ORIGINAL ARTICLE

Comparative study of thoracic epidural fentanyl with sufentanil for postoperative pain relief in thoracic surgery

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ABSTRACT

Objectives: Both fentanyl and sufentanil have been used, either alone or with local anesthetics, for thoracic epidural analgesia. This study was undertaken to compare quality and safety of thoracic epidural fentanyl and thoracic epidural sufentanil for providing postoperative analgesia for 48 hours after thoracic surgery.

Methodology: In a prospective randomized, controlled study, 70 patients age group between 20-60 years, of either gender, scheduled for routine thoracic surgery were randomly distributed into two groups of 35 patients each. Postoperatively, fentanyl 50 μg in Group-F and sufentanil 20 μg in Group-S, diluted in 10 ml of normal saline was injected in the thoracic epidural space (between T6 - T8) through the catheter and then repeated 6 hourly. Pain intensity score, onset of analgesia, number of top-ups required and overall patient satisfaction score were recorded.

Results: Mean onset of analgesia was 10.31 ± 1.5 min with sufentanil group as against 14.23 ± 1.2 min with fentanyl group. Pain Intensity (PPI) score ≤ 1 was observed in 78.21% observations belonging to sufentanil group and in 50 % observations belonging to fentanyl group. Twenty five patients (71.4%) from sufentanil group and 30 patients (85.7%) from fentanyl group required rescue analgesia. The patient's feedback on pain relief was graded as very good or good by 78.5% of the patients in Group-S and 69% patients in Group-F.

Conclusion: Though both drugs are equally safe, **s**ufentanil is faster acting, more potent and efficient analgesic than fentanyl when used for postoperative pain relief in thoracic surgeries via thoracic epidural approach.

Key words: Thoracic epidural; Postoperative analgesia; Fentanyl; Sufentanil

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INTRODUCTION

Postoperative pain and hypoxemia are common complications following thoracic and upper abdominal surgery. Inadequately treated pain results in an increased incidence of pulmonary complications and morbidity.[1] An ideal analgesic regimen should provide pain relief with minimal side effects and should allow early return of normal function. Regional analgesia provides superior quality of pain relief after thoracic surgery and avoids many of the side effects of conventional narcotic analgesics.[2] Thoracic epidural blockade using lipophilic opioids has advantages of better postoperative pain relief, minimal central nervous system depression, minimal somatic and visceral pain and abolition of the reflex muscle spasm.[3] Dawkins et al[4] found thoracic epidural superior to lumbar approach as dose of analgesic was decreased and duration was prolonged.

Both fentanyl and sufentanil have been used either alone or in combination with bupivacaine or ropivacaine for thoracic epidural analgesia.[5,6] There are few studies that directly compare these widely used drugs for postoperative pain relief via thoracic epidural approach in thoracic surgery. This study was undertaken to compare the clinical efficacy and safety of thoracic epidural using fentanyl or sufentanil to provide postoperative analgesia for a 48 hour period after thoracic surgery. The primary outcome measure compared was quality of analgesia expressed as Present Pain Intensity (PPI) score.[7]

METHODOLOGY

A prospective double-blind, randomized, study design with two parallel groups was used. After prior approval from Institutional Ethics Committee, this study was conducted at Gandhi Medical College and associated Hamidia Hospital, Bhopal during a period of 2 years on 70 patients, aged group between 20-60 years, of either gender, scheduled for routine thoracic surgery. Informed written consent was obtained from all patients. Exclusion criteria were severe systemic disorders including diabetes mellitus, hypertension, heart disease; addiction to narcotic drugs; chronic alcoholism; psychiatric disorders; allergy to study drugs and known contraindications to epidural anaesthesia. Patients were randomly distributed into two groups of 35 patients each and randomization was concealed.

Group-F (n=35): In this group, each patient received fentanyl 50 μg diluted in 10 ml normal saline via epidural catheter. This was considered as control group.

Group-S (n=35): In this group, each patient was given sufentanil 20 μg diluted in 10 ml normal saline via epidural catheter. This was considered as study group.

Method of Randomization was Blocked randomization. Thirty five blocks of two each with treatment allocation of 1:1 for Group-F and Group-S were created with the help of computer software. Coded envelopes (total 35) were used and each envelope was used for two patients leading to random assignment of one subject to one group. For sample size calculation a pilot study was done on 20 patients (each group containing 10 patients). Present Pain Intensity (PPI) score was recorded at 6 hourly intervals for 48 hours. PPI score ≤ 1 was observed in 34(42.5%) observations in Group-F as against 69(86.25%) observations from Group-S, out of total 80 observations made in each group. Sample size was calculated to detect effect size of 43.75% between two groups accepting alpha error 0.05 and β error 0.90 was 28.

In the operating room pre-operative parameters (pulse rate, blood pressure, respiratory rate and oxygen saturation) were noted. Patients were placed in sitting position and under aseptic precautions; a 17G epidural needle was inserted through the paramedian approach at a suitable space between T6-T8 depending on the level of surgical incision. Epidural space was identified by 'loss of resistance' technique and a disposable epidural catheter was inserted cephaloid 2-3 cm into the epidural space and secured with an adhesive. Its position was confirmed by a test dose of 2 ml lignocaine 2% with adrenaline and a possibility of subarachnoid or intravascular injection was excluded. After a negative test dose, patients were placed in the supine position and general anesthesia was induced with thiopentone (4-6 mg/kg) followed by succynyl choline (1.5 mg/kg) injected intravenously. Orotracheal intubation was done with a cuffed endotracheal tube of appropriate size and anesthesia was maintained with oxygen and nitrous oxide supplemented with halothane. Intraoperative analgesia was maintained with intravenous fentanyl 100 micrograms at the start and then if required. Muscle relaxation was provided with vecuronium. At the end of surgical procedure, patient was extubated after reversal of neuromuscular block with glycopyrrolate. 0.01 mg/kg and neostigmine 0.05 mg/kg. Physiological parameters e.g. pulse rate, blood pressure, respiratory rate and oxygen saturation, were recorded every 5 min during intraoperative period and before shifting to postoperative ward.

In the postoperative ward a bolus of either fentanyl 50 μg or sufentanil 20 μg diluted in 10 ml of saline was injected in the thoracic epidural space through the catheter when the patient complained of pain .The bolus was repeated 6 hourly. Both the patient and anesthesiologist were blinded to the study solutions. Syringes were prepared and coded just before injection by a third person. The observer was also blinded. Analgesia with epidural catheter was provided for two days postoperatively, then the catheter was removed and analgesia was maintained with conventional methods. Pulse rate, blood pressure and respiratory rate were recorded along with present pain intensity (PPI) score every 6 hours. The degree of pain was assessed by using the Present Pain Intensity (PPI) scale; 0=no pain; 1=mild pain; 2=discomfort; 3=distress; 4=horrible pain and 5=excruciating pain. Highest PPI score during the period of six hours between two top-ups was noted. Thus, there were 8 observations of PPI for each patient and total number of observations was 280 for each group. Percentage of different PPI scores out of total number of observations was used for comparison of two groups.

During this interval if any patient had PPI >3 ; 'rescue top-ups' of fentanyl 25 μg or sufentanil 10 μg were given in Group-F and Group-S respectively and number of such 'rescue analgesia top up' doses were noted. Catheter was removed after 48 hours.

Any side effect e.g. nausea, vomiting, backache, sedation or drowsiness, hypotension, sign of excessive block or numbness / weakness in limbs was noted.

On 5th postoperative day each patient was interviewed regarding feedback on overall pain relief during the first 2 postoperative days as very good, good, fair or poor. This scale was used to compare both groups as secondary outcome measure regarding quality of analgesia.

Statistical analysis: Statistical analysis was done using Stata 11 software. Demographic characteristics, hemodynamic parameters, onset of analgesia, quality of analgesia, level of sedation and side effects were compared between two groups and data was analyzed statistically. For continuous variables descriptive statistics (mean and

standard deviations) were computed. Comparison of means in Group-S and Group-F was done using unpaired t-test. For categorical data chi-square test was applied. P < 0.05 was considered significant.

RESULTS

Both groups were comparable in respect of demographic characteristics as shown in Table I. Groups were also comparable in type and duration of surgery (Table 2). Various surgical procedures performed included open window, decortications, pneumonectomy, hydatid cyst removal, excision of mediastinal mass, lobectomy and chest drain insertion. Table 3 compares the quality of analgesia among the groups. Sufentanil group was found to be faster in action as compared to fentanyl group. Mean onset of analgesia was 10.31 ± 1.5 min with sufentanil group as against 14.23 ± 1.2 with fentanyl group (p value < 0.05). Quality of analgesia was also better with sufentanil reflected by the fact that Present Pain Intensity (PPI) score was zero (means no pain at all) in only 11 observations out of 280 (3.93%) belonging to fentanyl group as against 49(17.5%) observations belonging to sufentanil group. PPI Score 1 (meaning slight pain) was observed in 129(46.07%) observations belonging to fentanyl group as against in 219(78.21%) observations belonging to sufentanil group. PPI score 3 and 4 was found in 105 and 35 observations respectively belonging to fentanyl group as against in 49 and 12 observations respectively belonging to sufentanil group.

Twenty five patients out of 35 from sufentanil group required rescue analgesia as against 30 patients from fentanyl group. Out of them 8 patients needed 3 top-ups, 15 patients needed 2 top-ups and 2 needed one top-up. Out of 30 patients from fentanyl group, 2 patients needed 4 top-ups, 6 patients needed 3 top-ups 17 needed 2 top-ups and 5 needed one top-up. This difference was not significant.

Overall feedback was graded as very good or good by 78.5% patients in Group-S and 69% patients in Group-F. Only one patient from Group-S and 4 from Group-F graded analgesia as poor. Mild hypotension was seen in 5 patients from Group-S and 8 patients in Group-F, which was easily corrected with crystalloid infusions. Two patients

Table 1: Patient characteristics

Characteristics		Group-F (n = 35) Mean ± SD	Group-S (n = 35) Mean ± SD	P value
Age (in years)		35.86 ± 13.17	33.57 ± 10.27	> 0.05
Height (in cm)		159.14 ± 6.86	161.29 ± 5.26	> 0.05
Weight (in Kgs)		62.57 ± 5.91	63.83 ± 6.82	> 0.05
Gender	Male n(%)	27 (77.14)	29 (82.86)	> 0.05
	Female n(%)	8 (22.86)	6 (17.14)	

Group-F = Epidural fentanyl 50 μg in 10 ml normal saline

Group-S = Epidural sufentanil 20 μg in 10 ml normal saline

Table 2: Types of surgical procedures performed

Type of Surgery	Group-F (n = 35)	Group-S (n = 35)	P value
Open window formation	14	10	> 0.05
Decortication	11	17	
Pneumonectomy	3	3	
Chest drain insertion	5	2	
Hydatid cyst removal	1	1	
Excision of Mediastinal mass	1	1	
Lobectomy	0	1	
Total	**35**	**35**	

Table 3: Quality of analgesia

Quality of analgesia		Group-F (n = 35)	Group-S (n = 35)	p Value
Onset of analgesia in min (Mean ± SD)		14.23 ± 1.2	10.31 ± 1.5	< 0.05
Rescue analgesia (Number of top-ups required)*	0	10	5	> 0.05
	1	5	2	
	2	17	15	
	3	6	8	
	4	2	0	
	Total	35	35	
Overall satisfaction regarding analgesia*	Very Good	1	5	> 0.05
	Good	14	19	
	Fair	16	10	
	Poor	4	1	
	Total	35	35	
PPI Score ≤ 1 [n(%)]		140 (50)	219 (78.21)	< 0.05
PPI Score 0 [n(%)]		11 (3.93)	49(17.5)	< 0.05
Total Number of observations		280	280	

* Number of patients

Table 4: Incidence of side effects. Data given as n(%)

Side effect	Group-F (n = 35)	Group-S (n = 35)
Hypotension	8(22.86)	5(14.29)
Pruritus	5(14.29)	411.43)
Nausea and vomiting	5(14.29)	3(8.57)
Respiratory depression	3(8.57)	2(5.71)
Sedation	0	2(5.71)
Gastrointestinal discomfort	1(2.86%)	0
Total	22(62.86%)	16(45.71)

from Group-S and 3 patients from Group-F had transient fall in oxygen saturation that responded to an increase in FiO_2. No significant difference was observed between the two groups. Table 4 shows the incidence of side effects in both the groups.

DISCUSSION

Sufentanil, an analogue of fentanyl, is an opioid analgesic which is highly selective for the μ-receptor site. It is a very potent analgesic; in animals it is 625 to 4,000 times more potent than morphine and 5 to 15 times more potent than fentanyl. It has shorter distribution and elimination half-lives and so produces a shorter duration of analgesia. Sufentanil has a better cardiovascular safety margin relative to morphine or fentanyl. For outpatient surgery, intravenous sufentanil produces equivalent anesthesia to isoflurane or fentanyl. Recovery tends to be more rapid after sufentanil and the requirement for postoperative analgesia is less.[8] Epidural sufentanil produces a more rapid onset and better initial quality of analgesia than other opioids like morphine, buprenorphine, fentanyl or hydromorphine when administered postoperatively, but the duration of analgesia is shorter.[8]

Blomberg et al demonstrated a less frequent incidence of difficulty in localization of epidural space, less incidence of paraesthesia & less resistance to catheter introduction, and anesthetic solution injection with paramedian approach. Chances of intravascular catheter placements are also less with paramedian approach.[9] So in our study we used paramedian approach to locazte epidural space with the patient in sitting position.

Fentanyl and sufentanil being lipophilic have less cephaloid spread necessitating administration close to the segmental level where analgesia is required. Keeping this in mind we placed the catheter at T6-T8 level, close to the incisional dermatome.

We used doses of fentanyl and sufentanil almost similar to Geller J Chrubasic et al[10] who used 15 μg bolus & 5 μg/hr infusion of sufentanil and 50 μg bolus & 10 μg/hr infusion of fentanyl in their study.

Sufentanil proved to be faster acting as compared to fentanyl (onset of analgesia 10.31 ± 1.5 vs. 14.23 ± 1.2 min). This was comparable with studies of Ionescue et al[11] and Chaney[12] who found that CSF concentration of fentanyl peaks in 20 min and sufentanil in 6 min. Stanton-Hicks et al[13] also found a rapid onset with a score >4.3 (inverse visual analog scale (IVAS) in 5 min and 7.3 at 15 min and a

mean maximum score of 9.3 with sufentanil used for high thoracic epidural analgesia. Mean duration of analgesia was 363 ± 25 min. Verborgh C et al[14] compared postoperative pain relief after cholecystectomy with epidural sufentanil at lumbar or thoracic level and found that pain scores were lower than three in both groups after 10 min, while mean pain scores remained below one from 20 min until 2 h following injection in both groups. Satisfactory pain relief lasted for 4 h. Analgesia lasted for 450 ± 46 min with epidural sufentanil 75 micrograms in the study of Verborgh et al.[14] Rosseel et al [15] used epidural sufentanil for intra and postoperative analgesia in thoracic surgery and observed sufentanil providing good analgesia with a very fast onset and a mean duration of almost 7 h. We found better quality of analgesia with sufentanil as compared to fentanyl. For maximum number of observations, patients from sufentanil group were found to be pain free (PPI score ≤ 1 in 95.71% observations). Though the difference between two groups was significant regarding PPI, no significant difference was observed in respect of number of rescue analgesia top-ups. Only 10 patients from fentanyl group and 5 patients from sufentanil group did not require any rescue analgesic top-up. This might be due to intermittent boluses given every 6 hourly instead of a continuous drip. Duration of action being for 4-7 hours, need for rescue top–up was increased equally in both groups. This is supported by the study of Cho et al[16] who compared epidural sufentanil with fentanyl in children undergoing urological surgery and found sufentanil providing better analgesia 24 hrs after surgery. The need for rescue analgesia during 24–72 hrs was higher in the fentanyl group than in the sufentanil group (6/32 vs. 0/32, *P*=0.012). They used continuous infusion of fentanyl or sufentanil instead of intermittent boluses.

In our study, no difference was observed between groups regarding patient satisfaction. All patients were hemodynamically stable. The incidence of side effects was remarkably minimal and both groups had comparable in this regard.

CONCLUSION

In conclusion, sufentanil is faster acting, more potent and efficient analgesic than fentanyl when used for postoperative pain relief in thoracic surgery via thoracic epidural approach.

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