

POST-THORACOTOMY ANALGESIA

- Comparison Epidural Fentanyl to Intravenous Pethidine -

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Summary

Background and Methods. To evaluate the efficacy of post-thoracotomy analgesia with intermittent epidural fentanyl. 50 patients were allocated randomly into 2 groups. The first group received intermittent epidural fentanyl and the second group received intermittent intravenous analgesia using pethidine. The variables studied were: pain score; total amount of additional intravenous opioid analgesia, and ventilatory function parameters [forced vital capacity (FVC), forced expiratory volume in the first second (FEV₁) and FEV₁/FVC ratio].

Results. In the first postoperative day, pain scores were higher in the epidural group ($P = 0.034$), but there was no significant difference between mean pain scores in the second and third days ($P = 0.61$, $P = 0.15$, respectively). On all three days, significantly more additional analgesics were required in the epidural group. A difference was found between both groups in the post- to pre-operative FEV₁, FVC and FEV₁/FVC ratios, with the better preservation of the ventilatory function in the epidural group ($P = 0.001$, 0.013 , <0.0001 , respectively).

Conclusion. The analgesic effect of intermittent epidural fentanyl is

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not adequate. and postoperative pain relief has not any significant advantage over the more easily-applied intravenous analgesia. However, better preservation of ventilatory function makes epidural fentanyl a useful adjunct analgesia in reduction of post-thoracotomy pulmonary complications.

Key words. Epidural Analgesia, Thoracotomy, Fentanyl, Post-operative Pain, Respiratory Function.

Introduction

Posterolateral thoracotomies are among the most painful procedures of surgery and may cause severe postoperative chest pain and impaired respiratory performance. Impairment of respiratory function following thoracotomies may produce lots of morbidities and in fact is multifactorial in etiology; however, severe postoperative pain substantially contributes to this impairment and therefore the effectiveness of analgesia may have a major effect on post-thoracotomy pulmonary function.

In the past few years, many trials have been performed to evaluate the efficacy of various analgesic regimens¹. Systemic opioids, non-steroidal anti-inflammatory drugs (NSAID), and regional analgesia including epidural, spinal, intercostals and interpleural techniques have been shown to be effective tools in preventing and overcoming on serious and sometimes life threatening complications of uncontrolled postoperative pain. Of these different available methods of analgesia, systemic opioids and thoracic epidural analgesia are of the most common techniques used to provide postoperative analgesia following posterolateral thoracotomies¹. It is uncertain which method has better pain control and fewer adverse effects.

Systemic opioids, as the most commonly used techniques to prevent post-thoracotomy pain, themselves result in adverse effects such as aggravation of respiratory depression and induction of somnolence, nausea, and vomiting and therefore are not the ideal method of analgesia in these situations.

On the other hand, it has been proven that epidurally given analgesic

agents could provide effective and relatively rapid-onset pain relief. Since the demonstration of opioid receptors in the peripheral nervous system, numerous studies have been performed to explore the efficacy of epidural analgesia with opioids for post-thoracotomy pain¹. It has been noted that thoracic epidural analgesia has replaced less invasive methods to manage postoperative pain² and it has been reported that after major surgeries (hysterectomy, thoracotomy, and knee arthroplasty) pain relief has been superior with the continuous epidural method compared to continuous intravenous analgesia³. However, there is a relative paucity of literature directly addressing the effects of intermittent epidural analgesia with fentanyl on postoperative pain and pulmonary function values in posterolateral thoracotomies.

Our clinical practice has been to use intravenous pethidine for pain relief after thoracotomies. However, often the patients are not completely satisfied. The objective of the present prospective randomized study was to compare the efficacy of these two analgesic techniques, epidural analgesia using fentanyl and the routine intravenous analgesia with pethidine, on the postoperative pain and pulmonary function values.

Methods

The present study is a part of a larger study, in which different methods of analgesia were compared with a same control group using intravenous protocol of analgesia and some results will be published elsewhere. Between March 2002 and March 2004 fifty consecutive patients scheduled for elective posterolateral thoracotomy were entered in this prospective study. All surgeries were performed by same surgeon and at two hospitals affiliated with Tehran University of Medical Sciences (Shariati Hospital, Imam Khomeini Hospital). Patients excluded from this study included any patient who had contraindication for epidural analgesia [patients who were drug abuser, obesity (weight greater than 100 kg), and who had significant central nervous system, hepatic, or renal disease] or who refused to enter the study.

The study protocol was approved by the Committee on Ethics at the

Faculty of Medicine, University of Tehran. Also informed consent was obtained from all participating patients.

The patients were randomly assigned into the two groups of 25 patients each according to the type of anesthesia given: Group 1 (G1) patients received epidural analgesia using fentanyl (50 µg every six hours), and Group 2 (G2) patients received intravenous analgesia using pethidine (25 mg every six hours). Because of the presence of an intravenous opioid group (no epidural catheter), it was impossible to double blind the study. All of the patients abstained from caffeine-containing beverages and alcohol for at least 24 h before the study. Surgery was performed via a standard posterolateral thoracotomy; all incisions were made in the posterior fifth or sixth intercostal spaces.

Postoperative Analgesia Protocol

In G1 patients, a standard thoracic epidural catheter was inserted at T3-4 interspace prior to the end of the surgery. The catheter was inserted 5 cm past the needle tip into the epidural space with the patient in the lateral position. Then, 50 µg fentanyl was administered and in the postoperative period, the injection was repeated every six hours. If analgesia was inadequate and pain score remained greater than 3 for 30 minutes, 25 mg pethidine was given intravenously and the total amount of this additional analgesia received, was recorded.

In the G2 patients, the analgesic protocol consisted of 25 mg intravenous pethidine every six hours. As in the case of G1 patients, if analgesia was inadequate and pain score remained greater than 3 for at least 30 minutes, 25 mg of pethidine was given intravenously and was registered.

Assessment of Analgesia Effectiveness

Recorded parameters by a blinded observer were pain score measurements (which were measured on arrival in the recovery room, and then every six hours up to 72 hours) and the amount of additional opioid analgesia required over the first 72 hours of the post-operative period.

Pain was evaluated after a deep inspiration 6 hours after the previous injection (i.e. immediately before the injection of the next dose of analgesics) and was classified according to the 5-point scale of Prince Henry (Table 1).

Table 1
5-point scale of Prince Henry for postoperative pain assessment

<i>Score</i>	<i>Severity of chest pain</i>
1	No pain on coughing
2	Pain on coughing or movement but not on deep breathing
3	Pain on deep breathing but not at rest
4	Slight pain at rest
5	Severe pain at rest

Moreover, the pulmonary function parameters [forced vital capacity (FVC), forced expiratory volume in first second (FEV₁) and FEV₁/FVC] were obtained using a simple portable monitor device of spirometry and through a mouth-piece, before surgery and on the third postoperative day. We evaluate these post-intervention values of the groups as a fraction of the corresponding preoperative controls.

Statistical Analysis

The differences between the groups were analyzed with the chi-square test and Fischer bicaudal exact test, analysis of variance; student's t-test and ANOVA. The administration of additional analgesics was analyzed using the Pearson χ^2 . SPSS for Windows (Release 11.5.0) was used for statistical analysis. All reported **P** values are two-tailed and **P** < 0.05 was considered to be statistically significant.

Results

Demographic data are shown in Table 2. Mean age and weight were 41.2 (18-60) yr and 71.2 (52-96) kg in the epidural group and 39.6 (19-57) yr and 69.1 (51-93) kg in the intravenous group (not statistically significant).

Table 2
Demographic data

	Epidural Group (n = 25)	Intravenous Group (n = 25)
Sex ratio; Female: Male	14/11	13/12
Age, years (mean range \pm SD)	41.2 \pm 15.3	39.6 \pm 15.2
Bodyweight, kg (mean (range))	71.2 (52-96)	69.1 (51-93)
ASA class (number of patients)		
1	9	7
2	9	10
3	7	8

* Demographic data as shown was comparable.

The range of the procedures was relatively similar in both groups. No neurological sequelae caused by thoracic epidural catheterization were seen in the early post-operative period. There were no complications of catheter placement or bupivacaine administration. Removal of the epidural catheters was also without incident.

The respective first day, second day, and third day mean pain scores of the G1 patients were 3.58/5, 2.69/5, and 2.18/5 and for the G2 patients those were 3.0/5, 2.8/5 and 2.55/5, respectively. No significant differences between the study groups were observed with regard to pain scores in the second and third postoperative days ($P = 0.61$ and $P = 0.15$, respectively), but in the first and postoperative day, pain scores were significantly higher in the G1 group than the G2 group ($P = 0.034$). In the whole 72 postoperative hours, the mean pain score was 2.81/5 in the G1 patients and 2.78/5 in the G2 patients. No statistical significance was found ($P = 0.85$).

The decrease in pulmonary function as assessed by FVC, FEV₁ and FEV₁/FVC, was significantly less with epidural fentanyl compared with the intravenous pethidine (Fig. 1, 2 and 3). FVC_{72/0}, FEV₁_{72/0} and FEV₁/FVC_{72/0} were all significantly higher in the G1 compared with G2 ($P = 0.001$, 0.013, and <0.0001 , respectively) (Table 3).

Fig. 1
Comparison of
Postoperative/Preoperative FEV₁
between two groups

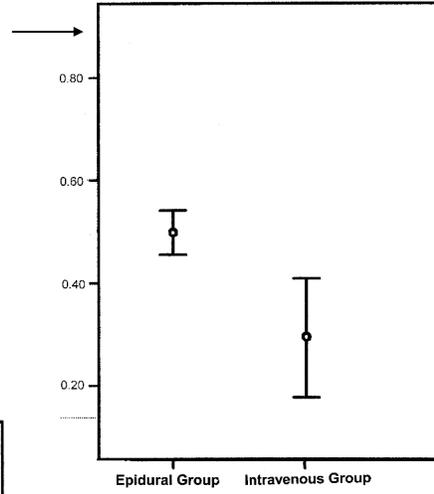
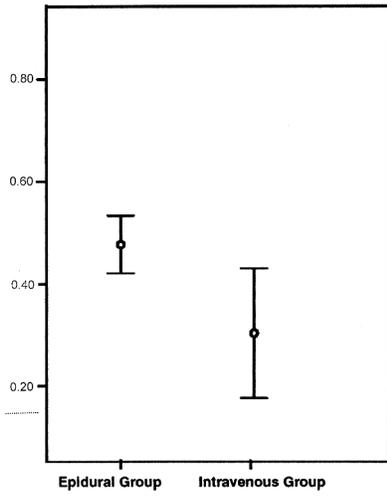


Fig. 2
Comparison of
Postoperative/Preoperative FVC
between two groups

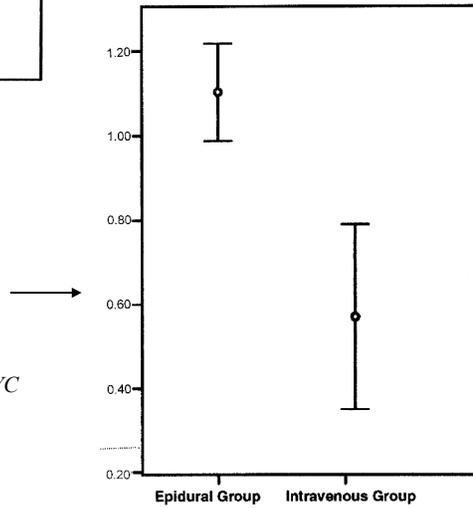


Fig. 3
Comparison of
Postoperative/Preoperative FEV₁/FVC
between two groups

Table 3
Comparison of the pre- and post-operative respiratory function parameters in the epidural analgesia (G1) and intravenous analgesia (G2) groups.

Respiratory Parameters	G1	G2	P Value
Postoperative to Preoperative FEV ₁	0.50 ± 0.10	0.29 ± 0.28	P = 0.001
Postoperative to Preoperative FVC	0.48 ± 0.14	0.30 ± 0.31	P = 0.013
Postoperative to Preoperative FEV ₁ /FVC	1.10 ± 0.28	0.57 ± 0.53	P < 0.001

** FEV₁, forced expiratory volume per 1 s; FVC, forced vital capacity; FEV₁/FVC, forced expiratory volume per 1 s/forced vital capacity.

** Data are given as mean ± SD.

The need for additional pethidine in the first, second and third days were significantly (**P** < 0.0001) higher in the G1 patients (Table 4).

Table 4
Mean additional opiate requirements

	G1	G2	P Value
First day	94 ± 48	30 ± 24	< 0.001
Second day	85 ± 46.8	22 ± 26.3	< 0.001
Third day	61 ± 47.4	6 ± 10.9	< 0.001
Total	240 ± 133.5	58 ± 48.3	< 0.001

** Data are expressed as mean ± SD in milligram.

The mean additional pethidine requirement during the whole 72 hours of the study was 240 mg in the G1 patients and 58 mg in the G2 patients. On the other hand, the patients of the intravenous group received basic and regular intravenous doses of pethidine (25 mg every six hours) as their primary analgesic method. Therefore, the total amount of the pethidine received by the patients (the total amount of basic doses plus the total amount of additional requirements) was significantly higher in the intravenous group than the epidural group (354 mg versus 240 mg respectively, **P** < 0.0001).

Discussion

More than 10 years ago Salomaki et al demonstrated that epidural fentanyl provided better analgesia than intravenous fentanyl after thoracic surgery⁴. Currently, thoracic epidural analgesia is considered to be the method of choice in the treatment of post-thoracotomy pain and no thoracotomy study has clearly shown any technique preferable to epidural analgesia. In fact different approaches can achieve the same goal, but it has been noted that postoperative epidural analgesia is a useful technique to control postoperative pain following thoracotomy because it allows reduction of postoperative respiratory and cardiovascular complications, and decreases chronic pain and morbidity⁵. Despite of all of these facts, epidural analgesia is still used by only a minority of thoracic surgeons.

On the other hand, intravenous analgesia is another widely used for postoperative pain control, and numerous studies indicate that both methods provide good analgesia after painful thoracotomies. However, because of the following reasons it is not completely determined whether one of the two modes of application is superior. First, there are conflicting data regarding the differences in pain relief and drug use between epidural and intravenous administration of opioids. Second, in many studies epidural analgesia is performed by a combination of local anesthetics and opioids. Third, reduced morbidity was observed only in some of the studies, in which epidural analgesia provided better pain relief than systemic opioid supply⁶.

According to our study results, it seems that intermittent epidural analgesia with only fentanyl, cannot provide adequate pain alleviation in the post-thoracotomy settings, and intravenous analgesia as a more practical and easily-performed method of analgesia, is superior. Both post-thoracotomy pain scores and the need for rescue medication were higher in the intermittent epidural group, which confirm the inadequacy of this method of analgesia.

Generally, there are remarkable drawbacks with the use of epidural analgesia. Epidural analgesia has to be supplemented by, or combined with, systemic analgesics in most patients. On the other hand, compared

to intravenous analgesia, epidural protocols are more invasive and more difficult to manage on general surgical wards. Even in the most experienced hands catastrophic complications are reported⁷. According to the report of Tiippana et al, technical problems occur in 24% of the epidural catheters². As it was previously noted by James et al, in 6-20% of the cases placement of an epidural catheter will be unsuccessful and in fact the procedure is extremely dependent to the expertise of the anesthesiologist⁸. Conversely, intravenous analgesia is easier to handle and may, perhaps, involve fewer problems and side effects⁹.

In fact, our results are not consistent with some of previous reports. Miguel and Hubbell concluded that post-thoracotomy pain is better relieved with epidural opioid compared to parenteral opioid¹⁰. However, the number of evaluated patients was insufficient to draw definitive conclusions. These reports reveal that controversy still remains and further comparison of the different analgesic methods in the larger series of patients is needed.

However, in our study the post-operative pulmonary function was better preserved by the application of the intermittent epidural analgesia protocol. We believe that this finding could be interpreted by the fact that intravenous opioids are a more potent depressant of central ventilatory centers than the epidurally administered narcotics.

As mentioned above, according to our results, the analgesic effect obtained with epidural fentanyl is not adequate, and regarding the postoperative pain relief, has not any significant advantage over the more easily-applied intravenous analgesia. However, better preservation of ventilatory function makes it useful in reduction of post-thoracotomy pulmonary complications. Although it was not examined in our study, but it can be concluded that with the insertion of few changes in this protocol, it could be possible to augment the advantages (e.g. less depression of respiratory function) and reduced the disadvantages. For example, it has been noted that the association of opioids and local anesthetics for spinal analgesia appears to have a synergistic effect^{3,6,11,12,13,14,15}. However, it should be noted that these results were not confirmed in other studies^{16,17,18}. Therefore, the controversy still remains and large scale

clinical studies are needed to provide more data and experience.

Conclusion

The fact that the difference in pain scores is probably not clinically significant and the fact that intravenous analgesia is more easily performed method of pain relief, show that intravenous analgesia is superior to intermittent epidural fentanyl alone. The authors do not recommend using intermittent epidural analgesia with fentanyl as the sole analgesic approach.

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Competing interests

The author(s) declare that they have no competing interests.

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