A comparison of epidural Butorphanol Tartrate and Tramadol hydrochloride for Postoperative analgesia using csea technique

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INTRODUCTION
Effective pain control is essential for optimal care of surgical patients, as these patients suffer from considerable pain in the postoperative period. Acute postoperative pain is a complex physiologic reaction to tissue injury or visceral distension. Its manifestation of autonomic, psychological and behavioral responses results in unpleasant, unwanted sensory and emotional experience. Combined spinal-epidural (CSE) analgesia is becoming increasingly used to provide pain relief in postoperative period. It combines both the rapid onset of the spinal analgesia and the flexibility of the epidural Reinforcement with continuous epidural anaesthesia.

ABSTRACT
BACKGROUND: The efficacy of epidurally administered tramadol hydrochloride and Butorphanol tartrate, a weak centrally acting analgesic, were studied for the relief of postoperative pain. MATERIALS AND METHOD: Sixty patients undergoing abdominal and lower limb surgery using CSEA technique were randomly allocated to two treatment groups to be given the following agents by the epidural route. In postoperative period if VAS ≥ 4, group A: patient’s received inj. Butorphanol tartrate 2mg in 10ml NS and group B patient’s received inj. Tramadol hydrochloride 100mg in 10ml NS through epidural catheter. Half top up doses i.e. 1mg of Butorphanol tartrate and 50mg of Tramadol hydrochloride in 10ml NS were given in respective group A and B when VAS score was ≥ 4, group 1 tramadol. The drugs were administered at the VAS score was ≥ 4 with each patient being allowed maximum doses in the first 24h and recorded total doses following surgery. Blood pressure, pulse rate, respiratory rate, SpO2, pain scores, the interval between doses and the occurrence of any side effects were recorded. Pain scores (assessed using a visual analogue scale) were significantly less (p < 0.05) at 3, 12, and 24h in patients receiving Butorphanol 2mg than tramadol 100mg epidurally. The mean interval between doses for groups 1, 2 and 3 was 7.40h, 9.36h and 5.98h respectively.

RESULTS: The mean interval in group B was significantly longer than in group A (p < 0.05). The incidence of nausea and vomiting in group B was significantly higher than in group A (p < 0.05). CONCLUSION: Epidural butorphanol has been shown to produce effective analgesia with less side effects than that of tramadol but relatively short duration.

Keywords: Butorphanol, Tramadol, CSEA, Postoperative pain

Epidural narcotics have been extensively used for post-operative analgesia. With discovery of newer opioids like Butorphanol tartrate, Tramadol hydrochloride and fentanyl citrate, a new era in pain relief has commenced. Butorphanol tartrate, a synthetic opioid derivative is a mixed agonist and antagonist non-narcotic opioid analgesic where as Tramadol hydrochloride is a synthetic 4-phenyl-piperidine analog of codeine with a dual mechanism of action. The advantage with these newer drugs is that their potency is comparable to that of morphine, produce lesser respiratory depression, easily available, larger margin of safety and lesser incidence of nausea, vomiting, urinary retention, pruritus compared to morphine. Hence it is feasible to conduct the present study to assess the safety and efficacy of postoperative analgesia with epidural Butorphanol tartrate compared with epidural Tramadol hydrochloride.
A comparison of epidural Butorphanol Tartrate and Tramadol hydrochloride

MATERIALS AND METHOD
The study was approved by Gujarat Cancer Institute IRB to do randomized clinical trial in 60 adult patients of physical status ASA grade I & II, of either sex, age group 18-69 years old, undergoing elective laparotomy and orthopedic lower limb surgery were divided in two groups, each of 30 patients who fulfill the inclusion and exclusion criteria.

Subject who met above criteria were examined in preoperative period which included patient’s detailed history, general physical examination systematic examination and necessary investigations. Written informed consent was taken from the patient. All patients received tablet lorazepam 1mg orally at previous night of surgery and tablet diazepam 5mg in the morning of surgery.

Under proper monitoring like ECG, NIBP, Pulse Oximetry baseline parameter were noted, all patients were preloaded with 10 ml/kg infusion of ringer lactate solution combined spinal epidural analgesia was initiated at L2-3 and L3-4 space, epidural space was identified by hanging drop method, epidural catheter (18G) was inserted and subarachnoid block was given in one segment lower using 4 ml of 0.5% heavy inj. bupivacaine hydrochloride. Level of sensory and motor block was noted and haemodynamic parameters were monitored intraoperatively. No narcotics were administrated throughout intraoperative period.

In postoperative period, if VAS ≥ 4, group A: patient’s received inj. Butorphanol tartrate 2mg in 10ml NS and group B patient’s received Inj. Tramadol hydrochloride 100mg in 10ml NS through epidural catheter. Half top up doses i.e. 1mg of Butorphanol tartrate and 50mg of Tramadol hydrochloride in 10ml NS were given in respective group A and B when VAS score was ≥ 4.

Patients were assessed at half-hourly intervals for first two hours then at 4, 8, 12, 24 hours after giving first dose of epidural opioid for the following variables

A. Visual analogue scale (VAS)
0-no pain,
1-3-mild pain,
4-7moderate pain,
8-10severe pain.

B. Sedation score
0 = Fully awake,
1 = Slightly drowsy,
2 = Asleep but easily arousable,
3 = Fully asleep but arousable,
4 = Fully asleep and not arousable.

C. HR and BP.

D. Monitoring of respiratory rate (RR) and SpO2.

E. Side effects such as nausea, vomiting, retention of urine, pruritis and respiratory depression.

Statistical Method
Using Medcal-caesarean software and taking an alpha error 0.01 and beta error of 0.01 for the parameter.

Duration of effective analgesia the minimum sample size required to conduct the study would be 22 per group. In order to compensate for greater variability, 30 patients were included in each group.

Statistical analysis;
- The results of the study were tabulated & statistically compared.
- Chi-square test was used for qualitative data.
- For rest of quantitative data student t test was used (unpaired).

The P-value was considered significant as shown below:
1. P >0.05 not significant
2. P <0.05 significant
3. P <0.001 highly significant

RESULTS
Sixty ASA risk I and II patients undergoing elective surgery were studied and randomly assigned into two groups of 30 patients each. They all received postoperative analgesia through epidural catheter in post anaesthesia care unit.

Table: 1 Demographic data (mean ± SD)

<table>
<thead>
<tr>
<th>Groups</th>
<th>Group 1</th>
<th>Group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of Pts.</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>Age(years)</td>
<td>56±10</td>
<td>58±9</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>158±7</td>
<td>160±5</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>48.6±8</td>
<td>51.6±3</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>8:22</td>
<td>10:20</td>
</tr>
</tbody>
</table>

Table-1 shows that there were no difference in the age, weight, height, sex,
in both groups and both groups are comparable using unpaired student T- test. (P> 0.05)

**Table: 2 No. of epidural dosages required to produce analgesia**

<table>
<thead>
<tr>
<th>No. of epidural dosages</th>
<th>Group A</th>
<th>Group B</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>0</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>5</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>25</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

Above table suggest that in Group a majority of patient required 4 doses while in Group B 3 doses required for pain relief and this difference was highly significant (P < 0.001).

**Table: 3 Duration of analgesia**

<table>
<thead>
<tr>
<th>Duration</th>
<th>Group A</th>
<th>Group B</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>30 min</td>
<td>1.8±0.8</td>
<td>1±0.47</td>
<td>0.0001</td>
</tr>
<tr>
<td>60 min</td>
<td>1.53±1.13</td>
<td>0.5±0.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>120 min</td>
<td>0.33±0.75</td>
<td>0±0.37</td>
<td>0.0348</td>
</tr>
<tr>
<td>4 hour</td>
<td>0±1.42</td>
<td>0±1.43</td>
<td>0.0015</td>
</tr>
<tr>
<td>8 hour</td>
<td>0.93±0.73</td>
<td>0.5±0.5</td>
<td>0.0100</td>
</tr>
<tr>
<td>12 hour</td>
<td>0.33±0.7</td>
<td>0±0.3</td>
<td>0.0210</td>
</tr>
<tr>
<td>24 hour</td>
<td>0.33±0.7</td>
<td>0±0.34</td>
<td>0.0253</td>
</tr>
</tbody>
</table>

Duration of drug effect was defined when VAS score reaches > 4 in observation period after giving the epidural dose. Table 3 shows there was statistically highly significant difference in duration of analgesia.

**Table: 4 Comparisons of VAS Score in both Groups**

VAS score of pain was not statistically different between the two groups before giving drugs. After 30 min VAS score in both Groups was significantly lower than previous reading. In Group A VAS score increased at 6 hours whereas in Group B it increased at 8 hours. VAS scores were significantly lower in Butorphanol group than in Tramadol group at many occasions which suggest that pain relief was significantly better in Butorphanol group than Tramadol group.

**Table: 5 Comparison of SEDATION Score in both groups**

<table>
<thead>
<tr>
<th>Baseline</th>
<th>Group A</th>
<th>Group B</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 min</td>
<td>1.84±0.8</td>
<td>1±0.47</td>
<td>0.0001</td>
</tr>
<tr>
<td>60 min</td>
<td>1.53±1.13</td>
<td>0.5±0.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>120 min</td>
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<td>0±0.37</td>
<td>0.0348</td>
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<td>0±0.34</td>
<td>0.0253</td>
</tr>
</tbody>
</table>

Table 5 shows that sedation score before giving drugs epidurally among both groups were comparable. (P>0.05). After giving drugs epidurally at 30 min sedation score in Group A was significantly higher than Group B(<0.0001).

**Table: 6 Side effects**

<table>
<thead>
<tr>
<th>Side effects</th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>2(6%)</td>
<td>6(18%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>1(3%)</td>
<td>2(6%)</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Nausea was observed seen in 2 patients in Group A and in 6 patients in Group B and Vomiting was found in 1 patient in Group A and in 2 patients in Group B which is statistically significant. Two out of 30 patients in Group B also had pruritus. No other complication was observed in either group.

**DISCUSSION**

Pain is one of the most important concern of mankind and one of the foremost factors that have influenced the course of history. Effective pain control is essential and has been recognized as a prime concern for anaesthesiologists. Epidural route is used extensively for postoperative pain control. No one can share the gravity and severity of others pain. Epidural opioids have been administered for hundreds of years to relieve anxiety and reduce pain associated with surgery. Combined spinal-epidural (CSE) anesthesia is commonly used now a days. Opioids are powerful, centrally acting agents which have peripheral effects also, so opioids have been administered for many years to allay anxiety and to reduce pain associated with surgery. Combined spinal epidural anaesthesia finds a common place for perioperative management of orthopaedic surgery. It combines the advantages of both spinal and epidural technique by initially providing an intense sensory and motor block of rapid onset. After the surgical procedure and regression of spinal analgesia, the epidural catheter can be used to provide post operative pain relief. A study using epidural narcotics like hydromorphone and morphine for postoperative analgesia concluded that analgesia produced by epidural narcotics was greater than IV narcotics and was relatively free of side effects. The first published report on opioids for intrathecal anaesthesia belongs to a Romanian surgeon, Racoviceanu-Pitesti, who presented his experience at Paris in

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1901. It was almost a century before the opioids were used for epidural analgesia. Behar et al 27 in 1979, reported epidural morphine therapy and since then they are very popular and are used extensively for postoperative analgesia. But the side effects produced by morphine were undesirable which lead to resurgence of newer drugs like Butorphanol tartrate and Tramadol hydrochloride.

Tramadol hydrochloride is 1/5 - 1/10th as potent as morphine and analgesic doses of Tramadol hydrochloride may produce less respiratory depression because of its non-opioid receptor mediated actions. However, the incidences of allergic rash, itching, and sedation were greater in the morphine group than in the Tramadol hydrochloride group in another study done by Anis Baraka in 1993.20

In our study Tramadol hydrochloride 100 mg selected because Siddik-Sayyid et al, 22 1999, stated that epidural Tramadol hydrochloride 100 mg can provide adequate post-operative analgesia without respiratory depression after cesarean delivery.

And also added by Wilder Smith CH et al, 1998, 20 mg Tramadol hydrochloride result in anti-analgesic and increase side effect.21

Butorphanol tartrate is a synthetic morphine derivative introduced into Indian market since 2002 is a mixed agonist and antagonist non-narcotic opioid analgesic. The analgesic potency of Butorphanol tartrate has been found to be greater than morphine and pethidine. Thus this study was conducted in an effort to assess efficacy of newer drug Butorphanol tartrate and compare it with Tramadol hydrochloride.

**Duration of Analgesia**

Our study shows that Tramadol hydrochloride had a longer duration of analgesia when compared to Butorphanol tartrate for postoperative epidural analgesia.

Abboud TK et al found an analgesia lasting 5.53 + 0.86 hours with epidural Butorphanol tartrate which is comparable to our study.17

In a comparative study of epidural morphine with epidural Butorphanol tartrate by Palacios QT 18 median time of duration of analgesia was 3, 2.5 and 4 hours for Butorphanol tartrate 1, 2 and 4 mg respectively.17

Sayyid S ET al 22 in their study on epidural Tramadol hydrochloride (100 mg) for postoperative pain relief found the duration of analgesia to be 4.5±3.1 hours. This result were different from our study may be because of the difference in the type of surgery.

**Quality of Analgesia (VAS)**

Pain assessment by VAS score suggest that no significant difference in the VAS before giving drug (Group a VAS= 7.1+/ -1.15 and Group B VAS =6.9+/ -1.33) (p>0.05). After drug injection pain relief was there in both the groups but after 30 min it was observed that VAS was significantly low in Group A(1.06 +/- 1.31) compared to Group B (3 +/- 0.76)up to 4 hrs suggesting that Butorphanol tartrate significantly reduced pain and increase quality of analgesia (p<0.05).

There was no need to administered rescue analgesia as none of the patient’s VAS was more than 4 within 30 minutes of drug administration.

Palacios Q et al 18 found decreased VAS score (0 +/- 1.4) with epidural Butorphanol tartrate, where as Anis Baraka 20,1991,found decreased VAS score (0.2 +/- 0.6 to 1.4 +/- 2.5) with epidural Tramadol hydrochloride 100 mg. Quality of analgesia was better with epidural Butorphanol tartrate (1mg) compared to that of epidural Tramadol hydrochloride (50mg).

**Cardiovascular and Respiratory Effects**

The significant decrease in mean pulse rates, systolic and diastolic blood pressure were observed from the baseline readings in both the groups after giving epidural drugs because adequate analgesia achieved resulting in less sympathetic discharge. Respiratory rate before giving drugs were comparable in both groups. After giving drugs there was fall in respiratory rate in both groups but difference between both groups was not significant.

Palacios ET al 18 found that no patients in their study group receiving epidural Butorphanol tartrate developed clinically important change in hemodynamic
parameters. Although none of patients developed respiratory rate below 12 breaths per minute, observation for clinical respiratory depression is indicated during period of analgesia as with other epidural opioid.

Way back in 1987 Abboud et al, stated the safety, efficacy and the ventilatory responses to carbon dioxide (CO2) of epidurally administered Butorphanol tartrate and it was compared with morphine and showed that ventilatory response to CO2 was depressed in both the groups but duration of depression was prolonged with morphine. As suggested by both, patients must be observed closely because of possibility of respiratory depression.

**Side Effects**

**Sedation**

Sedation Score was, (1.53+/−1.13) significantly higher with Butorphanol tartrate as compared to (0.5+/−0.6) with Tramadol hydrochloride in our study which is consistent with other study by Abboud. Mild sedation is desirable in the post-operative period, which is observed with the Butorphanol tartrate group.

**Other side effect**

Group B has significant propensity to cause nausea (18%), vomiting (10%) and pruritus (6%) which is comparable to Anis Baraka et al N/V 20 % and pruritus (10%) with epidural Tramadol hydrochloride. While in Group A only nausea was observed in (6%) in our study. In Vinita Singh et al, 2006, study Nausea / Vomiting (24%) and Pruritus (5%) with epidural Butorphanol tartrate which were comparable with our study.

**CONCLUSION**

In conclusion epidural Butorphanol tartrate (1mg) is a safe and effective in providing pain relief with minor side effects.

- Epidural Butorphanol tartrate provides a rapid, excellent but shorter duration of analgesia when compared to epidural Tramadol hydrochloride.
- Epidural Butorphanol tartrate had lesser side effects like nausea and vomiting but has sedation in milder degree which is an additional advantage in the post-operative period.
- Quality of analgesia in terms of patient satisfaction is also better with epidural Butorphanol tartrate.

**REFERENCES**

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