Fentanyl or Dexmedetomidine as an Adjuvant to Bupivacaine in Ultrasound Guided Supraclavicular Brachial Plexus Block: A Comparative Study

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Abstract: Peripheral nerve block as an anesthetic technique plays an important role in modern regional anesthesia. Upper limb surgeries are mostly performed under peripheral blocks such as the brachial plexus block. Peripheral nerve blocks not only provide intra-operative anesthesia, but also extend analgesia in the post-operative period without major systemic side-effects by minimizing stress response and using minimal anesthetic drugs. Ultrasound guidance has many advantages, as it can potentially improve the success rate up to 99%, fastens the onset time and reduce the risk of complications. In our study we compared between fentanyl and dexmedetomidine as adjuvants to bupivacaine in supraclavicular brachial plexus block as regards the onset and duration of the sensory and motor block as well as side effects. Fifty patients were included in this prospective, randomized, controlled, double blind study. Patients were randomly divided into two groups. Patients of group I (BD group) received 30 ml of bupivacaine 0.25% with dexmedetomidine 1 µg/kg while patients of group II (BF group) received 30 ml of bupivacaine 0.25% with fentanyl 1 µg /kg into the supraclavicular brachial plexus block. The two groups were compared regarding their demographic data (age, sex and body weight), the duration of surgery, onset and duration of sensory block and onset and duration of motor block. The duration of analgesia of the brachial plexus block was recorded. Hemodynamics were monitored through the operation. Observation of any side effects was done. Data were collected for each patient and statistical analysis was done. The present study showed that addition of dexmedetomidine to bupivacaine in ultrasound-guided supraclavicular nerve block shortened the onset times of both sensory and motor blocks and significantly prolonged their duration compared to fentanyl. Also dexmedetomidine prolonged the analgesia of brachial plexus block as well as postoperative analgesia with subsequent consumption of fewer amounts of analgesics. The use of ultrasonography in performing the supraclavicular nerve block abolished nearly the incidence of complication such as pneumothorax or intravascular injection. To conclude, we would like to state that dexmedetomidine prolongs the duration of sensory and motor block as compared with fentanyl when used as an adjuvant to bupivacaine in peripheral nerve block. Dexmedetomidine also increase time to first analgesic use, and decreases total analgesic use with no side-effects.

[Mohsen Abd Elghany Basiony, Sanaa Mohammed Elfawal, Marwa Ahmed Khairy, Ahmed Nageh Mohammed. **Fentanyl or Dexmedetomidine as an Adjuvant to Bupivacaine in Ultrasound Guided Supraclavicular Brachial Plexus Block: A Comparative Study.** *Nat Sci* 2019;17(6):9-14]. ISSN 1545-0740 (print); ISSN 2375-7167 (online). http://www.sciencepub.net/nature. 2. doi:10.7537/marsnsj170619.02.

Keywords: Fentanyl, Dexmedetomidine, Bupivacaine

1. Introductioon

Upper extremity surgeries are commonly performed under regional anesthesia. Regional anesthesia of the upper extremity has several advantages over general anesthesia such as improved postoperative pain management, decreased postoperative narcotic consumption, and reduced recovery time ***(Bruce et al., 2012)***.

The supraclavicular block provides an excellent anesthesia of all branches of the brachial plexus as they pass through a relatively confined area ***(Bruce et al., 2012)***.

Ultrasound guided (UG) supraclavicular block has been shown to be a safe alternative to the blind supraclavicular brachial plexus block as it overcomes its complications like pneumothorax or hematoma ***(McCartney et al., 2007).***

Different adjuvants are used with local anesthetics to prolong the duration of anesthesia with less adverse effects, for example; opioids, α2 agonists, and dexamethasone. Addition of fentanyl to local anesthetic is known to significantly improve the duration of sensory and motor blockade as well as visual analog scale (VAS) Scores ***(Madhusudan et al., 2011 & Nishikawa et al., 2009).***

Dexmedetomidine, a potent centrally acting α2 agonist, is widely used for anesthesia, analgesia, monitored anesthesia care, and as an adjuvant to local anesthetic for peripheral nerve block ***(Ammaeret al., 2012 & Swami et al., 2012).***

The purpose of the study will be to examine if dexmedetomidine added to bupivacaine enhances the duration of the motor block, sensory block, and duration of analgesia when compared to fentanyl added to bupivacaine for brachial plexus block.

Aim of the Work

The aim of this study was to compare between Dexmedetomidine and Fentanyl as an adjuvant to bupivacaine in supraclavicular brachial plexus block as regards the onset and duration of the sensory and motor block as well as side effects.

2. Patients and Methods

This prospective, randomized, controlled, double blind study was carried out in Ain-Shams University Hospitals on 50 adult patients between 18 and 55 years of both sexes with ASA physical status classification I & II who were scheduled for elective upper limb surgeries.

A written informed consent was obtained from all patients. Every patient received an explanation about the purpose of the study and had a hidden code number. Photos were taken only to the part of the body which was linked to the research to ensure privacy of the participants and confidentiality of the data. Procedures had been approved by both the institutional and the regional ethical committees.

Patients with known hypersensitivity to local anesthetic drugs, bleeding disorders, neuromuscular disease, uncontrolled diabetes mellitus chronic obstructive lung disease, underweight or cachectic patients, patients with neck abscess and patients with any neurological or joint disease affecting the operative limb movement like rheumatic arthritis were excluded from the study.

Patients were randomly assigned into two equal groups each formed of 25 patients using sealed envelope;

Group I: (BD) (n=25) patients received 30 ml of bupivacaine 0.25% (Sunnypivacaine, 20 ml vial contains Bupivacaine HCL Monohydrate 105.5 mg eq. to 100 mg Bupivacaine HCL, Sunny Pharmaceutical, Badr city- Cairo- Egypt) with dexmedetomidine 1 µg/kg (Precedex, Hospira, Inc., Lake Forest, IL60045USA)into the supraclavicular brachial plexus block.

Group II: (BF) (n=25) patients received 30 ml of bupivacaine 0.25% with fentanyl 1 µg /kg (Sunny pharmaceutical under license of Hameln pharmaceuticals- Germany).

Anesthetic management:

Preoperative evaluation was done to all patients which included history taking, full examination including general examination and local examination to detect any abnormality at the injection site. Laboratory investigations included complete blood count, coagulation profile, liver and kidney functions tests, chest x-ray and electrocardiogram (ECG) were done to all patients before the study.

Measurements

Measurements for all patients of two groups were as following:

1- Hemodynamics:

Baseline mean arterial blood pressure and heart rate values were recorded 5, 10, 15, 30, 45, 60, 120 min. after the injection. (If systolic blood pressure was <20% from base line or MAP <60 mmHg, it was treated firstly by bolus of IV fluid then IV ephedrine 5 mg incrementally. If the HR is <50 beats/min, 0.5 mg atropine sulfate was administrated).

2- Onset of sensory block:

Was defined as the time interval between the drug injection and complete loss of sensation, The anesthetized limb was hidden from the patient's sight with a drape, Sensory blockade of each nerve was assessed every 5 min up to 20 min by pin prick method in the different dermatomes according to its distribution ***(Musculocutaneous nerve*:** lateral side of the forearm, ***Radial nerve:*** dorsum of the hand over the 2nd metacarpophalangeal joint, ***Ulnar nerve****:* little finger, ***Median nerve****:* medial thenar eminence, and ***Medial cutaneous nerve:*** medial side of the forearm) on three point scale:

(0 = full sensation, 1 = partial loss of sensation, 2 = complete loss of sensation).

3- Onset of motor block (min): was defined as the time interval between the end of the drug injection and paresis in all of the nerve distributions, the degree of motor block was checked every 5 minutes up to 20 minutes by assessing the motor function as follows: elbow flexion for the ***musculocutaneous nerve***, extension and supination of arm and finger for the ***radial nerve***, flexion and pronation of wrist and 2-3rdfinger for the ***median nerve***, 4-5thfinger flexion and thumb adduction for the ***ulnar nerve***, The strength of voluntary movement was assessed according to a three grade scale: *(0= no block, 1= partial block, 2= complete block).*

4- Duration of sensory block (mins): was defined as the time interval between the onset of sensory block and complete recovery of sensation in the operative limb *(tested every 15 min postoperative) by pin prick method.*

5- Duration of motor block (mins): was defined as the time interval between the onset of motor block and complete recovery of motor function in the operative limb *(tested every 15 min postoperative).*

6- Duration of analgesia (DOA) of the brachial plexus block: was defined as the time interval between the complete sensory block and the

first postoperative analgesic request. Patients received 25 mg pethidine intravenously.

7- Postoperative analgesic requirement:

The number of doses of pethidine needed was recorded in the first 24 hours.

8- Complication:

The patients were observed for the occurrence of any adverse effect and/or complication related to procedure (e.g. pneumothorax, hematoma), or to the study drugs e.g. hypotension (20%decrease below baseline value), bradycardia (HR<50 beats/min), nausea, vomiting or Local anesthetics toxicity which was managed according to guidelines.

Statistical analysis:

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

3. Results

Demographic data of the patients and duration of surgery:

There was no significance difference between both groups regarding demographic data (age, sex, weight and ASA) and duration of surgery.

Assessment of hemodynamic changes:

Regarding hemodynamic parameters (HR, MBP), There was no significance difference between both groups regarding basal reading and after 5 or 10 minutes. However, patients in BD group showed lower heart rate and mean blood pressure when compared with BF group which were significant after 15, 30, 60 and 90 min. intraoperatively.

Assessment of onset sensory blockand motor block:

The onset of sensory block and motor block were earlier among patients in BD group when compared to patients in BF group, which were highly significant (p<0.001). **Table (1, 2)**.

Table (1): Comparison between both groups regarding onset of sensory block **(min).**

Onset of sensory block (min)	BD group *(n=25)*	BF group *(n=25)*	t-test	p-value
Mean±SD	18.36±2.56	22.32±2.19	14.440	<0.001**
Range	14-22	18-27		

*t-Independent Sample t-test; **p-value <0.001* highly significant

Table (2): Comparison between both groups regarding onset of motor block (min).

onset of motor block (min)	BD group *(n=25)*	BF group *(n=25)*	t-test	p-value
Mean±SD	22.04±2.72	24.52±2.16	8.760	<0.001**
Range	18-27	20-28		

*t-Independent Sample t-test; **p-value <0.001* highly significant

This table shows highly statistically significant decrease BD group compared to BF group according to onset of motor block.

Duration of sensory block and motor block:

Patients in BD group experienced longer duration of sensory and motor block than patients in BF group. which was highly significant (p<0.001) **Table (3, 4)**

Table (3): Comparison between both groups regarding duration of sensory block**.**

Duration of sensory block (min)	BD group *(n=25)*	BF group *(n=25)*	t-test	p-value
Mean±SD	919.60±30.75	802.20±29.16	9.871	<0.001**
Range	870-980	750-850		

*t-Independent Sample t-test; **p-value <0.001* highly significant

Table (4): Comparison between both groups regarding duration of motor block.

Duration of motor block (min)	BD group *(n=25)*	BF group *(n=25)*	t-test	p-value
Mean±SD	789.20±26.64	690.40±26.22	17.675	<0.001**
Range	725-850	640-750		

*t-Independent Sample t-test; **p-value <0.001 highly significant*

Assessment of the duration of analgesia of the block:

Patients in BD group experienced longer duration of analgesia when compared to patients in BF group, which was highly significant (p<0.001). **Table (5)**

Table (5): Comparison between both groups regarding duration of analgesia (min).

Duration of analgesia of the block (min)	Group A *(n=25)*	Group B *(n=25)*	t-test	p-value
Mean±SD	960.40±39.00	874.80±38.42	12.129	<0.001**
Range	900-1050	800-940		

*t-Independent Sample t-test; **p-value <0.001 highly significant*

Postoperative analgesic requirement:

Patients in BD group required less analgesic doses postoperatively than patients in BF group which was highly significant (p<0.001) **Table (6)**.

Table (6): Comparison between both groups regarding postoperative analgesic.

Postoperative analgesic requirement	BD group *(n=25)*	BF group *(n=25)*	x2	p-value
One dose of pethidine	21 (84.0%)	10 (40.0%)	10.272	<0.001**
Two doses of pethidine	4 (16.0%)	15 (60.0%)		

*x^2: Chi-square test; **p-value <0.001 highly significant*

Adverse effects and complications:

No adverse effects or complications related to procedure or to the study drugs were recorded in any patient in either group.

4. Discussion

Thehe current study shows that addition of dexmedetomidine to bupivacaine for ultrasound-guided supraclavicular nerve block significantly leads to earlier onset of sensory and motor block as well as increased duration of analgesia than addition of fentanyl. Dexmedetomidine also decreases postoperative analgesic doses.

Rajkhowa and his colleagues in 2016 found in their study on fentanyl as adjuvant in brachial plexus nerve block, that the mechanism of fentanyl in prolongation of analgesia may be due to the existence of peripheral functional opioid receptors, but this existence in peripheral tissue is still doubtful.

Furthermore, Rajkhowa *et al*. mentioned in their study that fentanyl used with ropivacaine prolonged the duration of sensory and motor blockade, probably by directly binding with opioid binding sites on the dorsal nerve roots aided with these axonal transports or by diffusing into surrounding tissues and subsequently into the epidural and subarachnoid spaces; it may also have been central opioid receptor mediated after systemic absorption of fentanyl.

Dexmedetomidine, a potent centrally acting α2 agonist, is widely used for anesthesia, analgesia, monitored anesthesia care, and as an adjuvant to local anesthetic for peripheral nerve block ***(Ammaer et al., 2012 & Swami et al., 2012).***

In our study we compared between Fentanyl and Dexmedetomidine as adjuvants to bupivacaine in supraclavicular brachial plexus block, Regarding assessment of onset of sensory block, adding dexmedetomidine in BD group significantly fastened the onset of sensory block when compared to adding fentanyl in BF group (18.36 ± 2.56 and 22.32 ± 2.19 minutes, p<0.001 respectively).

Not only dexmedetomidine fastened the onset of the sensory block, but also it prolonged the duration of the sensory block when compared to fentanyl (919.60±30.75 and 802.20± 29.16 minutes; p<0.001 respectively).

This result can be explained by two reasons; first, dexmedetomidine was found to have a local vasoconstriction effect which explains the prolongation of the block. Second, it augments the sodium channel blocking action of local anesthetics by opening potassium channels leading to membrane hyperpolarization. These actions explain the effect of α2 agonists when injected in various peripheral nerve blocks ***(Chakraborty et al., 2010).***

In our study we noticed that patients in dexmedetomidine group showed faster onset of motor block than patients in fentanyl group, similarly, the duration of motor block was significantly longer in

BD group (789.20±26.64 minutes) than in BF group. (690.40±26.22 minutes) p<0.001.

The results of our study came in agreement with the results of previous studies. **Esmaoglu and his colleagues in 2010** added dexmedetomidine to levobupivacaine for axillary brachial plexus block and showed that it shortened the onset time of both sensory and motor block and prolonged the duration of block.

Recently **Kaygusuz and his colleagues in 2012** evaluated the addition of dexmedetomidine 1 µg/kg to 0.5% levobupivacaine in axillary brachial plexus block and observed significantly earlier onset of sensory block, and longer sensory and motor block duration.

Concerning the duration of postoperative analgesia of the block, patients in BD group experienced longer pain free period than patients in BF group (960.40±39.00 min. versus 874.80±38.42 min). Additionally, patients in BD group needed less pethidine when compared to patients in BF group.

A similar result was obtained by **Das and his colleagues in 2014** who used 100 micrograms of dexmedetomidine added to 30 ml of ropivacaine (0.5%) in supraclavicular nerve block in upper limb surgery. The study included 84 patients and they used intramuscular diclofenac sodium for postoperative analgesia. They noticed that dexmedetomidine group received much less doses of rescue analgesia than other group (ropivacaine only group) with statistical highly significant difference.

Bharti and his colleagues in 2015 found in their study on dexmedetomidine as adjuvant with local anesthetic in supraclavicular nerve block that it prolonged anesthetic duration by 3 h and total analgesic duration by 4 h compared to the control group.

Ammar and his colleagues in 2012 used dexmedetomidine with bupivacaine and compared it with plain bupivacaine and demonstrated enhancement of onset of sensory and motor blockade, prolonged duration of analgesia, increased duration of sensory and motor block, lower VAS pain scores, and reduction in supplemental opioid requirements.

On the other hand**, Farooq and his colleagues in 2017** in their study showed that addition of fentanyl and dexmedetomidine were nearly equal effective in extending the duration of ropivacaine in ultrasound-guided brachial plexus block. This may be due to the use of ropivacaine rather than bupivacaine as ropivacaine has a longer duration of action, and the effect of adjuvants may not appear.

Regarding hemodynamics data in our study, MAP and heart rate were recorded althrough the operation. Patients in BD group showed lower heart rate and mean blood pressure when compared with BF group which were significant after 15, 30, 60 and 90 min. This negative chronotropic effect of dexmedetomidine did not require any anticholinergic drug therapy. **Abdallah and Brull in 2014** in the meta-analysis of perineural application of dexmedetomidine as a local anesthetic adjuvant stated that dexmedetomidine produced reversible bradycardia in 7% of brachial plexus block patients with no incidence of hypotension.

In contrast to the current study **Esmaoglu and his colleagues in 2010** recorded sever bradycardia in 7 patients out of 30 when they added 100 micrograms of dexmedetomidine to levobupivacaine 0.5% compared to control group in which 30 ml of levobupivacaine 0.5% was used alone.

Technical complications of supraclavicular brachial Plexus block such as hematoma and pneumothorax were not reported in our study. No respiratory depression was observed in any patient of the study.

In contrast to our study, **Das and his colleagues in 2014** recorded pneumothorax in 6 patients out of 84 when they used a nerve stimulator during performing supraclavicular nerve block.

The safety of ultrasound-guided nerve blocks explained the absence of such complication (pneumothorax) in the current study.

A limitation of our study was small sample size; more studies with larger sample sizes will be needed to confirm our results. The second was expense and unavailability of dexmedetomidine vials.

We recommend using dexmedetomidine as adjuvant with supraclavicular nerve block to provide earlier onset of the block and longer period of postoperative analgesia.

Conclusion:

In the current study, Addition of dexmedetomidine to bupivacaine in supraclavicular nerve block shortened the onset times of both sensory and motor blocks and significantly prolonged their duration. It also prolong the analgesia of brachial plexus block as well as postoperative analgesia with subsequent consumption of fewer amounts of analgesics.

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3/13/2019