EFFICACY OF ADDING FENTANYL TO LIGNOCAINE-ADRENALINE COMBINATION IN SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK FOR UPPER LIMB ORTHOPEDIC SURGERIES A MULTI-CENTER STUDY

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ABSTRACT: BACKGROUND: Brachial plexus block is a suitable alternative to general anesthesia for surgeries of upper limb and it can be performed even in patients who are not adequately fit for general anesthesia. The significance of brachial plexus block has increased in recent years due to renewed interest in day care surgery. Lignocaine hydrochloride has been used extensively for brachial plexus block and it has the disadvantage of having short duration of action. Opioids when added to anesthetic mixtures may improve and prolong the action of local anesthetics during peripheral nerve blocks. Such postoperative pain control can reduce both narcotic requirements and narcotic induced side effects. Studies have shown the efficacy of opioids as analgesic adjuvants in prolonging the duration of brachial plexus block. With this background in mind, this study was conducted to compare the onset and duration of sensory and motor block produced by a mixture of lignocaine and adrenaline with that produced by a mixture of fentanyl, lignocaine and adrenaline. Aims: To assess the effectiveness of addition of fentanyl to a mixture of lignocaine and adrenaline in prolonging the duration of analgesia and motor block for upper limb orthopedic surgeries. MATERIALS AND METHODS: This multi-center randomized control study was conducted in two tertiary care centers in 80 patients underwent elective upper limb orthopedic surgeries and they were allocated into two groups of 40 each group L and group F. the classical approach of supraclavicular brachial plexus block. Drug used were 30ml of lignocaine 1.5%+adrenaline 5mcg/ml +0.5ml normal saline in group L and 30ml of lignocaine 1.5% + adrenaline 5mcg/ml + fentanyl 50mcg in group F. Adequacy of block was assessed by the pin prick test and temperature test. Motor power was assessed by the modified Lowett scale. Sedation was monitored using the modified Ramsay scale. An assessment was made for onset of analgesia, onset of motor block, duration of analgesia, duration of motor block and occurrence of any side effects during the first 24 hours of the postoperative period. Subjective assessment of post-operative analgesia was done by direct questioning of the patient and by a five point pain scores. Data's were analyzed using computer software, Statistical Package for Social Science (SPSS) 16th version. **OBSERVATION AND RESULTS:** The mean onset of sensory block in the lignocaine group was 6.6±1.52 and in the lignocaine-fentanyl group 10.22±2.58. The mean onset of motor block was 8±1.97 in the lignocaine group and 11.39±3.57 in lignocaine-fentanyl group. The mean duration of sensory block was 105.73±9.45 in lignocaine group and 170.28±12.28 in lignocaine-fentanyl group. The mean duration of motor block motor block was 95.93±10.65 in lignocaine group and 178.33±12.37 in the lignocaine-fentanyl group. **CONCLUSION:** Addition of fentanyl to lignocaine-adrenaline in brachial plexus blocks will significantly delay the onset of sensory and motor block and significantly prolongs the duration of sensory and motor block. Addition of fentanyl produces high intraoperative sedation scores. There is

no incidence of hemodynamic instability or respiratory depression. So fentanyl can be used to improve the quality of anesthesia in brachial plexus block for upper limb surgeries.

KEYWORDS: Brachial plexus block, Lignocaine, Fentanyl, Sensory and motor block, Duration of analgesia.

INTRODUCTION: The technique of peripheral nerve blockade was developed in the early history of anesthesia and now it is a well-accepted component of comprehensive anesthesia care. Brachial plexus block is a suitable alternative to general anesthesia for surgeries of upper limb and it can be performed even in patients who are not adequately fit for general anesthesia during emergency.¹ The significance of brachial plexus block has increased in recent years due to increased number of trauma cases and renewed interest in day care surgery. With appropriate selection and sedation, these techniques can be used in all age groups. Skillful application of peripheral nerve blockade broadens the anesthesiologist's range of options in providing optimal anesthesia care.²

Among the various techniques of brachial plexus blocks, the supraclavicular and subclavian perivascular methods produce the most complete limb block.³

Lignocaine hydrochloride has been used extensively for brachial plexus block and it has the disadvantage of having short duration of action. Various methods have been adopted to prolong the effects of local anesthetics like addiction of vasoconstrictors and opioids. Opioids when added to anesthetic mixtures may improve and prolong the action of local anesthetics during peripheral nerve blocks.⁴ Such postoperative pain control can reduce both narcotic requirements and narcotic induced side effects.⁵ Studies have shown the efficacy of opioids as analgesic adjuvants in prolonging the duration of brachial plexus block. With this background in mind, this study was conducted to compare the onset and duration of sensory and motor block produced by a mixture of lignocaine and adrenaline.

AIM: To assess the effectiveness of addition of fentanyl to a mixture of lignocaine and adrenaline in prolonging the duration of analgesia and motor block for upper limb orthopedic surgeries. Onset and duration of sensory and motor block, side effects and intra operative sedation were observed during the study and compared with another group receiving lignocaine with adrenaline only.

MATERIALS AND METHODS: This multi-center study was conducted in two tertiary care centers for a period of two years after approval form institutional ethical committee. This randomized control study was conducted in 80 patients underwent elective upper limb orthopedic surgeries and they were allocated into two groups of 40 each group L and group F. ASA II&II, age group between 20-60 years, weight 50 to 70 kg were included in this study. Patients who are allergic to local anesthetic or opioids, patients with who have any anatomical abnormality of neck and shoulder region, patients with any bleeding disorders and alcoholic and psychiatric patients were excluded from the study.

Pre-anesthetic examination was carried out and relevant investigations were done. The procedure to be performed was explained to the patient in detail and written consent was taken. Patients in the two groups were premedicated with oral Diazepam 0.2mg/kg and Metoclopramide 0.2mg/kg one and half hours before surgery.

Under all aseptic precautions, the classical approach to supraclavicular block was used. Feeling of tingling or paraesthesia in the affected upper limb was considered as identification of brachial plexus during the classical approach of supraclavicular brachial plexus block. Drug used were as follows:

Group L: 30 ml of lignocaine 1.5 % + adrenaline 5mcg/ml + 0.5ml normal saline.

Group F: 30 ml of lignocaine 1.5 % + adrenaline 5mcg/ml + fentanyl 50mcg.

Adequacy of block was assessed by the pin prick test and temperature test. Motor power was assessed by the modified Lowett scale.

Modified Lowett Scale:

Score/Grade:

- (6) Normal.
- (5) Slightly reduced muscular force.
- (4) Pronounced reduction in muscle force.
- (3) Slightly impaired mobility.
- (2) Pronounced mobility impairment.
- (1) Almost complete paralysis.
- (0) Complete paralysis.

Vital parameters like pulse rate, BP and SPO₂ were monitored. Respiratory rate and abnormalities of respiration were looked throughout the surgery. Sedation was monitored using the modified Ramsay scale.

Modified Ramsay Scale:

Grade/Score:

- 1. Patient anxious, agitated or restless.
- 2. Patient cooperative, oriented and tranquil.
- 3. Patient responds to commands only.
- 4. Patient responds to gentle shaking.
- 5. Patient responds to noxious stimulus.
- 6. Patients has no response to noxious stimulus.

An assessment was made for onset of analgesia, onset of motor block, duration of analgesia, duration of motor block and occurrence of any side effects during the first 24 hours of the postoperative period.

Onset of sensory block was considered as the time taken from the injection of local anesthetic solution to the loss of sensation over the limb.

Onset of motor block was considered as the time taken from the injection of local anesthetic solution to the loss of motor power (Modified Lowett scale <2).

Duration of sensory block was taken as the time between the onset of analgesia and reappearance of pain or request for pain relief.

Duration of motor block was taken as the time between onset of motor block and the return of power (Modified Lowett scale >3).

Subjective assessment of post-operative analgesia was done by direct questioning of the patient and by a five point pain scores:

- 1. No pain.
- 2. Mild pain.
- 3. Moderate pain.
- 4. Severe pain.
- 5. Very severe pain.

Post-operative pain was assessed every hour for first 6 hours, every 2 hours for the next 6 hours and thereafter at 18 and 24 hours during the postoperative period. Pulse rate, blood pressure and respiration were monitored during each visit. Sedation status was monitored during the intraoperative period and graded according to the modified Ramsay scale. Side effects like drowsiness, nausea, vomiting, pruritus, urinary retention, hypotension, bradycardia and respiratory depression were over looked for 24 hours post operatively. Only those patients in whom a successful block is achieved were included in the study.

Statistical Analysis: Data's were analyzed using computer software, Statistical Package for Social Science (SPSS) 16th version. Data are expressed in its frequency and percentage. To elucidate the associations and comparisons between different parameters, Chi-Square test was used as a nonparametric test. Student's t test was employed to compare different parameters between two groups. For all statistical evaluations, a two tailed probability of value, 0.05 was considered as significant. Finally the results in the two groups were compared to draw the conclusion.

OBSERVATION AND RESULTS:

Age	Lignocaine (L)		Fentanyl (F)	
(years)	Total No.	% of Total	Total No.	% of Total
20-29	20	50.0%	11	27.5%
30-39	10	25.0%	17	42.5%
40-49	2	05.0%	4	10.0%
50-59	8	20.0%	6	15.0%
>60			2	5.0%
Table 1: Age distribution in each group				

Chi square = 7.3 P > 0.05.



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Gender	Lignocaine (L)		Fentanyl (F)		
denuer	Total No.	% of total	Total No.	% of total	
Male	26	65.0%	28	70.0%	
Female	14	35.0%	12	30.0%	
Table 2: Sex distribution in each group					

Chi square = 0.228 P > 0.05.



Fig. 2: Sex distribution of study population

Group	Weight (kg) Mean+SD	
Lignocaine(L)	61.8±4.73	
Fentanyl(F)	63.11±4.03	
Table 3 Weight distribution in each group		

T value 1.93 P value >0.05.

P value for age sex and weight distribution is >0.05. That means the variable age sex and weight of the patients do not vary amongst the groups. This means the two groups are comparable and therefore significant difference in the other variables under the study cannot be attributed to differences in these three external variables.

ONSET OF SENSORY AND MOTOR BLOCK

Parameter	Group	Mean+SD	t value	P value
Oncot of concorry block (mts)	Lignocaine	6.6±1.52	28 880	<0.001
Unset of sensory block (ints)	Fentanyl	10.22 ± 2.58	20.009	
Oncot of motor block (mts)	Lignocaine	8±1.97	6 020	<0.001
Oliset of motor block (mts)	Fentanyl	11.39±3.56	0.039	<0.001
Table 4: Comparison of onset of sensory and motor block				

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P value for the onset of sensory block is <0.001. Hence it can conclude that addition of fentanyl to lignocaine- adrenaline will significantly delay the onset of sensory block.

P value for the onset of motor block is <0.001.Hence it can conclude that addition of fentanyl to lignocaine- adrenaline will significantly delay the onset of motor block.

DURATION OF SENSORY AND MOTOR BLOCK

Parameter	Group	Mean±SD	t value	P value
Duration of concorry block (mts)	Lignocaine	105.73 ± 9.45	QQ Q/1	<0.001
Duration of sensory block (ints)	Fentanyl	170.28 ± 12.28	09.941	
Duration of concorry block (mts)	Lignocaine	95.93 ± 10.65	92 477	~0.001
Duration of sensory block (ints)	Fentanyl	178.33 ± 12.37	02.477	<0.001
Table 5: Comparison of the duration of sensory and motor block sedation score				



P value for the duration of sensory block is <0.001. Hence it can conclude that addition of fentanyl to lignocaine- adrenaline will significantly prolong the duration of sensory block.

P value for the onset of motor block is <0.001.Hence it can conclude that addition of fentanyl to lignocaine- adrenaline will significantly prolong the duration of motor block.

Sedation	Group			
Score	Lignocaine	Fentanyl		
Grade 1	8			
	20.00%			
Grade II	32			
	80.00%			
Crade III		7		
Grade III		17.50%		
Grade III		33		
		82.50%		
Table 6: Sedation score in different group				

Chi square = 66.768 P < 0.001



P value sedation score is <0.001, which means that addition of fentanyl to lignocaineadrenaline will produce increased sedation in study group.

DISCUSSION: The American surgeon Halstead and Hall^{6,7} described the injection of cocaine into peripheral nerve sites for minor surgical procedures in the 1880's. Matas of New Orleans⁸ and Crile of Cleveland⁹ in 1897 gave intraneural injection of local anesthetic to brachial plexus under direct vision. James Leonard Corning in¹⁰ in 1885, recommended the use of an esmarch band to arrest the local circulation, thus prolong the cocaine induced block and decreasing the uptake of that local anesthetic from tissues. Heinrich F.W Braun,¹¹ who substituted adrenaline, a "chemical tourniquet" in 1903, furthered this concept. Braun¹² also described the term "conduction anesthesia" in his 1905

text book on local anesthesia, which described all regional anesthetic techniques. In1912 Kulenkampff¹³ used the supraclavicular technique of brachial plexus block after experimenting on himself. In 1940, Patrick¹⁴ in Sheffield published a modification of Kulenkampff technique. This method involves blocking the plexus as it lies on the first rib lateral to the subclavian artery. In 1967, Macintosh and Mushin¹⁵ described the supraclavicular technique of brachial plexus block with excellent illustrations. In 1995, Stein¹⁶ described the mechanism of peripheral opioid peptides in controlling pain in peripheral tissues.

Lignocaine hydrochloride tis the most commonly used local anesthetic, synthesized by Nils Lofgren and Lundquist in 1943 in Sweden.¹⁷ It was first used by Gordh in 1948.¹⁸ It is a tertiary amine, which is an amide derivative of dimethyl amino acetic acid. Local anesthetics diffuse in their unchanged base form through neural sheaths and the axonal membrane to the internal surface of cell membrane sodium ion channels; there they combine with hydrogen ions to form a cationic species which enters the internal opening of the sodium channel and combines with a receptor. This produces blockade of the sodium ion channel, thereby decreasing sodium ion conductance and preventing depolarization of the cell membrane.¹⁹ Hydrophobicity appears to be a primary determinant of intrinsic anesthetic potency because the anesthetic molecules must penetrate the nerve membrane and must bind at a partially hydrophobic site on the sodium channel.²⁰⁻²³

Clinically this may not be true as in all circumstances as vasodilatation and tissue redistribution properties also affect the potency.²⁴

Factors influencing local anesthetic action

Dosage; Onset of action of a local anesthetic quickens as the concentration or dose of the drug is increased.²⁵ The volume per se of anesthetic solution probably influences the spread of anestrhesia.²⁶

Addiction of vasoconstrictors: The addiction of vasoconstrictors, usually adrenaline 1:200000 in the local anesthetic solution decrease the rate of vascular absorption, thereby allowing more anesthetic molecules to reach the membrane and so improve the depth and duration of anesthesia and also provide a marker for inadvertent intravascular injection.²⁷ When used with lignocaine in peripheral nerve blocks, adrenaline prolongs both sensory and motor blockade.^{28,29} Lidocaine acts in 2-20 minutes, dependent on the rate if administration and has a duration of action of 200-400 minutes dependent upon the presence of vasoconstrictors used.

Site of injection; Compared to intrathecal or local infiltration of local anesthetics, brachial plexus block produces longest latencies and duration of action. This is due to the particular anatomy of the area of injection, which in turn influences the rate diffusion and vascular absorption. Diffusion through the various tissue barriers before reaching the nerve membrane leads to delayed onset in brachial plexus block and the decreased rate of vascular absorption causes prolonged blockade.

Carbonation and pH of local anesthetics; Addition of sodium bicarbonate to local anesthetic solution decreases the onset time of conduction blockade and may produce a more complex blockade of the radial, median and ulnar nerves when they are employed for brachial plexus blockade. Increasing the pH increases the ionized form of drug enhancing the rate of diffusion of across the nerve sheath.

MIXTURES OF LOCAL ANESTHETICS: There is no clinical advantage to the use of mixture of local anesthetic agents. There is chance for exceeding dose of the toxic limits as the toxicities of the individual local anesthetic agents are additive.

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Signs and symptoms of toxicity.

Circumoral and tongue numbness, light-headedness and tinnitus, visual disturbances, muscular twitching's, convulsions, unconsciousness, coma, respiratory arrest and cardiac depression.

Fentanyl is a phenylpiperidine derivative, synthetic opioid, mu receptor agonist that is structurally related to meperidine and 75 to 125 times more potent than morphine as an analgesic. It has high lipid solubility, a rapid onset and short duration of effects. Opioids may also produce some analgesia via peripheral mechanism outside the CNS. Not all studies confirm this capacity in humans.

Factors affecting the efficacy of opioid actions in the periphery such as inflammation may be important. Opioid receptors located in the primary afferent neurons are likely site of action and immune cells infiltrating inflamed tissue may produce the endogenous ligands for these peripheral receptors.

Several other mechanism of opioid action has been suggested. Opioid agonist produces a local anesthetic like on the surface of excitable cell membranes that does not involve a stereospecific receptor and may contribute to some of their actions.³⁰ More recent works suggest that the local anesthetic effects of opioids, most prominent with pethidine, occur at the proximal end of the dorsal root as it passes the dorsal root entry zone. Serotoninergic pathways may also in part modulate opioid mediated analgesia.³¹ Some opioid effects may be elicited at GABA receptors.

Finally it has also been postulated that opioid anesthesia may involve a general membrane effect because of much closer correlations between EEG or anesthetic effects and membrane lipid content as opposed to serum opioid levels.

Several studies have been done using opioids in brachial plexus block. Viel et al in 1989³² studied 40 patients who were given supraclavicular brachial plexus block, comparing the effects of addition of morphine 50mcg/kg to buprenorphine 3mcg/kg. The studied concluded that buprenorphine provided prolonged analgesia compared to morphine.

Flory et al in 1995²⁹ studied 40 patients undergoing elective shoulder surgery for chronically painful conditions. Interscalene brachial plexus block with 0.5% bupivacaine with 5mg morphine was given. The study found no difference in quality of analgesia or patient satisfaction. Wajima et al in 1995²⁸ in a randomized double blind study compared two groups of patients getting intravenous infusion and brachial plexus infusion of butorphanol for postoperative analgesia. VAS score in two groups did not differ up to 6 hours and 24 hours after operation. From 9 hours until 24 hours, pain score were significantly higher in IV group than in brachial plexus infusion group. They concluded that continuous injection of butorphanol into the brachial plexus sheath provided superior analgesia compared with continuous IV injection.

Parikh et al in 1995 described a case of postoperative analgesia for 6 days in a patient undergoing arthrolysis of elbow joint. He used continuous infusion of 0.125% bupivacaine and subsequent addition of fentanyl to the infusate via a catheter inserted via supraclavicular approach into the sheath of brachial plexus. He described this as an ideal method for cases where immediate mobilization after surgery is essential. Wajma and Shitara et al in 1995³³ compared the analgesic effect of butorphanol alone, mepivacaine alone and mepivacaine – butorphanol mixture into the axillary sheath and found that pain relief was significantly higher when butorphanol is added to mepivacaine.

Kardash K et al in 1995³⁴ in study examined the effects of adding fentanyl to mepivacaine in supraclavicular blocks on block characteristic and postoperative analgesia. He concluded that adding fentanyl 75mcg to mepivacaine in supraclavicular blocks has no significant effects on block

characteristics. It may enhance postoperative analgesia, but the duration of this effect is too brief to be clinically useful. Gormley et al in 1996³³ studied the effect of addition of alfentanyl to lignocaine during axillary brachial plexus block. The incidence of satisfactory block was similar in both groups. Although the percentage of patients with complete anesthesia in the median nerve distribution was greater in the alfentanyl group, there was no significant difference in any other distribution. The time to return of sensation and motor function was prolonged significantly in the alfentanyl group.

Bazin J. E et al in 1997³⁴ compared the duration of analgesia produced by a mixture of lignocaine and bupivacaine either alone or combined with morphine, buprenorphine or sufentanil in 80 patients. He concluded that the addition of an opioid to local anesthetic mixture lengths the duration of analgesia. Fletcher et al in 1994³³ compared the effect of addition of Fentanyl 100 mcg to 1.5% lignocaine in axillary block in 51 patients. The study concluded that there was no significant difference in the two groups. Kapral et al in1999³⁴ studied the effect of addition of Tramadol 100 mg to 1% mepivacaine in axillary blocks in 60 patients. The study concluded that addition of tramadol to mepivacaine produced prolonged sensory and motor block. Nishikawa et al,³⁵ studied the effect of fentanyl 100 mcg added to 1.5% lignocaine for axillary block in 66 patients. The study concluded that addition of fentanyl caused an improved success rate of block, but a delayed onset of analgesia.

Antouncci in 200,³⁶ studied the effect of addition of tramadol 100 mg, clonidine and sufentanil 20 mcg to 0.75% ropivacaine in axillary block and concluded that tramadol produces significant reduction of onset time and prolongation of anesthesia and analgesia with lower incidence of side effects as compared to clonidine and sufentanil.

In our study the mean onset of sensory block in the lignocaine group was 6.6 ± 1.52 and in the lignocaine-fentanyl group 10.22 ± 2.58 . The mean onset of motor block was 8+1.97 in the lignocaine group and 11.39 ± 3.57 in lignocaine-fentanyl group. The mean duration of sensory block was 105.73 ± 9.45 in lignocaine group and 170.28 ± 12.28 in lignocaine-fentanyl group. The mean duration of motor block motor block was 95.93 ± 10.65 in lignocaine group and 178.33+12.37 in the lignocaine-fentanyl group.

CONCLUSION: Addition of fentanyl to lignocaine-adrenaline in brachial plexus blocks will significantly delay the onset of sensory and motor block and significantly prolongs the duration of sensory and motor block. Addition of fentanyl produces high intraoperative sedation scores. There is no incidence of hemodynamic instability or respiratory depression. So fentanyl can be used to improve the quality of anesthesia in brachial plexus block for upper limb surgeries.

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