SAFETY AND EFFICACY OF FENTANYL VERSUS SODIUM BICARBONATE IN AXILLARY BRACHIAL PLEXUS BLOCK
Darshna D Patel1*, Varsha N Swadia2
1Assistant professor, 2Professor and Head of Department, Dept.of Anaesthesia,S.S.G.Hospital,Medical college, Vadodara

ABSTRACT
BACKGROUND: Recent clinical studies have suggested that alkalinization of local anaesthetic mixture may shorten the time to onset and lengthen its duration of action. Purpose of this study is to see how PH change affects the onset time of sensory & motor block and duration of post operative analgesia.

MATERIALS AND METHODS: The patients were randomly allocated to two groups of 25 patients in each. Group F: patients received Inj. Lignocaine Hydrochloride 2% 15 cc +inj. Bupivacaine Hydrochloride 0.5% 15 cc +inj. Adrenaline (1:200,000) 5 mcg/ml +inj. Fentanyl Citrate 100 mcg +inj. Sterile water 5 cc. Group SB: patients received Inj. Lignocaine Hydrochloride 2% 15 cc +inj. Bupivacaine Hydrochloride 0.5% 15 cc +inj. Adrenaline (1:200,000) 5 mcg/ml +inj. Sodium Bicarbonate 7.5% w/v 2 cc +inj. Sterile water 5 cc.

RESULTS: The mean time for onset of sensory block was 226.6 ± 53.69 seconds in Group F and 144.8 ± 41.4 seconds (p<0.001) in Group SB. The mean time for onset of motor block was 338 ± 81.68 seconds in Group F and 256.2 ± 71.92 seconds in Group SB (p<0.001) and thus highly significant. At 9 hours, 14 patients were given rescue analgesia as they had a VAS score of 4.4+0.82. The duration of analgesia was 816.2 ± 87.49 minutes in Group F while it was 429+86.45 minutes in Group SB (p<0.001). In Group F, 64% patients required 2 doses and 36% required 1 dose of rescue analgesia. In Group SB, 96% patients required 3 doses and 4% required 2 doses.

CONCLUSION: We conclude that alkalinization of local anaesthetics significantly improved axillary brachial plexus block characteristics without any increase in side effects. It also prolongs duration of analgesia but fentanyl is better in this respect.

Keywords: Lignocaine, Bupivacaine, Sodium Bicarbonate, Fentanyl, Axillary brachial plexus block
axillary brachial plexus block, after approval by ethical committee.

**Exclusion criteria:**

1. Patients with known hypersensitivity to local anesthetic drugs.
2. Bleeding disorders
3. Patients on anticoagulant drugs
4. Progressive neurological disorder, nerve palsy, neuromuscular disease
5. Patient having opposite side pneumothorax or collapsed lung

The procedure was explained to the patients and written informed consent was taken. Blood pressure cuff, pulse oximeter and ECG electrodes were applied. The initial pulse, blood pressure, respiratory rate and arterial oxygen saturation were noted. Premedication was given in the form of inj. Atropine 0.01 – 0.02 mg/kg I.V. All the patients were given axillary brachial plexus block. The patients were randomly allocated to two groups of 25 patients in each.

- **Group F:** was given Inj. Lignocaine Hydrochloride 2% 15 cc +inj. Bupivacaine Hydrochloride 0.5% 15 cc +inj. Adrenaline (1:200,000) 5 mcg/ml +inj. Fentanyl Citrate 100 mcg +inj. Sterile water 5 cc.
- **Group SB:** was given Inj. Lignocaine Hydrochloride 2% 15 cc +inj. Bupivacaine Hydrochloride 0.5% 15 cc +inj. Adrenaline (1:200,000) 5 mcg/ml +inj. Sodium Bicarbonate 7.5% w/v 2 cc +inj. Sterile water 5 cc.

The pH of solution was measured with a digital pH meter.

To decide the volume of sodium bicarbonate 7.5% w/v to be added to local anesthetic mixture, we went on adding sodium bicarbonate drop by drop to a mixture of 15 cc 2% lignocaine with 15 cc 0.5% bupivacaine with adrenaline 1:200,000 5 mcg/ml till the solution became just turbid without causing precipitation and the pH approaching nearer to physiological pH.

1. 2%LignocaineHydrochloride+Bupivacaine Hydrochloride +Adrenaline 1:200,000 5 mcg/ml +Sterile water (pH 5.9)
2. 2% lignocaine Hydrochloride + 0.5% Bupivacaine Hydrochloride + Adrenaline 1:200,000 5 mcg/ml +Sterile water +Sodium bicarbonate 7.5% w/v 2cc (pH 7.6)
3. 2%LignocaineHydrochloride + 0.5% Bupivacaine Hydrochloride +Adrenaline 1:200,000 5 mcg/ml+ Sterile water + Fentanyl Citrate 100 mcg (pH 5.7)

The solution was freshly prepared just prior to performing a block. Sensory block was assessed by pin-prick method. Grade 0 – Sharp pain felt

Grade 1 – Analgesia: dull sensation felt
Grade 2 – Anaesthesia: no sensation felt

Assessment of sensory block was carried out every minute till 30 minutes after completion of drug injection. Time to sensory onset was considered when there was dull sensation to pinprick. Motor block was assessed as under:

- **Grade 0** – Normal grip strength
- **Grade 1** – Paresis: reduced grip strength and heaviness felt on raising arm above head
- **Grade 2** – Paralysis: no grip strength and inability to raise arm above head.

Onset of motor block was considered when there was Grade 1 blockade. Time to peak motor effect was considered when there was Grade 2 blockade. Success rate of block was assessed at 30 minutes after drug injection and was graded as:

**Complete:** When all segments supplied by median, radial, ulnar and musculocutaneous nerves had anaesthesia or anaesthesia.

**Incomplete:** When any of the segments supplied by median, radial, ulnar and musculocutaneous nerves did not have anaesthesia or anaesthesia.

**Failed:** When more than one nerve remained unaffected.

General anaesthesia was administered to patients in case of incomplete or failed blocks and these patients were excluded from the study. Patients were monitored for hemodynamic variables such as pulse, blood pressure, respiratory rate and SpO2 and sedation score intraoperatively as well as post operatively.

**Sedation score:**

1. Awake and alert
2. Sedated, responding to verbal commands
3. Sedated, responding to mild physical stimulus
4. Sedated, responding to moderate or strong physical stimulus
5. Not aroused

Post-operatively patients were examined at regular intervals to note the duration of analgesia. It is time from administration of block to 1st request of analgesics. Rescue analgesia was given when VAS ≥ 4/10 and it was given in the form of Inj. Diclofenac Sodium 1.5 mg/kg intramuscularly. The number of rescue analgesia doses were noted.

All the patients were observed for any side effects and complications like Nausea, Vomiting, Bradycardia, Hypotension, Pruritus, Respiratory depression, Urinary retention, Local anesthetic toxicity, Hypersensitivity, Inadvertent arterial
puncture, Hematoma, Post block neuropathy in the intra and post-operative period.

RESULTS
All qualitative data were analyzed using Chi-Square test and quantitative data using the Student’s t-test. Results were expressed as Mean ± SD. ‘p’ value ≤ 0.05 was taken as statistically significant.

Table 1: Demographic Data

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group F</th>
<th>Group SB</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>25</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Age in years (Mean ± SD)</td>
<td>38.12 ± 15.05</td>
<td>34.88 ± 11.07</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Sex (M:F)</td>
<td>21:4</td>
<td>20:5</td>
<td></td>
</tr>
<tr>
<td>Weight (kgs.)</td>
<td>57 ±4.84</td>
<td>56.36 ± 4.47</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

There was no statistically significant difference among two groups in terms of demographic data.

Graph 1: Mean onset time for sensory & motor blockade

The mean time for onset of sensory block was 226.6 ± 53.69 seconds in Group F and 144.8 ± 41.4 seconds (p<0.001) in Group SB. Thus it was found statistically highly significant. The mean time for onset of motor block was 338 ± 81.68 seconds in Group F and 256.2 ± 71.92 seconds in Group SB (p<0.001) and thus highly significant.

Table 2: Sedation score

<table>
<thead>
<tr>
<th>Sedation score</th>
<th>Group F</th>
<th>Group SB</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>9</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>16</td>
<td>64</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>2.92 ± 0.5</td>
<td>1.16 ± 0.38</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

In Group F majority of the patients (76%) were sedated but responding to mild physical stimulus, 4 patients (16%) were sedated and responding to verbal commands while 2 patients (8%) were sedated and responding to moderate or strong physical stimulus. In Group SB, majority of the patients (84%) were awake and alert while 4 patients (16%) were sedated and responding to verbal commands. There was no statistically significant difference in haemodynamic parameters and oxygen saturation measured intraoperatively as well as post operatively.

Graph 2 : Changes in mean VAS score

In Group F: only 4 patients were given rescue analgesia at the end of 12 hours. Majority of the patients (21) did not require rescue analgesia upto 12 hours. In Group SB: 9 patients were given rescue analgesia at the end of 6 hours. At 9 hours, 14 patients were given rescue analgesia. The remaining 2 patients were given rescue analgesia at the end of 12 hours.

Graph 3: Duration of analgesia

The duration of analgesia was 816.2 ± 87.49 minutes in Group F while it was 429 ± 86.45 minutes in Group SB, the p value being <0.001 i.e. highly significant.

Table 3: No. of rescue analgesic doses

<table>
<thead>
<tr>
<th>No. of doses</th>
<th>Group F</th>
<th>Group SB</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>9</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>16</td>
<td>64</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td>23</td>
<td></td>
</tr>
</tbody>
</table>

In Group F 9 patients (36%) required one dose and 16 patients (64%) required two doses of rescue analgesia in 24 hours post-operatively. In Group SB, 2 patients (8%) required two doses while 23 patients (96%) required three doses of rescue analgesia in 24 hours post-operatively. Intraoperatively, bradycardia was seen in two
patients and nausea and vomiting was seen in one patient in Group F, while no complications were observed in any patients of group SB. No complications were observed in any patients in either group in the postoperative period.

**DISCUSSION**

Peripheral nerve blocks with local anaesthetics provide excellent operating conditions with good muscle relaxation. However two major drawbacks encountered are latency of block and duration of post-operative analgesia. It is well known that relative alkalinity of local anesthetics may be a major determining factor in altering the onset of action of local anesthetics. Increasing the pH towards pKa of a drug by alkalinization increases the concentration of non ionized form and it is this non ionized fraction that diffuses rapidly to the inner axonal surface producing quicker onset of analgesia. The analgesia produced by opiates has classically been thought of as a centrally mediated phenomenon. However animal studies have shown that opiate receptors are present peripherally on primary afferent nerves and that activation of these receptors can produce analgesia. The mu-opioid receptor seems to be the most important receptor for antinociception and the majority of studies indicate that these receptors are located at the peripheral terminals of primary afferent nociceptive fibers. Fentanyl is available as Fentanyl Citrate, which is acidic in nature and having a pH of 4.7. Also, in contrast to morphine, Fentanyl is a highly lipid soluble compound. Fentanyl has also been studied in peripheral nerve blocks such as brachial plexus block by Kohki Nishikawa et al (2000), Karakaya Deniz et al (2001) and S.P. Singh et al (2009), femoral block by Md. Ashraf Abd Elmawgoud et al (2008) and in peribulbar block by Mostafa El Hamid El Enin et al (2009). Also Mark Tverskoy et al in 1998 and PT Vijay Kumar et al in 2006 demonstrated increased duration of analgesia by wound infiltration with fentanyl. Dr. B.N. Biswas et al 2002 used fentanyl as an adjunct for intrathecal anaesthesia and Chen-Hwan Chergn (2005) in their study on fentanyl as an adjuvant in epidural block demonstrated early onset of block by use of fentanyl. They attributed this effect to the increased lipophilic nature of the drug. In contrast, Kohki Nishikawa et al (2000) demonstrated the addition of fentanyl to lignocaine in axillary block prolonged the onset of block. They postulated that the acidic nature of Fentanyl caused a decrease in the pH of local anesthetic solution which increased the latency of the block. The amount of fentanyl used in our study was 100 mcg which is same as that used in the study of Fletcher et al (1994), Kohki Nishikawa et al (2000). In our study the change in pH after the alkalinization was from 5.9 to 7.6, while that after addition of fentanyl was from 5.9 to 5.7, which is in consonance with a study done by Ruby Mehta et al (2003) and Kohki Nishikawa et al (2000) and Mark Chow et al (1998). Majority of the patients (76%) were found to be sedated (sedation score 4) in Group F While in Group SB 84% of patients were alert (sedation score 1). The sedative effect of fentanyl can be explained by the peripheral uptake of fentanyl into the systemic circulation and its subsequent action in the CNS. Post-operative analgesia was judge on the basis of visual analogue score. The mechanism of action of opioids upon antinociception is not known. Mostafa Abdel Hamid Abo El Enin et al (2009) postulated the possible mechanisms of action for the improved analgesia produced by the peripheral application of fentanyl. First, fentanyl could act directly on the peripheral opioid receptor. Primary afferent tissues (dorsal roots) have been found to contain opioid binding sites. Because the presence of bidirectional axonal transport of opioid binding protein has been shown fentanyl may penetrate the nerve membrane and act at the dorsal horn. This could also account for the prolonged analgesia. However, fentanyl is reported to have a local anesthetic action. Gormley et al suggested that alfentanil also prolonged postoperative analgesia by local anesthetic action. Second, fentanyl may potentiate local anesthetic action via central opioid receptor-mediated analgesia by peripheral uptake of fentanyl to systemic circulation. We conclude that alkalinization of local anesthetics significantly improved axillary brachial plexus block characteristics without any increase in side-effects. It also prolongs duration of analgesia but fentanyl is better in this respect.

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