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ORIGINAL ARTICLE

Effect of adding Ketamine as adjuvant to lidocaine in Bier's block for below elbow surgeries

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ABSTRACT

Background: Bier's block is a simple, rapid and effective method with very high success rate. However, it has some drawbacks as great liability to systemic toxicity, tourniquet pain, and post- tourniquet deflation rapidly evolving postoperative pain. **Objective:** To reveal the effect of adding Ketamine to lidocaine on the characters of Bier's block. **Methods:** Fifty adults both sex patients, with physical status of ASA I and II and prepared for minor elective below elbow surgical procedures were enrolled in this study. Patients were randomly divided into two equal groups (25 patients for each one); Lidocaine group that received 3 mg/kg lidocaine and Lidocaine/Ketamine group that received 3 mg/kg lidocaine plus 0.1mg/kg ketamine. *The primary outcomes* were the characters of Bier's block (onset, potency, Tourniquet tolerance time, recovery time after tourniquet deflation, time to the 1st ask and the amount of the consumed analgesic in the 1st 24 hrs post-operatively) and secondary outcomes were the hemodynamic and respiratory changes, beside the rates of the associated side effects. **Results:** Ketamine significantly improved the characters of Bier's block (i.e. enhanced the block onset, increased intraoperative anesthetic potency, prolonged tourniquet tolerance time, prolonged the time to time to the 1st ask and decreased the amount of the consumed analgesic after surgery), without causing significant hemodynamic changes or any serious side-effects. **Conclusion:** Ketamine is a suitable adjuvant to local anesthetics. It improves the characters of Bier's block without causing significant hemodynamic changes or any serious side-effects.

Keywords: Adjuvant to local anesthetics; Bier's block; Ketamine, Tourniquet pain; Upper extremity surgery

INTRODUCTION

Nowadays, Bier's block or Intravenous regional anesthesia (IVRA), is frequently used to provide anesthesia for various short elective limbs' surgeries especially surgeries upon the upper limbs. It is considered a simple and reliable method with very high success rates [1]. The main drawbacks of Bier's block are great liability to systemic toxicity, tourniquet pain, and post-tourniquet deflation rapidly evolving postoperative pain [2,3].

For improving the characters of Bier's block, different adjuvant have been used such as opioids, tramadol, alpha 2 agonists, ketamine, dexamethasone, nonsteroidal anti-inflammatory drugs, non-depolarizing muscle relaxants,

magnesium sulfate and mixing two different types of local anesthetics [3]

Ketamine is a non-competitive antagonism of the N - methyl - D - aspartic acid (NMDA) receptors. It is used for acute pain management, chronic pain management, and as an anti-inflammatory agent. Nowadays, it is commonly added to local anesthetics to improve the characters of local anesthesia [4].

The aim of this study was investigating the effect of adding ketamine to lidocaine on the characters of Bier's block for elective minor forearm and hand surgeries.

METHODS

This prospective randomized double-blind controlled trial was carried out at Zagazig University Hospitals from December 2022 to May

2023 after getting the approval of Institutional Review Board (IRB# 9679-1-7-2022) and the informed consent from each patient. This study applied the Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Fifty adults both sex patients which were enrolled in this study. *The criteria of inclusion* included patients' with physical fitness of class I and II according to the classification of American Society of Anesthesiologists (ASA), age of 21-64 years and body weight of 65-85Kg, and prepared for minor elective forearm and hand surgeries that did not need more than 60 min. *The criteria of exclusion* from this study included patient refusal, difficult vein, infection at the site of needle insertion, sickle cell anemia, crush injury, allergy to the used drugs, peripheral neuropathy, peripheral vascular disorders, myasthenia gravis, coagulopathy, hepatic and renal disorders, pregnancy, abnormalities in cardiac conduction and operations that need more than one hour.

All patients were visited at the night of operation for clinical evaluation, explaining the Bier's block technique and recording the base lines of heart rate (HR), mean arterial blood pressure (MABP), respiratory rate (RR), and peripheral arterial oxygen saturation (SpO₂). Premedication was not given to all patients.

In the theater, a suitable size sphygmomanometer cuff was applied around the arm of non-operated upon limb for continuous measurement of MABP and electrocardiogram (ECG) leads were fixed to the chest of patient, and pulse oximeter probe was applied to one of the big toes for continuous observations of HR, rhythm, RR and SpO₂.

Two intravenous cannulas were inserted: one in a one of the veins on the dorsum of the hand of the operated upon limb for injection of the local anesthetic and the other one in one of the veins on the dorsum of the opposite limb for fluids infusion and injection of any medications. After that, suitable size pre-checked double-cuffed pneumatic tourniquet (i.e. 40% more than the arm circumference in length and 5–6 cm in width) was fastened on a well-padded upper third of the arm of the operated upon limb. Exsanguinations of this limb was performed by its elevation above heart level and wrapping it tightly with the Esmarch bandage. Immediately after exsanguinations, the upper cuff of the pre-applied tourniquet was inflated to 150 mmHg higher than the baseline systolic blood pressure and absence of radial pulse was considered as a sign of sufficient tourniquet pressure. After tourniquet securing, Esmarch bandage was removed, and the

exsanguinated limb was lowered down and the fitness of the applied tourniquet was proved by absence of radial pulse and the pale color of the limb. The patients of this study were randomly divided into two equal groups via a computer-generated random numbers table. These two groups were Lidocaine (L) group that was injected by 3mg/kg of lidocaine [lidocaine 2% 50ml vial: 20mg/1ml, sigma-Tec Pharma-ceutical Industries Co.] and Lidocaine/Ketamine (L/K) group that was injected by 3mg/kg of lidocaine plus 0.1mg/kg of Ketamine [Ketamine, 50 mg/ml vial, Sigma EG, Egypt]. The injected volume of either lidocaine or Lidocaine/Ketamine was diluted up to 40ml by 0.9% Sodium Chloride solution and this volume was injected over 60 seconds in the patients of the two groups. When block of sensation reached to the middle third of the arm, the lower tourniquet cuff was inflated to a pressure of 150 mmHg above the baseline systolic blood pressure, then this was followed by deflation of the upper one.

In this study, the following parameters were recorded by an anesthesiologist who was unaware to which group the patient was related:

The primary outcomes (characters of Bier's block)

The block onset time (min): Sensory and motor blocks were tested every 30 second by pinprick test with needle gauge No. 22 for the first and by testing the ability of patient to flex his fingers, wrist and elbow for the later. *Sensory block time* was calculated from the start of local anaesthetic injection to the moment of loss of pinprick sensation at the middle third of the arm. *Motor block time* was calculated from the start of local anaesthetic injection to the moment at which the patient was unable to flex his fingers, wrist, and elbow.

Onset time sensory and motor block

Onset time of sensory block was calculated per minute from the moment of local anesthetic administration to the moment of loss of pin prick sensation at the middle third of the arm.

Onset time of motor block was calculated per minute from the moment of local anesthetic administration to the moment at which the patient was unable to flex his fingers, wrist and elbow joint.

Intra-operative analgesic potency

Intra-operatively, pain score was assessed via Visual Analogue Scale (VAS) firstly at skin incision, then every 5 minutes intraoperatively and lastly at skin closure. The mean of the allover VAS score values at various times of measurements were calculated in each group. Tourniquet tolerance time was calculated by minutes from the start of inflation of tourniquet to the moment at which patient reported that, the score of pain that exerted by tourniquet on

the applied area was above 3 according to VAS. Intraoperatively, surgical pain with score above 3 according to VAS was relieved by intravenous (iv) administration of 50 mcg fentanyl. Tourniquet pain with score above 3 according to VAS was relieved by alternating inflation and deflation of tourniquet cuffs and if this was not sufficient, 50mcg of fentanyl was intravenously injected to relieve it.

Block recovery times after deflation of tourniquet

These were assessed every 2 minutes after tourniquet deflation. Sensory block recovery time was calculated from the start of deflation of tourniquet to the start of returning sensation to pinprick. Motor block recovery time was calculated from the start of deflation of tourniquet to the start of ability of patient to flex his fingers, wrist, and elbow.

Time to the 1st ask to post-operative analgesia and the amount of the consumed analgesic during the 1st 24 hrs post-operatively

Post-operative pain intensity was assessed every 15 minutes. Time to the 1st ask to post-operative analgesia was calculated by minutes from the start of tourniquet deflation to the moment at which VAS score became above 3.

Postoperative pain was relieved by intramuscular injection of 75 mg of diclofenac sodium every 8 hours, The amount of diclofenac sodium for that required for relieving pain in the 1st 24 hours postoperatively was also recorded.

Secondary outcomes

Haemodynamic changes: Mean HR (beat per minute) and MAP (mmHg) had been detected and recorded immediately before operation (base line), then at 2, 5 and 15 and 30 minutes after Tourniquet deflation.

Bradycardia was considered when the decrease in HR became > 30% of basal reading and hypotension was considered when the decrease in MAP became > 30% of basal reading [5].

Atropine (0.5 mg iv) and ephedrine (5 to 10-mg iv) were considered for treatment of bradycardia and hypotension respectively.

Respiratory changes: Mean respiratory rate (breath per minute) and SpO₂ were detected and recorded immediately before operation (base line), then at 2, 5 and 15 and 30 minutes Tourniquet deflation.

Hypopnea was considered when respiratory rate became <8 breaths/min and hypoxemia was considered when peripheral oxygen saturation (SpO₂) became < 92% (on room air) for 30 seconds or more.

Assisted ventilation and face mask 100% oxygen administration till return back of respiratory rate and SpO₂ to normal levels were considered for treatment of hypopnea and hypoxemia respectively [5].

The rates of the various side effects:

Side effects as systemic toxicity of local anesthetic, bradycardia, hypotension, hypopnea, hypoxemia and sedation i.e. sedation score > 2 during and after surgery, were recorded. Sedation score was determined by Ramsay sedation scale (Table 1 [6]).

After finishing the surgical procedure, deflation of tourniquet was done by intermittent deflation technique. This technique consists of 3 repeated cycles of deflation and inflation. Each cycle was complete tourniquet deflation for 10 seconds then re-inflation for 50 seconds [7]. Following deflation and removal of tourniquet, the patient was closely monitored for 30 min in post anesthesia care unit (PACU).

Deflation of tourniquet was never performed before passing 30 minutes after injection of local anesthetic.

One hour after tourniquet deflation, all patients were shifted from PACU to the ward of surgery.

Estimation of the sample size

It was calculated using Open Epi program. According to the study of **Elmetwaly et al.**, [8], the sensory block onset times was 4.4±1.2 min in Lidocaine/ketamine group and 6.5 ± 1.1 min in Lidocaine group. At 80 % power and 95% CI, the estimated of sample size was 75 patients, 25 in each group.

STATISTICAL ANALYSIS

The values of the various data were statistically analyzed by using SPSS software program. The values of the various data were expressed as Mean ± Standard Deviation (SD), ratio and numbers (%). Quantitative values were statistically analyzed by Student *t*-test. The values that were expressed by either ratios or percentage were analyzed statistically by Chi-square test., P value below 0.05, in all tests, was considered significant.

RESULTS

Patients' characteristics of the two groups were statistically comparable (Table 2).

Onset times of sensory and motor block were significantly shorter in L/K group (3.74±0.81 min.

and 4.53 ± 0.85 min. respectively) than in L group (6.60 ± 1.50 min. and 10.5 ± 3.70 min. respectively). Intra-operative VAS score in L/K group (0.79 ± 0.25) was significantly lower than that in L group (2.61 ± 0.84). Intra-operative fentanyl consumptions in L/K group (24.5 ± 3.50 μ g/patient) was significantly lesser than in L group (77.20 ± 5.32 μ g/patient). The mean duration of tolerance to tourniquet pain in L/K group (29.36 ± 3.45 min.) was significantly longer than in L group (12.32 ± 2.10 min). Recovery times of both sensory and motor block in L/K group (7.90 ± 1.34 min. and 8.52 ± 1.14 min. respectively) were significantly longer than in L group (12.32 ± 2.10 min and 5.35 ± 0.45 min. respectively). Time to ask for the 1st post-operative analgesia in L/K group (71.25 ± 6.32 min.) was significantly longer than in L group (50.36 ± 5.36 min.). The amount of the consumed Diclofenac Na⁺ as pain killer in the 1st 24 hrs post-operatively in L/K group (88.60 ± 10.25 mg/patient) was significantly lesser than that in L group (180.25 ± 55.36 mg/patient) (**Table 3**).

The corresponding values of the heart rate (

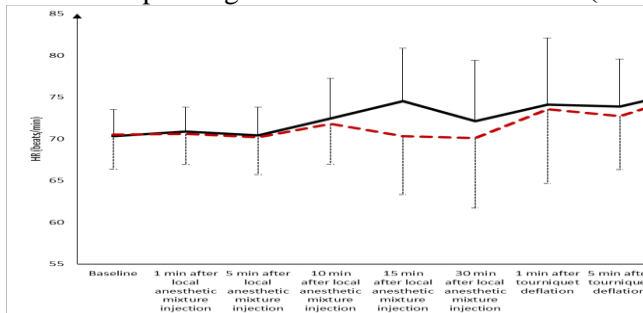


Table (1): Ramsay sedation scale [6].

Response to stimuli	Sedation score
Patient anxious or agitated or both	1
Patient cooperative, oriented and tranquil.	2
Patient respond to commands.	3
A brisk response to light glabellar tap.	4
A sluggish response to light glabellar tap.	5
No response to stimulus.	6

Table (2): Patients' characteristics in the two groups.

	L group (n=25)	L/K group (n=25)
Age (years).	34.12 ± 10.16	34.04 ± 9.55 NS
Weight (kg).	74.83 ± 4.13	76.48 ± 6.29 NS
Height (cm).	173.36 ± 5.16	174.32 ± 6.11 NS
BMI (Kg/m ²)	23.47 ± 2.92	24.5 ± 3.42 NS
Sex ratio (Male/Female ratio).	18:7	19:6 NS
ASA ps classes (Class I/II ratio).	21: 4	20:5NS
Duration of surgery (min.).	45.5 ± 6.52	44.22 ± 6.28 NS

Figure1), and the mean arterial blood pressure (**Fig. 2**), at various times of measurements of the two groups were statistically comparable.

The corresponding values of the respiratory rate (

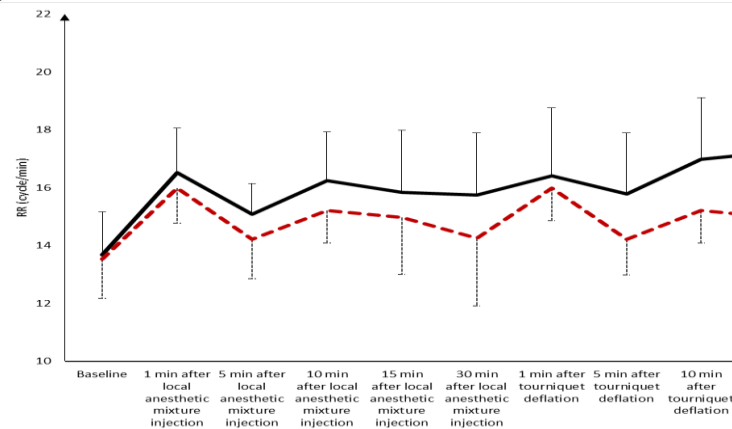


Figure ()), and the SpO₂ (**Figure ()**), at various times of measurements in the two studied groups were statistically comparable.

Each of bradycardia and hypotension were detected in one patient (i.e. in 4% of patients) in **L group**, however no side effects were detected (0.00%) in **L/K group**. The rates of the occurred side effects in **L group** (4%) were statistically significantly higher than in **L/K group** (0.00%).

Tourniquet time (min).	52.60 ± 7.63	51.32 ± 7.72 NS
Distribution of the various types of surgeries [N (%)]:		
- Carpal tunnel release.	3 (12.0%)	4 (16.0%) NS
- Ganglion excision.	3 (12.0%)	2 (8.0%) NS
- Fracture fixation.	5 (20.0%)	6 (24.0%) NS
- Tendon repair.	5 (20.0%)	3 (12.0%) NS
- Foreign body removal.	3 (12.0%)	5 (20.0%) NS
- Plate and screw removal.	4 (16.0%)	3 (12.0%) NS
- Tendon lengthening.	2 (8.0%)	2 (8.0%) NS

Data were expressed as Mean ± Standard Deviation (SD), ratio, and numbers (%).n =Group number. N= Number of each surgery type. L group = Lidocaine group. L/K group =Lidocaine/Ketamine group.

ASA ps class =American Society of Anesthesiology physical status class. NS = P > 0.05 i.e. non-significant difference between the two groups.

Table (3): The characters of the produced anesthesia in the two groups.

Variable	L group (n=25)	L/K group (n=25)
Onset of sensory block (min).	6.54 ± 1.14	4.74±1.81*
Onset of motor block (min).	10.63±2.40	6.53±1.85*
The mean of intra-operative VAS scores.	2.61±0.84	0.79±0.25*
The mean of intra-operative fentanyl consumptions (µg/patient).	77.2±5.32	24.50±3.50*
Tourniquet tolerance time (min).	12.32±2.10	29.36±3.45*
Sensory block recovery time after tourniquet deflation (min).	5.35±0.45	7.90 ±1.34*
Motor recovery time after tourniquet deflation (min).	6.75 ± 1.15	8.52±1.14*
Time to ask for the 1st post- operative analgesia (min).	50.36 ± 5.36	71.25 ± 6.32 *
The consumed amount of Diclofenac Na+ during the 1st 24 hrs post-operatively (mg/patient).	180.25 ± 55.36	88.60 ± 10.25*

Data are expressed as Mean ± Standard Deviation (SD). n =Group number. L group= lidocaine group. L/K group =Lidocaine/Ketamine group. *= P <0.05 i.e. Significant difference between the two groups.

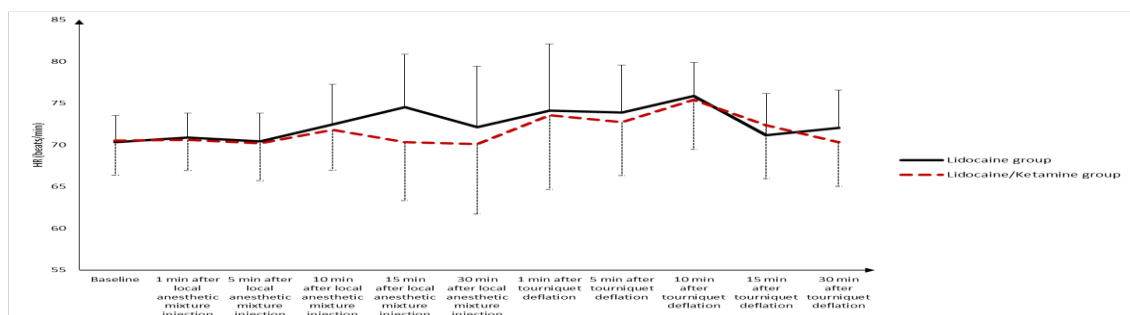


Figure (1): The heart rate (beats/min) at various times of measurements among the two studied groups.

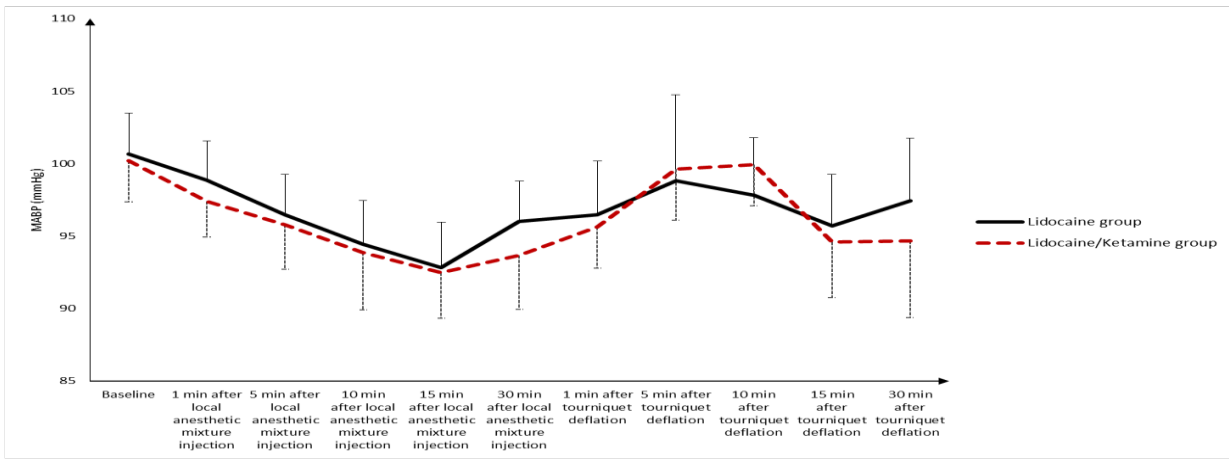


Figure (2): The mean arterial blood pressure (mmHg) at various times among the two studied groups.

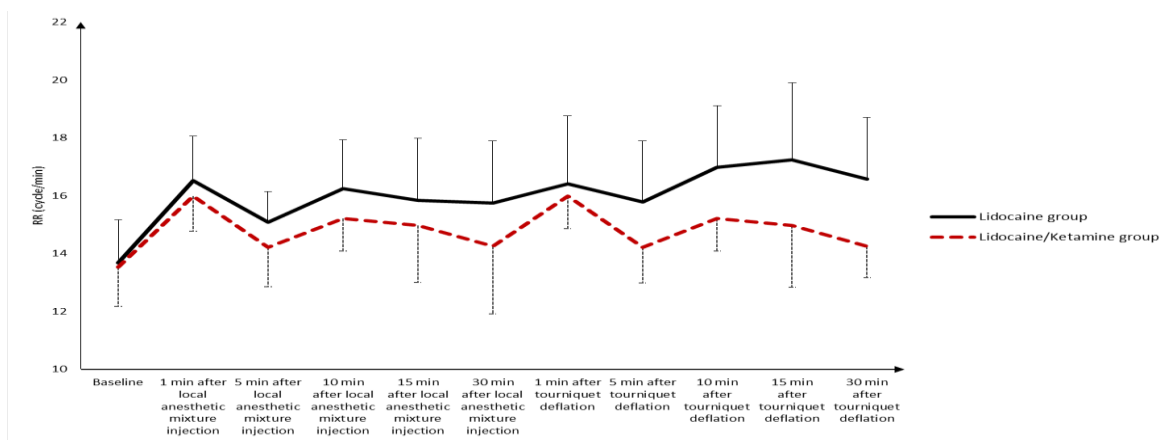


Figure (3): The mean respiratory rate (Cycles/min.) at various times among the two studied groups.

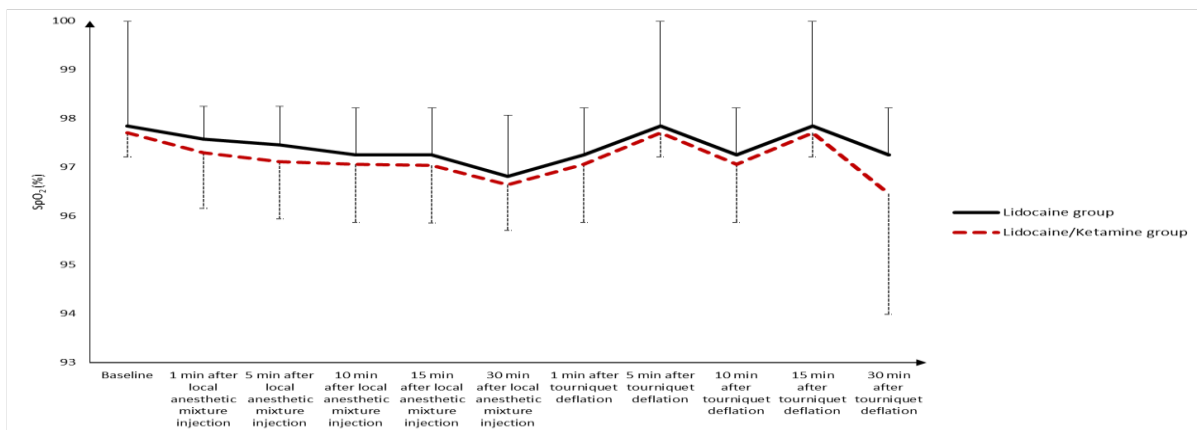


Figure (4): The mean peripheral oxygen saturation (SpO₂) at various times among the two studied groups.

DISCUSSION

The present study revealed that, adding of ketamine to lidocaine for Bier's block, produced significant decrease in block onset time, increase intra-operative anesthetic potency, increase of

Tourniquet tolerance time, decrease in the amount of intra and post-operative analgesic consumption, delay in the time to the first ask for post-operative analgesia, no significant changes in hemodynamic, respiration and no associated side effects.

The detected decrease in block onset time was in accordance with many reported studies. Kumar et al. [9], Haider and Mahdi [10], and Opda et al. [11] reported that, adding sub-anaesthetic doses of ketamine to lidocaine decreased the block onset of IVRA. EL-Soudy et al. [12] reported that, adding 25µg/kg ketamine to bupivacaine decreased the block onset time of Ultrasonic guided supraclavicular brachial plexus in patients undergoing various below elbow surgical procedures.

The detected, significantly lower mean of surgical pain score, longer duration of tolerance to tourniquet pain and a lesser intra-operative fentanyl consumption in L/K group than in L group was in accordance with many reported studies. Gorgias et al. [13] reported that addition of 0.1mg/kg ketamine to lidocaine in IVRA, significantly increased the intra-operative anesthetic potency, decreased Tourniquet pain and delayed the first request of post-operative analgesia. Viscomi et al. [14] reported that adding 0.1mg/kg of ketamine to lidocaine for IVRA, significantly prolonged tourniquet tolerance time and significantly decreased the analgesic consumption for relieving the pain that exerted by tourniquet. Haider and Mahdi [10] reported that, using a mixture of ketamine (0.5 mg/kg) atracurium and lidocaine for IVRA produced a significant increase in the intra-operative anesthetic potency. Abdel-Ghaffar et al. [15] reported that, adding ketamine to lidocaine for IVRA, significantly reduced the required amount intraoperative and postoperative analgesia. EL-Soudy et al. [12] reported that, adding 25 µg/kg of ketamine to bupivacaine for Ultrasonic guided supraclavicular brachial plexus prolonged postoperative analgesia and decreased the post operative analgesic requirement in patients undergoing various forearm and the hand surgical procedures. Tverskoy et al. [16] and Loix et al. [17] reported that, adding ketamine to bupivacaine produced a significant increase in the time of postoperative analgesia.

In contrast, some workers reported that, the adding ketamine as to local anesthetics did not potentiate the peripheral, regional, or local analgesia. Zohar et al. [18] declared that, adding of ketamine to bupivacaine for wound infiltration of the surgical incision of Cesarean section did not potentiate its analgesic potency. Clerc et al. [19] reported that, adding of ketamine to local anesthetics for intra-articular injection for knee arthroscopy did not improve their analgesic potencies and its mixing to bupivacaine for nerve block and for wound infiltration after repair of inguinal hernia did not significantly improve its analgesic potency. Rahimzadeh et al. [20] declared

that, adding 1mg/kg ketamine to 0.1% Ropivacaine for peri-femoral nerve infusion postoperatively, in patients who underwent repairing the anterior cruciate ligament, under intrathecal anesthesia, did not improve its analgesic potency and duration.

The cause of the contradictory between the reported findings of Zohar et al., [18], Clerc et al. [19], and Rahimzadeh et al. [20] and the findings of the present study, may be came from usage or not of premedication, different doses and concentrations of ketamine, different types, doses and concentrations of local anesthetics, different types of regional blocks, and different sample sizes.

The detected no significant changes in hemodynamics and respiration in L/K group agreed with some workers. Haider and Mahdi [10] revealed that, adding 0.5 mg/kg ketamine to lidocaine for IVRA, had no significant effect on hemodynamics. El Mourad and Amer [21] reported that, adding of ketamine to bupivacaine in Thoracic paravertebral block (TPVB) for modified radical mastectomy did not significantly affect the hemodynamic at the various times of measurements.

The detected absence of ketamine well-known side effects in L/K group was in accordance with the reporting results of some workers [13, 15]. This could be attributed to usage of low dose of ketamine and slow release of it into the systemic circulation.

The improved anesthetic quality that was detected in L/K group than in L group indicates that, ketamine has synergistic effect on the action of lidocaine on peripheral nerves.

This synergistic effect of ketamine to lidocaine was attributed to its' local and central anesthetic beside anti-inflammatory effects [22, 23].

Tourniquet pain is a well-known drawback of Bier's block. It is thought to be transmitted by slow-conducting small, unmyelinated, C fibers which are normally inhibited by fast-conducting large, myelinated A-delta fibers, but mechanical compression by tourniquet reduces transmission through these larger A-delta fibers [24]. Beside spinal cord, NMDA receptors are also detected on a small, unmyelinated C fibers. It is well known that, ketamine has noncompetitive antagonist of NMDA receptors Zorumski et al. [25] and local anesthetic effect [26]. This can explain why in L/K group, tourniquet tolerance time was statistically significant longer than that in L group.

The detected longer post-operative analgesia, and smaller analgesic consumption during the 1st 24 hrs. postoperatively after tourniquet deflation in L/K group than L group were in agreement with detected finding of Gorgias

et al. [13]. This finding may be attributed to the more stay of the combined lidocaine/ketamine than lidocaine alone in the operating limb because Ketamine might increase the binding capacity of local anesthetic to albumin alpha acid glycoprotein [27].

The limitations of this study were small number of the enrolled patients, uni-center study, lack of assessment of patient and surgeon's satisfaction about the quality of the produced anesthesia and lack of control groups that received systemic ketamine as adjuvant to lidocaine for Bier's block to compare its central with its peripheral sites of action.

CONCLUSION

Ketamine is a suitable adjuvant to local anesthetics. It improves the characters of Bier's block without causing significant hemodynamic changes or any serious side-effects.

CONFLICTS OF INTEREST

The authors report no conflicts of interest. The authors along are responsible for the content and writing of the paper.

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