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Comparative Study of Intravenous Regional Anaesthesia Lignocaine with Ketorolac versus Plain Lignocaine

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Abstract

Aim: To prove the effectiveness of ketorolac as an adjuvant in intravenous regional anaesthesia. To know the effect of ketorolac on the tourniquet pain & post operative analgesia in IVRA. *Materials and Methods:* This is a prospective double blinded study conducted at Government Rajaji Hospital attached to Madurai Medical College. After approval by the ethical committee 50 patients of ASA grade I & II age between 20-70 years who came for upper limb surgeries which lasting for less than 60 minutes were included in this study. Patients with history of allergic to local anaesthetics, sickle cell disease, raynaud's disease, scleroderma, local infection, pagets disease and patients with inadequate starvation <6 hours and patients who had contraindication to ketorolac were excluded from this study. *Results:* A (lignocaine only) and group B (lignocaine with ketorolac) patients were comparable in respect of age, sex, weight and duration of surgery. The onset of sensory blockade was similar in both the groups. But there was rapid onset of motor blockade in ketorolac group in this study. 24% patients (6 patients out of 25 patietns) need supplementation due to tourniquet pain compared to 64% patients (16 patients out of 25 patients) in the control group. The incidence of tourniquet pain in the ketorolac group was less and which statistically significant. The duration of sensory blockade after cuff deflation in study group and control group were 5.28+/- 5.34 miutes and 4.4+/- 2.44 minutes respectively. The duration of motor blockade after cuff deflation in study group and control group were 9.04+/-6.1 minutes and 7.6+/-3.1 minutes. Though the duration of blockade found to be superior than that of control group, the difference in the effects between them were not statistically significant. The time for first analgesic requirement in study group and control group were 123.1+/-49.4 miutes and 19.4+/-11 miutes respectively. The differences between them were statistically significant. The lowest duration achieved in ketorolac group was 85 minutes and longest duration was 156 minutes. The difference between the group with respect to mean arterial pressure and pulse rate at 1minute and at 5 minutes was not statistically significant. Hence the groups were comparable with respect to mean arterial pressure and pulse rate at 1 minute and at 5 minutes after cuff deflation. There were no side effects noted in both the groups after cuff deflation. *Conclusion:* Ketorolac 20 mg which was added to lignocaine for IVRA provides less incidence of tourniquet pain, increases the duration of post operative analgesia and no significant increase in side effects and there was no haemodynamic changes.

Keywords: Lignocaine; Ketorolac; Plain Lignocaine.

Introduction

IntraVenous Regional Anaesthesia (IVRA) since its birth in the hands of August Bier in 1908 has become a valuable instrument in the repertoire of anaesthesia providers. This method enjoyed wide popularity for a time. It is not long before simple and reliable techniques for brachial plexus developed, and the intravenous method declined in popularity. It was revived in 1963 by Holmes, who used lignocaine because it appeared to give more reliable anaesthesia than procaine [1]. With slight technical modifications IVRA, today, is an ideal method of providing anaesthesia for minor surgical procedures to the extremities performed

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on an ambulatory basis. It has the advantages of speed of onset, rapid recovery, reliability of blockade & cost effectiveness. Adjuvants to local anaesthetics have greatly expanded the potential applications of regional anaesthesia by providing faster onset time, inhibition of tourniquet pain, prolonged post-operative anaesthesia and improved peri-operative analgesia apart from decreasing risk of local anaesthetic toxicity. In this regard, ketorolac – a parenterally administered NSAID by decreasing tissue prostaglandin (PG) synthesis, decrease peri-operative pain in combination with LA [2]. Being a peripherally acting drug, not crossing the blood brain barrier in significant degree, it has the specific advantage of minimal CNS side effects. Cumulative effects of these agents result in greater patient satisfaction, rapid hospital discharge , cost effectiveness and minimal risks [9,10].

Materials and Methods

This is a prospective double blind study conducted at Government Rajaji Hospital attached to Madurai Medical College. After approval by the ethical committee 50 patients of ASA grade I & II age between 20-70 years who came for upper limb surgeries which lasting for less than 60 minutes were included in this study. Patients with history of allergic to local anaesthetics, sickle cell disease, raynaud's disease, scleroderma, local infection, pagets disease and patients with inadequate starvation < 6 hours and patients who had contraindication to ketorolac were excluded from this study. Preanaesthetic evaluation was done. All patients were premedicated with Inj. Midazolam 2 mg IM 45 minutes before surgery. Resuscitation equipment and drugs were kept ready. Initial PR, BP, SPO2 were estimated continuously. A 22 G cannula was placed intravenously as distal as possible in the arm to be anaesthetized. Venous access is established in the opposite arm to allow administration of fluids or drugs if necessary. The double tourniquet was applied on the arm with generous layers of padding, ensuring that no wrinkles are formed and the tourniquet edges do not touch the skin. The arm was exsanguinated by using Esmarch bandage. If this was impossible, exsanguination was achieved by elevating the arm for 2-3 minutes while compressing the axillary artery. The proximal tourniquet was inflated to at least 100 mm Hg higher than the patients systolic blood pressure. Before injecting local anaesthetic, radial pulse was palpated and confirmed that there was no pulse. The local anaesthetic is then injected slowly over 90 secs. A standard volume of 40 ml of 0.5% lignocaine or 40 ml of 0.5 mg ligcocaine with ketorolac was injected. Patients were divided into two groups according to the drug which they received. Group A patients received 40 ml of 0.5% lignocaine and group B patients received 40 ml of 0.5% lignocaine with 20 mg of ketorolac. After achieving surgical anaesthesia, the distal tourniquet which overlies part of the anaesthetized arm was inflated and the proximal one was deflated. After that the surgeons were allowed to proceed. Intraoperatively PR, BP, SpO2, signs of drug toxicity were monitored regularly. If patient complained of tourniquet pain, they were supplemented with Inj. Midazolam IV (In titrated doses, max. upto 2 mg) and intercostobrachial N block with local infiltration around the cuff. The cuff was not deflated until 20 minutes after local anaesthetic injection even if surgery was completed before 20 minutes. Cuff deflation was performed in cycles with deflation/inflation times of less than 10 seconds until the patient no longer exhibits signs of systemic toxicity. Patients were observed for 30 minutes after surgery. Intraoperatively the following parameters were noted : Onset action with sensory and motor, PR, BP, SpO2 were monitored regularly at frequent intervals, duration of surgery, need of supplementation, side effects, duration of blockade after cuff deflation both sensory & motor, Post operatively the following parameters were noted and Time to first analgesic need.

Results

In this study totally 50 patients were studied. Patients were divided into two groups according to the drug which they received. Group A patients received 40 ml of 0.5% lignocaine and group B patients received 40 ml of lignocaine with ketorolac 20mg. Computer analysis of statistical data was done utilizing Epidemiological Information Package (EPI 2003) developed by World Health Organisation. Frequencies, percentages, mean, S.D. and 'p' values were calculated using this package.

Table 1 shows that the difference between the group with respect to age is not statistically significant. Hence the groups are comparable with respect to age. The difference between the group with respect to sex is not statistically significant. Hence the groups are comparable with respect to sex. The difference between the group with respect to weight is not statistically significant. Hence the groups are comparable with respect to weight.

Table 2 shows the onset of sensory blockade in study group and control group were 3.64 +/- 2.3mins and 4.28+/- 3.24 minutes respectively. Though the effects of ketorolac appears to be superior, the effect was not statistically significant. The effects were almost same. The onset of motor blockade in study group and control group were 7.12+/- 3.32 and 9.48+/- 5.46 minutes respectively which was statistically significant. The duration of surgery in study group and control were 45.72+/- 21.3 and 45.48+/- 19.76 minutes respectively. The difference between the groups with respect to duration of surgery is not statistically significant. Hence the groups were comparable with respect to duration of surgery.

Table 3 shows need of supplementation in the intraoperative period due to tourniquet pain, duration of blockade after cuff deflation-sensory, duration of motor blockade in minutes.

Table 3 shows that the 24% patients (6 patients out of 25 patietns) need supplementation due to tourniquet pain compared to 64% patients (16 patients out of 25 patients) in the control group. The incidence of tourniquet pain in the ketorolac group was less and which statistically significant. The duration of sensory blockade after cuff deflation in study group and control group were 5.28+/- 5.34 miutes and 4.4+/- 2.44 minutes respectively.

Table 1: Shows age distribution, sex distribution, weight distribution

Age Group	Study Group		Controls	
	No.	%	No.	%
<20	4	16	2	8
20-29	12	48	11	44
30-39	4	16	5	20
40-49	2	8	-	-
50 & above	3	12	7	28
Total	25	100	25	100
Mean	28.4		35.1	
S.D.	12.5		15.7	
Range	10-55		16-70	
'p'	0.0692 (Not significant)			

Sex	Study Group		Controls	
	No.	%	No.	%
Male	10	40	12	48
Female	15	60	13	52
P	0.7757 (Not significant)			

Weight in kg	Study group	Control group
Range	42-64	46-68
Mean	52.9	55.3
S.D.	5.8	5.2
P	0.1443 (Not significant)	

Table 2: Shows onset of sensory blockade, onset of motor blockade, duration of surgery

Onset of sensory in minutes	Study group	Control group
Range	2-7	2-7
Mean	3.64	4.28
S.D.	1.15	1.62
'p'	0.2940 (Not significant)	
Blockade motor in min		
Range	3-11	5-15
Mean	7.12	9.48
S.D.	1.66	2.73
'p'	0.0014 (Significant)	
Duration of surgery in minutes		
Range	32-71	30-76
Mean	45.72	45.48
S.D.	10.65	9.88
'p'	0.938 (Not significant)	

Table 3: Shows need of supplementation in the intraoperative period due to tourniquet pain, duration of blockade after cuff deflation-sensory, duration of motor blockade in minutes

Supplementation	Study Group	Controls
Given	6	16
Not given	19	9
'p'	0.0103 (Significant)	
Duration of sensory blockade after Cuff deflation in minutes		
Range	3-13	3-7
Mean	5.28	
S.D.	2.67	
'p'	0.4263 (Not significant)	
Duration of motor blockade in minutes		
Range	5-17	5-11
Mean	9.04	7.6
S.D.	3.05	1.55
'p'	0.0933 (Not significant)	

Table 4: Shows time to first analgesic in minutes

Time of first Analgesic (in minutes)	Study Group		Controls	
	No.	%	No.	%
≤60	1	4	25	100
61-120	9	36	-	-
121-180	15	60	-	-
>180	-	-	-	-
Range	85-156		11-28	
Mean	123.1		19.4	
S.D.	24.7		5.5	
'p'	0.0001 (Significant)			

Table 5: Mean arterial pressure and pulse rate after cuff deflation at 1, 5 minute

1 minutes MAP	Study group	Control group
Range	90-111.33	80-104.67
Mean	109.8	103.9
S.D.	15.2	6.7
P	0.2045 (not Significant)	
1 minutes PR		
Range	62-104	60-94
Mean	86.2	80.7
S.D.	12.5	8.1
P	0.2463 (not Significant)	
5 minutes MAP		
Range	78.33-110.33	70-109.33
Mean	93.1	87
S.D.	9.8	6.8
P	0.3166 (Not significant)	
5 minutes PR		
Range	58-99	58-92
Mean	80.8	79
S.D.	12.9	7.9
P	0.2756 (Not Significant)	

The duration of motor blockade after cuff deflation in study group and control group were 9.04+/-6.1 minutes and 7.6+/-3.1 minutes. Though the duration of blockade found to be superior than that of control group, the difference in the effects between them were not statistically significant.

Table 4 shows the time for first analgesic requirement in study group and control group were

123.1+/-49.4 miutes and 19.4+/-11 miutes respectively. The differences between them were statistically significant. The lowest duration achieved in ketorolac group was 85 minutes and longest duration was 156 minutes.

Table 5 shows the difference between the group with respect to mean arterial pressure and pulse rate at 1minute is not statistically significant. Hence the groups were comparable with respect to mean arterial pressure and pulse rate at 1 minute after cuff deflation. There were no side effects noted in both the groups after cuff deflation. The difference between the group with respect to mean arterial pressure and pulse rate which was recorded at 5minutes after cuff deflation was not statistically significant. Hence both the groups were comparable. There were no side effects noted after cuff deflation in both the groups.

Discussion

Intravenous regional anaesthesia uses local anaesthetics administered to one particular limb by occluding the arm proximally to provide conduction blockade. It must be safe, not threatening or unpleasant to the patient, allow adequate surgical access to the operative site, and cause as little disturbance as possible to the internal homeostatic mechanisms. Intravenous regional anaesthesia has many advantages. It is simple, reliable with rapid onset and recovery. Despite these advantages intravenous regional anaesthesia has its own limitations like lack of postoperative analgesia and tourniquet pain which causes discomfort to the patient. In this study, we attempted to eliminate these disadvantages by adding ketorolac as an adjuvant. In this study both group A (lignocaine only) and group B (lignocaine with ketorolac) patients were comparable in respect of age, sex, weight and duration of surgery. The onset of sensory blockade was similar in both the groups. But there was rapid onset of motor blockade in ketorolac group in my study. This is contrary to the findings of Andrew choyce et al, who showed that ketorolac added to IVRA produces similar onset profile in both the groups. Duration of blockade after cuff deflation, both sensory and motor has similar recovery profile. This results correlate with studies conducted by Scott S. Reuben et al. Incidence of tourniquet pain which was assessed by supplementation during surgery was significantly less in ketorolac group (24%) than lignocaine group (64%) which was statistically significant. The p value is 0.0103. Similar study conducted by Scott S. Reuben et al, Duprat KM et al, James R. Hebel et al shows incidence of tourniquet pain was less with when ketorolac as an additive. The duration of post operative analgesia which was assessed by time to first analgesic, in ketorolac group is 123.1+/-49.4 minutes and lignocaine group is 19.4+/-11 minutes. The p value is 0.0001, $p < 0.5$, which is statistically highly significant. The results correlate favourably with the studies conducted by Scott S. Reuben et al in which the mean duration of analgesia was 701+/-133 minutes. Other study conducted by Andrew choyce et al, the mean duration of analgesia was 624+/-80minutes. Surgical trauma results in release of intracellular contents from damaged and inflammatory cells. Nociceptor stimulation cause a neurogenic response with release of mediators such as substance P and neurokinin A. This results in an "inflammatory soup" containing histamine, serotonin, bradykinin and metabolites of the cyclooxygenase and lipooxygenase pathways. Ketorolac inhibit the production of prostaglandins from arachidonic acid in phospholipid membranes. The result is decreased afferent nociceptive signals arising from the site of surgery. Whether interfering with the synthesis of inflammatory mediators has a preemptive analgesic role in preventing sensitization of nociceptors remains controversial. The role of ketorolac in the management of postoperative pain is well established. Clinical studies have demonstrated an enhanced analgesic effect from ketorolac when concentrated at a peripheral site compared to the systemic administration of the same drug. This would suggest a predominantly peripheral site of action. It is interesting to note that the plasma half-life of ketorolac is four to six hours yet the duration of analgesia reached a plateau at over ten hours. It may be that by concentrating the dose of ketorolac at the site of surgery, either as part of IVRA or wound infiltration, the resulting analgesic benefit is longer lasting than the same dose administered parenterally. Presumably there is a persistent drug level in the tissues, and this coupled to the lower dosage could result in reduced systemic side effects. Considering all the above said factors ketorolac in the dose of 20 mg can be used as a adjunt for intravenous regional anaesthesia with improved duration of postoperative analgesia duration and decreased incidence of tourniquet pain. Many studies have been reported regarding Lidocaine with Ketoralac versus plain lignocaine.

Andrew Choyce et al [3], tested the use of adjuncts for intravenous regional anaesthesia (IVRA) for surgical procedures in terms of their intraoperative effects and postoperative analgesia.

They concluded that, there is good evidence to recommend NSAIDS in general and ketorolac in particular for improving post operative analgesia after IVRA. Clonidine also appears to improve post operative analgesia and prolong tourniquet tolerance. Opioids are disappointing by this route. Only 30 mg meperidine has substantial postoperative benefit but at the expense of post deflation side effects. Muscle relaxants improve motor block and aid fracture reduction.

Scott S. Reuben et al [4], assessed the analgesic efficacy of administering IVRA by administrating lidocaine and ketorolac with either a forearm or upper arm tourniquet for outpatient hand surgery. They concluded that forearm tourniquet intravenous regional anaesthesia with 0.5% lidocaine and ketorolac provides both a longer duration of sensory block and prolonged postoperative analgesia compared with upper arm IVRA.

James R. Hebl et al [5], studied about various local anaesthetic additives such as opioids, alpha – 2 agonists (clonidine), acetylcholine esterase inhibitors(neostigmine) and N methyl – D aspartate receptor antagonists (Ketamine) and NSAIDS. They demonstrated that more effective postoperative analgesia can be achieved when Ketorolac is used in conjunction with lidocaine for IVRA. They hypothesized that more effective analgesia was obtained during IVRA administration because a higher concentration of ketorolac existed at the site of surgical trauma, where inflammatory mediator synthesis occurred.

Reuben et al [6], assessed the analgesic effectiveness of ketorolac administered with lidocaine via intravenous regional anaesthesia (IVRA) or via wound infiltration following ambulatory hand surgery. They concluded that ketorolac provides similar postoperative analgesia after ambulatory hand surgery when administered with lidocaine either by IVRA or by wound infiltration.

A. Turan et al [7], conducted a study in which thirty patients undergoing hand surgery were randomly assigned to two groups to receive IVRA. They have used 0.5 mg of neostigmine as a additive. They found shortened sensory and motor block onset times, improved quality of anaesthesia and prolonged sensory and motor block recovery times, and prolonged time to first analgesic requirement were found in neostigmine group.

Stephan C. Marsch et al [8], conducted a prospective randomized, double blinded trial in which they tested the hypothesis that compared with 40ml chloroprocaine 0.5%, 40ml chloroprocaine 1% results in an earlier onset of analgesia duration and improves distal tourniquet tolerance during IV reginal anaesthesia. These beneficial effects must be weighed against a fourfold increase in signs of systemic local anaesthetic toxicity.

Conclusion

Ketorolac 20 mg which was added to lignocaine for IVRA provides less incidence of tourniquet pain, increases the duration of post operative analgesia and no significant increase in side effects and there was no haemodynamic changes.

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