Original Article

Comparitive study of Buprenophine and Fentanyl for Postoperative Pain Relief after Thoracotomy by Continuous Thoracic Epidural Infusion

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Abstract Lateral thoracotomy results in severe pain and deleterious changes in pulmonary physiology. Intrathecal and epidural administration of opioid drugs have been extensively investigated since the discovery of spinal opiate receptors and shown to produce acceptable analgesia after thoracotomy. The present study was designed to compare the efficacy of different doses of buprenorphine and fentanyl for postoperative pain management after thoracotomy by continuous thoracic epidural infusion in 60 patients of either sex. Patients were divided into two groups of 30 each and subdivided into two subgroups of 15 each. Group I received bolus epidural buprenorphine 0.1 mg followed by infusion of buprenorphine 0.03µg/kg/hr(subgroup IA)and 0.36µg/kg/hr(subgroup IB). Group II received bolus epidural fentanyl 50 µg followed by infusion of fentanyl0.40µg/kg/hr (subgroup IIA) and 0.60µg/kg/hr(subgroup IIB).Pain assessment was done by VAS score. VAS was noted at 0,0.5,1.5,2,4,8,12,24 and 36 hours postoperatively. In Group I (Buprenorphine) visual analogue score was significantly lesser while incidence of nausea and urinary retention was more in comparison of Group II (Fentanyl).

Keywords: Thoracic epidural, Buprenorphine, Thoracotomy.

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INTRODUCTION

Surgery produces local tissue damage with consequent release of analgesic substances (prostaglandins, histamine, serotonin, bradykinin, 5- hydroxytryptamine, substance P) and generation of noxious stimuli that are transduced by nociceptors and transmitted by A delta and C nerve fibers to the neuraxis. Further transmission is determined by complex modulating influences in the spinal cord. Some impulses pass to the anterior and anterolateral horns to provoke segmental reflex responses. Others are transmitted to higher centers via the spinothalamic and spinoreticular tracts, where they produce supra segmental and cortical responses. Pain causes stimulation of sympathetic neurons and subsequent tachycardia, increased stroke volume, cardiac work, and myocardial oxygen consumption. The risk of myocardial ischaemia and infarction may be increased, as the risk of deep vein thrombosis when fear of aggravating pain results in reduced physical activity, venous stasis, and platelet aggregation[1]. Blockade of the cardiac sympathetic innervations (T1-T5) should have a myocardial protective effect and reduce cardiac morbidity. Clinical consequences of the "Stress response" also include myocardial ischemia, protein catabolism, immune system suppression and impaired renal excretory function. The most definitive clinical benefits of suppression of the stress response with epidural analgesia include prevention of hyperglycemia, and prevention of the protein catabolic tissue breakdown state, which may have implications with respect to wound healing and risk of infection. Preservation of baseline immune function may be an important benefit of epidural analgesia. Surgery involving the upper abdomen or thorax produces a number of pulmonary changes including reduced vital

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capacity, tidal volume, residual volume, functional residual capacity (FRC) and forced 1 second expiratory volume (FEV1). The epidural route had been used much more extensively for peri-operative pain control. Improved pulmonary outcome has been observed following the use of thoracic epidural analgesia (TEA) for postoperative analgesia. Several studies have demonstrated an improvement in pulmonary function tests when epidural opioids or local anesthetics are administered after thoracotomy, upper abdominal surgery, or lower abdominal surgery[2,3]. Fentanyl is widely used for epidural analgesia. Since lipid soluble opioids like fentanyl have a short duration, continuous infusion is preferred to single dose. Fentanyl produces "segmental analgesia" and rostral spread is very little because of redistribution[4]. Epidural opioid with mixed agonist-antagonist actions (e.g. Buprenorphine) are also popular. Buprenorphine is highly lipophilic, its opiate receptor association and dissociation are slow. Buprenorphine has prolonged duration of action.

MATERIAL AND METHODS

After approval of the institutional ethical committee, informed consent was obtained from each patient. The study was performed in a randomized fashion on 60 ASA grade II and III patients of either sex, aged between 15-60 years posted for elective thoracotomy for different cardio-thoracic procedures under general anesthesia. Patients were divided into two groups of 30 each and subdivided into two subgroups of 15 each. Group I received a bolus epidural administration of buprenorphine 0.1mg diluted to 10 ml with normal saline and thereafter received continuous thoracic epidural infusion of two different dose of buprenorphine according to subgroup (subgroup IA-0.03µg/kg/hr and subgroup IB-0.036µg/kg/hr). Group II received a bolus epidural administration of fentanyl 50 µg diluted to 10 ml with normal saline and thereafter received continuous thoracic epidural infusion of two different doses of fentanyl according to subgroup(subgroup IIA-0.4µg/kg/hr and subgroup IIB-0.6µg/kg/hr). For Group I infusion, buprenorphine was diluted with normal saline to make a concentration of 10µg/ml. For group II infusion, fentanyl was diluted with normal saline to make a concentration of 10µg/ml. After thorough preanaesthetic checkup,relevant investigations were done. The patients were familiarized with the visual analogue scale (VAS) for pain. A day before surgery, 18G epidural catheter was placed under local anesthesia at T7-T8 or T8-T9 levels, utilizing loss of resistance technique with Touhy needle of 18G.

Anaesthetic technique: All patients were pre-medicated with ing. glycopyrolate(0.2mg) and midazolam 0.03mg/kg intravenously 15 minutes before induction. General anaesthesia was induced with thiopentone sodium 4-6 mg/kg and endotracheal intubation accomplished with succinylcholine 1.5mg/kg. Anaesthesia was maintained with nitrous oxide, oxygen, halothane and vecuronium bromide. Muscle relaxation was maintained with vecuronium. Intra-operative analgesia was achieved with a bolus epidural administration of buprenorphine 0.1mg diluted to 10ml with saline in group I and a bolus epidural administration of fentanyl 50 µg diluted to 10 ml with saline in group II. Intraoperative monitoring consisted continuous electrocardiogram, heart rate, pulse oximetry and invasive blood pressure measurements.

No repeat bolus of buprenorphine was given before or after extubation. An infusion of buprenorphine according to sub groups started. Considering short duration of action of fentanyl repeat bolus dose of fentanyl 50 µg diluted to 10 ml with NS was given in fentanyl group and followed by infusion of fentanyl according to subgroup.

Fentanyl 25µg diluted to 5ml with normal saline as a rescue analgesic was administered if VAS > 3 through epidural catheter in the postoperative period in both group I and group II.

Pain was estimated by visual analogue score(VAS) on 0-10 scale.

A sedation scale (Pasero and McCaffery)[5] that can be used to monitor patients receiving opioids is:

S = Sleep, easy to arouse

1 = Awake and alert

2 = Slightly drowsy, easily aroused

3 = Frequently drowsy, arousable, drifts off to sleep during conversation

4 = Somnolent, minimal or no response to physical stimulation

Sedation scale >2 was noted as side effect.

VAS, pulse, blood pressure, respiratory rate were assessed at - 0, 0.5, 1, 1.5, 2, 4, 8, 12, 24 and 36 hours postoperatively. Adverse effects, if any noted. Total dose of fentanyl and buprenorphine noted.

RESULTS

Table 1: Demographic Characteristics

S.No.		Group I_A	Group I_B	Group II_A	Group II_B
1.	No. of patients	15	15	15	15
2.	Sex	9:6	8:7	7:8	7:8
3.	Age (Years)	32.20 ± 12.27	29.40 ± 9.92	30.40 ± 10.78	29.06 ± 10.76
4.	Weight (Kg)	50.1 ± 5.68	47.53 ± 5.44	47.33 ± 6.91	46.53 ± 5.6
5.	Height (cm)	157 ± 8.262	156.67 ± 9.26	154.53 ± 7.83	152.6 ± 6.88
6.	Duration of surgery (mins.)	115 ± 28.19	114.33 ± 33.43	116.0 ± 29.33	103 ± 21.61
7.	Duration of Anesthesia (min)	127 ± 30.16	126.00 ± 34.60	131.3 ± 31.48	117.3 ± 23.13

Table 2: Visual Analogue Score

Group	0 min	30 min	1 hr	1.5 hr	2 hr	4 hr	8 hr	12 hr	24 hr	36 hr
I_A	2.00±1.69	1.40±1.12**	1.13±0.99**	0.80±0.86**	0.80±0.94**	0.80±0.94**	2.13±1.68	1.73±1.33	0.73±1.10**	0.47±0.74**
I_B	2.27±2.02	1.47±1.25**	1.07±1.10**	0.53±0.83**	0.47±0.83**	0.87±1.68*	1.27±1.49**	1.07±1.44*	0.60±1.12**	0.27±0.59**
II_A	3.67±1.05	2.47±0.52**	1.93±0.26**	1.73±0.46**	1.73±0.59**	2.20±1.01**	2.33±0.82**	1.93±0.80**	2.33±1.05**	1.93±0.46**
II_B	3.60±1.40	2.20±0.56**	1.73±0.70**	1.60±0.74**	1.60±0.74**	2.07±1.49*	2.07±1.10*	1.33±0.90**	1.53±1.36**	1.13±0.92**

*P<0.05(Significant);**P<0.01 (Highly Significant) from Baseline

Table 3: Intergroup Analysis of VAS (Supine)

Group	0 min	30 min	1 hr	1.5 hr	2 hr	4 hr	8 hr	12 hr	24 hr	36 hr
I_A –I_B	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
I_A-II_A	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	NS	NS	<0.001	<0.001
I_A-I_B	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	NS	<0.05	<0.001	<0.001
I_B-II_A	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
I_B-II_B	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
II_A-II_B	NS	<0.001	<0.001	NS	NS	NS	NS	<0.001	<0.001	<0.001

NS-Not Significant

Table 4: Rescue Analgesic

Group	No. of patients									
	0 min	30 min	1 hr	1.5 hr	1 hr	4 hr	8 hr	12 hr	24 hr	36 hr
I_A (n=15)	4 (26.7%)	0	0	0	0	0	4 (26.7%)	3 (20.0%)	0	0
I_B (n=15)	5 (33.3%)	0	0	0	0	2 (13.3%)	1 (6.7%)	2 (13.3%)	1 (6.7%)	0
II_A n=15)	6 (40.0%)	0	0	0	0	2 (13.3%)	1 (6.7%)	1 (6.7%)	1 (6.7%)	0
II_B (n=15)	5 (33.3%)	0	0	0	0	3 (20.0%)	1 (6.7%)	0	1 (6.7%)	0

Table 5: Incidence of Side-Effects

Group	I_A	I_B	II_A	II_B
Resp. Depression	0	0	0	0
Nausea	3 (20.0%)	4 (26.7%)	2 (13.3%)	2 (13.3%)
Urinary Retention	6 (40.0%)	6 (40.0%)	1 (6.7%)	1 (6.7%)
Sedation	0	0	0	0
Pruritus	0	0	1 (6.7%)	0

There was no statistically significant difference in demographic variables among the four subgroups (Table-1). There was a statistical significant decrease in VAS in all subgroups ($p<0.05$) but the mean VAS increased to 2.13±1.68 and 1.73±1.33 at 8 and 12 hours respectively in subgroup IA.(Table-2).The mean VAS in buprenorphine group (IA, IB) showed statistical significant difference ($p<0.001$) from fentanyl group (IIA, IIB). No statistical significant change in mean VAS between buprenorphine subgroups IA and IB was seen. No statistical significant change in mean VAS between fentanyl subgroups IIA and IIB at 0, 1.5, 2, 4 and 8 hours but showed statistical significant change at 0.5, 1, 12, 24 and 36 hours were seen (Tabe-3). Table 4 shows time for rescue analgesic requirement in postoperative 36 hours in all subgroups. The percentage of patients who needed rescue analgesic at 0 hour were 26.7%, 33.3%, 40% and 33.3% respectively in subgroups IA, IB, IIA and IIB. The incidence of nausea was less in fentanyl group (IA and IB 13.3%) in comparison to buprenorphine group (IIA 20% and IIB 26.7%). The incidence of urinary retention was less in fentanyl group (IA and IB 6.7%) in comparison to

buprenorphine group (IIA and IIB 40%). The pruritus was associated only with fentanyl sub group IIA (6.7%)[Table-5].

DISCUSSION

Lateral thoracotomy results in severe pain and deleterious changes in pulmonary physiology. Intrathecal and epidural administration of opioid drugs have been extensively investigated since the discovery of spinal opiate receptors and shown to produce acceptable analgesia after thoracotomy. Epidural local anesthetics can also produce selective analgesia but after thoracic surgery there is a considerable risk of hypotension[6]. While a combination of local anesthetic and opioid improves the quality of pain relief but the problem of cardiovascular instability and profound respiratory depression still remains[7-9]. Although the side effects of opioids may still be a problem, the most dangerous of which is delayed respiratory depression. Other methods of postoperative analgesia following thoracotomy include intrapleural, intravenous and cryoanalgesia. Advantages of epidural over intravenous analgesia regarding pain relief include improvement in postoperative pulmonary complications, endocrine and metabolic response. Both thoracic and lumbar epidural infusion have been reported to provide good pain relief after thoracic operations but uncertainty remains about the best site and dose. Chamberlain and associates[10] reported that thoracic epidural fentanyl infusions provided better pain scores at smaller doses than lumbar epidural fentanyl infusion in a group of 20 patients. We used the fentanyl 10 µg/ml, which has been shown by Welchew[11] to be the optimal concentration for fentanyl administrated at the T7-T8 interspace for pain relief following upper abdominal surgery. We also used the buprenorphine at a concentration of 10 µg/ml. We compare the two different doses of fentanyl and two different doses of buprenorphine as a continuous thoracic epidural infusion. Hirabayashi *et al*[12] examined the analgesic efficacy in patients who underwent thoracotomy and infused buprenorphine 15 µg/hr for 48 hours. VAS was22 ± 2 mm (0-100 scale) at rest on the postoperative day 1 and 16 ± 2 mm on postoperative day 2. These results are comparable with subgroup 1A(buprenorphine infusion 0.30µg/kg/hr) of our study. In subgroup IA mean VAS at zero hour was 2.00 ± 1.69, thereafter decreasing trend in VAS upto 4 hours and at 24 and 36 hours. The mean VAS at 8 hour and 12 hour was 2.13 ± 1.68 and 1.73 ± 1.33. Hirabayashi *et al*[12] also compared postoperative analgesia after two buprenorphine infusoion regimen in thoracotomy. All patients received buprenorphine 0.1 mg in 8 ml of 0.25% bupivacaine.. Following this epidural bolus, buprenorphine 15 µg in 1 ml of 0.25% bupivacaine (group E) or buprenorphine 18 µg in 1 ml of 0.25% bupivacaine (group F) with a rate of 1 ml/hour for 48 hours. The percentage of patients who did not require additional narcotics for the first 24 hours postoperatively in group E and F, were 60% and 70% respectively. In our study, the percentage of patients who did not require additional narcotics were 60% (Subgroup IA, Continuous epidural infusion of buprenorphine at 0..30 µg/kg/hour) and 66.7% (Subgroup IB, continuous infusion of buprenorphine at 0.36 µg/kg/hour) which is comparable with above study. Swaroop *et al*[13] evaluated thoracic epidural fentanyl for post-thoracotomy pain. The mean infusion of fentanyl was 0.44 ± 0.08 µg/kg/hr.. The median VAS was 7.0 at zero hour and 3,3,2,2,1,1 at 2,4,6,8,16 and 24 hour respectively and78% of patients required no additional analgesia. Pain score is comparable to subgroup 11A(fentanyl infusion 0.4µg/kg/hr)of our study at all time intervals except at zero hour. VAS at zero hour in our study was 3.67 ± 1.05 because we gave 50 µg of fentanyl just before extubation. 60% of patient required no addition narcotic in our study. Kaetsu *et al*[14] compared the efficacy of epidural administration of fentanyl and that of buprenorphine for postoperative pain relief. In fentanyl group (F), patients receiving 0.1 mg with 9 ml NS, followed by constant rate of infusion of 25 µg/hr for 24 hours. In buprenorphine (B) group, patients received buprenorphine 0.2 mg with saline 9 ml epidurally. 76.7% in F group and 52.9% in B group obtained satisfactory analgesia. In our study, patients who did not need additional analgesic were 60%, 67.7%, 60% and 60% in Subgroups IA, IB, IIA and IIB respectively. The most common adverse effects of epidural opioids are nausea and vomiting, pruritus, urinary retention, sedation and respiratory depression. Patients receiving epidural analgesia usually experience a lower incidence and less severe opioid induced adverse effects than patients receiving opioids systemically. Gough *et al*[15] examined the side-effects of fentanyl infusion at a rate of 0.6 µg/kg/hr after thoracotomy. The incidence of itching, urinary retention and nausea were 44%, 6%, and 22% respectivevely.In our study, incidence of nausea and urinary retention were less in fentanyl group as compared to buprenorphine group. Pruritis (6.7%) was observed in fentanyl group only. Fentanyl has a segmental effect when administered spinally[4]. So thoracic epidural improves the quality of analgesia.In addition this has been shown to reduce the amount of fentanyl infused and its side effects. Kaetsu[14] compared the efficacy of epidural fentanyl (25 µg/hr) and buprenorphine (17 µg/hr) and percentage of patients having respiratory depressions were 6.8% in fentanyl group and 28.2% in buprenorphine group. No patients had respiratory depression in our study.Fentanyl,a liphophilic drug,reduces the risk of

respiratory depression,because its rapid absorption into the spinal cord and nearby blood vessels decreases the concenterations in cerebrospinal fluid(CSF) and reduces the risk from cephalad CSF spread[16]. We conclude that continuous thoracic epidural infusion of buprenorphine and fentanyl both are effective in post thoracotomy pain relief. There was significant lesser VAS score of buprenorphine group than to fentanyl group probably because of long duration of buprenorphine. There is no significant difference in VAS score of two different doses of buprenorphine as continuous infusion. There is significantly lesser VAS score in fentanyl subgroup IIB because of higher infusion rate of fentanyl i.e. 0.6 µg/kg/hr in comparison to 0.4 µg/kg/hr in subgroup IIA. The incidence of side-effects are less with fentanyl.

REFERENCES

1. Modig J: Thrombo-embolism and blood loss: Continuous epidural versus general anesthesia with controlled ventilation. Reg. Anesth. 7: 584, 1982.
2. Bromage PR, Camporesi E, Chestnut D: Epidural narcotics for postoperative analgesia. Anesth. Analg. 59: 473-480, 1980.
3. Cuschieri RJ, Morran CG, Howie JC, *et al*: Postoperative pain and pulmonary complications: Comparison of three analgesic regimens. Br J. Surg. 72: 495-498, 1987.
4. Welchew EA, Breen DP:Patient controlled on demand epidural fentanyl:A comparison of patient controlled on demand fentanyl delivered epidurally or intravenously.Anaesthesia46:138-441,1991.
5. Pasero C, McCaffery M.. Preventing opioid induced respiratory depression. Am J of Nursing 1994: 94(4), 25-31.
6. Conacher ID, Paes ML, Jacobson L, Phillips PD, Heaviside DW. Epidural analgesia following thoracic Surgery. Anaesthesia 1983: 38, 546-551.
7. Cicala RS, Voeller GR, Foy T, Fabian TC, Kudsk K, Mangiante EC. Epidural analgesia in thoracic trauma: effect of lumbar epidural morphine and thoracic bupivacaine on pulmonary function. Crit Care Med 1990: 18, 229-231.
8. Brockway MS, Noble DW, Sharwood-Smith GH, *et al*. Profound respiratory depression after extradural fentanyl. Br J Anaesth 1990: 64, 243-245.
9. Weightman WM. Respiratory arrest during epidural infusion of bupivacaine and fentanyl. Anaesthesia 1991: 19, 282-284.
10. Chamberlain DP, Bodily MN, Olssen GL, Ramsev DH. Comparison of lumbar vs thoracic epidural fentanyl for post thoracotomy analgesia using patient controlled dosage. Reg Anesth 1989: 14, 26.
11. Welchew E.A.: The optimum concentration for epidural fentanyl. Anaesthesia 38: 1037-1041, 1983.
12. Hirabayashi Y, Mitsuhata H: Postoperative analgesia service by continuous epidural infusion with buprenorphine. Masui 44(4):493-8, 1995 April.
13. Swaroop NS, Batra YK, *et al*: A comparative evaluation of thoracic and lumbar epidural fentanyl for post thoracotomy pain. Annals of Cardiac Anaesth 5:53-58, 2002
14. Kaetsu H, Takeshi M, Chigusa S: Analgesic effects of epidurally administered fentanyl for postoperative pain relief- comparison with buprenorphine. Masui 41 (12): 1870-4, 1992 Dec.
15. Gough J.D., Williams A.B.: The control of postthoracotomy pain. A comparative evaluation of thoracic epidural fentanyl infusions and cryo-analgesia. Anaesthesia 43:780-783, 1988.
16. Cousins MJ,Mather LE:Intrathecal and epidural administration of opioids.Anesthesiology.61:276-310, 1984.

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