

ORIGINAL ARTICLE

COMPARISON BETWEEN EPIDURAL MORPHINE VERSUS MORPHINE + FENTANYL IN LUNG RESECTION SURGERY

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Background – Use of narcotics in the epidural space has dramatically changed patient care after surgery because it provides suitable analgesia with fewer complications than other methods. Morphine is a narcotic widely used in the epidural space for pain management, but its use is associated with several complications such as urinary retention, nausea, and vomiting. This study was designed to determine whether the addition of fentanyl to epidural morphine would reduce the associated complications.

Methods – Of patients prepared for lung surgery, 72 were selected for epidural analgesia. Twelve patients met the exclusion criteria, but the remaining patients were randomized in a double-blind manner to receive morphine plus fentanyl (n = 30) or morphine alone (control group; n = 30). Drugs were injected when requested by patients, when the visual and verbal pain scores reached 2. Vital signs were checked and complications were recorded in a predefined questionnaire.

Results – At the end of the study, there was a higher prevalence of complications in the morphine group than in the morphine plus fentanyl group ($p < 0.05$). There was no significant difference in analgesic time between the two groups, and analgesic time was more than expected in the morphine plus fentanyl group ($p < 0.000$).

Conclusion – The results of this study showed that adding fentanyl to morphine in epidural analgesia can reduce the complications with at least equal analgesic time. Thus, we can consider this combination as a good choice for epidural analgesia in thoracotomy patients.

Keywords • anesthesia • analgesia • epidural morphine • lung surgery

Introduction

The use of epidural narcotics has dramatically changed patient care after surgery because it provides suitable analgesia with fewer complications than other methods. Morphine administration to the epidural space can provide effective pain relief after most surgical procedures, such as thoracic and abdominal surgery and limb amputation.^{1, 2} However, the pain relief is often accompanied by a high incidence of side effects.³⁻⁵

Fromme et al compared lumbar morphine with thoracic morphine for relief of postthoracotomy

pain and concluded that the thoracic approach was more useful.⁶ However, we could not find any studies of morphine versus morphine plus fentanyl for thoracotomy pain relief. In an attempt to decrease the side effects of epidural morphine, the narcotic fentanyl was added to morphine and administered as mixed doses to the epidural space for pain relief in postoperative thoracotomy patients.

Patients and Methods

Seventy-two patients scheduled to undergo pulmonary resection between October 1999 and October 2000 were scheduled to receive epidural analgesia. Of these, 60 were randomized into two groups, following the approval of the ethics committee of Masih Daneshvari Hospital. The

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Epidural Morphine vs Morphine + Fentanyl in Lung Resection Surgery

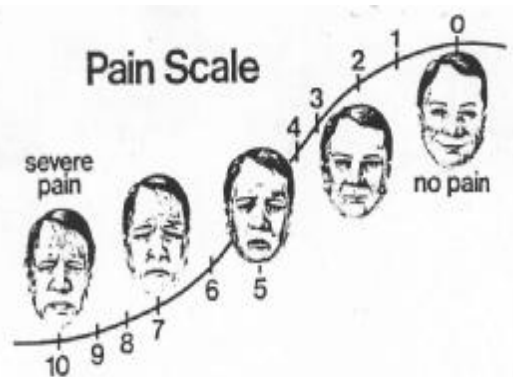


Figure 1. Visual pain analogue.¹

advantages and probable disadvantages of the treatments were completely explained to participants before they gave informed consent.

At the end of surgery, patients were placed in the lateral position and an epidural catheter was inserted in the L₃-L₄ or L₄-L₅ lumbar epidural space. At the end of insertion, catheters were checked for correct position by administering 3 mL lidocaine 2% with epinephrine 1:200,000. Morphine (30 patients, Group M) or morphine plus fentanyl (30 patients, Group MF) was slowly injected.

In Group M, the first injection of morphine was 0.05 mg/kg morphine sulfate in 20 mL normal saline, while the same dose in 10 mL normal saline was used for subsequent injections. In Group MF, the initial injection was 0.25 mg/kg morphine sulfate plus 0.00125 mg/kg fentanyl in 20 mL of normal saline, while the same dose was used in 10 mL of normal saline for subsequent injections.

The agents were administered at the patient's request, but at intervals of not less than 1 hour.

Four-hourly follow-up started at the first injection. This was provided by a team of five nurse anesthetists, both in the intensive care unit and the surgical ward. If any complications were detected, naloxan 0.2 mg was injected intravenously and this was recorded in the patient's file. During the study period, patients were assessed for pain intensity every 6 hours using both a visual pain analogue (VPA) and a verbal pain analogue (WPA) scale (Figures 1 and 2).

Two pain scales (VPA and WPA) were used to reduce bias, which might have occurred if either of these systems were applied separately. The health care team was blinded to the drugs used. During the 3 days of follow-up, patients were asked for symptoms of probable opioid overdose, such as pruritus and catheter-related complications, and other pains (muscle pain, incisional pain, etc.)

Catheter tips were checked for an intact head after removal from the epidural space at the end of the 3-day follow-up.

Chi-square, Student's *t* ($p < 0.05$) and Fisher's exact tests were used to determine the comparability of the treatment groups. Both pain complications and the length of pain-free periods, determined from the pain questionnaire, were analyzed. Results of Chi-square tests were considered significant at 0.05 or less. There was no significant difference in the duration of painlessness in each group, so the Student's *t*-test was used to test the mean duration of pain relief interval and the Chi-square test was used to analyze complications, that is, if the *p* value was 0.05 or less in any mentioned test, it would be meaningful.

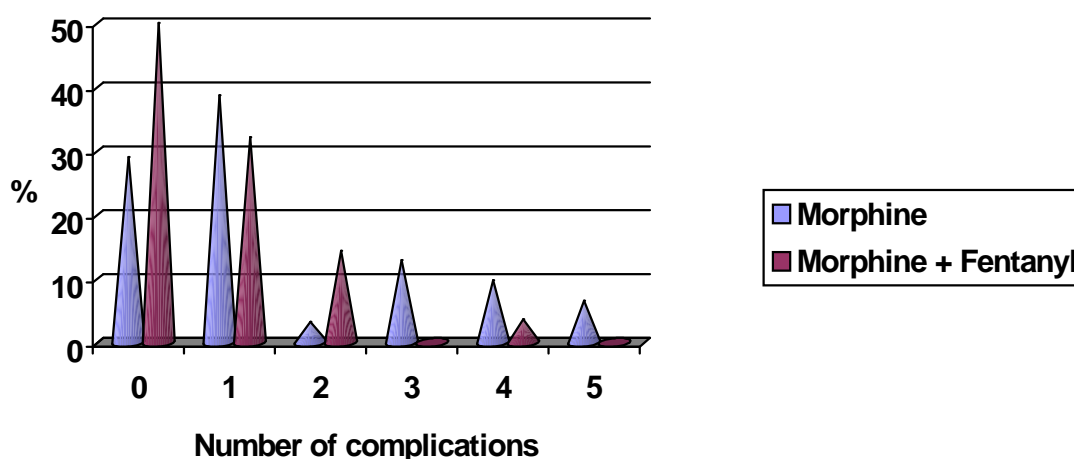


Figure 2. Frequency of the number of complications in two groups.

Table 1. Distribution of the two groups by age.

Patient/Age (yr)	A		B		Total	
	F (n)	%	F (n)	%	F (n)	%
5 – 15	1	3.2	2	7.7	3	5.3
15 – 25	4	12.9	3	11.5	7	12.3
25 – 35	7	22.6	6	23.1	13	22.8
35 – 45	8	25.8	4	15.4	12	21.1
45 – 44	5	16.1	2	7.7	7	13.3
> 55	6	19.4	9	34.6	15	26.3
Total	31	54.4	26	45.6	57	100

A = morphine group; B = morphine + fentanyl group; F = frequency.

Results

Three patients were excluded from the experiment because of a malpositioned epidural catheter in both groups. Of the 57 patients, most were males [31 (58%) in Group M and 26 (64%) in Group MF]. There was no significant difference between the groups in age and sex ($p = 0.65$) (Table 1).

Females in Group M had statistically more complications than females in Group MF ($p = 0.02$).

The number, percentage and validity of each complication are shown in Figure 2. There was a trend towards not statistically significant more complications in Group M than Group MF (Table 2).² In Group M, 71% of patients had at least one complication, while in Group MF, this figure was 50%. There was a statistically significant difference between females in Group MF and females in Group M (92.3 % vs 50%, $p < 0.05$).

These results show that the combination of morphine and fentanyl had greater efficacy in

females than in males. In addition, low back pain during epidural injection was more frequent in Group M than Group MF. However, the only meaningful statistically significant complication was related to other pains (i.e. incisional pain, radiculopathy, etc).

Discussion

Initially, the duration of analgesia (analgesic time) was not considered important, but was measured as a quantitative variable. It was expected that patients in Group MF would have a much shorter analgesia than those in Group M.⁷

Because the dose of morphine in Group MF was half that in Group M and fentanyl (duration of action, 1.5 – 3 hours) was used as an adjuvant to morphine in Group MF, the expected analgesic times in Groups M and MF were 4.5 and 6 hours, respectively.⁷ However, the analgesic time was 8 ± 4.8 hours in Group M and 9 ± 4.5 hours in Group MF (Table 1), an increase of 2 and 4.5 hours, respectively, over the expected analgesic times.

Table 2. Frequency of complications in two groups.

Treatment groups/Complications	A		B		p Value
	No.	%	No.	%	
Low back pain	12	37.7	7	25	0.26
Headache	1	3.2	1	3.6	0.72
Other pains	5	16.1	0	0	0.034*
Flushing	5	16.1	2	7.1	0.428
Nausea and Vomiting	6	19.4	3	10.7	0.477
Pruritus	9	29	4	14.3	0.172
Urinary retention	6	19.4	5	17.9	0.883
Total	22	71	14	50	0.09

A = morphine group; B = morphine + fentanyl group; * $p < 0.05$.

Epidural Morphine vs Morphine + Fentanyl in Lung Resection Surgery

Thus the extended was enhanced is 9 ± 4.5 hours, a difference of 5.5 hours. Thus, the pain-free period was longer in Group MF than in Group M ($p < 0.00$) implying that fentanyl could have had a synergistic effect on morphine pain reduction.

There were no significant differences between the two groups in sex and age, and more complications occurred in Group M as compared to Group MF (Tables 1 and 2; Figure 2) ($p > 0.05$).

There was no statistically significant difference between the groups in complication rate, other than the incidence of radiculopathy and incisional pain. This was due to various factors. There was a limited number of thoracotomy cases and case gathering took more than 14 months. This sample scattering over a long period of time reduced the internal validity, hence it would have been better if the experiment had been carried out over a specific limited period.

In order to reduce complications in both groups, the lowest doses of both morphine (0.05 mg/kg morphine in Group M and 0.025 mg/kg morphine in Group MF) and fentanyl (0.00125 mg/kg) were used. Had the recommended dose of 0.1 mg/kg morphine been used, the complication rates would have been dramatically increased and any significant differences would have been more easily detected.

The complication rate in females in Group MF was lower than that of females in Group M (50% vs 92.3%; $p = 0.02$). Thus, the MF regimen can be prescribed for females undergoing thoracotomy.

More patients in Group M than Group MF discontinued epidural therapy. This may have been because the time to onset of action of morphine is 20 minutes compared with 5 minutes for fentanyl⁷ and because of the higher frequency of low back pain in Group M after injection. There were fewer complaints of low back pain in Group MF than in Group M because it took about 20 minutes in Group M to suppress the pain caused by dilation of the epidural space during forceful injection compared with 5 minutes in Group MF.

In summary, there was a longer duration of pain reduction (5 hours vs 2 hours in Groups MF and M, respectively) ($p < 0.000$) and faster onset of action in Group MF than in Group M.

In addition, there was a higher complication rate in Group M than in Group MF ($p > 0.05$); complication rates were significantly lower in females in Group MF than in females in Group M ($p = 0.02$).

Nonetheless, more cases are needed to evaluate

whether all of the useful items discussed can be attributed solely to fentanyl or whether other unknown factors are involved.

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