COMPARISON OF EPIDURAL BUTORPHANOL VERSUS EPIDURAL MORPHINE IN POSTOPERATIVE PAIN RELIEF

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Abstract

Introduction: Epidural route is preferable for postoperative pain relief in thoraco-abdominal and lower limb surgeries. We aimed to compare epidural butorphanol versus morphine for post-operative analgesia up to 24 hours in open nephrectomy surgery.

Methods: 80 ASA physical status I and II adult patients were selected for this randomized double blind prospective study. A standard balanced general anesthesia technique was applied for all patients. Epidural catheter was placed in lower thoracic inter-vertebral space before the start of surgery. Injection butorphanol 0.04 mg/kg in group B (n=40) or morphine 0.06mg/kg in group M (n=40) was given in a double blind manner after completion of surgery and before extubation through the epidural catheter. Patients were observed for pain relief by Visual Analogue Scale (VAS) for the next 24 hours. Dose was repeated when VAS was > 4. The onset and peak effect of pain relief, duration of analgesia of 1st dose, frequency of drug administration and side effects if any were observed.

Results: The average onset of analgesia was 26.5± 7.61 minutes with butorphanol and 62.5±13.4 minutes with morphine group which was statistically significant ($p<0.05$). The mean peak effect of pain relief following 1st dose was 173 ± 51.25 minutes with butorphanol and 251 ± 52.32 minutes with morphine group. The duration of pain relief after 1st dose was statistically significant and was 339.13 ± 79.57 minutes in group B and 709.75 ±72.12 minutes in group M which was gradually increased on repeated dosing in group B while it was almost same in Group M. Number of doses required in 24 hours was significantly higher ($p<0.05$) in butorphanol group than morphine group. Somnolence was the main side effect in group B while pruritus was the main side effect with group M.

Conclusion: Epidural butorphanol appears to provide safer and faster postoperative analgesia without much untoward effects but its analgesic action is short so more repeated doses are required than morphine via epidural catheter up to 24 hours.

Keywords: epidural technique, butorphanol, morphine, post-operative analgesia.

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Introduction

Post-operative pain is maximum during the initial 48-72 hours of post-operative period and it declines thereafter[1]. The goal of post-operative pain management is to reduce an individual patient's pain to a tolerable level.

From all routes of pain relief, epidural remains the best route for thoraco-abdominal and lower limb surgeries since it preserves the pulmonary function and provides early ambulation with lower risk of postoperative deep venous thrombosis. Epidural morphine, a potent narcotic analgesic, produces profound postoperative analgesia but it is associated with the occurrence of undesirable side effects including pruritus, nausea, vomiting, urinary retention, and respiratory depression. Butorphanol tartrate is a potent partial agonist antagonist narcotic analgesic. When administered parenterally, it provides pain relief similar to morphine but with shorter duration and with lesser side effects[3,4]. This study was undertaken to compare the onset, quality and duration of pain relief and side effects of butorphanol versus morphine given by epidural route.

Methods

This prospective double blind randomized study was conducted in adult patients with ASA physical status of I-II who were scheduled for open nephrectomy. After ethical committee approval, 80 patients were recruited for the study. The exclusion criteria included history of allergic reaction to study drugs, contraindication to epidural catheter, difficult localization of epidural space or catheter blockage during the study period. All patients were familiarized with standard 0-10 visual analogue scale (VAS) prior to study where 0 stood for " no pain at all" while 10 stood for "worst pain imaginable". Potential side effects were also described.

A standard balanced general anesthesia technique was applied with intravenous fentanyl 2 μg/kg as premedication. After induction of general anesthesia, epidural catheter was placed in the lower thoracic inter-vertebral space. Anesthesia was maintained with 50% N2O in oxygen and isoflurane with intravenous atracurium as muscle relaxant. An epidural bolus dose of 7mL 0.25% bupivacaine was injected prior to surgical incision. Intravenous tramadol 1.0 mg/kg was given during closure of the wound. After completion of surgery and before extubation, dose of study drug was given by double blind method. Randomization was done by closed envelope method. In group B, epidural butorphanol 0.04 mg/kg in 10 ml saline was given while group M patients received epidural morphine 0.06 mg/kg in 10 ml saline.

After the surgery, patients were shifted to the recovery room and monitored for vital signs, VAS score, sedation and any side effects like pruritus, nausea, vomiting and respiratory depression initially every half an hour for the first two hours followed by every two hours for 24 hours. Urinary retention was not elicited because per-urethral catheter was kept for 24 hours in all patients undergoing nephrectomy.

When the patient complained of uncomfortable pain (i.e. VAS score >4), same drug at the same dose was given. Total number of doses required in 24 hours was recorded. Nausea and vomiting were treated with intravenous ondansetron and pruritus was treated by intravenous chlorpheniramine. If respiratory rate went below ≤ 9/min, further doses were withheld and O2 was supplemented. Sedation was graded as 0 to 3 with 0 being fully awake and 3 being extremely sleepy. After 24 hours, the epidural catheter was removed.

Sample size calculation was done by power analysis. This analysis was based on two samples with statistical significance of 0.05 & 80% power. The sample size required was 40 in each group. Statistical analysis was performed using SPSS version 12. Continuous variables were described as Mean ± SD and categorical variables are given as number (%). Continuous variables were compared using t-test for two independent samples. Percentages were compared using Chi-square analysis. P value < 0.05 was considered to be statistically significant.

Results

There were no significant difference in demographic data and hemodynamic changes between the two groups (Table 1, figure 1, 2). Duration of surgery in both the groups was comparable.

Table 1
Demographic data

	Group-B	Group-M	P-value
Age (years)	52 ± 2.1	50.4 ± 2.22	0.65
Weight(kg)	56.1 ± 1.54	55.9 ± 1.2	0.5190.93
Height (cm)	158 ± 1.1	156 ± 1.2	0.32
Sex(M/F)	30/10	28/12	0.617
Duration of surgery (min)	111.12±17.99	112.87±16.82	0.65

The VAS scores were lower for 1st 4 hours in butorphanol group while 4 hours onwards in morphine group after 1st dose administration (figure 3). The

Fig. 1
Hemodynamics

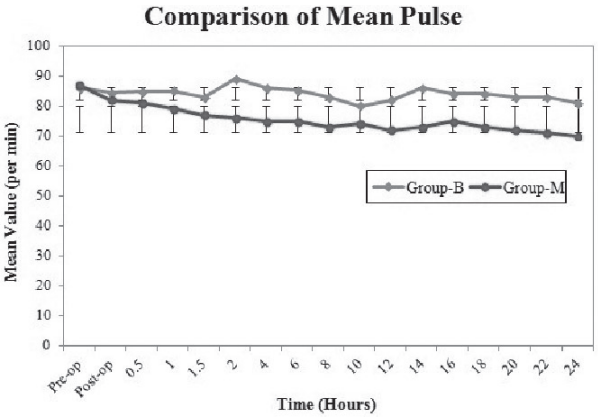

Fig. 2
Hemodynamics

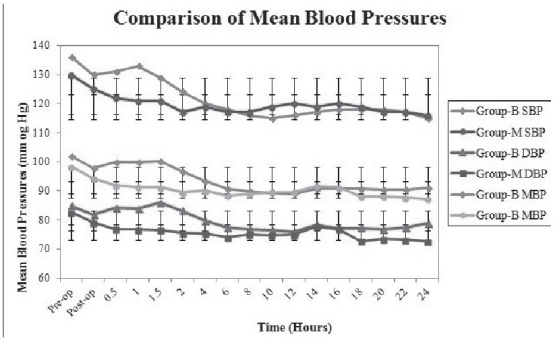

Fig. 3
Mean Visual Analogue Score (VAS)

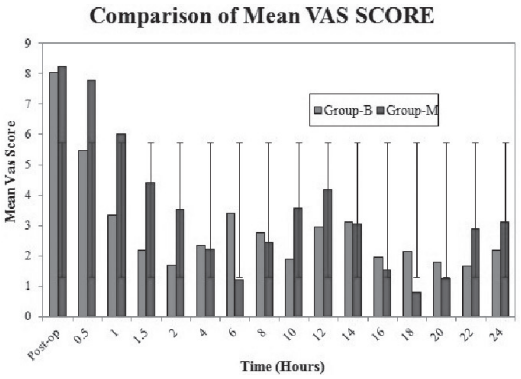

Fig. 4
Mean sedation score

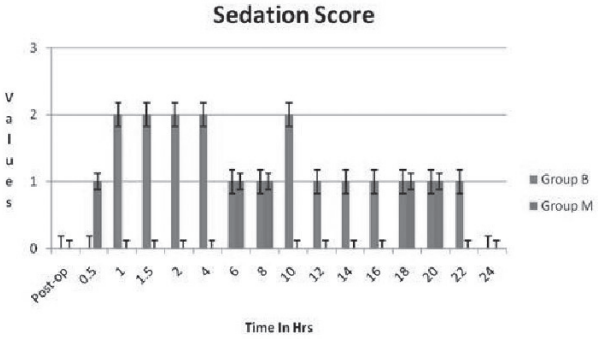

Table 2
Onset and duration of pain relief

Pain relief (minutes)	Group-B (Mean±SD)	Group-M (Mean±SD)	P-value
Onset of pain relief following1st dose	26.5 ± 7.61	62.5 ± 13.4	**<0.0001**
Duration of pain relief following 1st dose	339.13±79.57	709.75±72.119	**<0.0001**
Duration of pain relief following 2nd dose	440.3 ± 76.9	710.1 ± 55.6	**<0.0001**
Duration of pain relief following 3rd dose	504.7 ± 149.1	721.1 ± 41.8	**<0.0001**
Duration of pain relief following 4th dose	506.6 ± 70.7	--	**<0.0001**

mean onset of pain relief was 26.5 ± 7.61 minutes in group B compared to 62.5 ± 13.4 minutes in group M suggesting faster & statistically significant onset in Group B compared to Group M ($p<0.05$). The mean peak effect of pain relief following 1st dose was 173± 51.25 minutes in Group B while in Morphine group, it was delayed and 251± 52.32 minutes ($p< 0.05$).The mean duration of pain relief following 1st dose was significantly longer in group M than group B (709.75 ± 119 v/s339.13 ± 79.57 minutes, $p< 0.05$) which was gradually increased on repeated dosing in group B while it was almost same in Group M (table 2). All 40 patients required 3 doses in butorphanol Group and two doses in morphine group while 24 patients required the 4th dose in B Group & 27 patients required 3rd dose in morphine group in 24 hours (table 3).

The patients in Group B had overall higher sedation score as compared to Group M. Pruritus, respiratory depression & hypotension were only observed in Group M in 37.5 %, 7.5 % & 5 % of cases respectively while somnolence was seen in 75%cases in Group B as compared to 12.5 % cases in Group M. Nausea & vomiting were seen in both groups but higher in Group M. Dizziness, warm sensation & blurring of vision was seen in one patient of Group B only (Table 4). No bradycardia was noted in either of the group.

Table 3
Total no. of doses required in 24 hours

Number of doses	Group-B(40)	Group-M(40)	P-value
3 doses	40	27	0.00008
4 doses	24	00	< 0.0001

Table 4
Side effects

	Group-B	Group-M	P-value
Pruritus	0	15	< 0.0001
Somnolence	30	5	< 0.0001
Nausea	1	3	0.305
Vomitting	1	2	0.556
Respiratory depression	0	3	0.077
Dizziness	1	0	0.314
Warm sensation	1	0	0.314
Blurred vision	1	0	0.314
Hypotention	0	2	0.152

Discussion

Epidural morphine has been used since long but it has many side effects as it is a μ receptor agonist. Butorphanol is a μ receptor agonist/antagonist & κ agonist so it produces analgesia with fewer side effects except somnolence. In our study, there was no statistical difference in hemodynamic parameters like mean values of pulse, systolic, diastolic and mean arterial pressure during study period. Morphine is hydrophilic & has a low lipid partition co-efficient, hence crosses blood brain barrier with difficulty. So, it has got slow onset and prolonged duration of action. As Butorphanol is lipophilic, it has faster onset, faster peak of analgesia and short duration of action. The lowest VAS score following the first dose in group B was observed at 2 to 4 hours while at 6 to 8 hours in group M. The mean duration of analgesia was gradually prolonged on repeated dosing with butorphanol while it remained almost similar with morphine which could be due to lipophilicity of butorphanol and hydrophilic nature of morphine.

Side effects like pruritus was observed only in 37.5% cases in morphine group in our study because it is pure μ receptor agonist. Bromage et al[9] found itching 3 hours after administration of epidural morphine. Somnolence is the main side effect observed in 75% patients of butorphanol group which is κ receptor mediated & 12.5 % in morphine group. Abdoud et al.[5] found somnolence in 67% patients with 4 mg epidural butorphanol & in 21 % patients with 5 mg epidural morphine and respiratory depression (≤10/minute) was observed in 7.5 % cases of group M. Morphine being a hydrophilic agent, spreads rostrally leading to delayed respiratory depression while butorphanol is lipophilic having minimum respiratory depression. Butorphanol has a ceiling effect for respiratory depression. Increasing the dose of butorphanol causes increase in duration of effect, not the degree of respiratory depression. In our study, only in morphine group, two patients had a fall in respiratory rate to 10/minute at 4 hours and one patient had at 6 hours but that time SpO_2 was maintained. Nausea (7.5%) & vomiting (5%) were observed more in morphine group than butorphanol (2.5 %). This could be due to modulation of the afferent input at the area postrema or at the nucleus of tractus solitarius which might be affected by morphine.

Palacios[3] found duration of analgesia > 24 hours with 5mg morphine and 4 hours with 4mg butorphanol. The VAS score was constantly lower in group B than group M while number of doses required during 24 hours are more with butorphanol than with morphine suggesting short duration of action of butorphanol. He also could not found any statistical difference in hemodynamic parameters. He found pruritus in 43% with morphine & 1.4 % with butorphanol group.

Ackerman et al[4] reported more prolonged duration of analgesia with morphine (5mg) and shorter duration with butorphanol (1mg) than ours which might be due to dose variation. They found pruritus in 60% patients of morphine & 6.66% of butorphanol (1mg).

Abboud et al[5] found analgesia of approximately 8 hours with 4 mg epidural butorphanol and 21 hours with 5 mg morphine. Mok et al[6] also found faster onset of action and peak effect due to higher dose of butorphanol (4mg) and morphine (5mg) while duration of action was almost similar to ours (324minutes) in B group but prolonged in group M (912minutes). Martin et al[7] studied with different doses of epidural morphine and concluded 2.0 mg morphine as optimum dose because higher doses were more effective but with more side effects in the form of nausea &vomiting. Rawal et al[8] found 10.7 hours duration of analgesia with 2mg and 4mg of epidural morphine but 4mg had systemic responses so more than 2 mg should be avoided in elderly and fragile patients. Bromage[9] found maximum itching after 3 hours of epidural morphine Binsted[10] found pruritus with 5 mg morphine without any respiratory depression. Fuller[11] found pruritus in 58 % of patients.

The limitation in this study is to administer more frequent number of doses of butorphanol as compared to morphine group.

Conclusion

Epidural butorphanol is safe and effective in providing post-operative pain relief having faster onset and shorter duration of action as compared to morphine. Butorphanol is associated with only minor side effects like sedation where the patient is arousable at any time which may be advantageous to the patient in early postoperative period.

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