ABSTRACT

Background: Alpha-2 agonists are mixed with local anesthetic agents to extend the duration of spinal, extradural and peripheral nerve blocks. Ketamine is an N-Methyl D-Aspartate antagonist with analgesic properties which modulates central sensitization of nociceptive stimulation. Aim of the work: This study compared Dexmedetomidine and Ketamine as an adjuvant to local anesthetic agent in axillary brachial plexus block with respect to onset and duration of sensory and motor block and duration of analgesia. Patients and Methods: Sixty ASA I and II patients scheduled for elective upper limb surgeries under supraclavicular brachial plexus block were divided into two equal groups in a randomized, double-blinded fashion. Group D received dexmedetomidine 1 μg/kg and group K received Ketamine 2 mg/kg added to bupivacaine 0.25% (25cc). Onset and recovery time of sensory and motor block, duration of analgesia and quality of block were studied in both two groups. Results: Duration of sensory block and motor block was 413.97±87.13 and 472.24±90.06 min, respectively, in group D. while it was 227.00±48.36 and 292.67±59.13 min, respectively, in group K. There was no statistically significant difference in onset of sensory and motor block between the two groups. The duration of analgesia (time to requirement of rescue analgesia) in group D was 456±97 min, while in group K, it was 289±62 min. statistically, this difference was significant
The number of patients achieving grade IV quality (excellent) of block was higher in group D (86.6%) as compared with group K (46.6%) (P<0.05).

**Conclusion:** Dexmedetomidine when added to local anesthetic in axillary brachial plexus block enhanced the duration of sensory and motor block and also the duration of analgesia. The time for rescue analgesia was prolonged in patients receiving dexmedetomidine. It also enhanced the quality of block as compared with ketamine.

**Keywords:** dexmedetomidine, ketamine, axillary block.

**INTRODUCTION**

The axillary block is particularly useful in providing anesthesia and postoperative analgesia for surgery to the elbow, forearm, wrist, and hand. The axillary block is also the safest of the four main approaches to the brachial plexus, as it does not risk paresis of the phrenic nerve, nor does it have the potential to cause pneumothorax (Satapathy and Coventry, 2011). In the axilla, the nerves of the brachial plexus and the axillary artery are enclosed together in a fibrous sheath, which is a continuation of the deep cervical fascia. The easily palpated axillary artery thus serves as a reliable anatomical landmark for this block, and the injection of local anesthetic close to this artery frequently leads to a good block of the brachial plexus. The axillary block is commonly performed due to its ease of performance and relatively high success rate (Winnie, 1990).

Adjuvants to the regional nerve block with drugs that prolong the duration of analgesia always a subject for researches as it lessens the adverse effects of local anesthetics.

Alpha-2 adrenergic receptor agonists have been the focus of interest for their sedative, analgesic, perioperative sympatholytic and cardiovascular stabilizing effects with reduced anaesthetic requirements. Furthermore, various methods of administration, such as epidural, intrathecal and peripheral injections, have been
tried either alone or in combination with another drug to prolong and intensify the anaesthesia. (Elliott et al., 1997) and (Popping et al., 2009).

Dexmedetomidine, a potent $\alpha_2$ adrenoceptor agonist, is approximately eight-times more selective towards the $\alpha_2$ adrenoceptor than clonidine. (Raimo et al., 1988). In previous clinical studies, intravenous dexmedetomidine resulted in significant opioid sparing effects as well as a decrease in inhalational anaesthetic requirements (Keniy et al., 2011).

Dexmedetomidine, a selective $\alpha_2$-adrenoceptor agonist, has been used as an adjuvant during regional and local anesthesia (Ebert et al. 2000) and (Yoshitomi et al, 2008). Studies have shown safety and efficacy of adding dexmedetomidine to local anesthetics in various regional anesthetic procedures, such as subarachnoid, epidural, and caudal injections (Brummett et al., 2010).

Amany et al., 2012, have concluded that improved parameters of analgesic efficacy support the use of dexmedetomidine as an adjunct mixed with local anesthetics for brachial plexus blockade to improve pain management and prolong anesthesia duration of local anesthetics.

N-Methyl D-Aspartate (NMDA) receptors play an important role in neuronal plasticity leading to central sensitization and in the intensity of perceived postoperative pain. Ketamine is an NMDA antagonist with analgesic properties which modulates central sensitization of nociceptive stimulation (Sunder et al., 2008). Kulkarni et al. found ketamine to be a safe and effective adjuvant for stellate ganglion blocks when combined with LA solution for relief of pain and ischemia in patients suffering from peripheral vascular disease of the upper limbs (Kulkarni et al., 2010).

This study was designed to compare the efficacy of dexmedetomidine versus ketamine as an adjuvant in combination with local anesthetic solutions during an axillary Block for upper extremity surgery.
PATIENTS AND METHODS

After approval from ethical committee and written informed consent from the patients, this study was in Al-Azhar university hospital through a double-blind randomized prospective clinical study was carried out on 60 American Society of Anesthesiologist (ASA) Grade I and II patients of either sex, aged 18–65 years, undergoing various bony orthopedic surgeries on the upper limb under axillary brachial plexus block. The study was conducted in two groups of 30 patients each. The patients were randomly assigned using “slips in a box technique” to one of the following groups:

Group D: Bupivacaine 0.25% (25 cc) + dexmedetomidine 1 μg/kg
Group K: Bupivacaine 0.25% (25 cc) + ketamine 2 mg/kg

Patients on adrenoreceptor agonist or antagonist therapy, with known hypersensitivity to local anaesthetic drugs, bleeding disorders, uncontrolled diabetes mellitus, and pregnancy and pre-existing peripheral neuropathy, were excluded from the study.

On arrival in the operation room, baseline heart rate, blood pressure and oxygen saturation were recorded. An intravenous line was secured in the unaffected limb and Ringer's lactate was started.

All the patients received brachial plexus block through the axillary approach by an experienced anesthesiologist different from the one assessing the patient intra- and post-operatively. Both were blinded to the treatment groups. Neural localization was achieved by using an ultrasound (sonosite).

Following negative aspiration, 25 mL of a solution containing local anesthetic combined with dexmedetomidine or ketamine as mentioned above was injected. A 3-min massage was performed to facilitate an even drug distribution.

Sensory block was assessed by the pinprick method. Assessment of sensory block was done at each minute after completion of drug injection in the dermatome areas corresponding to median nerve, radial nerve, ulnar nerve and
musculocutaneous nerve till complete sensory blockade. Sensory onset was considered when there was a dull sensation to pin prick along the distribution of any of the above-mentioned nerves. Complete sensory block was considered when there was complete loss of sensation to pin prick.

Sensory block was graded as-

**Grade 0:** Sharp pin felt

**Grade 1:** Analgesia, dull sensation felt

**Grade 2:** Anesthesia, no sensation felt.

Assessment of motor block was carried out by the same observer at each minute till complete motor blockade after drug injection. Onset of motor blockade was considered when there was Grade 1 motor blockade. Peak motor block was considered when there was Grade 2 motor blockade. Motor block was determined according to a modified Bromage scale for upper extremities on a 3-point scale (Ramsay et al., 1974).

**Grade 0:** Normal motor function with full flexion and extension of elbow, wrist and fingers

**Grade 1:** Decreased motor strength with ability to move the fingers only

**Grade 2:** Complete motor block with inability to move the fingers

The block was considered incomplete when any of the segments supplied by median, radial, ulnar and musculocutaneous nerve did not have analgesia even after 30 min of drug injection. These patients were supplemented with intravenous fentanyl (1 μg/ kg) and midazolam (0.02 mg/kg). When more than one nerve remained unaffected, it was considered a failed block. In this case, general anaesthesia was given intraoperatively. Patients were monitored for hemodynamic variables such as heart rate, blood pressure and oxygen saturation every 30 min after the block intraoperatively and every 60 min post-operatively. Sedation of patient was assessed by the Ramsay Sedation Score. At the end of the
procedure, quality of operative conditions was assessed according to the following numeric scale (Memis et al., 2004).

**Grade 4:** (Excellent) No complaint from patient

**Grade 3:** (Good) Minor complaint with no need for the supplemental analgesics

**Grade 2:** (Moderate) Complaint that required supplemental analgesia

**Grade 1:** (Unsuccessful) Patient given general anesthesia

Assessment of blood loss was done and fluid was administered as per the loss. Duration of surgery was noted.

The intra- and post-operative assessment was done by an anaesthesiologist who was unaware of the drug used. Patients were assessed for duration of analgesia as per a numeric rating scale of 0 to 10. The numeric rating scale was recorded post-operatively every 60 min till the score of 5. The rescue analgesia was given in the form of intravenous paracetamol 500 mg at the Numeric Rating Scale of 5 and the time of administration was noted. All patients were observed for any side-effects like nausea, vomiting, dryness of mouth and complications like pneumothorax, haematoma, local anaesthetic toxicity and post-block neuropathy in the intra- and post-operative periods.

The duration of sensory block was defined as the time interval between the end of local anaesthetic administration and the complete resolution of anaesthesia on all nerves. The duration of motor block was defined as the time interval between the end of local anaesthetic administration and the recovery of complete motor function of the hand and forearm.

**Statistical analysis**

The data was analyzed by SPSS version (Statistical Package for Social Sciences) software. Unpaired t-test was applied for demographic data, haemodynamic parameters, onset and duration of sensory and motor blockade and duration of analgesia. Fisher exact test was applied for assessment of quality of
block. P-value was considered significant if <0.05 and highly significant if <0.001.

**RESULTS**

There were a total number of 60 patients fulfilling the inclusion criteria were randomly assigned to one of the two groups. There was no protocol deviation pre-operatively and intraoperatively,

Both groups were comparable in terms of age, gender, weight and type of surgeries [Table 1] (P>0.001).

**Table 1: Patient characteristics**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group C (Mean±SD)</th>
<th>Group D (Mean ± SD)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>33.25 ± 9.63</td>
<td>32.58 ± 8.63</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>73.96 ± 5.06</td>
<td>70.54 ± 5.54</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>11/19</td>
<td>8/22</td>
<td>NS</td>
</tr>
<tr>
<td>Types of surgery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cole’s wrist fracture</td>
<td>7</td>
<td>9</td>
<td>**NS</td>
</tr>
<tr>
<td>Olecranon fracture</td>
<td>8</td>
<td>11</td>
<td>NS</td>
</tr>
<tr>
<td>Radial head fractures</td>
<td>13</td>
<td>12</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Cole’s’ wrist fracture It’s also known as a distal radius fracture

**NS: non significant.

The baseline haemodynamic parameters were comparable in both groups. Significantly lower pulse rate was observed at 60, 90 and 120 min, but not less than 60 beats/min, in Group D as compared with Group K (Figure 1) (P<0.001). Systolic and diastolic blood pressure were found to be significantly lower than baseline from 30 to 120 min in Group D as compared with Group K (Graph II) (P<0.001). No treatment was required for this fall in blood pressure. The hemodynamic parameters were comparable at the end of 180 min. [Figure 2].
Onset of sensory block was faster in Group D than in Group K, while onset of motor block was faster in Group K than in Group D, but the difference was not statistically significant [Table 2] (P>0.001).

**Table 2: Sensory and motor block onset time, block and analgesia durations in both groups**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group D (n = 30)</th>
<th>Group K (n = 30)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of surgery (minutes)</td>
<td>47 ± 17.53</td>
<td>43.08 ± 10.48</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Onset of Sensory block (seconds)</td>
<td>1.88 ± 1.38</td>
<td>2.35± 1.23</td>
<td>&lt;0.085</td>
</tr>
<tr>
<td>Onset of Motor block (minutes)</td>
<td>12.46 ± 3.31</td>
<td>7.83 ± 1.37</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Duration of sensory block</td>
<td>413.97±87.31</td>
<td>227.00±48.36</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Duration of motor bloc</td>
<td>472.24±90.06</td>
<td>292.67 ±59.13</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Duration of analgesia (min)</td>
<td>456.21 ± 97.99</td>
<td>289.67 ± 62.50</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Post recovery pain score (VAS)</td>
<td>3.21 ± 0.41</td>
<td>3.21 ± 0.41</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Satisfaction score</td>
<td>2.75 ± 0.44</td>
<td>3 ± 0</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Sedation Score</td>
<td>2.67 ± 0.48</td>
<td>2.29 ± 0.62</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
Duration of sensory block was 413.97±87.31 min in Group Das compared with 227.00±48.36 min in Group K. Statistically significant longer duration of sensory block was observed in Group D [Table 2 and Figure 3] (P=0.001).

![Figure 3: Comparison of duration of sensory block, motor block and analgesia in both the groups](image)

The duration of motor block was 292.67±59.13 min in Group C as compared with 472.24±90.06 min in Group D. Again, duration of motor block was significantly longer in Group D [Table 2 and Figure 3] (P=0.001).

There was significant increase in duration of analgesia in Group D (456.12±97.99 min) as compared with Group K (289.67±62.50 min). The difference was statistically significant [Table 2 and Figure 3] (P=0.001).

In Group D, 87% of the patients achieved Grade IV quality of block as opposed to 47% in Group K (P<0.05). There were a total 17 patients in Group C with Grade II and III block and six patients in Group D who required sedation or sedation with analgesia. One patient in Group k required general anaesthesia as the block was inadequate [Table 3].

**Table 3: Quality of block**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Group D (number %)</th>
<th>Group K (number %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>-</td>
<td>1 (3.4)</td>
</tr>
<tr>
<td>II</td>
<td>1 (3.4)</td>
<td>7 (23.3)</td>
</tr>
<tr>
<td>III</td>
<td>3 (10)</td>
<td>8 (26.7)</td>
</tr>
<tr>
<td>IV</td>
<td>26 (86.6)</td>
<td>14 (46.6)</td>
</tr>
</tbody>
</table>
No side-effects (nausea, vomiting, dry mouth) were reported during the first 24 h in the post-operative period in both the groups.

**DISCUSSION**

In this randomized, double-blinded trial, we compared dexmedetomidine and ketamine as an adjuvant to Bupivacaine in axillary brachial plexus block

The use of ultrasound-guided blocks helped us to lower the dosages and volumes of local anaesthetic (25 cc)

The efficacy of peripheral perineural dexmedetomidine added to bupivacaine and ropivacaine for sciatic nerve blocks in rats has been established (Brummett et al., 2010)

The increase in duration of analgesia is dose dependent and the effect is peripheral (i.e., not caused by centrally mediated or systemic analgesia) (Brummett et al., 2008).

In this study, we compared the addition of dexmedetomidine (Group D 1 μg/kg) of ketamine (Group K 2 mg/kg) to bupivacaine in axillary brachial plexus block. The result of this study shows that all patients in both groups were comparable with respect to demographic profile, duration of surgery and type of surgery. With these doses, we had stable hemodynamics in patients except significant lower pulse rate in Group D at 60, 90 and 120 min as compared with Group K, but not less than 60 beats/min.

This is in contradiction to another study which showed dexmedetomidine decreased mean arterial and diastolic blood pressures and heart rate during the procedures Alireza M. et al., (2014).

There is a study showed that when dexmedetomidine added to bupivacaine for axillary brachial plexus block is more superior than Ketamine in shortens of
the onset time of sensory block, prolongs the duration of block and the duration of
post-operative analgesia (Esmaoglu et al., 2010)

This may be because peripheral $\alpha_2$ agonist produces analgesia by reducing
release of norepinephrine, leading to $\alpha_2$ receptor-independent inhibitory effects on
nerve fiber action potentials. However, in this study, we found that postoperative
pain score is not significant statistically.

The concern of prolongation of motor block was minimal patient discomfort
on movement in the post-operative period.

Memis et al. in their study showed that addition of dexmedetomidine to
lignocaine for intravenous regional anaesthesia improves both the quality of
anaesthesia as well as intraoperative and post-operative analgesia. In this study,
the quality of block in 87% of the patients in Group D was grade IV, i.e. excellent
block without any supplementary sedation or analgesia, while 47% in Group K
achieved grade IV quality (Memis et al., 2004).

None of the patients in Group D required sedation intraoperatively and they
were comfortable throughout the surgery with arousable sedative effects. This can
be explained on the basis that some amount of systemic absorption of drug could
be present.

Previous studies have indicated that the addition of ketamine (10-50 mg) to
epidural bupivacaine or lidocaine prolongs the duration of regional anesthesia.
They suggested that the enhancement of lidocaine epidural anesthesia by
ketamine is more likely the result of the direct action of ketamine on the nerve
root fibers rather than the action on the spinal cord (Loix et al., 2011).

Local anesthetic properties of ketamine were demonstrated and reported
that ketamine could produce reversible inhibition of the compound action
potential in the stimulated frog sciatic nerve(Dowdy et al., 1973). Also, dogs
injected with ketamine rapidly developed reversible segmental paralysis (with no alteration of the state of consciousness). The effect of ketamine on nerve conduction was confirmed by Weber et al., 1975.

In contrast, in some studies, the addition of ketamine to local anesthetics has not improved the peripheral, regional, or local analgesia (Rahimzadeh et al., 2013) compared the analgesic effects of peri-femoral nerve infusion of ketamine plus ropivacaine versus ropivacaine, after operation, in patients who underwent elective knee surgery for repairing the anterior cruciate ligament, under spinal anesthesia. They reported that the addition of ketamine 1 mg/kg to 0.1% ropivacaine could not improve postoperative pain relief in the first 48 hours after the operation. Luban I et al., 2002, reported that ketamine added to local bupivacaine did not enhance analgesia after wound infiltration following Cesarean section.

The addition of ketamine to local anesthetics failed to improve analgesia after intra-articular injection for knee arthroscopy (Rosseland et al., 2003).

The explanation of various effects of Ketamine may be due to different dose used in searches. This study administered 2 mg/kg ketamine and it was more than what the previously mentioned studies had used without complications and alterations in the level of consciousness.

This study showed that ketamine decreased the severity of postoperative pain till 24 hours after surgery. As Tverskoy and colleagues (Tverskoy et al., 1996).

This is in agreement with a recent study which showed that the addition of ketamine 2 mg/kg to lidocaine in the brachial plexus block did not improve the onset and duration of the sensory or motor block, but it decreased the postoperative pain and need for analgesics, without significant adverse effects.

Therefore, it could be considered as an option to enhance the analgesic
effects of the brachial plexus block. (Mohammad L. et al., 2014). It showed, the effect of ketamine on the inhibition of central sensitization explained the long-lasting analgesic effect of ketamine on postoperative pain.

In the Tverskoy et al. study, the analgesic efficacy of ketamine when added to bupivacaine infiltration before inguinal hernia repair, by the same mechanism, lasted for one week after infiltration (Tverskoy et al. 1996). In this randomized, double-blinded trial, we compared ketamine and dexmedetomidine as an adjuvant to Bupivacaine in axillary brachial plexus block, and found that there was a significantly increased duration of sensory and motor blockade in the dexmedetomidine group than in the ketamine group without any adverse effects.

**CONCLUSION**

This study would like to state that dexmedetomidine prolongs the duration of sensory and motor block and enhances the quality of block as compared with ketamine when used as an adjuvant to Bupivacaine in axillary brachial plexus nerve block.
REFERENCES


استخدام عقار الكتلار وعقار الديكساميتوتودين في تخدير الأعصاب العضدية بواسطة الأشعة التليفزيونية

مصطفى محمد صبره - بدر إسماعيل فضل الله - عبد الوهاب صالح - علي الكميتي
وحاتن الكناني
كلية الطب - جامعة أزهر بنيـن - القاهرة

تم استخدام عقار الكتلار وعقار الديكساميتوتودين في تخدير الأعصاب العضدية بواسطة الأشعة التليفزيونية في مشفى جامعة الأزهر. أظهرت الدراسة تأثير هذه الأدوية في تسكين الألم والقدرة على الانتظار بخاصة لتخدير الأعصاب.

وبفضل التوجيه من الدكتور أحمد نزال، رائد الجراحة العصبية في وجامعي الجزيرة والأنف، تم إعطاء الأدوية داخل الأوعية الدموية، مما أدى إلى تحسين الألم بسرعة وتأثيرها على الانتظار. وتم إعطاء ملاحظات فردية لل bóأب وتحقيق النتائج الإيجابية في معظم الحالات.

وقد تم تنفيذ الدراسة على 60 حالة، تأثرت نسبة الانتظار بخذ العينات عند 30 حالة، وتم إعطاء الأدوية في الأفراد الذين تتراوح أعمارهم بين 20 إلى 60 سنة.

وقد أعربت بعضويتي الجراح عن شكرهم على الإلتزام بأعمالهم وتفانيهم في تقديم الخدمة الصحية للأفراد في بيئة الأزهرية.