Comparative Evaluation of Efficacy of Plain Lignocaine 0.5%(3mg/kg) with Lignocaine 0.5%(3mg/kg) + Buprenorphine (3µg/kg) in IV Regional Anaesthesia

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ABSTRACT

Introduction: The main objective of the anaesthesiologist is to provide analgesia for surgery. Even though general anaesthesia was the earliest technique adopted to provide analgesia for surgery, the search for an alternative was made in order to overcome the problems and complications related to situations like ‘full stomach’, in emergency surgeries. This Study aimed to evaluate the usefulness of adding an opioid analgesic, Buprenorphine, Lignocaine, IVRA, Limb Surgery

Material and methods: This clinical study was conducted for a period of 2 years (2002–2003) at SV Medical college, SVRRGGH, Tirupati. 50 patients of ASA Grade - I and II of either sex undergoing upper limb (forearm and hand) surgery under intravenous regional anaesthesia, were randomly assigned to one of the 2 groups (25 each). Patients in Group - A received IVRA with Lignocaine 0.5% 3 mg/kg (0.6 ml/kg) and those in Group - B received IVRA with Lignocaine 0.5% 3 mg/kg (0.6 ml/kg) and 3µg/kg Buprenorphine. Onset and recovery times of sensory blockade (as assessed by pinprick), onset and recovery times of motor blockade (as assessed by flexion and extension movements of wrist and fingers and hand grip), postoperative duration of analgesia (as assessed by numerical pain rating scale score) and tourniquet times were compared between the two groups by chi – square test.

Results: The mean onset time (i.e., injection to analgesia time) of sensory blockade (analgesia) in Buprenorphine + Lignocaine group (Group-B) was considerably less (3.72 ± 1.48 minutes) compared to that in Lignocaine group (Group-A) (6.24 ± 1.94 minutes) and the difference was also statistically significant (t = 5.26; p<0.001). Postoperative duration of analgesia in Buprenorphine + Lignocaine group (Group-B) was considerably more prolonged (447.4 ± 57.9 minutes) compared to that in Lignocaine group (8.92 ± 2.69 minutes) and the difference was statistically significant (t= 37.83; p<0.001). The recovery time of sensory blockade and the onset and recovery times of motor blockade and the tourniquet times were comparable between the two groups and yielded no statistical significance. Amongst all the complications compared between the two groups in the post operative period, only the incidence of vomiting in Group-B (12 cases) was statistically significant (p2 = 8.03; df = 1; p=0.01, s).

Conclusion: Intravenous regional anaesthesia with addition of Buprenorphine to Lignocaine results in early onset of analgesia, prolonged residual (postoperative) analgesia and is free from any significant side effects.

Keywords: Buprenorphine, Lignocaine, IVRA, Limb Surgery

INTRODUCTION

Regional anaesthesia may provide an ideal operative condition when used optimally. It is said to cause the least interference with the vital physiological functions of the body with reduced stress response, avoids polypharmacy and provides an alert, awake and co-operative patient when compared to conventional methods.

The adequately administered regional anaesthesia provides excellent intraoperative pain control and also good relief of postoperative pain. Since regional blocks are less stressful for the patients, they could form the ideal anaesthesia of choice for emergency surgery in unprepared patients apart from their appreciated role even for elective surgical procedures. However, the main drawbacks are that the long acting agents used for regional anaesthesia have delayed onset of action, varying quality of blockade and unpredictable duration of action and the need for systemic analgesics for postoperative pain relief.

The technique of intravenous regional anaesthesia was discovered by August Bier,1 in 1908 using 0.5% procaine. It was revised in 1963 by Holmes,2 who used lignocaine and applied a second tourniquet (below the first one) over already anaesthetised area, instead of Bier’s ring block above the first one to avoid tourniquet discomfort (Holmes’ modification

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of Bier’s block). IVRA remains one of the safe and simple
techniques to use. Inability to provide effective postoperative
analgesia remains major disadvantage of IVRA.3-6
The peripheral administration of opioid at the site of acute
inflammation was observed to produce analgesia. This
effect was postulated to be peripherally mediated, opioid
specific and dose related.7 A lot of research work in the
field of peripheral opioid analgesia revealed that human
peripheral nerves contain opioid ligands as well as opioid
receptors and that immune cells produce endogenous opioids
during inflammation. These could be the targets for opioids
to exert their analgesic effects without causing various
side effects when they are given systemically.8-12 A variety
of opioids have been tried along with local anaesthetic
agents to improve postoperative analgesia in IVRA.13-18 In
contrast to other μ-opioid receptor agonists, in some recent
experiments, buprenorphine potentially blocked multiple
isolated voltage gated alpha subunits of sodium channels via
the local anesthetic binding sites. This property is likely to be
relevant when buprenorphine is used for pain treatment and
for local anaesthesia.19
An attempt was made in this prospective double-blind study
to evaluate the effect of adding an opioid to lignocaine
and compare the results with respect to onset time, quality,
duration of block and post operative analgesia.

MATERIAL AND METHODS
This clinical study was conducted at S.V.R.R. Govt. Gen.
Hospital attached to S.V. Medical College, Tirupati, in the
years 2002-2003. 50 patients of ASA Grade - I and II of either
sex undergoing upper limb (forearm and hand) surgery were
randomly assigned to group - A and B, each group consisting
of 25 patients and surgery was done under intravenous regional
anaesthesia.

Exclusion criteria: Patients with progressive neurologic
disease or neurologic injury, known sensitivity to the local
anaesthetic or other drugs used, sickle cell anaemia or trait,
ischemic or infected limbs, Berger’s disease, Raynaud’s
disease, peripheral arteriopathy or gangrene.

General procedure
30 ml of saline was added to 10 ml of 2% preservative free
xylcaine to yield 40 ml of 0.5% xylocaine. The calculated
dose of buprenorphine was added to the requisite volume of
this solution in the study group.
Intravenous regional anaesthetic was given according to the
following combinations:
Group – A (control group) - Received lignocaine 0.5% 3 mg/
kg (0.6 ml/kg).
Group – B (study group) - Received lignocaine 0.5% 3 mg/kg
(0.6 ml/kg) with 3µg/kg buprenorphine.

It was made sure that the patients fasted for at least 8 hours
before the elective surgery. Procedure was explained to
patients including the feeling of tourniquet application.
Patients received no pre-medication. In the operating room,
patients were monitored for non invasive blood pressure
(NIBP), oxygen saturation (Spo2) and pulse rate (PR). Two

Kumar, et al.
Plain Lignocaine 0.5%(3mg/kg) with Lignocaine 0.5%(3mg/kg) + Buprenorphine (3µg/kg)
later in the ward, patients were observed for any side effects or complications, and if encountered were noted and treated. Patients were observed for complications like drowsiness (assessed by Ramsay sedation scale), nausea, vomiting, pruritus, respiratory depression and convulsions. The recovery times of sensory and motor blockade, postoperative duration of analgesia and the incidence of complications were noted by another anaesthesiologist blinded to the study.

**STATISTICAL ANALYSIS**

The differences between means and proportions were analysed using unpaired 2 sample students ‘t’ test and Chi-square tests and a P value < 0.05 was considered statistically significant.

**RESULTS**

Both the groups were comparable with respect to age, weight and sex as the differences between the two groups were not statistically significant (table-1).

The groups were also compared with respect to mean onset time and mean recovery time of sensory and motor blockade. The mean onset time (i.e., injection to analgesia time) of sensory blockade (analgesia) in Buprenorphine + Lignocaine group (Group-B) was considerably less (3.72 ± 1.48 minutes) compared to that in Lignocaine group (Group-A) (6.24 ± 1.94 minutes) and the difference was also statistically significant (t = 5.26; p<0.001). The mean onset time of motor blockade and the mean recovery times of sensory and motor blockade were comparable between the two groups (table-2).

The mean tourniquet time and residual analgesia were compared between the two groups. The mean tourniquet time was comparable between two groups. Postoperative duration of analgesia in Buprenorphine + Lignocaine group (Group-B) was considerably more prolonged (447.4 ± 57.9 minutes) compared to that in Lignocaine group (8.92 ± 2.69 minutes) and the difference was statistically significant (t=- 37.83; p<0.001) (table-3).

| Age(Mean±SD in years) | P- Value |
|-----------------------|----------|
| Group-A 31.52 ± 10.55 | t = -0.81; p>0.05, ns |
| Group-B 33.68 ± 8.04 |

| Weight(Mean±SD in kgs) | P- Value |
|------------------------|----------|
| Group-A 52.72 ± 6.93 | t = 0.41; p>0.05, ns |
| Group-B 51.88 ± 7.37 |

| Sex (Male:Female) | P- Value |
|-------------------|----------|
| Group-A 16:9 | χ² = 2.00; df =1; p>0.05; ns |
| Group-B 10:15 |

| Mean onset time in minutes | Sensory | Motor |
|----------------------------|---------|-------|
| Mean                     |         |       |
| Group-A 6.24             | 1.94    | 8.68  |
| Group-B 3.72             | 1.48    | 8.72  |
| t' value                 | t = 5.26, p<0.001, s | t = -0.06, p>0.05, ns |

| Mean recovery time in minutes | Sensory | Motor |
|------------------------------|---------|-------|
| Mean                        |         |       |
| Group-A 3.64                 | 1.29    | 4.04  |
| Group-B 3.40                 | 1.32    | 3.84  |
| t' value                     | t = 0.65, p>0.05, ns | t = 0.48, p>0.05, ns |

| Tourniquet time in minutes | Mean | SD |
|----------------------------|------|----|
| Group-A 52.28               | 8.77 |
| Group-B 52.68               | 10.73|
| t' value                    | t = -0.14, p>0.05, ns |

| Residual (Postoperative) analgesia in minutes | Mean | SD |
|-----------------------------------------------|------|----|
| Group-A 8.92                                 | 2.69 |
| Group-B 447.4                                | 57.9 |
| t' value                                     | t = -37.83, p<0.001, s |

| No. of patients | Statistical Significance |
|-----------------|-------------------------|
| Group-A         | Group-B                  |
| 1. Respiratory Depression | Nil | Nil |
| 2. Nausea       | Nil | 5 |
|                  | χ² = 3.55; df = 1; p>0.05, ns. |
| 3. Vomiting     | 2 | 12 |
|                  | χ² = 8.03; df = 1; p<0.01, s. |
| 4. Pruritus     | Nil | 3 |
|                  | χ² = 1.41; df = 1; p>0.05, ns. |
| 5. Convulsions  | Nil | Nil |
| 6. Drowsiness   | Nil | Nil |

Table-1: Demographic distribution

Table-2: Mean onset and recovery time in minutes

Table-3: Tourniquet time and Residual (Postoperative) analgesia in minutes

Table-4: Complications in the study
The incidence of complications as compared within the two groups. The difference in the proportions of incidence of vomiting between the two groups was statistically significant \( \chi^2 = 8.03; \)  df = 1; p<0.01, s) while the incidence of either pruritus or nausea was not statistically significant. Other complications like respiratory depression, convulsions or drowsiness weren’t observed in either of the group (table-4).

**DISCUSSION**

With the increasing awareness of the hazards of theatre pollution, various methods were envisaged to minimize the risk to the theatre personnel. One such method was introduction of scavenging system of the anaesthetic gases when general anaesthesia was given. A better approach for the avoidance of general anaesthesia was the employment of regional technique by use of local anaesthetic solutions. The surgeries of lower abdomen and below were done with spinal or epidural analgesia with ease, but the surgeries in upper limb required the use of various nerve blocks which are technically difficult and are not without their complications. IVRA is a preferred technique for regional anesthesia for upper extremity surgery due to ease of application, safety and low failure rate. Inability to provide effective postoperative analgesia remains major disadvantage of IVRA. Lidocaine 0.5%–1% is one of the commonly used local anaesthetic for IVRA. Numerous attempts to reduce the severity of tourniquet discomfort, improve the quality of block and to prolong postoperative analgesia have been made by adding a wide range of adjuvant drugs (apart from opioids) like ketorolac, clonidine, dexmedetomidine, magnesium, ketamine, paracetamol and neostigmine to the local anaesthetic (lidocaine) in IVRA.

Tourniquet pain was not the major concern in our study probably as a result of using double-cuff tourniquet technique (Holmes’ modification). Tsai YC et al., compared EMLA cream, subcutaneous ring anesthesia and double cuff technique in the prevention of tourniquet pain and concluded double cuff technique to be most effective.

The peripheral perineural injection of morphine for chronic intractable pain was found to produce local analgesia without the use local anaesthetic and its duration of action was found to be longer than that of systemic morphine and that of bupivacaine. Contrary to the traditional view that opioid antinociception takes place exclusively within central nervous system, there are peripheral opioid receptors that mediate analgesia, when activated by exogenous opioid agonists applied in the vicinity. This understanding of the concept of peripheral opioid receptors in sensory afferent neurons has emerged from a series of studies in animals as well humans. Research trials by Stein C et al., revealed that small, systemically inactive doses of exogenous opioids when administered in the vicinity of peripheral-nerve terminals had beneficial analgesic effects. This concept has already been exploited in regional anesthesia like brachial plexus blocks with much promise. A variety of opioids have been tried so far as adjuncts to local anaesthetics for IVRA including morphine, meperidine and fentanyl in attempts to improve postoperative analgesia but reports are conflicting. Buprenorphine is a synthetic partial μ-receptor agonist derived from thebain, one of the opioid alkaloid. It has a rapid onset and prolonged duration of action. It is 25-40 times more potent than morphine on parenteral administration. It is potentially safe in conditions of over dosage due to its bell shaped dose response curve and has a low abuse potential. Researchers have reported analgesic synergy between buprenorphine and lidocaine. The duration of response from the lidocaine - buprenorphine combination exceeded that seen with any of the other opioid tested as an adjuvant. In our study, the mean onset time (i.e., injection to analgesia time) of sensory blockade (analgesia) in Buprenorphine + Lignocaine group (Group-B) was considerably less (3.72 ± 1.48 minutes) compared to that in Lignocaine group (Group-A) (6.24 ± 1.94 minutes) and the difference was also statistically significant (t = 5.26; p<0.001). This early onset of analgesia might be attributed to buprenorphine's ability to significantly modify the action of local anaesthetic on peripheral ‘C’ fibres.

Also, postoperative duration of analgesia in Buprenorphine + Lignocaine group (Group-B) was considerably more prolonged (447.4 ± 57.9 minutes) compared to that in Lignocaine group (8.92 ± 2.69 minutes) and the difference was statistically significant (t=37.83; p<0.001). This prolonged duration of analgesia could be attributed to peripheral perineural and or pre-emptive analgesic effect of buprenorphine. Complications which were reported sporadically with IVRA, were usually due to technical failure. We did not observe any adverse reaction in this study. The complications noted in this study were pruritus in 3 cases, mild nausea in 5 cases and occasional vomiting which occurred in 12 cases in the postoperative period in Buprenorphine + Lignocaine group (Group-B).

The difference in the proportions of incidence of vomiting between the two groups was statistically significant \( \chi^2 = 8.03; \)  df = 1; p<0.01, s) while the incidence of either pruritus or nausea was not statistically significant. Though the incidence of vomiting was statistically significant it could be easily managed with inj. metoclopramide 10 mg IM. No complications of any other nature were noted in this study. The findings in our study are supported by the study by Jitendra M et al., where in the addition of buprenorphine 0.3mg to 40ml 0.5% lidocaine for IVRA resulted in early onset of sensory block (4±0.35mts vs 6±0.6mts, p=0.001) and prolonged postoperative analgesic duration (6.7±1.2hrs vs 3.3±0.2hrs, p=0.001). As in our study, complication rates were higher in the buprenorphine group (p=0.002) with 5 patients having nausea and vomiting and 2 having sedation. In the study by Swarnkar N et al., 75 patients undergoing hand and forearm surgery were randomly allocated into three groups of 25 each: group A received 0.5% 40 ml lidocaine for IVRA, group B received 0.5% 40 ml lidocaine for IVRA and Buprenorphine 0.3 mg intramuscularly and group C received 0.5% 40 ml lidocaine with Buprenorphine 0.3 mg for IVRA. Duration of postoperative analgesia was significantly longer.
in group C (20 ±2 hrs) as compared to 0.7±0.2 and 7±0.6 hrs for group A and B respectively (p=0.001) and incidence of nausea/vomiting and sedation was much higher in group B as compared to other groups (p=0.002). They concluded that addition of Buprenorphine 0.3 mg to lidocaine for IVRA significantly prolongs analgesia without causing systemic side effects.31

Similarly to our study, Gupta S et al., in their study too found out that, when buprenorphine (1.5 μg/kg) was given along with bupivacaine (0.25%, 1.5 mg/kg) for IVRA, onset of analgesia was significantly faster (4.15±1.66 mts vs 6±1.66 mts, p< 0.001) and residual analgesia was significantly prolonged (99±7.3 mts vs 42.5±8.09 mts, p< 0.001).32

Similarly to our study, wherein the use of buprenorphine as an adjuvant in IVRA resulted in marked prolongation of analgesia, Candido KD et al., observed marked prolongation of analgesia extending up to 30 hrs when buprenorphine was used in brachial plexus block, supporting the enhanced peripheral opioid antinociception.33 Similarly, YaDeau JT et al., in their study, wherein they used dexamethasone and buprenorphine as adjuvants to bupivacaine in sciatic nerve block, observed that perinerveal buprenorphine and dexamethasone prolonged the duration of block, reduced the amount of opioids used and the worst pain experienced.34 Other studies too, wherein buprenorphine was used as an adjuvant to local anesthetics in central neuraxial blocks, reported similar findings.35-37

CONCLUSION

It can be concluded that the technique of intravenous regional anaesthesia with addition of Buprenorphine to Lignocaine results in early onset of analgesia, prolonged residual (postoperative) analgesia and is free from any significant side effects. Thus one of the main disadvantages of intravenous regional anaesthesia, rapid onset of postoperative pain after tourniquet release when using only local anaesthetic solutions could be circumvented by the addition of an opioid like buprenorphine to the solution.

Lastly, in the present health care scenario where cost effectiveness is important, this technique would be a best and suitable alternative to general anaesthesia wherever feasible.

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Kumar, et al. Plain Lignocaine 0.5%(3mg/kg) with Lignocaine 0.5%(3mg/kg) + Buprenorphine (3µg/kg)

Section: Anaesthesiology

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