ASSESSMENT OF ANALGESIC EFFICACY OF CLONIDINE AND FENTANYL WITH ROPIVACAINE IN THE SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK

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Abstract:
Ropivacaine, the S (-) enantiomer of N-(2,6- dimethylphenyl)-1-propyl-2-piperidinecarboxamide is a new long-acting local anesthetic like bupivacaine. Ropivacaine, compared to bupivacaine blocks pain transmitting A-delta and C fibers to a greater extent than A-beta fibers (controlling motor function). Ropivacaine has a wider margin of safety and is less cardiac & neurotoxic compared to bupivacaine with similar duration of action. The fentanyl and clonidine given with local anaesthetic in regional nerve block enhances the block by acting perineurally or it is because of systemic absorption of fentanyl and clonidine administered in block. The current study was planned to compare the efficacy of fentanyl and clonidine as an adjuvants and as an intravenous administration in supraclavicular plexus block with 0.75% ropivacaine.

The study was planned in the Department of the Surgery undergoing the Anaesthesia in Sri Krishna Medical College and Hospital, Muzaffarpur, from Jan 2017 to Jun 2017. After obtaining proper informed consent, 40 adult patients of both sexes, aged 18 to 65 years, belonging to ASA I or II and undergoing supraclavicular brachial plexus block were enrolled for this study.

The data from the present study concludes that the earliest onset of sensory and motor blockade as well as longer duration of analgesia resulted when clonidine 150 µg was used as a perineural adjuvant to Ropivacane 0.75% with minimal side effects compared to its same dose given intravenously.

Keywords: supraclavicular block, clonidine, fentanyl, ropivacaine, etc.

Introduction:
Brachial plexus block is a regional anesthesia technique that is sometimes employed as an alternative or as an adjunct to general anesthesia for surgery of the upper extremity. This technique involves the injection of local anesthetic agents in close proximity to the brachial plexus, temporarily blocking the sensation and ability to move the upper extremity. The subject can remain awake during...
the ensuing surgical procedure, or s/he can be sedated or even fully anesthetized if necessary.

There are several techniques for blocking the nerves of the brachial plexus. These techniques are classified by the level at which the needle or catheter is inserted for injecting the local anesthetic — interscalene block on the neck, supraclavicular block immediately above the clavicle, infraclavicular block below the clavicle and axillary block in the axilla (armpit).[1]

General anesthesia may result in low blood pressure, undesirable decreases in cardiac output, central nervous system depression, respiratory depression, loss of protective airway reflexes (such as coughing), need for tracheal intubation and mechanical ventilation, and residual anesthetic effects. The most important advantage of brachial plexus block is that it allows for the avoidance of general anesthesia and therefore its attendant complications and side effects. Although brachial plexus block is not without risk, it usually affects fewer organ systems than general anaesthesia.[2] Brachial plexus blockade may be a reasonable option when all of the following criteria are met:

- Surgery is expected to be limited to a region between the midpoint of the shoulder and the fingers
- There are no contraindications to a block such as infection at the intended injection site, significant bleeding disorder, anxiety, allergy or hypersensitivity to local anesthetics
- There will not be a need to perform an examination of the function of the blocked nerves immediately following the surgical procedure
- The patient prefers this technique over other available and reasonable approaches

Brachial plexus block is typically performed by an anesthesiologist. To achieve an optimal block, the tip of the needle should be close to the nerves of the plexus during the injection of local anesthetic solution. Commonly employed techniques for obtaining such a needle position include transarterial, elicitation of a paresthesia, and use of a peripheral nerve stimulator or a portable ultrasound scanning device.[3] If the needle is close to or contacts a nerve, the subject may experience a paresthesia (a sudden tingling sensation, often described as feeling like "pins and needles" or like an electric shock) in the arm, hand, or fingers. Injection close to the point of elicitation of such a paresthesia may result in a good block.[3]

Providing a rapid onset of dense anesthesia of the arm with a single injection, the supraclavicular block is ideal for operations involving the arm and forearm, from the lower humerus down to the hand. The brachial plexus is most compact at the level of the trunks formed by the C5–T1 nerve roots, so nerve block at this level has the greatest likelihood of blocking all of the branches of the brachial plexus. This results in rapid onset times and, ultimately, high success rates for surgery and analgesia of the upper extremity, excluding the shoulder.[4]

Surface landmarks can be used to identify the appropriate location for injection of local anesthetic, which is typically lateral to (outside) the lateral border of the sternocleidomastoid muscle and above the clavicle, with the first rib generally considered to represent the limit below which the needle must not be directed (the pleural cavity and uppermost part of the lung are located at this level). Palpation or ultrasound visualization of the subclavian artery just above the clavicle provides a useful anatomic landmark for locating the brachial plexus, which is lateral to the artery at this level.[9] Proximity to the brachial plexus can be determined using by elicitation of a paresthesia, use of a peripheral nerve stimulator, or ultrasound guidance.[5]

Compared to the interscalene block, the supraclavicular block — despite eliciting a more complete block of the median, radial ulnar and musculocutaneous nerves — does not improve postoperative analgesia. However, the supraclavicular block is often quicker to perform and may result in fewer side effects than the interscalene block. Compared to the
infraclavicular block and axillary blocks, the successful achievement of adequate anesthesia for surgery of the upper extremity is about the same with supraclavicular block.[5]

Unlike the interscalene block — which results in diaphragmatic hemiparesis in all subjects — only half of those who undergo supraclavicular block experience this side effect. Disadvantages of the supraclavicular block include the risk of pneumothorax, which is estimated to be between 1%–4% when using paresthesia or peripheral nerve stimulator guided techniques. Ultrasound guidance allows the operator to visualize the first rib and the pleura, thereby helping to ensure that the needle does not puncture the pleura; this presumably reduces the risk of pneumothorax.[5]

Clonidine treats high blood pressure by stimulating α2 receptors in the brain stem, which decreases peripheral vascular resistance, lowering blood pressure. It has specificity towards the presynaptic α2 receptors in the vasomotor center in the brainstem. This binding has a sympatholytic effect, suppresses release of norepinephrine, ATP, renin, and neuropeptide Y which if released would increase vascular resistance.

Fentanyl binds to opioid receptors these are G-protein coupled receptors (GPCR) which regulate synaptic transmission. Binding of fentanyl activates the GPCR which initiates signalling to result in the inhibition of the release of nociceptive neurotransmitters. This inhibits the ascending pathways in the CNS to increase pain threshold by changing the perception of pain, therefore decreasing propagation of nociceptive signals resulting in analgesic effects. [6]

Ropivacaine, the S (-) enantiomer of N-(2,6-dimethylphenyl)-1-propyl-2-

piperidinecarboxamide is a new long-acting local anesthetic like bupivacaine. Ropivacaine, compared to bupivacaine blocks pain transmitting A-delta and C fibers to a greater extent than A-beta fibers (controlling motor function). Ropivacaine has a wider margin of safety and is less cardiac & neurotoxic compared to bupivacaine with similar duration of action. [7]

The fentanyl and clonidine given with local anaesthetic in regional nerve block enhances the block by acting perineurally or it is because of systemic absorption of fentanyl and clonidine administered in block.

The current study was planned to compare the efficacy of fentanyl and clonidine as an adjuvants and as an intravenous administration in supraclavicular plexus block with 0.75% ropivacaine.

Methodology:

The study was planned in the Department of the Surgery undergoing the Anaesthesia in Sri Krishna Medical College and Hospital, Muzaffarpur, from Jan 2017 to Jun 2017. After obtaining proper informed consent, 40 adult patients of both sexes, aged 18 to 65 years, belonging to ASA I or II and undergoing supraclavicular brachial plexus block were enrolled for this study. A written informed consent was obtained from each patient after explaining the procedure, the possible outcomes and complications. Patient unwilling to participate in the study, suspected coagulopathy, hypersensitivity to the study drugs, localized or systemic infection, cardiovascular disease, renal disease and patients having chronic pain were excluded from the study.

Following was the groups and the administration details in each group.
Table 1:

<table>
<thead>
<tr>
<th>Groups</th>
<th>No. of Cases</th>
<th>Ropivacaine (0.75%)</th>
<th>Supraclavicular block</th>
<th>Intravenously</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>10</td>
<td>24 ml</td>
<td>1ml fentanyl (50µg/ml)</td>
<td>5ml normal saline</td>
</tr>
<tr>
<td>Group 2</td>
<td>10</td>
<td>24 ml</td>
<td>6ml normal saline</td>
<td>1 ml fentanyl (50µg/ml)</td>
</tr>
<tr>
<td>Group 3</td>
<td>10</td>
<td>24 ml</td>
<td>1 ml clonidine (150µg/ml)</td>
<td>5ml normal saline</td>
</tr>
<tr>
<td>Group 4</td>
<td>10</td>
<td>24 ml</td>
<td>6ml normal saline</td>
<td>1 ml clonidine (150µg/ml)</td>
</tr>
</tbody>
</table>

Onset of sensory block was defined as time elapsed from injection of drug to complete loss of cold perception of upper limb elicited by using spirit soaked cotton or pinprick. Duration of sensory block was defined as duration between injection of drug and return of pinprick sensation.

Onset of motor block was defined as time elapsed from injection of drug to complete motor block elicited by asking the patient to adduct the shoulder, flex the forearm and hand against gravity. Duration of Motor block was defined as duration between drug injections to complete return of motor power with movement of all upper limb joints.

Results & Discussion:

The data from the all the 4 groups is collected and presented as below.

Table 2: Demographic Details

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>Group IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Cases</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Administration</td>
<td>Inj. ropivacaine (0.75%) 24 ml +1ml fentanyl (50µg/ml) + 5ml normal saline in Supraclavicular block; and 1ml normal saline intravenously</td>
<td>Inj. Ropivacaine (0.75%) 24 ml +6ml normal saline in Supraclavicular block; and 1ml fentanyl (50µg/ml) intravenously</td>
<td>Inj. ropivacaine (0.75%) 24 ml +1ml clonidine (150µg/ml) + 5ml normal saline in Supraclavicular block; and 1ml normal saline Intravenously.</td>
<td>Inj. ropivacaine (0.75%) 24 ml +6ml normal saline in Supraclavicular block; and 1ml clonidine (150µg/ml) intravenously.</td>
</tr>
<tr>
<td>Age</td>
<td>31 – 45 years</td>
<td>28 – 39 years</td>
<td>32- 48 years</td>
<td>31 – 50 years</td>
</tr>
<tr>
<td>Weight in kg</td>
<td>53 – 79 kg</td>
<td>58 – 75 kg</td>
<td>60 – 71 kg</td>
<td>58 – 68 kg</td>
</tr>
<tr>
<td>ASA I Cases</td>
<td>8</td>
<td>7</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>ASA II Cases</td>
<td>2</td>
<td>3</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Duration of Surgery</td>
<td>45 – 68 mins</td>
<td>48 – 76 mins</td>
<td>53 – 76 mins</td>
<td>57 – 69 mins</td>
</tr>
</tbody>
</table>
Table 3: Onset and duration of sensory and motor block among the groups

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>Group IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Cases</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Administration</td>
<td>Inj. ropivacaine (0.75%) 24 ml +1ml fentanyl (50µg/ml) + 5ml normal saline in Supraclavicular block; and 1ml normal saline intravenously</td>
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<td>Inj. ropivacaine (0.75%) 24 ml + 1ml clonidine (150µg/ml) + 5ml normal saline in Supraclavicular block; and 1ml normal saline Intravenously.</td>
<td>Inj. ropivacaine (0.75%) 24 ml + 6ml normal saline in Supraclavicular block; and 1ml clonidine (150µg/ml) intravenously.</td>
</tr>
<tr>
<td>Onset of Sensory block (in min.)</td>
<td>11.2 – 18.2</td>
<td>10.6 – 17.3</td>
<td>10.5 – 15.9</td>
<td>11.4 – 15.7</td>
</tr>
<tr>
<td>Onset of Motor block (in min.)</td>
<td>17.3 – 22.8</td>
<td>19.5 – 23.7</td>
<td>14.8 – 21.4</td>
<td>15.1- 22.2</td>
</tr>
<tr>
<td>Duration of Sensory block (in hrs)</td>
<td>5.1- 6.5</td>
<td>5.4 – 6.3</td>
<td>5.9 – 8.2</td>
<td>5.5 – 7.6</td>
</tr>
<tr>
<td>Duration of Motor block (in hrs)</td>
<td>5.5 – 6.8</td>
<td>5.6 – 7.1</td>
<td>6.0 – 7.5</td>
<td>5.4 – 6.7</td>
</tr>
<tr>
<td>Rescue analgesia (in hrs)</td>
<td>6.5 – 8.3</td>
<td>7.2 – 8.4</td>
<td>7.9 – 9.8</td>
<td>7.2 – 9.5</td>
</tr>
</tbody>
</table>

Opioids and α2 agonist have been used frequently as adjuvants with local anaesthetic intrathecally, in epidural space as well as in various nerve blocks to ensure good perioperative anaesthesia as well as analgesia without major side effect, but opinion differs on the side effect like nausea, vomiting, pruritus, bradycardia, hypotension, sedation etc. associated with these were due to systemic absorption of locally administered adjuvants or due to some other mechanism. So this study was planned to define effect of clonidine and fentanyl, when they were given with 0.75% ropivacaine in Supraclavicular brachial plexus block perineurally and also intravenously in the same dose. [8]

Madusudhan et al [9] demonstrated a significant increase in the duration of sensory, motor blockade on addition of fentanyl to ropivacaine 0.75% for brachial plexus blocks compared to ropivacaine used alone. Study by Fletcher et al [10] however concluded that there was no additional benefit on addition of fentanyl to lidocaine with epinephrine for axillary brachial plexus block except for faster block onset along the musculocutaneous nerve trunk. The delayed onset of sensory and motor block in ropivacaine with fentanyl (RF) group could be due to a change in the pH of the local anaesthetic solution on addition of fentanyl, resulting in the slower block onset. To confirm this hypothesis, further studies are required comparing the effects of Fentanyl on the pH of local anaesthetic used for brachial plexus block.
Clonidine acts synergistically with local anesthetic. Clonidine enhances both sensory and motor blockade of neuraxial and peripheral nerves after injection of local anaesthetic solution. This is thought to be due to blockage of conduction of delta A and C fibers, increase in the potassium conductance in isolated neurons in vitro and intensification of conduction block achieved by local anaesthetics. [11]

Casati A et al added clonidine (1 µg/kg) to 0.75% ropivacaine for foot surgery under sciatic-femoral nerve block. They observed that there was no difference in the time required to achieve surgical anesthesia between patients receiving only 0.75% ropivacaine and those receiving the ropivacaine-clonidine mixture. [12]

Andrea Casati A et al. observed that the mean time from block placement to first request for pain medication was shorter in group Ropivacaine (13.7 h; 25th –75th percentiles: 11.8-14.5 h) than in group Ropivacaine Clonidine (16.8 h; 25th -75th percentiles: 13.5-17.8 h) (P = 0.038). [12]

Jacques T. Ya Deau et al compared addition of clonidine (100 µg) to local anaesthetic, systemic (intramuscular) 100 µg of clonidine and placebo. They found that clonidine resulted in a statistically significant prolongation of analgesia when included with the local anesthetic for popliteal fossa nerve block. [13] These findings are at variance with the study by Duma et al, which showed no difference in analgesia after addition of clonidine 0.5 µg/kg to levobupivacaine in axillary block. [14]

Probable explanation for this inconsistency may relate to inter-patient variations in the anatomy of the plexus sheath and difference in the spread of local anesthetics in the plexus sheath depending upon the block technique.

**Conclusion:**

The data from the present study concludes that the earliest onset of sensory and motor blockade as well as longer duration of analgesia resulted when clonidine 150 µg was used as a perineural adjuvant to Ropivacane 0.75% with minimal side effects compared to its same dose given intravenously.

**References:**


