DISCUSSION

The present study revealed the employment of dexmeditomidine and paracetamol as adjuvant to lignocaine hydrochloride for intravenous regional anesthesia (IVRA) and to provide postoperative analgesia after lower limb surgeries is safe and effective with less postoperative pain and analgesic requirement during the primary 24hr compared to lignocaine hydrochloride alone. It was observed that dexmedetomidine is related to significant lower pain scores and longer time for first analgesic required, with reduced analgesic usage as compared with paracetamol as adjuvant with lignocaine hydrochloride and lignocaine hydrochloride alone because dexmedetomidine acts through spinal, supraspinal and peripheral actions as an alpha-2 agonist to produce its effects.[9] The direct local action of dexmeditomidine makes it favorable analgesic agent in IVRA. However, because of systemic absorption a central analgesic effect of dexmeditomidine can't be excluded. The mechanism of action for analgesic effect of dexmeditomidine for lower limb surgeries could be like that of clonidine which produces analgesia mainly through inhibition of the transmission of nociceptive stimulation within the dorsal horn of spinal cord.[8] Clonidine is described to take off the effect of noradrenaline release by descending inhibitory control pathways.[10] Local anesthetic effect provided by Dexmedetomidine, like clonidine, could also be the results of inhibition of the conduction of nerve signals through C and Ad fibers and will stimulate the discharge of enkephalin-like substances at peripheral sites .[11] Our study was in accordance with,[12] work demonstrated the intra-articular injection of 1 mcg/kg dexmedetomidine as adjuvant to bupivacaine significantly increase the postoperative analgesia after arthroscopic knee surgery, with an increased time to first analgesic required (450±85min) compared with bupivacaine alone (230±85 min).[13] Intra-articular injection of magnesium against dexmedetomidine for postoperative pain relief after knee arthroscopic meniscectomy concluded that both intra-articular injection of dexmedetomidine and magnesium sulfate increases postoperative analgesia after knee arthroscopic meniscectomy with significantly more time to postoperative analgesic requirement without adverse systemic complications of those agents.[14] One study concluded that, injection of dexmedetomidine as adjuvant to anaesthetic agent ropivacaine enhance the standard and duration of postoperative analgesia and reduces the consumption of opioids, with prolong the time 10.84±2.6 hrs between intra-articular injection of ropivacaine with dexmedetomidine and supplementary analgesic administration by PCA pump.[15] Similarly, this study depicts a more pronounced analgesic effect of paracetamol as adjuvant with lignocaine hydrochloride.[16] Paracetamol acts during a similar fashion to selective inhibitors of COX II as every week inhibitor of prostaglandin synthesis, however, it lacks their anti-inflammatory effects.[17,18] Several mechanisms are proposed for the analgesic effects of Paracetamol when used as adjuvant with other local agents as intravenous anaesthesia. The results of our study was almost like work reported that by mixing 300 mg of IV paracetamol into 0.5% lignocaine hydrochloride that although sensory block onset time was shorter within the group where paracetamol was mixed compared with the control group, there was no difference in terms of sensory block offset times after the surgery, intra-operative analgesia requirement was less, and intraoperative and postoperative visual analogue scale values were lower.[19,20] Similarly, motor block and sensory block onset periods were observed to be shorter in our study in patients to whom paracetamol was mixed compared with the group without adjuvant addition. Furthermore, the requirement for intraoperative analgesia and visual analogue scale values were similarly found to be lower.

CONCLUSION

In this study, it had been concluded that the addition of dexmeditiomidine and paracetamol to the lignocaine hydrochloride in intravenous regional anesthesia given for lower limb operations produce significantly effective postoperative analgesia. Both dexmedetomidine and paracetamol are safe and effective when added to lignocaine hydrochloride but dexmedetomidine/Lignocaine hydrochloride has better

analgesic profile with lower perception of pain, as assessed by the visual pain score, longer time to analgesic required and less total dose of analgesia during first 24 h after lower limb operations compared with paracetamol/Lignocaine hydrochloride or lignocaine hydrochloride alone.

Conflict of interest: None.

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

MAMM: Study design, drafting the manuscript, data interpretation, critical review, approval of the final version to be published.

KA: Data acquisition, data analysis, approval of the final version to be published.

LA: Critical review, concept, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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