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Comparison of dexmedetomidine and Clonidine as an adjuvant to 0.5% bupivacaine in Ultrasound Guided Supraclavicular Brachial Plexus Block – A Randomised Clinical Trial

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ABSTRACT

Background: In this study, we have compared the analgesic effect of addition of dexmedetomidine and clonidine as an adjuvant to 20 ml solution of 0.5% bupivacaine in ultrasound guided supraclavicular brachial plexus block .Dexmedetomidine is an α-2 adrenoreceptor agonist and it can prolong the motor and sensory block for local anaesthesia. It acts by binding to presynaptic C- fibre and postsynaptic dorsal horn neurons. The analgesic action is a result of depression of release of C- fiber transmitters and hyperpolarization of postsynaptic dorsal horn neurons.

Methodology: Patient were randomly grouped by close-envelope technique into the three equal group of 30 in each group. Total 90 patients were including in this study. The blind nature of the study was maintained and the study drug is given according as,
Group -1: 20 ml of 0.5% bupivacaine.(Control group).
Group -2: 20 ml of 0.5% bupivacaine with 1mcg/kg of clonidine and.
Group -3: 20 ml of 0.5% bupivacaine with 1mcg/kg dexmedetomidine for spinal anesthesia.
Result: Patients in dexmedetomidine group-3 had a significantly longer sensory.

Results: Patients in dexmedetomidine group-3 had a significantly longer sensory (546±32.5min) and motor block (442± 42.2min) time as compared to patients in clonidine and control group.($P<0.001$). The time for first request of analgesic in the post-operative period was also longer in dexmedetomidine group (445±33.6 min) when compared to bupivacaine (control group) and clonidine group in which it was (292±18.5min) and (362±22.6 min)respectively. ($P<0.001$).

Conclusion: We concluded that dexmedetomidine with bupivacaine for local anaesthesia is associated with more prolonged motor and sensory block than clonidine with bupivacaine and bupivacaine alone.

Keywords: Dexmedetomidine, Clonidine, Bupivacaine, Supraclavicular brachial plexus block.

INTRODUCTION

Peripheral nerve blocks used is a new technique for upper limb orthopaedic surgery as it is very economical and easy to administer. However, post-operative pain control is a major problem because using only local anaesthesia is associated with relatively short duration of action, and early analgesic intervention is needed in the postoperative period. A number of

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adjuvants such as midazolam , clonidine and others have been studied to prolong the effect of anaesthesia.[1,2] A common problem during upper Limbs surgery under local anaesthesia is visceral pain, nausea and vomiting.[3] The addition of dexmedetomidine and clonidine to bupivacaine improves the quality of intraoperative and early postoperative block.[4] The addition of opioids to local anaesthetic solution have disadvantages such as vomiting and respiratory depression. Dexmedetomidine a newly highly selective α- 2 agonist, is under evolution as a neuraxial adjuvant as it provides stable hemodynamic conditions, good quality of intraoperative and post-operative analgesia with minimal side effects.[5,6] It has been approved by food and drug administration as a short term sedative for mechanically ventilated Intensive care Unit patients. Based on earlier human studies, it is hypothesized that local anaesthesia with 1 mcg/kg dexmedetomidine would produce more postoperative analgesic effect with bupivacaine with minimal side effects.[5,6] It acts on the alpha 2 receptors on the dorsal horn cells and reduces the sympathetic neurotransmitter release. The duration of motor block may be increased when it binds to the motor neurons in the spinal cord.[7] In our study we have evaluated the effect of adding dexmedetomidine and clonidine to bupivacaine separately for local anaesthesia.

MATERIAL & METHODS

The study was conducted in Rama medical college hospital and research centre, Hapur, after approval of ethical committee of the institution. Written and informed consent was obtained from all patients. Total 90 patients male and female who were in the age group between 20-60 years belonging to the American Society of Anaesthesiologists (ASA) class I and II scheduled for upper limb orthopaedic surgery under local anaesthesia were enrolled.

Exclusion Criteria

Patients who refused to participate in the study, patients with history of bleeding disorder, local infection at the site of block, who were documented with neuromuscular disorder were excluded from study. Also patients with respiratory compromise, post pneumonectomy cases having only one functional lung and who were known allergic to local anaesthesia drugs and pregnant patient were excluded from the study.

The anaesthesia technique, the visual analogue (VAS) scale for pain and other relevant things were explained to the patients in the preoperative room and in the operation theatre. An18 Gauge intravenous cannula was inserted in the hand, and preloaded with 10 ml/ kg Ringer lactate solution. Electrocardiogram pulseoximeter,non-invasive arterial pressure monitor were applied. Patients were randomly grouped by close envelope technique into the three equal group of 30 each. The blind nature of the study was maintained and the study drug is given as below

Group 1: 20 ml of 0.5% hyperbaric bupivacaine.

Group 2: 20 ml of 0.5% hyperbaric bupivacaine with 1 mcg/kg of clonidine for local anaesthesia.

Group 3: 20 ml of 0.5% hyperbaric bupivacaine with1mcg/kg dexmedetomidine for local anaesthesia.

The demographic data of the patient´s age in years, sex, weight, height, and ASA physical status were noted. Hemodynamic parameters heart rate, mean arterial blood pressure were recorded before the anaesthesia. After anaesthesia, the heart rate and mean arterial blood pressure were measured every 5 minute for the first 20 minutes and then every 10 minutes intraoperatively till the patient is shifted to the recovery room. Hypotension was said to have occurred when systolic blood pressure decreased by more than 20% from baseline measurement or a fall below 90 mmHg. It was treated with bolus intravenous infusion of normal saline 300 ml. Bradycardia was said to have occurred if heart rate less than 50 beats/min. It was treated with 0.6 mg of intravenous atropine .Total number of patient who

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required atropine or vasopressure in the intraoperative period were recorded. Ultrasound guided supraclavicular brachial block was performed under all antiseptic precautions with 22 G echogenic needle, using linear probe of 8-12 MHZ transducer with Mindray M-8 ultrasound machine was used. The block was performed with the patient in supine position with patient head turned towards opposite site. Skin transducer was placed in transverse plane in supraclavicular fossa and under ultrasound guidance the brachial plexus, subclavian artery, cervical pleura, and first rib were identified.2 ml of 2% lignocaine was injected in the skin, lateral to transducer. The bunch of grape appearance on ultrasound was noted and 22G, 5cm needle was inserted in plane towards the brachial plexus, in a lateral to medial direction. After careful negative aspiration 20 ml of solution containing study drug was injected. Sensory and motor block evaluation was done every minute after completion of drug administration until complete sensory and motor block .Sensory level were tested by pinprick test every min for the first 10 min in the distribution of ulnar, median, radial and musculocutaneous nerves using a 3 point scale as
0 = Normal sensation
1 = Loss of sensation of prick (analgesia)
2 = Loss of sensation of touch (anaesthesia)
The block was considered incomplete when any of the segment supplied by radial, ulnar, median and musculocutaneous nerve did not have analgesia even after 30 minute of drug injection. When more than one nerve remained unaffected, it was considered a failed block. In this case, general anaesthesia was given intraoperatively. Onset time for sensory block was defined as the time interval between the end of total local anaesthetic administration and complete sensory block (score 2) on all nerve. Duration of sensory block defined as the interval between the end of local anaesthetic administration and complete resolution of anaesthesia (score 0).Motor block was assessed by thumb abduction (radial nerve), thumb adduction (ulnar nerve) thumb opposition (medial nerve) and flexion of elbow (musculocutaneous nerve) with modified Bromage Scale with onset at grade 2 and peak motor block at grade 3. The motor block was assessed and recorded using modified Bromage Scale score 1,2,3 and time to reach Modified Bromage(MB) score 3 was recorded.
Grade 1 = normal motor function with full flexion and extension of elbow, wrist, and fingers.
Grade 2 = reduced motor strength with ability to move fingers only.
Grade 3 = complete motor block with inability to move fingers. Time to regress of motor blockage to modified Bromage score 1 was assessed and recorded in the postoperative period. Sedation level were assessed using Modified Ramsay sedation scale.
Score 1 = patient is awake
Score 2 = patient drowsy but respond to commands
Score 3 = asleep, but with brisk responds to glabellar tap or tactile stimulation.
Score 4= asleep with a sluggish responds to light glabellar tap or tactile stimulation.
Score 5= asleep and no responsive.
The post-operative pain scores were recorded for 24 hours at 1,6, 12,18,and 24 hour using Visual analogue scale (VAS). The time for the first request for analgesia was recorded. statistical analysis, SSPS 21.0 software was used. Data were given as means and standard deviation (SD) median and range. Chi-square and Fischer´s exact probability test for significance of associations. ANOVA test was used for continuous data. P value < 0.05 is taken as significant in the limit of 95% confidence interval.

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RESULTS

There was no significant difference with respect to the patient's demographic data, ASA status and duration of surgery among the three groups. Among the local block characteristics, the time to regress sensory block was longer in group 3 when compared with the group 1 and group 2 which is highly significant. (<0.001) The time of the motor block regression to modified Bromage 1 was significantly longer in group 3 when compared with group 1 and group 2. Time to the first request for analgesia was longer in group 3 then group 1 and 2 which is strictly highly significant (P<0.001) There was no significant difference in variation of heart rate of patient in all three group observed. With regards to intraoperative mean blood pressure, respective study groups showed no significant difference. So hemodynamic parameters were stable in all the groups and there were no complication in any patient among the three group. No statically significant difference was seen among the study groups in the number of patients who required atropine, diclofenac and tramadol in 24 hours. The VAS score was higher in group 1 and 2, as compared to group 3 at any time interval but which was statically non-significant(P>0.05).

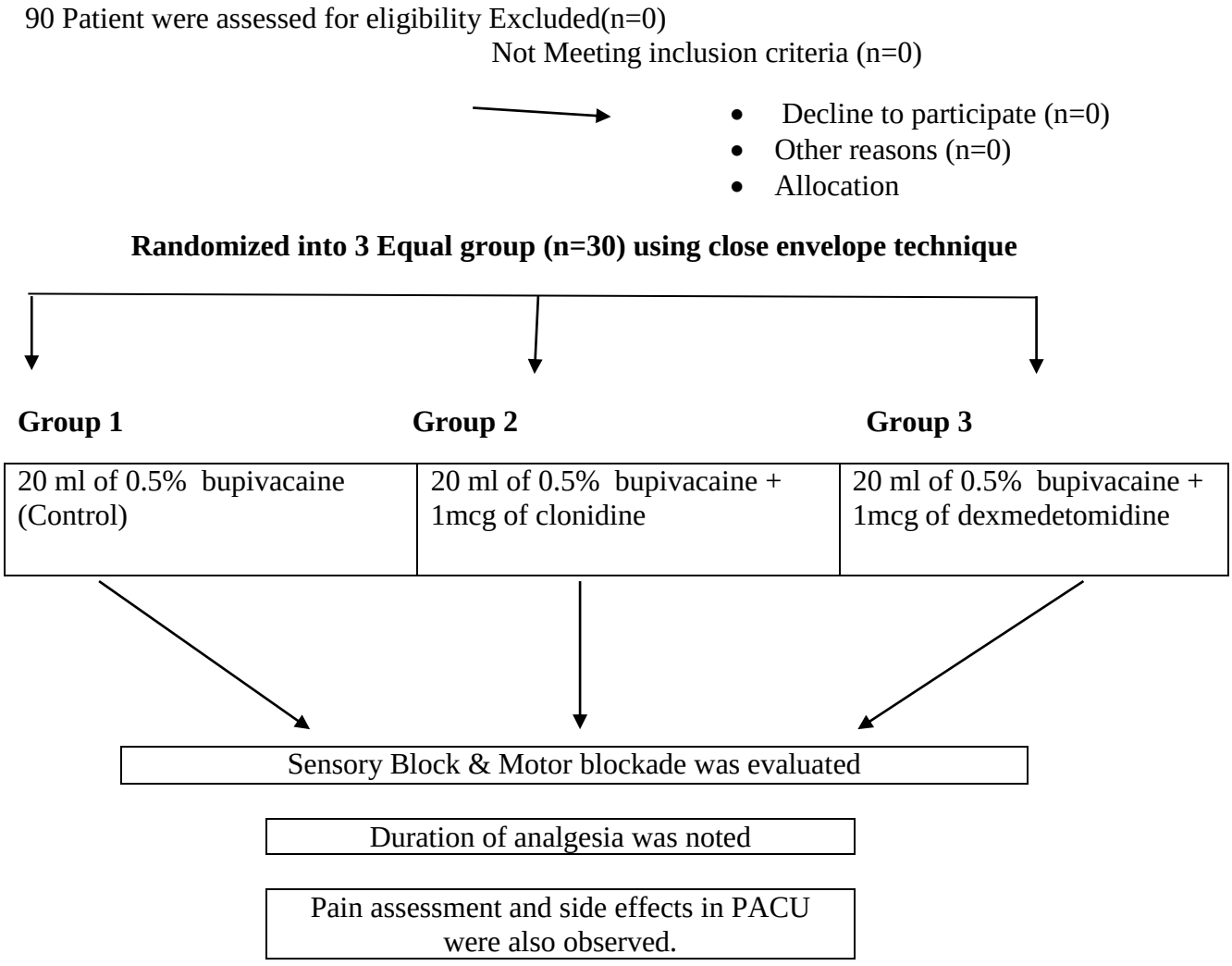

Figure1: The CONSORT flow diagram of the study

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Table 1: Comparison of demographic and surgical duration

	Group-1	Group-2	Group-3	P value
Age	41.21±13.6	37.3±12.06	39.23.3±13.8	0.304
Sex(M/F)	18/12	21/9	19/11	0.836
Height	158±2	159.21±1.8	157.21±1.01	0.606
ASA grade I and II	21/9	19/11	18/12	0.931
Weight	61.08±5.84.	64.4±1.3	65.23±1.01	0.952
Duration of surgery	120±20.0	115±10.5	112±15.5	0.005

Table 2: Block characteristics of patients

Block characteristics	Group 1	Group 2	Group 3	P-value
Time to reach highest sensory level (min)	15.5±1.8	12.2±1.6	10.9±1.8	P<0.001
Sensory block time to regression (min)	270±26.3	432±30.2	546±52.5	P<0.001
Total analgesic dose in first 24 hrs (drug % in mg)	219±66	154±73	81±63	P<0.001
Time to rescue analgesia (min)	145±19.9	175±26.42	240±28.45	P<0.001
Motor block- time to reach modified bromage 3(min)	20.2±1.6	15.5±1.6	13.6±1.4	P>0.05
Motor block- regression to modified bromage 0 (min)	210±28.2	336±32.6	442±42.5	P<0.001
Time to first request of analgesic (min)	292±18.5	362±22.6	445±33.6	P<0.001

Table 3: Postoperative Visual Analogue Scale

Variables	Group-1	Group-2	GROUP-3	P value
1h	0	0	0	0
6h	5	3	3	>0.05
12h	5	4	3	>0. 05
18h	5	3	2	>0. 05
24h	5	4	1	>0.05

Table 4: Complications

	GROUP-1	GROUP-2	GROUP-3	P VALUE
No complication	19	27	27	P>0.05
Hypotension	2	1	1	P>0.05
Bradycardia	1	0	1	P>0.05
Hypotension+ bradycardia	4	2	1	P>0.05
Shivering	1	0	0	P>0.05
Nausea + vomiting	2	0	0	P>0.05
Pruritus	1	0	0	P>0.05
Total	30	30	30	

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DISCUSSION

We observed that the use of Alpha- 2 agonists dexmedetomidine and cloning as an adjuvant to bupivacaine in supraclavicular brachial plexus block, apart from hasting the onset of sensory and motor block also significant prolonged the duration of sensory and motor block, duration of analgesia, provide significantly lower postoperative VAS pain score as well as provided comparable overall satisfaction score among patients as compared to the control group. The mechanism of the action of Alpha- 2 agonist is probably multifactorial. The analgesic effect of Alpha- 2 agonist is mediated through stimulation of Alpha 2c and Alpha 2a receptor in dorsal horn, thus directly suppressing pain transmission by reducing the release of pronociceptive transmitters substance P and glutamate and hyperpolarization of interneurons. During perineural administration the effect of dexmedetomidine and clonidine on nerve is likely elicited by prolonged hyperpolarization of unmyelinated C fibres (sensory) and to a lesser extent the A fibre(motor function). In animal modles the analgesic effect of perineural dexmedetomidine and clonidine have been shown to be caused by enhancement of the hyperpolarisation activated cation current, which prevents the nerve from returning from a hyperpolarized state to resting membrane potential for subsequent firing.[8,9] In our study patient receiving dexmedetomidine as an adjuvants with bupivacaine reported higher sedition score compared to the clonidine. No patient suffered airway compromising or required airway assistance. Similar to our study Swami et al. in their study reported that the patients in dexmedetomidine and clonidine group are comfortable throughout the surgery with arousable sedative effects. Alpha 2 agonist produce sedation by central action through activation of α- 2 adrenoreceptor in locus coeruleus. The sedative effect can be explained on the basis that some amount of systemic absorption of drug could be present which can we do to the lipophilic nature of cloning and dexmedetomidine.[10] The brachial plexus block consists of injecting a local anaesthetic drugs in the fascial spaces surrounding the brachial nerve plexus. It is simple, safe and effective technique of anesthesia having distinct advantage over general and IV regional anaesthesia. In this study we compared the efficacy and complications of recently introduced adjuvants, α- 2 agonist dexmedetomidine 1µg/ kg(group 3) and clonidine 1 µ/kg (group 2) added to 0.5% bupivacaine with a total volume of 20 ml in ultrasound guided supraclavicular approach of brachial plexus block of upper limb surgeries. Dexmedetomidine showed faster onset of sensory (10.9±1.8) and motor (13.6±1.4) blockage, prolonged duration of action with longer duration of analgesia(445±33.6) as compared to clonidine sensory (12.2±1.6),motor (15.5±1.16) and total duration (362±22.6) and control group sensory(15.5±1.8,), motor (22.2 ±1.6) and total duration(292±18.5).

In our study patient demographic characteristics and the duration of surgery was comparable. There were no significant differences with respect to hemodynamic characters (heart rate, blood pressure) among the all three groups and there were also no significant side effects (sedation, hypotension etc).

We use 20 ml volume in present study and compared to the other study which is used higher volume. A same study done by Swami S et al.[11] in 2012 reported that the onset of sensory block was shorter with dexmedetomidine 1µg /kg group than clonidine 1µg/kg group. While the onset of motor block was faster in group 2 than group 1, but the difference was not statistically significant. In this study authors used 35 ml drugs to achieve adequate analgesia in ultrasound guided Supra clavicular block.

In other study done by Ammar AS et al.[12] 30 ml of volume was used to achieve the adequate effect in ultrasound guided infraclavicular block, lower VAS pain scores, and reduction in supplemental opioid requirements. The reason behind using low volume was that direct visualisation of bundles leading to infiltration of these bundles directly.This lead to requirement of low volume of local anaesthesia by ultrasounded guided. Similar low volume was used another study where 2 to 4 ml of drug was used in axillary brachial plexus block

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under USG guided and achieved adequate blockade. The pain free period was significantly more in the dexmedetomidine group as compared to clonidine and control group and this increase may be due to the use of 1µg/kg of drug. The increase in pain free interval was beyond the pharmacological effect of either of the drugs individually and may be explained by direct modulation of activity of sensory nerve fibers.
Tripathi A et al[13] in 2016 compared 1 mcg/ kg clonidine and 1 mcg/kg dexmedetomidine as adjuvant to 0.25% bupivacaine in supraclavicular brachial block, concluded that dexmedetomidine prolong the duration of sensory and motor block as compared to clonidine with hemodynamic stability and lack of side effects. Our study showed the similar finding.
EL Boghdadly K et al[14] in 2017 conducted a systematic review and meta-analysis to compare the efficacy of perineural dexmedetomidine and clonidine when added to local anesthetics in supraclavicular brachial plexus block, they observed that compared with clonidine, dexmedetomidine prolonged the duration of sensory and motor block and also duration of analgesia. Dexmedetomidine also hastened the onset of sensory and motor block. Their finding corroborates our study.
Yoshitomi et al[15] demonstrated that α-2 agonist enhanced the local anaesthetic action via peripheral α- 2A adenoceptors. Studies have shown that clonidine when added to the bupivacaine can prolongs the duration of anaesthesia and analgesia in brachial plexus block but was associated hypotension, respective depression as a side effects. Our study also two patients developed but did not require any treatment.
Khadeet al[16] 2013 concluded that the dexmedetomidine when added to the bupivacaine for supraclavicular brachial plexus block resulted in prolongation of the duration of anaesthesia then clonidine. No hemodynamic derangements, and no sedation.
Usha K Chaudhary et al[17] 2017 has shown that the addition of dexmedetomidine and clonidine with bupivacaine in USG guided supraclavicular brachial plexus block and conclude that dexmedetomidine significantly prolongs both sensory and motor block as compared to clonidine and control group which is similar to our study. Both dexmedetomidine and clonidine provided good quality intraoperative analgesia and hemodynamic stability. The analgesia was clinically better in group 3 as compared to group 1 and group 2 but it was not statistically significant. Small dose of dexmedetomidine used in combination with bupivacaine in human have been shown to shorten the onset of motor block with hemodynamic stability and lack of sedation.
Our study showed that the motor regression to modified Bromage score 1 and time for request of first analgesia was significantly longer in dexmedetomidine group than group 1 and 2 respectively.
The α-2 adrenergic agents also have antishivering property as observed by Talke et al.[18] We too did not find any incidence of shivering in group 2 and 3 respectively.
It was observed that the addition of dexmedetomidine or clonidine to bupivacaine was not associated with post-operative nausea and vomiting in the present. Bakhamees et al[19], 2007 in a similar study compared intraperitoneal installation of 50 ml of bupivacaine 0.25%(125mg) + 1µg/kg of dexmedetomidine the observed that the incidence of post-operative nausea and vomiting was comparable in both groups.[13] Similarly in our study, the incidence of the PONV was insignificant.
The present study finding suggests that both dexmedetomidine and clonidine can be safely and effectively used as an adjuvant to bupivacaine for the local anaesthesia. Both drugs achieved a similar level of blockage and produce almost similar side effects profile. However adding dexmedetomidine with bupivacaine showed a better profile for duration of blockade and time to the requirement of post-operative rescue analgesia. Further the hemodynamic profile of patients receiving dexmedetomidine had a faster onset of sensory action (10.9±1.8 min) which was statistically significant. Our finding are consistent with studies of those of

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Sarita S et al[16] 2012.And of Karthic G S et al in 2015.[17] That also found a better onset of time for dexmedetomidine.

In the present study, 1µg dexmedetomidine as an adjuvant has provided a prolong duration of analgesia in the form of sensory blockade up to 240 minutes, reducing the need of rescue analgesics and polypharmacy in the post-operative period. Swami et al[19] reported increasing the dose of dexmedetomidine would show better and longer sensory and motor block with longer duration of anaesthesia and comparable hemodynamic and side effect profile. Only two cases of bradycardia and one case of hypotension were noticed in the study which was insignificant and not required any medication. Our study showed that the onset of sensory and motor block is faster with dexmedetomidine compared to clonidine, both dexmedetomidine and clonidine prolong the duration of sensory and motor block, more prolongation seen with dexmedetomidine. None of the patients in any group required intraoperative supplementation with analgesia or general anaesthesia during the surgical procedure. Thus both dexmedetomidine and clonidine of postoperative analgesia. Significant prolongation of duration of analgesia is seen with dexmedetomidine as compared to clonidine and control group.

CONCLUSION

Instillation of bupivacaine in combination with 1 µg/kg dexmedetomidine or with 1µg/kg clonidine significantly reduces postoperative pain score and provide longer duration of sensory and motor blockage. They also provide hemodynamically stable conditions with minimal side effect in comparison to bupivacaine alone in patients undergoing upper limb orthopaedic surgery.

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