Comparison of Ketamine, Nelbuphin, and Ondansetron as Adjuncts in Bier’s block.

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ABSTRACT... Objective: To find out the better adjunct in bier’s block. **Study Design:** Comparative, Qualitative. **Setting:** Aziz Fatima Hospital and Faisal Hospital. **Period:** August 2021 to May 2022. **Material & Methods:** This study was carried out in Faisal Hospital and Aziz Fatima Hospital Faisalabad. Patients electively undergoing hand and forearm surgery with expected duration less than or equal to one hour had been selected and randomly divided in three groups, group 1 LK means lignocaine and ketamine, group 2 LN means lignocaine and nalbuphine and group 3 LO that is lignocain and ondeansetron. All patients selected were ASA 1,2 between 22 to 60 yrs of age. An informed consent was taken. Patients were monitored with standard non-invasive monitoring like pulse oximeter, NIBP and ECG. Onset of sensory block was assessed by pin prick and motor by movement at 0, 1, 2 minutes of drug given. Pain was assessed by using Numeric Rating Scale (NRS 0-10) Post-operative pain as well as systemic effects of drugs administered at 10,20,30 and 60 minutes recorded. Patients then shifted to parent ward and need for systemic analgesia recorded for 24 hours. **Results:** Ketamine is more effective drug in terms of providing longer duration and improving quality of anesthesia with little side effects. **Conclusion:** The results of this study showed that ketamine is a better adjunct in Bier’s block as compared to nelbuphine and ondansetron. The least effective drug is ondansetron in terms of prolonging duration of anesthesia and post operative analgesia. But all three do not have many systemic side effects.

**Key words:** Nelbuphin, Ondansetron.

INTRODUCTION
Bier’s block is a type of regional anesthesia which has been first described by a German scientist August Bier in 1963. Later it was again popularized by Holmes. This is a simple and safe technique for short procedures of distal parts of limbs lasting less than 40 minutes performed on ambulatory basis. It avoids all the side effects of general anesthesia and is particularly useful in patients with systemic illness. There are disadvantages of this technique as well, including local anesthetic toxicity risk, tourniquet pain, poor muscle relaxation. Ideally, the drug being used for this technique should have rapid onset, low dosage requirement, less tourniquet pain, and prolonged post operative analgesia. None of the currently available single drug has all these properties. So, the need arises to combine two or more drugs to fulfill the objective. Several adjuncts have been used time to time to get desired results. Different drugs have different advantages and disadvantages.¹ ² ³ ⁴

Ketamine a well known drug in anesthesia is a phenyl pipperidine derivative. At sub anesthetic doses it acts as NMDA receptor antagonist which provides local analgesia by blocking peripheral NMDA receptors in sensory nerves. NMDA receptors plays a role in peripheral spasticity and in central sensitization of pain. Therefore NMDA receptor antagonist can be used as analgesics by modulating central sensitization of pain. It is widely used as perioperative analgesia. Ketamine, when combined with local anesthetic in bier’s block, has effects of prolonging the duration and quality of analgesia. Ketamine when otherwise used as anesthetic or analgesic agent has systemic side effects of hypertension and tachycardia as well as
hallucinations. But because of use of tourniquet in bier,s block it does not produce such effects.\textsuperscript{5,6,7}

Nelbuphine, which is a semi synthetic opioid having both agonist and antagonist properties is also a drug which causes prolongation of the effects of local anesthetic by improving analgesic action.\textsuperscript{8} It acts as agonist at kappa receptors and antagonist at mu receptors and has less side effects then pure opioids.\textsuperscript{9}

Ondansetron, a serotonin receptor antagonist also possesses some local anesthetic effects and causes prolongation of their effects. It has its role in anesthesia commonly as antiemetic by antagonising serotonin receptors both centrally and peripherally. Multiple studies have shown that serotonin has analgesic effects by interfering with peripheral effects of serotonin on nociception as well as can bind mu opioid receptors and provide analgesia.\textsuperscript{10,11,12}

This study is designed to find out which of these drugs has better effects on onset (sensory and motor block), duration and quality of analgesia as well as less post operative side effects.

\textbf{MATERIAL & METHODS}

This study was carried out in Faisal hospital and allied hospital Faisalabad. Patients electively undergoing hand and forearm surgery with expected duration less than or equal to one hour had been selected and randomly divided in three groups, group 1 LK means lignocaine 0.5% 30ml and ketamine 50 mg, group 2 LN means lignocaine 0.5% 30ml and nalbuphine 10mg and group 3 LO that is lignocaine 0.5% 30ml and ondansetron 8mg. All patients selected were ASA 1,2 between 22 to 60 yrs of age, with no history of allergy to any of above drugs and no contraindication to regional anesthesia. An informed consent was taken. Patients were monitored with standard non invasive monitoring like pulse oximeter, NIBP and ECG.

An intravenous line was placed in the dorsum of hand to be operated on for regional block. Another intravenous line passed on other side for i/v fluids and systemic drugs administration. No premedication was given. The limb to be operated had been exanguinated by elevating and applying esmarch,s bandage, a double, pneumatic cuff applied, esmarch bandage removed and the proximal cuff inflated 100 mm Hg above systolic blood pressure. The absence of radial artery pulsation and loss of pulse oximetry in the ipsilateral index finger was noted and 25ml of study drug was then injected. Distal tourniquet was inflated 15-20 min after injecting drug or when patient complained about tourniquet pain and proximal tourniquet then released. Distal tourniquet was released after at least 45 min of drug or at the end of procedure if it took more than 45 minutes.

All patients then shifted to recovery room and monitored for post operative pain as well as systemic effects of drugs administered at 10,20,30 and 60 minutes. Patients then shifted to parent ward and need for systemic analgesia recorded for 24 hours.

Onset of sensory block was assessed by pin prick and motor by movement at 0, 1, 2 minutes of drug given. Pain was assessed by using Numeric Rating Scale (NRS 0-10). Need for systemic analgesia during procedure had recorded and patient excluded. Duration of block was assessed by restoration of normal sensation and movement after tourniquet release. Any systemic complication of drugs (tachycardia, hypertension, hallucinations, dizziness, nausea, vomiting) had been noted.

Patient received injection Diclofenac 75mg postoperatively if NRS >5.

Results are calculated with a confidence Interval >95%. Mean+- std was calculated for demographic data like age, sex. p value<0.05 was considered significant.

Analysis of variance (ANOVA) was applied for duration of analgesia, post operative complications. All the data was calculated by using SPSS 16.0.
RESULTS
Ninety patients were included and divided in 3 sub groups randomly. There was no significant difference in demographic data (age, sex, ASA status). In groups LK, LN and LO there was significant difference in onset of pinprick sensation loss and motor block, as showed in Table-I in group LK onset was rapid 20% patients showed onset in 40 seconds with maximum of 23% in 45 seconds. Similarly, in terms of duration of analgesia LK was better then other 2. Duration of block extended upto 90 minutes in 13.3% of pts with a maximum of 75 minutes in 30%. Group LO had least prolongation of duration in 3 groups suggesting that ketamine and nalmiphine have better peripheral analgesic effect than ondansetron. Post operative analgesia and need for systemic analgesia was also better in the LK and LN groups. There were no systemic complications of any of three drugs used.

Onset S/M block (seconds)

| Groups | 40 | 45 | 50 | 55 | 60 | 65 | 70 | 75 | 80 | 85 | 90 | Total |
|--------|----|----|----|----|----|----|----|----|----|----|----|-------|
| Group A | 6 (20.0%) | 7 (23.3%) | 6 (20.0%) | 6 (20.0%) | 3 (10.0%) | 1 (3.3%) | 0 (0.0%) | 1 (3.3%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 30 (100.0%) |
| Group B | 2 (6.7%) | 5 (16.7%) | 2 (6.7%) | 3 (10.0%) | 5 (16.7%) | 3 (10.0%) | 5 (16.7%) | 1 (3.3%) | 0 (0.0%) | 1 (3.3%) | 3 (10.0%) | 30 (100.0%) |
| Group C | 0 (0.0%) | 1 (3.3%) | 1 (3.3%) | 0 (0.0%) | 3 (10.0%) | 5 (16.7%) | 5 (16.7%) | 6 (20.0%) | 5 (16.7%) | 1 (3.3%) | 3 (10.0%) | 30 (100.0%) |
| Total | 8 (8.9%) | 13 (14.4%) | 9 (10.0%) | 9 (10.0%) | 11 (12.2%) | 9 (10.0%) | 10 (11.1%) | 8 (9.5%) | 5 (5.6%) | 2 (2.2%) | 6 (6.7%) | 90 (100.0%) |

Table-I. Sensory/Motor Block Onset

Duration of Block (Minutes)

| Groups | 45 | 50 | 54 | 55 | 60 | 65 | 70 | 75 | 80 | 85 | 90 | 95 | 120 | Total |
|--------|----|----|----|----|----|----|----|----|----|----|----|----|-----|-------|
| Group A | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 6 (20.0%) | 9 (30.0%) | 4 (13.3%) | 2 (6.7%) | 4 (13.3%) | 4 (13.3%) | 1 (3.3%) | 30 (100.0%) |
| Group B | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 5 (16.7%) | 7 (23.3%) | 9 (30.3%) | 7 (23.3%) | 2 (6.7%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 30 (100.0%) |
| Group C | 3 (10.0%) | 3 (10.0%) | 1 (20.0%) | 9 (30.3%) | 11 (36.7%) | 3 (10.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 30 (100.0%) |
| Total | 3 (3.3%) | 3 (3.3%) | 1 (1.1%) | 9 (10.0%) | 16 (17.8%) | 10 (11.1%) | 15 (16.7%) | 16 (17.8%) | 6 (6.7%) | 2 (2.2%) | 4 (4.4%) | 4 (4.4%) | 1 (1.1%) | 90 (100.0%) |

Table-II. Block duration

Post-Operative analgesia (Hours)

| Groups | 5 | 10 | 15 | 20 | 25 | 30 | 35 | Total |
|--------|---|----|----|----|----|----|----|-------|
| Group A | 0 (0.0%) | 2 (6.7%) | 6 (20.0%) | 11 (36.7%) | 6 (20.0%) | 4 (13.3%) | 1 (3.3%) | 30 (100.0%) |
| Group B | 0 (0.0%) | 3 (10.0%) | 13 (43.3%) | 9 (30.0%) | 4 (13.3%) | 1 (3.3%) | 0 (0.0%) | 30 (100.0%) |
| Group C | 12 (40.0%) | 11 (36.7%) | 7 (23.3%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 30 (100.0%) |
| Total | 12 (13.3%) | 16 (17.8%) | 26 (28.9%) | 20 (22.2%) | 10 (11.1%) | 5 (5.6%) | 1 (1.1%) | 90 (100.0%) |

Table-III. Duration of analgesia

DISCUSSION
Addition of adjuncts to IVRA effects the onset of block, duration of analgesia and quality of anesthesia. There has been many studies to find out the best drug out of NSAIDS, OPIOIDs, Muscle relaxants, NMDA antagonists. We decided to find out which one is better amongst opiod, NMDA antagonist and 5HT3 antagonists.

Different studies on IVRA adjuncts has been performed and gave different results. Purpose of adjuncts are to potentiate onset of block, provide better block, prolonged post operative analgesia. Different drugs provide different benefits. Ketamine provides better block and post operative prolonged analgesia. Abdel Ghaffar HS et al showed the similar results when they compared ketamine and dexmedetomidine as adjuncts in bier,s block, they found ketamine having better analgesic effects as well as better quality of anesthesia. Addition of nalmiphin to lidocaine as an adjunct in Intravenous regional anesthesia also shows prolonged duration of analgesia Addition of 8mg ondansetron as adjunct found to improve quality of block and lessens post operative analgesic requirements. In another study performed by Badeaux et al showed that addition of 4mg ondansetron to lidocaine
reduces analgesic requirements and improved intraoperative conditions but the analgesic requirements were reduced for 4 hrs only.\textsuperscript{20} Quality of block by these three drugs were not compared when we did, we found that it is better with ketamine as well as duration of analgesia was also more prolonged with ketamine, then with nolbuphine and ondansetron proved to be least effective both in quality of block it had less effect and less prolonged duration of analgesia.

When we add NMDA antagonist or opioid there is a risk of systemic side effects after the release of tourniquet. No studies yet found any systemic effects after the addition of adjuncts as there may be reduced dose or tourniquet use prevents the drug to enter in systemic circulation rapidly. Viscomi CM et al found that addition of ketamine to low dose lidocaine for IVRA to systemic toxicity of local anesthetic is a safe adjunct.\textsuperscript{16} Similarly, vishma k et al showed that addition of nolbuphine to lidocaine in IVRA significantly prolongs duration of analgesia with minimum side effects.\textsuperscript{18}

CONCLUSION
The results of this study showed that ketamine is a better adjunct in Bier’s block as compared to nolbuphine and ondansetron. The least effective drug is ondansetron in terms of prolonging duration of anesthesia and post operative analgesia. But all three do not have many systemic side effects.

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