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 3µg/kg to 0.5% xylocaine 3 mg/kg (0.6 ml/kg) in intravenous regional anaesthesia (Holmes' modification of Bier's Block) for forearm and hand surgeries in providing postoperative analgesia without increased incidence of side effects and complications.

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 t – test. The incidence of complications (respiratory depression, nausea, vomiting etc.,) were also 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 ($\chi 2 = 8.03$; $df = 1$; $p<0.01$, 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.[13-16] 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.[17]

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 xylocaine 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 cannulae were placed, one (22G) in a vein on the dorsum of the operative hand and the other (18G) on the non operative hand for intra venous fluids. The operative arm was elevated for 3 min and was then exsanguinated with an Esmarch bandage. Two padded pneumatic tourniquets with individual pressure gauges were then placed around the upper arm, and the proximal cuff was inflated to 100 mm Hg above systolic BP. Circulatory isolation of the arm was verified by inspection, absence of a radial pulse, and a loss of the pulse oximetry tracing in the ipsilateral index finger.

The prepared IVRA solution was injected over 90 s. Proximal tourniquet inflation time and drug injection time were noted. When the patient complained of tourniquet discomfort or pain after sometime through the surgical procedure distal tourniquet was inflated and the proximal was released (Holmes' modification). Tourniquet pressure was monitored and maintained throughout the surgical procedure. A different anesthesiologist, who was blinded to the constituents of the local anaesthetic solution evaluated the blockade. After injection, sensory block was evaluated with pinprick testing with a 22-gauge short bevelled needle every minute in the median, ulnar, and radial nerve innervated areas of the hand and forearm. Motor function was assessed by asking the patient to flex and extend his wrist and fingers, grip the examiners fingers and complete motor block was noted when any voluntary movement proved impossible. Onset time for sensory and motor blocks was the duration from the injection of the drug to loss of appreciation of pin prick and loss of voluntary movements respectively. Surgery commenced after establishing an adequate sensory and motor block.

At the end of surgery a note was made about the pulse rate, BP, O_2 sat, pattern of respiration and the level of consciousness. Following completion of surgery, tourniquet cuff was deflated with cyclic deflation-reinflation technique, wherein, cuff was deflated for 10 seconds and then re-inflated again for one minute and this sequence was repeated three times. This technique was adopted, as it was noted in some studies to delay the peak arterial concentration of local anaesthetic, as opposed to single stage let down of tourniquet cuff.[18] In any case cuff was not deflated within 30 minutes of drug injection and was not kept inflated for more than 1.5 hrs. Tourniquet time was noted. All the patients were then observed for 2 hrs postoperatively for signs of any untoward reaction. Recovery of sensory and motor blocks was noted at one minute intervals and the recovery time for sensory and motor blockade was the duration from the final deflation of the distal tourniquet to appreciation of pin prick and return of motor movement of digits and hand grip.

The postoperative duration of analgesia was assessed by numerical pain rating scale, having 10 cms length, numbered from 0-10 cms. Patients were asked to score their pain between 0 and 10, where 0 = no pain and 10 = worst pain ever, when they felt the pain in postoperative period. The postoperative duration of analgesia measured was the time in minutes from the release of tourniquet to the numerical pain rating scale score ≥ 5, at the point of which patients were given Inj. Diclofenac 1mg/kg, IM. In the post anaesthesia care unit and

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	
Group-A	52.72 ± 6.93	t = 0.41; p>0.05, ns
Group-B	51.88 ± 7.37	
	Sex (Male:Female)	
Group-A	16:9	χ^2 = 2.00; df =1; p>0.05; ns
Group-B	10:15	

Table-1: Demographic distribution

Mean onset time in minutes	**Sensory**		**Motor**	
	Mean	SD	Mean	SD
Group-A	6.24	1.94	8.68	2.15
Group-B	3.72	1.48	8.72	2.07
`t'value	t = 5.26, p<0.001, s		t = -0.06, p>0.05, ns	
Mean recovery time in minutes				
Group-A	3.64	1.29	4.04	1.56
Group-B	3.40	1.32	3.84	1.37
`t'value	t = 0.65, p>0.05, ns		t = 0.48, p>0.05, ns	

Table-2: Mean onset and recovery time in minutes

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	

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

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

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 (χ^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 techniqually 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.[3-6] Lidocaine 0.5%–1% is one of the commonly used local anaesthetic for IVRA.[3-6] 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.[19-25]

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.[26]

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 bupivacine.[27] 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 have 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.[11-12] 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.[13-16] 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.[28] Researchers have reported analgesic synergy between buprenorphine and lidocaine.[29] 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 ocassional vomiting which occured 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 (χ^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 0.33±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.[30]

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]

Similar 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±7.3mts vs 42.5±8.09 mts, p< 0.001).[32]

Similar 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 upto 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 perinueral 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 anaesthetics 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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