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A Comparative Study of 0.25% Bupivacaine with Clonidine, Fentanyl, Midazolam, as Adjuvants for Brachial Plexus Block

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Abstract
several local anaesthetic drugs used for brachial plexus block, Bupivacaine is used most frequently as it has a long duration of action varying from 3-8 hours. To prolong the duration of analgesia various drugs have been studied as adjuvants to local anaesthetic solution and techniques like the continuous catheter placement in the plexus have evolved. The aim of the present study is to evaluate the effects of addition of 1 mcg/kg of preservative free clonidine to the maximum of 75 mcg, 1 mcg/kg of preservative free fentanyl to the maximum of 50mcg and 50mcg/kg of preservative free midazolam to 30ml of 0.25%. 60 adult patients of both sexes in the age group of 20-60 years belonging to ASA I/II category and their weight ranging between 40-70 kgs posted for various types of upper limb surgeries at the Department of Orthopedics and Department of surgery at sree Mookambika institute medical sciences the study group. This study was designed as a prospective randomised comparative study. Supra clavicular technique was chosen for this study because it provides a rapid onset, dense and predictable anaesthesia with a high success rate. Clonidine an α2-adrenergic agoinst has been extensively used an adjunct to general anaesthesia and regional anaesthesia. When added to 1% mepivacaine6 with 1:2,00,000 epinephrine 150mcg of clonidine prolongs the duration of both anaesthesia and analgesia after axillary brachial plexus blockade. In conclusion, clonidine 1mcg/kg to a maximum of 75mcg added to 0.25% Bupivacaine solution for supra clavicular brachial plexus block, quickens the onset of sensory and motor blockade, prolongs the duration of sensory blockade, improves the quality of postoperative analgesia when compared to fentanyl and midazolam group.

INTRODUCTION

Regional anaesthesia as the name implies is the blocking of peripheral nerve conduction in a reversible manner by using local anaesthetic agents thereby one region of the body is made insensitive to pain and is devoid of reflex response to surgical stimuli. The central nervous system is spared, so the patient is conscious during the surgical procedure. Regional anaesthesia offers many advantages over general anaesthesia for surgery on upper extremities particularly in emergency operations. William Steward Halsted first performed brachial plexus block is 1885. In 1911 Kulemkampff and Hirschel described the first per cutaneous brachial plexus block by supra clavicular and axillary routes respectively[1]. Since then several techniques of brachial plexus block have been described with the purpose of improving the efficacy and success rate and minimizing the risk and rate of complications. Of the various techiques the most widely used methods are classical technique described by Patrick (1940), Vertical plump bob approach described by Brown, 1st rib walk over technique described by Bonica and Moore and subclavian peri vascular technique described by Winnie and Collins (1964). Of the several local anaesthetic drugs used for brachial plexus block, Bupivacaine is used most frequently as it has a long duration of action varying from 3-8 hours. To prolong the duration of analgesia various drugs have been studied as adjuvants to local anaesthetic solution and techniques like the continuous catheter placement in the plexus have evolved. These adjuvant drugs ideally are expected to prolong the analgesic effect without causing any systemic side effects or prolonging motor blockade. Commonly used additives to local anaesthetic solutions are epinephrine, clonidine and opioids[2,3] benzodiazepines and phenylephrine. Clonidine[8-12] an α2 adrenergic agonist has been extensively studied as an adjunct to general and regional anaesthesia. It has been shown to produce this effect by activation of post synaptic adrenergic receptors[13]. Fentanyl an-receptor agonist has also been used widely in intra the cal, extra dural and peripheral nerve plexus blockade. Midazolam, a water soluble benzodiazepine, is known to produce antinociception[4] and to enhance the effect of local anaesthesia when given epidurally or intrathecally. Midazolam produces this effect by its action on GABA-A receptors .The presence of GABA receptors in peripheral nerves is also demonstrated[5-7]. This study is intented to determine and compare the effects of adding additives like clonidine, fentanyl and midazolam to bupivacaine in brachial plexus blockade by supra clavicular approach with regard to onset and blockade duration of blockade along with its analgesic efficacy and quality of analgesia and sedation.

Aims of the Study: The aim of the present study is to evaluate the effects of addition of 1 mcg/kg of preservative free clonidine to the maximum of 75 mcg, 1 mcg/kg of preservative free fentanyl to the maximum of 50mcg and 50mcg/kg of preservative free midazolam to 30ml of 0.25%.

MATERIALS AND METHODS

60 adult patients of both sexes in the age group of 20-60 years belonging to ASA I/II category and their weight ranging between 40-70kgs posted for various types of upper limb surgeries at the Department of Orthopedics and Department of surgery at sree Mookambika institute medical sciences the study group. This study was designed as a prospective randomised comparative study. After receiving the institutional ethical committee approval and informed consent, the patients were randomly allocated into 4 groups brachial plexus block with Nerve Stimulator was performed with supra clavicular block technique. Group 1-BC-15 patients received 30ml of 0.25% Bupivacaine with 1mcg/kg of preservative free clonidine to the maximum of 75 mcg. Group 2-BF-15 patients received 30ml of 0.25% Bupivacaine with preservative free fentanyl 1 mcg/kg to the maximum of 50 mcg. Group 3-BM-15 patients received 30ml of 0.25% Bupivacaine with preservative free midazolam 50 mcg/kg. Group 4-B-15 patients received 30ml of 0.25% bupivacaine. Clonidine an α2 adrenergic agonist has been extensively studied as an adjunct to general and regional anaesthesia. It has been shown to produce this effect by activation of post synaptic adrenergic receptors .Fentanyl an m-receptor agonist has also been used widely in intrathecal, extra dural and peripheral nerve plexus blockade. Midazolam, a water soluble benzodiazepine, is known to produce antinociception (48,49) and to enhance the effect of local anaesthesia when given epidurally or intrathecally (50)-54. Midazolam produces this effect by its action on GABA-A receptors (48,51,54). The presence of GABA receptors in peripheral nerves is also demonstrated (44,46,55). This study is intented to determine and compare the effects of adding additives like clonidine, fentanyl and midazolam to bupivacaine in brachial plexus blockade by supra clavicular approach with regard to onset and blockade duration of blockade along with its analgesic efficacy and quality of analgesia and sedation. Statistical analysis was done using the statistical package for social sciences (SPSS). Different statistical methods were used as appropriate. Mean±SD was determined for quantitative data and frequency for categorical variables. The independent t-test was performed on all continuous variables. The normal distribution data was checked before any t-test. The Chi-Square test was used to analyze group

difference for categorical variables. A p-value <0.05 was considered significant.

RESULTS AND DISCUSSIONS

Table 1: Analysis of Age Among the Groups

S. No.	Age Group in years	Group 1 (BC)	Group 2 (BF)	Group 3 (BM)	Group 4 (B)
1.	20-25	4	6	2	1
2.	26-35	4	2	6	4
3.	36-45	1	2	2	5
4.	46-55	3	5	3	3
5.	56-65	3	0	2	2

Table 2: Onset of Sensory Block

Group	Count	Mean	Standard Error
1 (BC)	15	4.733333	0.1972027
2 (BF)	15	6.466667	0.1972027
3 (BM)	15	5.8	0.1972027

Table 3: Onset of Motor Block

Group	Count	Mean	Standard Error
1 (BC)	15	6.266667	0.2510296
2 (BF)	15	7.733333	0.2510296
3 (BM)	15	7.33333	0.2510296
4 (B)	15	10.13333	0.2510296
P=0.0000 <0.005	Significant		

Table 4: Duration of Sensory Block

Group	Count	Mean	Standard Error
1 (BC)	15	602	6.549264
2 (BF)	15	452	6.549264
3 (BM)	15	421	6.549264
4 (B)	15	332	6.549264
P=0.0000 <0.005	Significant		

Table 5: Duration of Motor Block

Group	Count	Mean	Standard Error
1 (BC)	15	557.3333	7.245962
2 (BF)	15	414	7.245962
3 (BM)	15	389	7.245962
4 (B)	15	292	7.245962
P=0.0000 <0.005	Significant		

Brachial plexus blockade offers an excellent alternative technique to general anaesthesia for upper limb surgical procedures. Various approaches for successful performance of the blocks and for reducing the complication have been described. The technique chosen in this study was supra clavicular brachial plexus technique. Kulemkampff in Germany in 1911 performed the first per cutaneous supra clavicular approach. This technique was later published in 1928 by Kulemkampff and Persky (Classical) approach). Supra clavicular technique was chosen for this study because it provides a rapid onset, dense and predictable anaesthesia with a high success rate. Clonidine an α2-adrenergic agonist has been extensively used an adjunct to general anaesthesia and regional anaesthesia. When added to 1% mepivacaine6 with 1:2,00,000 epinephrine 150mcg of clonidine prolongs the duration of both anaesthesia and analgesia after axillary brachial plexus blockade. The minimum dose of clonidine 8 required to prolong significantly the duration of analgesia and anaesthesia for brachial plexus block with 1% mepivacaine is respectively 0.1mcg/kg and 0.5mcg/kg. At this dose, clonidine may be used without important reported adverse effects even in outpatients. In this present study 1mcg/kg to the maximum of 75mcg of clonidine is used. It is postulated that clonidine added to local anaesthetics for peripheral nerve block prolongs postoperative analgesia and duration of block owing to a direct action on the nerve[13]. Two mechanisms of action may be proposed. This effect might be due to clonidine mediated activation of post synaptic adrenergic receptors leading to vasoconstrictor thus prolonging local anaesthesia by decreasing the systemic absorption of the local anaesthetic. When applied on the rabbit cornea, clonidine is approximately 140 times more potent as a surface anaesthetic than procaine. This might indicate that C fibers or Ad fibers, which exclusively in nervate the rabbit cornea are especially sensitive to clonidine. Butter worth and Strichartz hypothesized that analgesia seen after neuraxial application of clonidine might result from direct inhibition of impulse conduction in primary afferent nerve fibers. They speculate that part of the efficacy of α2-adrenergic agonists at producing analgesia after their regional injection may result from their local anaesthetic actions on A a and especially C fibers[14]. Fentanyl a synthetic opioid and a m receptor agonist has been extensively studied for its use in brachial plexus block. Nishikawa *et al* have concluded in their study that fentanyl improves analgesia but prolongs the onset of brachial plexus block by peripheral mechanism[5]. Mostafa *et al* have studied the effects of addition of fentanyl to local anaesthetic in peribulbar block and concluded that addition of fentanyl to local anaesthetic mixtures fastens the onset and prolong the duration of akinesia and improve the quality of postoperative pain in peribulbar block. Karakaya *et al* have studied the analgesic and anaesthetic effects of fentanyl with 0.25% bupivacaine and concluded that addition of 100 mcg/ml fentantyl to 0.25% bupivacaine almost doubles the duration of analgesia following axillary brachial plexus block when compared to 0.25% bupivacaine alone. Midazolam as an additive to local anaesthesia has been studied in intrathecally, epidural and caudal routes. It has been proved in these studies that midazolam is as useful additive by way of improved analgesia and with sedation. 50mcg/kg midazolam in central neuraxial blockade did not produce any significant adverse effects. Studies in animals have showed no neurotoxic effects of intrathecally administered midazolam. Potentiation of analgesic effects of intrathecal fentanyl with midazolam in labouring patients has been demonstrated. Intrathecal midazolam 2mg did not increase the occurence of neurologic or urologic symptoms. Hence 50mcg/kg dose was chosen in this study[15,8]. In this prospective

randomised comparative study, 60 patients satisfying the selection criteria underwent brachial plexus with or without adjuvants. Comparison of the onset, completion and duration of the block and sedation scores between the three groups and hemodynamic variables were observed and statistically analysed. The onset and completion of the sensory and motor blockade was quicker in group I (Bupivacaine+ clonidine) followed by group II (Bupivacaine + fentanyl) and group III (Bupivacaine+midazolam)[16]. Similarly the duration of sensory block was prolonged to last longer than motor block in group I (BC) followed by group II (BF) and group (III) (BM). This is in line with the observations made by Dejong et al who explained that large fibers require a higher concentration of local anaesthetic than small fibres. The minimum effective concentration of local anaesthetic for large motor fibres is greater than for small sensory fibres. Thus motor function return before pain perception and duration of motor block is shorter than the sensory block[8]. In this study, the pain scores as assessed by the visual analog scale were significantly lower in group I (BC) when compared to the other groups. Sedation scores was higher in group III (BM) when compared to group I (BC) and group II (BF). This is due to partial vascular uptake of the drug and its transport to the central nervous system where it acts and produces sedation. The limited duration of sedation could be explained by the fact that it is highly lipophilic and diffuses faster in to the blood vessels, by its rapid clearance and short halflife. Highest sedation score was 3 ie patient was asleep and arousable by mild physical stimuli. No patient required airway compromise or required airway assistance due to sedation[17-21]. Hemodynamic variables like pulse rate, blood pressure was found to altered much in group I (BC) than group II (BF) and group III (BM), during the first 30 mins of the intraoperative period. But no patient required vassopressor support. The hypotension was only mild and corrected only with intravenous crystalloids. No complications with regard to the techniques or drug was observed.

CONCLUSION

In conclusion, clonidine 1mcg/kg to a maximum of 75mcg added to 0.25% Bupivacaine solution for supra clavicular brachial plexus block, quickens the onset of sensory and motor blockade, prolongs the duration of sensory blockade, improves the quality of postoperative analgesia when compared to fentanyl and midazolam group.

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