ORIGINAL RESEARCH PAPER
Volume-6 | Issue-12 | December-2017 | ISSN No 2277 - 8179 | IF : 4.176 | IC Value : 93.98
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

COMPARISON OF THREE DIFFERENT DOSES OF DEXMEDETOMIDINE AS ADJUVANT TO BUPIVACAINE IN SUPRA CLAVICULAR BRACHIAL PLEXUS BLOCK FOR UPPER LIMB ORTHOPAEDIC SURGERIES

Anesthesiology

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ABSTRACT

BACKGROUND AND AIMS: The aim and objective of the study is to compare three different doses of dexmedetomidine and to know the optimal dose of dexmedetomidine as adjuvant to bupivacaine in supra clavicular brachial plexus block for upper limb orthopaedic surgeries.

METHODS: We studied 60 ASA l & ll patients undergoing upper limb orthopaedic surgeries under supra clavicular brachial plexus block done by ultrasound technique. . Patients were randomly allocated to three groups. Group A :(n-20) – 30 ml 0.33% bupivacaine with dexmedetomidine 30µg.Group B :(n-20) – 30ml 0.33% bupivacaine with dexmedetomidine 50µg.Group C: (n-20) – 30ml 0.33% bupivacaine with dexmedetomidine 100µg. Patients were evaluated for sensory & motor block onset and duration, duration of analgesia, sedation score, and complications. Haemodynamic parameters including non-invasive blood pressure, pulse rate, oxygen saturation were noted intra operative and post operative period.

RESULTS: The sensory and motor block onset was delayed in group A (16.3±3.31/ 20.4±2.7 min) than group B (12.4±2.5/ 16.15±2.89 min) but shortest in group C (7.35±1/12.15±2.81 min). The duration of both sensory and motor block was longest with group C (sensory 722.5±55.1min, motor 704±41.4 min) compared with group B (sensory 625.5±72.7 min, motor 604±98.6 min) and group A (sensory 432±69.8 min, motor 426.5±81.8 min). The mean duration of analgesia was dose dependent with highest in group C (736±67.1) than group B (642±76.5) and group A (480.5±81.3) in minutes.

CONCLUSIONS: We conclude that dexmedetomidine 100µg is an optimal dose to provide prolonged post-operative analgesia without much significant side effects.

KEYWORDS

Dexmedetomidine, supra-clavicular brachial plexus block, as adjuvant to bupivacaine.

KEY MESSAGES: Dexmedetomidine 100µg is an optimal dose as adjuvant to bupivacaine in supra clavicular brachial plexus block for upper limb orthopaedic surgeries without significant side effects.

INTRODUCTION :

The first supraclavicular route for brachial plexus block was introduced by kullenkampff in 1911 which was later modified as Winnie block [1]. Supraclavicular brachial plexus block via Winnie's approach is a very popular mode of anaesthesia for various upper limb surgeries. In this technique block is given at the level of distal trunk and proximal division where they are compact in structure so just 30ml volume of local anaesthetic solution is adequate in an adult person.

The currently available local anaesthetics, potentially results in block resolution before the period of worst postoperative pain. Although continuous catheter-based nerve blocks can extend postoperative analgesia, their placement requires additional cost, time and skill. While a novel sustained-release encapsulated (liposomal) preparation of bupivacaine is presently undergoing investigation in phase III trials [2], a variety of perineural adjuvants, including buprenorphine, clonidine, dexamethasone, magnesium, and midazolam, have been used to prolong the duration of analgesia of nerve blocks with varying degrees of success. Memis¸ and colleagues [3] was first to propose Dexmedetomidine, an alpha 2 adrenoreceptor agonist, as an adjuvant capable of prolonging duration of sensory and motor block produced by nerve blocks.

There are differences existed in the doses of perineural dexmedeto idine; doses varied between 30µg [4], 100 mg [5], 0.75, or 1 µg kg^{-1} [6] for the peripheral nerve blocks. In this study we have made an attempt to compare the efficacy and side effects between three doses of dexmedetomidine 30µg,50µg and 100µg as adjuvant to bupivacine in supra clavicular brachial plexus block for upper limb orthopaedic surgeries.

The onset and duration of sensory and motor block and duration of analgesia are taken as primary outcome and sedation score with complications like hypotention and bradycardia are taken as secondary outcome in this study.

METHODS:

This prospective randomized double blinded study was conducted in the orthopaedic department of our institution from Feb 2015 to Dec. 2015 after obtaining institutional ethical committee approval. After obtaining informed written consent 70 adult patients of either gender, American Society of Anaesthesiology (ASA) grade 1 and 2 between ages of 18-60 years, posted for various upper extremity orthopaedic surgeries under supraclavicular brachial plexus block were enrolled in this prospective, randomized, double-blinded, trial. The flow chart of the participants is given in the Fig 1.

Exclusion criteria included the following: patient refusal, coagulopathy, allergy to the study drugs, patients taking other medications with α-adrenergic blocking effect, renal or hepatic insufficiency, pregnancy, infection at the site of injection, and shoulder surgery.

Simple randomized sampling was done by computer generated random numbers. Seventy patients were enrolled for the study. Five patients excluded after decline to participate in the study. Remaining 65 patients were randomized into three groups, Dexmedetomidine hydrochloride (Dextomid,Neon Laboratories Ltd, India) is supplied in 100 µg/mL. Group A (n-22) – 30 ml 0.33% bupivacaine + dexmedetomidine 30µg (30µg dexmedetomidine made into 1 ml in saline), Group B (n-21) – 30ml 0.33% bupivacaine + dexmedetom idine 50µg (0.5ml saline plus 0.5ml Dexmedetomidine) and Group C (n-22) – 30ml 0.33% bupivacaine + dexmedetomidine 100µg (1 ml Dexmedetomidine). The anaesthesiologist who prepared the drug and the observer were blinded to the study. Local anaesthetic, study drug mixture was prepared by another Anaesthesiologist not participating in the study. The intra operative monitoring and post operative observation was done by the same anaesthesiologist who performed the block and was unaware of the group allocation.

Brachial plexus block was performed by supraclavicular approach before the planned surgery using SonoSiteM-Turbo (SonoSite, Bothell, Washington). Intravenous access and routine monitoring (electrocardiogram; arterial oxygen saturation, SpO2; and non invasive arterial blood pressure) were established prior to the bock.

Patients were positioned in the supine position, with the arms by the side and the head turned slightly to the contralateral side. A SonoSiteM-Turbo ultrasound system with multi beam (compound imaging) capability and with a high frequency linear array transducer (HFL25, 13–6 MHz), was used for the ultrasound guidance. The transducer was placed just cephalad and parallel to the clavicle, and the ultrasound beam was insonated toward the posterior aspect of the clavicle. Initially, the subclavian artery was identified as a hypoechoic and pulsatile structure, on top of the first rib. In the optimized sonogram, the trunks and division of the brachial plexus were visualized as multiple hypoechoic round to oval structures lying superolateral to the subclavian artery. The brachial plexus elements were also embedded in a hyperechoic connective tissue and collectively surrounded by a hyperechoic fascial layer, the brachial plexus sheath.

A 5-cm, 22-gauge, short-bevelled (17 degrees) nerve block needle (pajunk) was used to perform the block. The brachial plexus was approached with the nerve block needle (pajunk) inserted either in-plane or out-of-plane depending on the ergonomics achieved and the operators convenience. During injection of the drug solution, negative aspiration was done every 5 ml to avoid intravascular injection.

The effect of three different dose of dexmedetomidine as adjuvant to bupivacaine in supra clavicular brachial plexus block was assessed in terms of onset and duration of sensory block, onset and duration of motor block, duration of analgesia, peri operative haemodynamics and complications. Immediately following the administration of the drug, patient was evaluated for the onset of sensory and motor blockade every minute. Onset time for sensory block is the time from completion of injection to loss of cold and pain sensation (score 2). Sensory loss is assessed by cold sensation using alcohol swab in all dermatomes of brachial plexus and Atraumatic Pin Prick test which is graded in to Score 0 – normal sensation, Score 1 : loss of sensation to pin prick and Score 2 : loss of sensation to touch. Onset time for motor block is the time from completion of injection to complete motor blockade with inability to move fingers and graded by using Modified Bromage Scale for upper extremities on a three point scale[7]: Score 0 – normal motor function with full flexion, extension of elbow, wrist and fingers, Score 1 – decrease motor strength with ability to move fingers and/or wrist only and Score 2 – complete motor blockade with inability to move fingers. Sedation is assessed using Ramsay Sedation score and if the patient is anxious even 1 h after blocking the plexus, 1mg midazolam was given to achieve a sedation score of 2-3.When the saturation falls below 92% supplemental oxygen was given.

Only patients with complete sensory & motor blockade are included in the study. Failure of block to be established even after 20 min was taken as block failure. Block failure patients were managed with local anaesthetic supplementation or general anaesthesia as appropriate and those patients were excluded from the study. Vital signs heart rate, non-invasive blood pressure, sedation score and oxygen saturation were measured every minute for the first 5 min and every 5 min for 1 h, every 15 min thereafter until the end of surgery and in the post-operative period. For statistical purposes they were documented at 0,5,10,15,30,45,60,90,120,150 min. Patients were monitored for local anaesthesic toxic reactions like circumoral numbness, tinitus, twitching, and convulsions. Patients were also monitored for complications associated with the technique and the drug like intravascular injection, Intrathecal injection, pneumothorax, hypotension & bradycardia. Post-operatively heart rate, NIBP, oxygen saturation, sedation score recorded at 0,30,60 min, 2 h, 3 h, 4 h, 6 h, 12 h, 24 h. The time from onset of sensory block to Visual Analogue Scale score of 4 is taken as duration of Analgesia. Diclofenac 75mg is given intramuscularly as a rescue analgesic when the pains score (VAS) is more than four. Patients were followed for up to 24 h for any adverse effects.

A pilot study was conducted in each group before the study. The mean ± standard deviation for the time of sensory block onset was 17.5 $\pm$ 3.1 min, 12.1 $\pm$ 2.8 min and 9.5 $\pm$ 2.2 min in Group A, Group B and Group c respectively. Fifteen needed to be enrolled in each group to have a confidence level of 99.9% and power of 95%. For the sake of greater accuracy a minimum of 20 cases were enrolled in each group. The information collected regarding all the selected cases were recorded in a Master Chart. Data analysis was done with the help of computer using Epidemiological Information Package (EPI 2010) developed by Centre for Disease Control, Atlanta. Using this software range, frequencies, percentages, means, standard deviations, chi square , 'F' value and 'P' values were calculated. ANOVA test was used to test the significance of difference between quantitative variables and Yate's and Fisher's chi square tests for qualitative variables. A 'P' value less than 0.05 is taken to denote significant relationship.

RESULTS:

There were two cases in group A and C and one case in group B lost follow up due to block failure. The demographic data and surgical characteristics were comparable in all three groups (P>0.05) as shown in Table 1. The mean onset time of sensory blockade of group A was significantly longer than group B and group B was significantly longer than group C; A (16.3±3.31 min) >B (12.4±2.5 min) >C (7.35±1min); The mean onset time of motor blockade group A was significantly longer than group B which was significantly longer than group C; A (20.4±2.7 min) >B (16.15±2.89 min) >C (12.15±2.81 min). The mean duration of sensory block of group C was significantly longer than group B and group B was significantly longer than group A; C (722.5±55.1 min) >B (625.5±72.7 min) >A (432.5±69.8 min). The duration of motor block of group C was significantly higher than group B and group B was significantly higher than group A; C (704.5±41.4 min) > B (604.5±98.6 min) > A (426.5±81.8 min). The duration of analgesia between the three groups was 480±81.3, 642±76.5 and 736±67.1 min respectively. The mean duration of analgesia of C group was significantly longer than the B group and B group was significantly longer than the A group C; (736±67.1 min)>B (642±76.5 min)>A (480±81.3 min). The sedation score of three groups are compared in table 1.The C group achieved more sedation level than group B and group B achieved more sedation level than group A; C (4.65±10.4)>B (3.8±1.15)> A (2.95±1.05). The table 2 compares the adverse effects between three groups.

One case in group A, three cases in group B and four cases in Group C went for bradycardia. Hypotension was observed in two cases in group B and one case in group C. But the association within the groups did not have any statistical significance (P>0.05). The mean systolic, diastolic blood pressure and pulse rate at different times between the three groups are not statistically significant (P>0.05) (Fig 2)

DISCUSSION:

Several researches have revealed that the administration of an alpha 2 adrenergic agonist in the peripheral nerve blockade produces prolonged post-operative analgesia without much complication. Previously several mechanism have been hypothesized to explain the analgesic effect of alpha 2 adrenergic agonist including complex interaction with axonal ion channels which result in direct suppression of impulse propagation ,vasoconstriction around injection site and local release of encephalin like substances. But recent studies found that the effect of dexmedetomidine in peripheral nerve blocks is not because of central nervous system effects or vasoconstriction. Instead, the effect of peripheral perineural dexmedetomidine is because of blocking an activity-dependent cation current (the I_h current), which normally acts to reset the nerve from a hyperpolarized state back to the resting membrane potential [8,9]. By keeping the nerve in a hyperpolarized state, the nerve is unable to generate a new action potential. This effect is thought to be greater in unmyelinated C-fibers (pain fibers), and small myelinated fibers (A-delta fibers, skin-receptors for temperature sensitivity and 'fast' pain), instead of the large, myelinated motor fibers [9]. As such, dexmedetomidine was thought to possibly confer more sensory analgesia with motor sparing.

The differences existed in the doses of perineural dexmedetomidine; doses varied between 30µg, [4] 100 µg, [5] 0.75, [10] or 1 µm/ kg [6] for adjuvant to peripheral nerve blocks. These dosing inconsistencies most likely reflect the absence of human dose–response studies and/or extrapolation from animal studies [11]. Significantly prolonged durations of sensory and motor blocks and also time to first analgesic request were achieved even with the lowest doses of dexmedetomi dine, namely 30µg of peripheral nerve block administration. But pharmacodynamic data in volunteers suggest a dose of 100µg dexmedetomidine is ideal for peripheral regional anesthetic blocks [12].

As literature suggested different doses of dexmedetomedine for peripheral nerve blocks we investigated the efficacy and occurrence of side effects between three different doses namely 30µg, 50µg and 100µg to establish the safe dose of dexmedetomidine for peripheral nerve blocks.

In our study the onset time of sensory and motor block is shortened in dose depended manner; Sensory A (16.3±3.31 min) >B (12.4±2.5 min) >C (7.35±1 min) and Motor A (20.4±2.7 min) >B (16.15±2.89 min) >C (12.15±2.81 min) onsets. Likewise the duration of sensory and motor blockade also increased in dose depended manner; the mean duration of sensory block is C (722.5±55.1 min) >B (625.5±72.7 min) >A (432.5±69.8 min), the mean duration of motor block is C (704.5±41.4 min) > B (604.5±98.6 min) > A (426.5±81.8 min). The duration of analgesia is highest in 100µg dexmedetomidine group as 736±67.1 min and lowest in 30µg group as 480±81.3 min.

Rachana Gandhi et [13] al study with 30µg dexmedetomedine as adjuvant in supraclavicular brachial plexus blocks prolonged duration of analgesia as 732.4 ± 95.1 min which is higher than in our study. Dr Amit R. Khade [14] et al study with 50µg dexmedetomedine as adjuvant in supraclavicular brachial plexus block found the duration of analgesia as 970.36±80.7 which is higher than in our study. The long duration in both studies may be due the usage of higher volume (40 ml) and higher concentration of the local anaesthetics (0.5% bupivacaine). Sandhya Agarwal et al [15] used 100µg dexmedetomidine in supraclavicular brachial plexus block and found that the duration of analgesia was 776.4±130.8 min which is comparable with our study (736±67.1 min).

The side effects were found to be insignificant in 30µg dexmedetomi dine group in Rachana Gandhi et al [13] study and no evidence of respiratory depression, bradycardia, or hypotension reported in Amany S. Ammar et al [10] study with 0.75µg/kg dexmedetomidine in infraclavicular brachial plexus block. Bradycardia was observed in only one patient in the group of 100µg dexmedetomidine in supraclavicular brachial plexus block of Sandhya Agarwal et al [15] study.

In our study one case in group 30µg, three cases in group 50µg and four cases in Group 100µg went for bradycardia. Hypotension was observed in two cases in group 50µg and one case in group 100µg. These shows that the incidence of side effects are not raises with increasing the dose of dexmedetomidine in peripheral nerve blocks.

The increasing sedation score from ideal 3 in the group with 30µg dexmedetomidine to a sedation score of 4-5 in 100µg dexmedetomidine in our study is really a worrisome fact. Most of the other studies are failed to notice this and paid less importance.

So, the earlier onset of sensory and motor blockade with much increased duration of analgesia with lesser side effects can be achieved with 100µg of dexmedetomidine as adjuvant in peripheral nerve blocks compared to other doses of 30µg and 50µg of dexmedeto midine. Our study proves that a dose of 100µg dexmedetomidine is ideal for peripheral regional anaesthetic blocks but with caution on higher side of sedation score. The limitations in our study are there is no control group and the sample size may be small in each group. Further studies with large sample sizes are warranted to validate our finding of 100µg dexmedetomidine as ideal for peripheral regional anaesthetic blocks.

CONCLUSION:

To conclude, in our study we found that among the different doses of dexmedetomidine 30µg, 50µg and 100µg when added to bupivacaine for supraclavicular brachial plexus block, 100µg dose is superior in terms of onset of sensory and motor blockade and the duration of analgesia but with significant increase in sedation score. When considering the dose of 100 µg dexmedetomidine as an ideal adjuvant to peripheral nerve blocks caution should be paid to higher sedation score as well.

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