To assess the efficacy of verapamil 5mg as an adjuvant to 0.5% plain Bupivacaine in Lumbar Epidural Anaesthesia for elective inguinal surgeries in comparison with 0.5% plain Bupivacaine

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Abstract: Pain is an unpleasant sensation which is almost totally subjective. It is a physiologically protective mechanism, but in excess, it becomes destructive and even fatal. Pain is the result of sensory perception and cortical integration of the stimuli that threaten the integrity of the body tissues. The International Association for the Study of Pain defines pain as an "unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage". An ideal technique should provide effective pain relief with minimal side effects and a reasonable level of patient satisfaction in the post operative period. Epidural analgesia is one of the entities practised to provide post operative pain relief. Central neuraxial blockade with a "combination therapy" of local anaesthetics and non opiates yield near total pain relief while diminishing or avoiding side effects from each component alone. This newer dimension in pain management can be called balanced epidural analgesia. It offers the most complete form of analgesia. This study was undertaken to assess the efficacy of verapamil 5mg as an adjuvant to 0.5% plain Bupivacaine and found that epidural bupivacaine (0.5%) with verapamil prolonged the postoperative analgesic period when compared to 0.5% bupivacaine alone for elective inguinal herniorrhaphy surgeries under lumbar epidural anaesthesia.

I. Introduction

Pain is an unpleasant sensation which is almost totally subjective. It is a physiologically protective mechanism, but in excess, it becomes destructive and even fatal. Pain is the result of sensory perception and cortical integration of the stimuli that threaten the integrity of the body tissues. The International Association for the Study of Pain defines pain as an "unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage".

The perception of pain has two main components:
1. The original sensation (in response to stimuli)
2. The reaction or processing component.
Post operative pain lies between these two modalities.

An ideal technique should provide effective pain relief with minimal side effects and a reasonable level of patient satisfaction in the post operative period. Epidural analgesia is one of the entities practised to provide post operative pain relief.

Central neuraxial blockade with a "combination therapy" of local anaesthetics and non opiates yield near total pain relief while diminishing or avoiding side effects from each component alone. This newer dimension in pain management can be called balanced epidural analgesia. It offers the most complete form of analgesia. Local anaesthetics may be used alone or in combination with opiates or non opiates epidurally to prevent pain and attenuate the stress response intra operatively and to provide good post operative pain relief.

Bupivacaine has traditionally been the longest acting local anaesthetic commercially available and widely used. Its prolonged duration of action reduces the need for repeated administration of top up doses. Furthermore, Bupivacaine has a differential sensory to motor blockade. This is important for its use in post operative pain relief. The primary mode of action of local anaesthetics is through sodium channel and axonal conduction blockade. Local anaesthetics also have extensive effects on presynaptic calcium channels that must function to stimulate the release of neurotransmitters. Thus interference with calcium channel conductance may enhance epidural anaesthesia with local anaesthetics.

Excitatory aminoacids involved in nociceptive transmission in the dorsal horn of the spinal cord are mediated by N-methyl D-aspartate receptors (NMDA). Activation of NMDA receptors leads to Ca$^{2+}$ entry into the cell and initiates a series of Central sensitization. This central sensitization may be prevented by calcium channel blockers that block calcium entry into the cell.

This study is aimed at adding verapamil, a L-type calcium channel blocker to epidural Bupivacaine, to improve...
quality of analgesia and prolong the post operative period of analgesia in patients undergoing herniorraphy.

**Aim of The Study**

This study was undertaken to assess the efficacy of verapamil 5mg as an adjuvant to 0.5% plain Bupivacaine in Lumbar Epidural Anaesthesia for elective inguinal surgeries in comparison with 0.5% plain Bupivacaine with regard to the following parameters:

1. Time of Onset
2. Duration of analgesia
3. Hemodynamic changes
4. Respiratory changes
5. Level of sensory blockade
6. Quality of motor blockade
7. Complications

**II. Materials And Methods**

This study was done at Coimbatore medical college hospital, Coimbatore. The aim of this study was to assess the efficacy of Verapamil –5mg as an adjuvant to 0.5% Bupivacaine in Lumbar Epidural Anaesthesia for elective inguinal herniorraphy surgeries.

**Study Design**

This study is a randomized, prospective, double blinded study.

**Inclusion Criteria**

40 Patients of ASA grade I or grade II between the age group of 20-50 years scheduled for herniorraphy surgeries were included in the study. The patients were assigned to two groups. Group I received 16 ml of 0.5% Bupivacaine with 2ml of normal saline. Group II received 16 ml of 0.5% Bupivacaine with 2 ml of Verapamil (5 mg).

**Exclusion Criteria**

- Patients not willing for regional anaesthesia
- ASA Grade III/ Grade IV patients
- Patients with cardiac disease
- Patients with neurological illness
- Patients with impaired hepatic function
- Patients with impaired renal function
- Spine deformity
- Local sepsis
- Bleeding disorders
- Technical failure - Dural tap, Bloody tap.
- Any H/O allergy
- Hearing impairment

**Consent**

The Institutional Ethics Committee approval and the patients informed consent were obtained prior to the study.

**Pre Operative Visit**

A careful history and physical examination of the patient was done. The following routine preoperative investigations were assessed:

- **Blood**: Haemoglobin% Total count Differential count Erythrocyte Sedimentation rate Blood grouping and typing Bleeding Time an Clotting time Blood-urea, sugar Serum Creatinine Liver function tests
- **Urine**: Albumin, Sugar
- **Chest**: X-ray ECG

Patients vital signs and weight were noted down. Patients were taught about the visual analogue scale during the pre-operative visit. Here the patients were shown a 100 mm scale and it was explained to them that the
score of 0 meant no pain and the score of 100 meant worst possible pain that can be imagined. Pre operative fasting of 6 hours for solid food and 4 hours for clear liquid was advised.

**Premedication**

No premedication was prescribed during the pre-anaesthetic evaluation.

**Lumbar Epidural Block**

On the day of surgery after the pre-operative examination, the patient was shifted to the operating room and an ECG monitor, non invasive blood pressure and pulseoximeter were connected. Base line heart rate, blood pressure and oxygen saturation were noted.

Patients was preloaded with 10ml/kg body weight of Ringer Lactate solution using a 16 gauge iv Cannula. Local anaesthetic samples were prepared by an anaesthesiologist who was not involved in the clinical study. The observer was not aware of the type of local anaesthetic in each preparation.

Patient was then positioned in the right lateral position. The Thoraco lumbar area was thoroughly cleaned with Povidone-Iodine solution and sterile drapes were placed around the site. Skin and subcutaneous tissue infiltration with 0.5-1ml of 1% lignocaine was done at the L3 L4 level using a 26 gauge needle. A 16 Gauge size Tuohy needle was introduced into the lumbar epidural space through the mid line approach. The extradural space was identified using a loss of resistance to air technique with a 5ml syringe. A standard 18G epidural catheter was threaded into the epidural space. Four cm of the catheter was advanced cephalad into the space.

A test dose of 0.5% bupivacaine 1 ml with adrenaline 1: 200,000 was injected after negative aspiration for CSF or blood through epidural catheter. The total calculated dose of local anaesthetic solution was then injected 3 mins after the test dose if there was no significant change in the heart rate or arterial pressure. The case was excluded from the study if there was any significant change in the heart rate subsequent to the test dose. The patient was turned from the lateral to the supine position. SpO2 and ECG were monitored throughout the procedure, intraoperatively and post operatively. Heart rate, blood pressure and respiratory rate were recorded every 5 mins for the first 30 mins, every 15 mins for next 30 mins. every 30 mins for next 2 hours and every hour for next 3 hours.

**Onset of Sensory Analgesia**

It was noted as the time taken for the disappearance of pinprick pain from the administration of local anaesthetics into the epidural space, at the puncture dermatomal level.

**Maximum Level of Sensory Blockade**

It was taken to be the upper level of absence to pinprick pain 20 mins after the epidural injection.

**Duration of Sensory Analgesia**

Sensory analgesia was assessed as per visual analogue scale scoring at 2,4,6,12, 24 hours post operatively. Rescue analgesia was given by injecting 6 to 8 ml of 0.25% bupivacaine at VAS 4 through the catheter. The duration of sensory analgesia is calculated from the time of administration of local anaesthetic drug till the time rescue analgesia is sought.

**Assessment of Motor Blockade**

Motor blockade was assessed using Bromage scale

<table>
<thead>
<tr>
<th>Score</th>
<th>Motor block</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0%</td>
<td>Nil</td>
</tr>
<tr>
<td>1</td>
<td>33%</td>
<td>Partial</td>
</tr>
<tr>
<td>2</td>
<td>66%</td>
<td>Almost complete</td>
</tr>
<tr>
<td>3</td>
<td>100%</td>
<td>Complete</td>
</tr>
</tbody>
</table>

The scores were recorded every 15 mins after the epidural injection till a score of 0 was obtained.

**Duration of Surgery**

It was the time from skin incision to the end of surgery.

**Complications**

Post operatively patients were observed for

- Nausea, vomiting
- Respiratory depression
- Hypotension (drop of more than 25% from the base line)
To assess the efficacy of verapamil 5mg as an adjuvant to 0.5% plain Bupivacaine in Lumbar epidural anaesthesia

• Bradycardia (equal to or less than 60/mt)
• Urinary retention
• SpO₂ decrease (below 90%)
• Shivering
• Arrhythmias
• Conduction defects
• Pain at injection site

III. Observation And Results
This study was conducted on forty patients undergoing elective herniorraphy surgeries. The observations were recorded during the intra operative and the post operative period. All these patients were grouped in to two categories.

Group I: Patients who had received 16 ml of 0.5% Bupivacaine + 2 ml of normal saline
Group II: Patients who had received 16 ml of 0.5% Bupivacaine + 2 ml of Verapamil (5 mg).

Patients Characteristics
In Group I there were 20 male patients and in Group II there were 20 male patients.

Table 1 Age (In Years)

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean age (in years)</th>
<th>± SD</th>
<th>t-test</th>
<th>P value</th>
<th>Statistical Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>32.80</td>
<td>5.85</td>
<td>0.11</td>
<td>0.9146</td>
<td>NS</td>
</tr>
<tr>
<td>Group II</td>
<td>33.00</td>
<td>5.87</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NS: Not Significant

The mean age in Group I was found to be 32.80 ± 5.85 years and the mean age in Group II was found to be 33.00 ± 5.87 years.

Table 2 Weight (In Kgs)

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean weight in Kgs</th>
<th>± SD</th>
<th>t-test</th>
<th>P value</th>
<th>Statistical Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>55.25</td>
<td>4.41</td>
<td>1.01</td>
<td>0.3196</td>
<td>NS</td>
</tr>
<tr>
<td>Group II</td>
<td>54.00</td>
<td>3.36</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NS: Not Significant

The mean weight in Group I was 55.25 ± 4.41 kgs and in Group II was 54.00 ± 3.36 kgs.

Table 3 Height (In Cms)

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean height in Cms</th>
<th>± SD</th>
<th>t-test</th>
<th>P value</th>
<th>Statistical Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>156.70</td>
<td>2.89</td>
<td>1.95</td>
<td>0.0584</td>
<td>NS</td>
</tr>
<tr>
<td>Group II</td>
<td>159.20</td>
<td>4.95</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NS: Not Significant

The mean height in Group I was 156.70 ± 2.89 cms and in Group II was 159.20 ± 4.95 cms.

Table 4 Sex Distribution

<table>
<thead>
<tr>
<th>Group</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>20</td>
<td>-</td>
</tr>
<tr>
<td>Group II</td>
<td>20</td>
<td>-</td>
</tr>
</tbody>
</table>

NS: Not Significant

The distribution of age, weight, height and the sex of patients in both the groups were similar and comparable.

Table 5 Pulse Rate (Beats/Minute)

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean pulse rate (Beats/min)</th>
<th>SD</th>
<th>t-test</th>
<th>P value</th>
<th>Statistical Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>77.96</td>
<td>4.13</td>
<td>1.52</td>
<td>0.1648</td>
<td>NS</td>
</tr>
<tr>
<td>Group II</td>
<td>78.95</td>
<td>5.05</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NS: Not Significant

DOI: 10.9790/0853-1504030416 www.iosrjournals.org
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The mean pulse rate in Group I was found to be 77.96 /mt with standard deviation of 4.13. The mean pulse rate in Group II was found to be 78.95 /mt with standard deviation of 5.05.

### Table 6
<table>
<thead>
<tr>
<th>Group</th>
<th>Mean respiratory rate (nos/min.)</th>
<th>± SD</th>
<th>t-test</th>
<th>P value</th>
<th>Statistical Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>14.24</td>
<td>1.85</td>
<td>1.18</td>
<td>0.3326</td>
<td>NS</td>
</tr>
<tr>
<td>Group II</td>
<td>14.70</td>
<td>1.93</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NS : Not Significant

The mean respiratory rate in Group I was found to be 14.24 / mt with SD of 1.85. The mean respiratory rate in Group II was found to be 14.70 / mt with SD of 1.93.

### Table 7
<table>
<thead>
<tr>
<th>Group</th>
<th>Mean systolic BP (in mm of Hg)</th>
<th>± SD</th>
<th>t-test</th>
<th>P value</th>
<th>Statistical Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>114.47</td>
<td>7.30</td>
<td>0.76</td>
<td>0.5458</td>
<td>NS</td>
</tr>
<tr>
<td>Group II</td>
<td>113.93</td>
<td>7.16</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NS : Not Significant

The mean Systolic BP in Group I was found to be 114.47 mmHg with SD of 7.30 mmHg. The mean systolic BP in Group II was found to be 113.93 mmHg with SD of 7.16 mmHg.

### Table 8
<table>
<thead>
<tr>
<th>Group</th>
<th>Mean diastolic BP (in mm of Hg)</th>
<th>± SD</th>
<th>t-test</th>
<th>P value</th>
<th>Statistical Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>73.88</td>
<td>5.21</td>
<td>0.78</td>
<td>0.4954</td>
<td>NS</td>
</tr>
<tr>
<td>Group II</td>
<td>74.33</td>
<td>5.17</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NS : Not Significant

The mean Diastolic BP in Group I was found to be 73.88 mmHg with SD of 5.214 mmHg. The mean Diastolic BP in Group II was found to be 74.33 mmHg with SD of 5.17 mmHg.

The difference in mean pulse rate, respiratory rate, systolic blood pressure and diastolic blood pressure were not statistically significant and were comparable.

The Heart Rate, Respiratory Rate and Blood Pressure were recorded every 5 mins. of first 30 mins. after epidural injection every 15 mins till 1 hour and every 30 mins. there after.

There was no significant differences in heart rate between Group I and Group II. Through out the intraoperative and post operative period the blood pressure was similar in both groups.

### Onset Of Analgesia

### Table 9
<table>
<thead>
<tr>
<th>Group</th>
<th>Mean onset of analgesia (in minutes)</th>
<th>± SD</th>
<th>t-test</th>
<th>P value</th>
<th>Statistical Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>16.90</td>
<td>2.49</td>
<td>0.27</td>
<td>0.7892</td>
<td>NS</td>
</tr>
<tr>
<td>Group II</td>
<td>17.10</td>
<td>2.20</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NS : Not Significant

The mean onset of analgesia for Group I was 16.90 ± 2.49 mins and for Group II 17.10 mins ± 2.20. The mean time to onset of action in both the groups were statisitcally not significantly different.

### Maximum Sensory Level
To assess the efficacy of verapamil 5mg as an adjuvant to 0.5% plain Bupivacaine in Lumbar epidural anaesthesia

### Table 10
**Maximum Sensory Level (Segments)**

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean maximum sensory level (segments)</th>
<th>± SD</th>
<th>t-test</th>
<th>P value</th>
<th>Statistical Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>6.80</td>
<td>0.77</td>
<td>0.60</td>
<td>0.5554</td>
<td>NS</td>
</tr>
<tr>
<td>Group II</td>
<td>6.95</td>
<td>0.83</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NS : Not Significant

The mean maximum sensory level in Group I was found to be 6.80 ± 0.77. The mean maximum sensory level in Group II was found to be 6.95 ± 0.83. This is also not significantly different.

### Maximum Motor Blockade

### Table 11
**Maximum Motor Block (According To Bromage Scale)**

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean maximum motor block</th>
<th>± SD</th>
<th>t-test</th>
<th>P value</th>
<th>Statistical Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>2.50</td>
<td>0.51</td>
<td>0.31</td>
<td>0.7590</td>
<td>NS</td>
</tr>
<tr>
<td>Group II</td>
<td>2.55</td>
<td>0.51</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NS : Not Significant

The mean maximum Motor blockade in Group I was found to be 2.50 ± 0.51. The mean maximum Motor blockade in Group II was found to be 2.55 ± 0.51. This was also Not significantly different. The sensory level and motor blockade were statistically Not significantly different in the 2 groups.

### Duration Of Surgery

### Table 12
**Duration Of Surgery (In Minutes)**

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean duration of surgery (in minutes)</th>
<th>± SD</th>
<th>t-test</th>
<th>P value</th>
<th>Statistical Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>92.85</td>
<td>5.07</td>
<td>0.58</td>
<td>0.5663</td>
<td>NS</td>
</tr>
<tr>
<td>Group II</td>
<td>91.90</td>
<td>5.31</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NS : Not Significant

The mean duration of surgery in Group I was found to be 92.85 ± 5.07 mins. The mean duration of surgery in Group II was found to be 91.90 ± 5.31 mins. The mean duration of surgery is not statistically significantly different.

### Duration Of Analgesia

### Table 13
**Duration Of Analgesia (In Minutes)**

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean duration of analgesia (in minutes)</th>
<th>± SD</th>
<th>t-test</th>
<th>P value</th>
<th>Statistical Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>175.70</td>
<td>13.21</td>
<td>16.13</td>
<td>0.000</td>
<td>S-Significant</td>
</tr>
<tr>
<td>Group II</td>
<td>323.20</td>
<td>38.71</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

S : Significant

In Group I the patients who have received only epidural Bupivacaine, the mean duration of analgesia was 175.70 mins, with SD of 13.21 i.e. around 3 hrs.

In Group II the patients who have received Bupivacaine with verapamil, the mean duration of analgesia was 323.20 with SD of 38.71 i.e. around 6 hours.

Duration of analgesia was found to be significantly different. In the verapamil group the duration of analgesia was prolonged and the requirement of post operative analgesics was reduced.

**SpO₂**

SpO₂ was maintained in both the groups between 96 to 99%. No patients needed supplemental oxygenation.

### Complications

There was no incidence of complications like

- Nausea
• Vomiting
• Retention of urine
• Hypotension (25% below the baseline level)
• Brady cardia (Rate less than 60/min.)
• AV conduction defects or arrhythmias,
• Pruritis
• Respiratory depression (less than 8/bmt).

IV. Discussion

Providing intra operative pain relief is the “raison –d- etae” of anaesthesia. It would be advantageous if this pain relief could be extended into the post operative period as well. The prevention of pain is much simpler to achieve than the treatment of pain once established. Epidural analgesia is the presently favoured method to provide intra operative and post operative analgesia.

Epidural anaesthesia and analgesia have been evolved now with novel analgesic agents. Opioids, Ketamine, Clonidine, neostigmine, adenosine, midazolam and tramadol are now being used as adjuvants with local anaesthetics to provide pain relief by epidural administration. These adjuvants provide more potent action in reducing pain and in prolonging post operative analgesia.

Recent studies show that calcium channel blockers like verapamil can also be used to provide pain relief. Normal calcium movement is essential for normal sensory processing. A disruption of calcium influx will interfere with normal sensory processing, thus contributing to reduced pain. Inhibition of calcium influx by calcium channel blockers produces antinociception at the level of the spinal cord.

In this study, epidural administration of bupivacaine and verapamil in herniorraphy surgeries produced effective analgesia and increased the post operative duration of analgesia.

All patients suffering from cardiac illness had been excluded. P.Foex say that the rate of sinus node discharge is depressed and atrioventricular time is prolonged by verapamil. Myocardial contractility decreases in a dose dependent fashion. Patients who are receiving beta blockers for cardiac illness or anxiety or Hyperthyroidism, were carefully excluded from our study. The concomitant use of verapamil and beta blockers may potentiate negative ionotropy, chronotropy and dromotropy.

Preoperative and Post operative 12 lead ECG were recorded. Intraoperative ECG monitoring was done as verapamil may produce conduction abnormalities like prolongation of PR interval. Non-invasive blood pressure and pulseoximeter were connected. Baseline heart rate, blood pressure and oxygen saturation were noted. Our study concurs with the double blind study done by Huhnchoe, Jin song kim, Seong Hoon Ko, Young chin Han, He -Sun song on how epidural verapamil reduces analgesic consumption after lower abdominal surgery during the Post operative period.

The patients selected for our study were exclusively male patients undergoing inguinal herniorrhaphy surgeries for the purpose of uniformity. The age, weight and height were also similar and comparable so that the study of the level of sensory blockade should not be affected in our study. Kapur et al., 1984 say a verapamil and Fentanyl combination produced marked vasodilation. As Kapur stated, opiates for premedication were prevented. No premedication was given in our study as it may influence the heart rate, duration of analgesia and haemodynamic changes.

At present pain during the intra operative and post operative period are of more concern. B.L. Kidd and L.A. Urban say that nociception may be defined as the detection of noxious stimuli and the subsequent transmission of encoded information to the brain. The responses to noxious stimuli may be enhanced (hyperalgesia) or normally innocuous stimuli may produce pain (allodynia). This pain will stimulate the sympathetic nervous system after surgical incision and produce an increase in pulse rate and blood pressure. This increase in heart rate leads to increased myocardial oxygen consumption. In both the groups of our study, we experienced neither tachycardia nor Hypertension due to an adequate epidural blockade.

Purnel RJ 1985 in his study demonstrated bradycardia after verapamil and spinal analgesia. The total incidence of bradycardia (ventricular rate less than 50 beats/minute) was 1.4%, in controlled studies, through IV administration of verapamil. Verapamil did not produce significant bradycardia in ideal dosages. As in both the groups, the maximum level of sensory blockade was only at T6 to T7 level bradycardia was not experienced. The mean pulse rate in Group I (0.5% bupivacaine alone) was found to be 77.96 ± 4.13/min and in Group II (0.5% bupivacaine + 5 mg of verapamil) was found to be 78.95 ± 5.05/min. Verapamil is a much less powerful vasodilator than nifedipine and therefore causes less reflex increase in ß adrenoreceptor activity. It reduces peripheral vascular resistance usually without reflex tachycardia. So undue tachycardia was not seen.

Due to pain, the respiratory rate will increase. The tidal volume to perfusion ratio will reduce and may result in hypoxemia. In our study the mean respiratory rate in Group I (0.5% bupivacaine alone) was found to be
Verapamil is a potent smooth muscle relaxant with vasodilatory properties, as well as a depressant of myocardial contractility and these effects are largely independent of autonomic influences. It reduces peripheral vascular resistance without reflex tachycardia. Epidural verapamil did not produce hypotension. The mean systolic pressure in Group II (0.5% bupivacaine + 5 mg of verapamil) was 113.93 ± 7.16 mm of Hg and the mean diastolic pressure was 74.33 ± 5.17 mm of Hg. The maximum sensory level in both the groups were between T6 to T7 level. So neither hypotension nor bradycardia was seen.

Onset of sensory analgesia and Motor blockade was neither prolonged nor reduced by addition of verapamil epidurally to bupivacaine. The onset of analgesia in Group I (0.5% bupivacaine alone) was found to be 16.90 ± 2.49 mins and Group II (0.5% bupivacaine + 5 mg of verapamil) was found to be 17.10 ± 2.20 minutes. The motor blockade in Group I (0.5% bupivacaine alone) was 2.50 ± 0.51 and Group II (0.5% bupivacaine + 5 mg of verapamil) was found to be 2.55 ± 0.51 according to the bромгам scale. Since we had selected inguinal herniorrhaphy surgery for our study, we did not find major differences in the duration of surgery.

Addition of verapamil to bupivacaine in epidural administration had a significant influence on the duration of analgesia. The duration of analgesia in Group II (0.5% bupivacaine + 5 mg of verapamil) was 323.20 ± 38.71 minutes i.e around 6 hours. The duration of analgesia is Group I (0.5% bupivacaine alone) was 175.70 ± 13.21 minutes i.e around 3 hours. The mean duration of surgery in Group I and Group II was around one and a half hours. Addition of 5 mg of verapamil to 0.5% bupivacaine had produced post operative analgesia for four and half hours where as Group I (0.5% bupivacaine alone) had produced post operative analgesia for one and a half hours. These results simulate the study done by Huhn Choe and Jin-song Kim, in which they say that post operative analgesic consumption was less by the addition of verapamil to 0.5% bupivacaine.

Many studies have been done to demonstrate the usage of verapamil with local anaesthetics spinally and epidurally to produce antinociception. Himes, Difacio and Burney 1977 say verapamil causes some blockade of sodium channels also. Iwasaki H, Onote K, Kavamata M 1995 says that sensory blockade produced by lignocaine is potentiated by calcium channel blockers. They also demonstrated in rats that local sensory block produce by lignocaine injection at its tail base was potentiated by verapamil in a dose dependent manner.

Hara K and Saito Y evaluated the effects of verapamil on somatic and visceral nociception at the level of the spinal cord. In Sprague-Dawley rats 50 μgms of verapamil injected, with isotonic normal saline as control in to the intrathecal lumbar catheters. Intrathecally administered verapamil increased both tailflick latency and colorectal distension threshold where as isotonic normal saline does not. This indicates verapamil produced both somatic and visceral nociception. It suggests a possible clinical application of verapamil to pain.

Bingurann D, Lipinski HG, Hagemann G, Speckmann 1990 concluded in their study that local anaesthetics block sodium channels primarily from the intracellular side. The primary mode of action of Local anaesthetics is through sodium channel and axonal conduction blockade. It also has extensive effects on presynaptic calcium channels that must function to stimulate the release of neurotransmitters. Thus if we add verapamil and interfere with calcium conductance it may enhance epidural anaesthesia with local anaesthetics due to its synergistic effect.

Omote K, Iwasaki 1995 investigated the effects of intrathecal verapamil on spinal anaesthesia with local anaesthetics. Male Sprague Dawley rats were chronically implanted with Lumbar intrathecal catheters. Tail flick and mechanical paw pressure tests were used to assess thermal and mechanical pain threshold respectively. Motor function was assessed through modified Langerman's scale. Intrathecal lidocaine showed prolongation of tail flick latency i.e. thermal threshold, increase in mechanical paw pressure i.e. mechanical threshold and increase in motor function. Intrathecal verapamil alone (50-200 microgram) did not produce sensory or motor block. When combination of 50 μgm of verapamil and 200 μgm of lidocaine produced more potent and prolonged antinociception and motor blockade. Their study indicate that intrathecal verapamil potentiates spinal anaesthesia with local anaesthetics. Thus epidural Ca" channel blockers potentiate the analgesic effects of local anaesthetics. Toxic doses of local anaesthetics can be reduced and may be used synergistically for clinical pain management by adding verapamil.

Wong CH, Dey P. 1994, Department of Anaesthesiology, New Jersey Medical School, New York explored the analgesic effect of epidural nifedipine (20 μg) a L type calcium channel blocker in male Sprague - Dawley rats. Analgesia was measured by tail flick involving spinal reflexes and by hot plate requiring intact central nervous system. They conclude that nifedipine given epidurally, possesses antinociceptive properties at the dose of 5 micrograms, and higher and it is more prominent at the spinal than the supraspinal level.

Hirota and colleagues studied the effect of lidocaine, bupivacaine on L type voltage activated calcium channels in cerebro cortical membranes prepared from rat brain. They found an interaction between local anaesthetics agents and L types calcium channel.
Sugiyama and Mutelai showed that tetracaine, at concentrations required for spinal anaesthesia, depressed high and low voltage activated calcium channels of dorsal root ganglion cells of rat sensory neurones, the most susceptible being the L-Type Calcium Channel.

A.Fassaulaki, M.Zotou 1998 investigated the effect of IV infusion of nimodipine on the spread of spinal anaesthesia in 50 patients undergoing TURP. His study was associated with a delay in regression of sensory block produced by intrathecal injection of lidocaine.

Calcium channel blockers, including verapamil potentiate the antinociceptive effects of opioids at the spinal cord level. It has also been demonstrated that morphine inhibits calcium ion influx through receptor operated calcium channel in neuronal cells. A proposed mechanism for opioid mediated analgesia at the spinal level is thought to involve reducing presynaptic calcium ion influx, resulting in suppression of neurotransmitters release from primary afferents conveying nociceptive formation. This indicates that antinociceptive effects of intrathecally administered opioids could be increased by intrathecal calcium channel blockers.

Omore K, sonada H., Kawamata M, Namiki 1993 studied the potentiation of antinociceptive effects of morphine by verapamil at the level of spinal cord. They say opioids inhibit voltage dependant calcium conductance which is essential for the nervous system to be able to signal a painful event. Accordingly interference with calcium channel conductance may enhance opioid analgesia. Rats were chronically implanted with lumbar intrathecal catheters. Intrathecally administered drugs were morphine, calcium channel blockers - verapamil, and a combination of morphine and verapamil. Intrathecal morphine showed a significant dose dependant antinociception. In contrast intrathecal verapamil did not show any antinociception. When morphine (5 µgms) and verapamil (50 µgms) were injected together and produced significant antinociception. These interactions were synergistic. The author interpreted these results to indicate that calcium channel blockers synergistically potentiate the analgesic effects of morphine at the level of the spinal cord.

Zarausa R, Tribarren MJ 1991 at University of Navarra, Department of Anaesthesiology, Spain tested the ability of L-type calcium channel blockers and NMDA receptor antagonist magnesium to decrease morphine requirement and pain in post operative period in 92 patients undergoing colorectal surgery. Increase of intracellular calcium plays a key role in spinal transmission of pain and in the establishment of central sensitization. They found no differences in post operative morphine consumption by using verapamil or magensium. But in our study the post operative analgesic period is prolonged.

Santillin R, Mastre JM, Hure MA 1994, Department of Anaesthesiology, Santander, Spain studied the ability of nimodipine, a L type calcium channel blocker, to enhance morphine analgesia or modify the development of tolerance. They studied in patients with cancer pain who had needed successive increments of morphine for periods ranging from 21 to 780 days. Assessment of daily morphine requirement was the primary effect parameter. Nimodipine succeeded in 23 patients in reducing daily dose of morphine, these results support the pharmacological interference with Ca²⁺ related events which may modify chronic opioid effects, including expression of tolerance.

Weizman and Getslev 1999 evaluated, the opioid antinociceptive mechanism of Ca²⁺ channel blockers verapamil and flunarizine in groups of mice, with hotplate test. Both produced naloxone sensitive dose dependent analgesia. Both enhanced the antinociceptive activity of morphine implying a role of mu receptors. They also found in their study that the antinociceptive activity of verapamil is also mediated by delta receptor agonistic activity. Verapamil is a partial agonist of Kappa 1 and Kappa 3 receptors. Verapamil's analgesia was explained by agonistic activity at the mu, delta and kappa 3 receptors subtypes. Flunarizine exhibited agonist - antagonistic property. It has agonistic activity at the mu 1 receptor and antagonistic activity at delta, kappa 1 and kappa 3 subtypes.

All these various studies indicates how verapamil produces antinociception. These studies only initiated us to use verapamil epidurally to enhance the duration of analgesia along with bupivacaine. The altered sensory processing caused by high intense noxious stimuli results in a decrease in thresholds of dorsal horn neurons, an increase in gene expression and increased response of dorsal horn neurons elicited by repetitive C-fiber stimulation.

There is activation of excitatory aminoacid receptors followed by release of glutamate and aspartate in the dorsal horns of spinal cord. These amino acids actions are mediated by NMDA receptors. Activation of NMDA receptors leads to Ca²⁺ entry in to the cell through NMDA receptor operated by Ca²⁺ channels and activates phospholipase C. Phospholipase C catalyzes the formation of intracellular second messengers, which causes the release of Ca²⁺ from endoplasmic reticulum.

The increase in intracellular calcium results in increased gene expression and central sensitization including wind up phenomenon and long term potentiation. Thus calcium channel conductance is required for the nervous system to signal a painful situation. A disruption of calcium ion movement interferes with sensory
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processing and contributes to antinociception. This principle holds good for the use of verapamil, a L type calcium channel blocker to reduce post operative pain.

This series of reactions may be prevented or attenuated presynaptically by reducing the release of neurotransmitters by using opioids and local anaesthetics or post synaptically by NMDA receptor antagonist like ketamine. There is evidence that ketamine, a clinical NMDA receptor antagonist reduces post operative pain. Magnesium a physiological calcium channel blocker and NMDA receptor antagonist suppresses NMDA induced adverse behavioural reactions. Nowek et al., 1984 says that extracellular application of Mg$^{2+}$s in the vertebrate central nervous system.

NMDA receptor antagonists may pre

current of NMDA receptors. It has been suggested that substances with calcium channel blocking effects and NMDA receptor antagonists may prevent pain and facilitate treatment for established pain states.

Conduction abnormalities were carefully watched during our study with continous ECG monitoring and preoperative as well as post operative 12 lead ECG. Verapamil will slow the conduction around AV node and rarely may produce second or third degree AV block, bradycardia and in extreme cases, asystole. Verapamil causes dose dependent suppression of the SA node and produce bradycardia. But with this 5 mg of verapamil given epidurally we did not experience bradycardia or conduction abnormalities.

There are only limited informations are available on verapamil's effect on pain in humans. In our study we showed that bupivacaine and verapamil administered epidurally produced good analgesic quality and increased the post operative analgesic period in elective herniorraphy surgeries.

V. Summary

This study assessed the clinical efficacy of Verapamil 5mg added to 0.5% plain bupivacaine in Lumber epidural Anaesthesia for elective inguinal surgeries.

The onset time, duration of analgesia, level of sensory blockade, quality of motor blockade. Hemodynamic parameters, Respiratory changes were assessed and the results showed that Verapamil had

- Significant prolongation in the duration of analgesia
- No effect on the time to onset of analgesia
- No effect on the highest level of sensory block
- No significant effect in the degree of motor blockade
- No significant effect on Hemodynamics
- No significant effect on Respiration.

VI. Conclusion

From this study we conclude that epidural bupivacaine (0.5%) with verapamil prolonged the postoperative analgesic period when compared to 0.5% bupivacaine alone for elective inguinal herniorraphy surgeries under lumbar epidural anaesthesia.

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