Respiratory Depression following a Cervical Epidural Opioid Injection

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(Key words: respiratory depression, epidural opioid, epidural anesthesia)

Morphine administered epidurally produces excellent pain relief, although it may cause a respiratory depression[1-7], and too great a dose of an opioid has been found to be a risk factor of such a depression[3]. To the best of our knowledge, however, there has been no report thus far on whether a respiratory depression occurs after an opioid has been administered epidurally in the cervical region.

Therefore, we have examined the respiratory effects of an opioid in the cervical region by monitoring the end-tidal CO_2 tension ($P_{ET}CO_2$) and the respirataory rates (RRs) in patients slated for surgery who received an epidural anesthesia combined with a light, general anesthesia.

Materials and Methods

This study, which was approved by the hospital research committee, consisted of 29 ASA class I or II female patients who underwent elective surgery under an epidural anesthesia combined with a light general anesthesia. These patients had given their informed consent, and those with a preexisting respiratory disease were excluded. The operations they underwent are presented in table 1.

Depending on whether an epidural anesthesia or saline administered in the cervical region, the patients were divided into three groups: 7 patients in Group I received morphine, 5 patients in Group II received fentanyl, and 7 patients in Group III, which served as our controls, received saline through an epidural catheter. The remaining 10 patients were designated as belonging to Group IV, since they were given morphine through an epidural catheter sited in the lumbar region.

Table 1. Operations performed

Operation	Epidural Anesthesia	N
Mastectomy	Cervical	14
Removal of thyroid nodule	Cervical	6
Transabdominal hysterectomy	Lumbar	6
Orthopedic surgery of the leg	Lumbar	4

All patients were given oral flunitrazepam, 1.0 mg, 90 min before their respective operations. Prior to the induction of anesthesia, their sedation level was scored by one of the authors, based on the following scale: 1, None (alert and/or apprehensive); 2, Mild (occasionally drowsy); 3, Moderate (sleeping but easily aroused); and 4, Severe (sleeping and difficult to arouse).

For groups I, II, and III, 12 to 15 ml of 1.5% lidocaine with epinephrine (1:200,000) was injected through an epidural catheter introduced at the C7-Th1 interspace, and within 10–15 min the area in which analgesia (determined by the pin-prick method) resulted extended from the C3 to the Th6 region. For group IV, 15 to 20 ml of 2% lidocaine with epinephrine (1:200,000) was

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Table 2. Demographic data, sedation scores, and doses of lidocaine administered epidurally

Group	cervical			lumbar
	morphine	fentanyl	normal saline	morphine
Cases (n)	7	6	7	10
Age (yr)	49 ± 5	52 ± 4	55 ± 6	41 ± 5
Height (cm)	153 ± 2	150 ± 4	152 ± 3	155 ± 2
Weight (kg)	55 ± 3	50 ± 2	49 ± 4	55 ± 2
Sedation score				
1 (n)	1	2	0	1
2	3	2	5	9
3	3	3	2	0
4	0	0	0	0
lidocaine ($mg \cdot kg^{-1}$)	7.05 ± 0.30*	8.40 ± 0.69	9.62 ± 0.72	9.69 ± 0.56

Mean ± SE.
*$P < 0.05$, vs the cervical saline and the lumbar morphine groups.

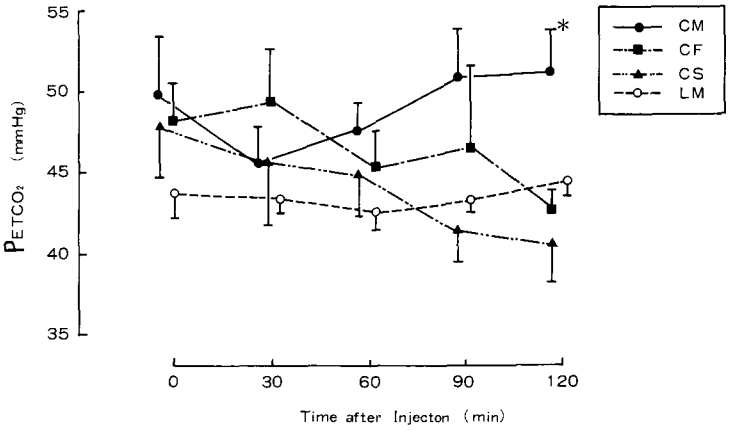

Fig. 1. P_{ETCO_2} following a cervical, epidural injection of morphine 4 mg (—●—, CM); a cervical, epidural injection of fentanyl 100 μg (—■—, CF); a cervical, epidural injection of normal saline (—▲—, CS); and a lumbar epidural morphine 4 mg (—○—, LM). Values are expressed in means ± SE. *$P < 0.05$ vs the cervical saline group.

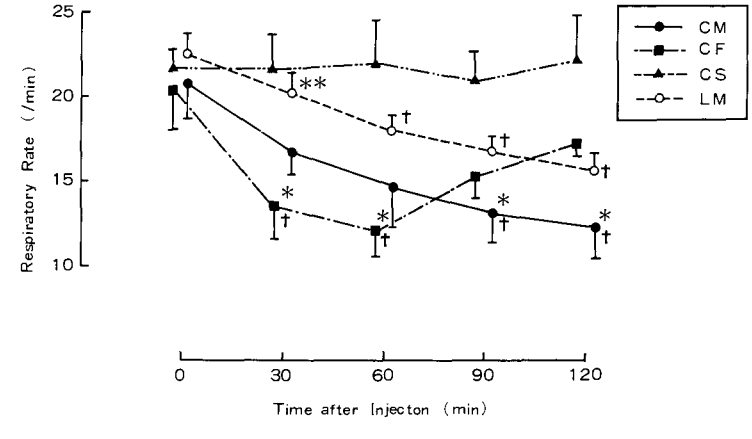

Fig. 2. Respiratory rates following a cervical, epidural injection of morphine 4mg (—●—, CM); a cervical, epidural injection of fentanyl 100 μg (—■—, CF); a cervical epidural injection of saline (—▲—, CS); or a lumbar, epidural injection of morphine 4 mg (—○—, LM). Values are expressed in means ± SE. *$P < 0.05$ vs the cervical saline group. **$P < 0.05$ vs the cervical fentanyl group. †$P < 0.05$ vs the control value of each group.

injected through an epidural catheter that had been introduced at the L2–3 interspace, and within 10–15 min the area in which analgesia occurred extended from the Th6 to the S1 region. Half of the initial lidocaine dose was incrementally administered every 50 min or whenever there was a blood pressure increase of 20 per cent or more.

Anesthesia was induced with thiopental, 5 $mg \cdot kg^{-1}$, i.v., after which endotracheal intubation was facilitated with succinylcholine, 1 $mg \cdot kg^{-1}$, i.v. and a lidocaine topical spray. Anesthesia was maintained with nitrous oxide (67%) and oxygen. Fifteen min after induction, the patients were left to respire on their own, after which, using an epidural catheter, each group was administered the medication that follows: Group I, morphine hydrochloride 4 mg in 5 ml of a normal saline solution (NS); Group II, fentanyl citrate 100 μg in 3 ml NS (total 5 ml); Group III, 5 ml NS; and Group IV, morphine hydrochloride 4 mg in 5 ml NS.

The $P_{ET}CO_2$ and RR responses were recorded prior to the injection, and at intervals of 30, 60, 90, and 120 min after the injection. $P_{ET}CO_2$ was monitored using an infrared CO_2 analyzer (Normocap®, Datex, Finland), which had been precalibrated with standard gas (7% CO_2).

Differences in age, height, and weight, the dose of lidocaine administered for 120 min after the opioid or saline injection, and the $P_{ET}CO_2$ and RR responses were compared by using a one-way analysis of variance and the t test modified by Bonferroni's method. Differences in each patient's sedation score were compared by using the Kruskal–Wallis test, and a P value of less than 0.05 was considered as statistically significant.

Results

Before their epidural injection, no significant differences were found among the 4 groups with regard to their age, height, weight, sedation score (table 2), mean $P_{ET}CO_2$, and mean RRs (fig. 1, 2). The effect of the epidural injection of lidocaine in the cervical group given morphine was significantly lower than in either the cervical group given saline or the lumbar group morphine during the 120 min following the injection.

In the cervical group given morphine, the mean $P_{ET}CO_2$ at 120 min was significantly higher and the mean RRs at 90 and at 120 min was significantly lower than in the cervical group given saline. Two patients in cervical group given morphine developed RRs of less than 10 per min (one patient, 6 per min at 60 min; the other, 9 per min at 90 min).

In the cervical group given fentanyl, the mean RRs were significantly lower than the mean RRs of the cervical group given saline at 30 and at 60 min. Two patients in the fentanyl group developed RRs of less than 10 per min (one patient, 8 per min at 30 min; the other, 8 per min at 60 min).

In contrast, no patient in the cervical group given saline or in the lumbar group given morphine developed RRs of less than 10 per min during the study regimen. Only one patient in the cervical group given morphine required naloxone to alleviate respiratory depression, nausea, and vomiting at the end of surgery. Finally, no patient from any group complained of incisional pain at the end of the surgery.

Discussion

The aim of this study has been to assess the respiratory effects of morphine or fentanyl administered epidurally in the cervical region of patients when this administration is combined with a light general anesthesia. A patient's respiratory status is said to be modified by a number of drugs, such as the premedicant benzodiazepine[8], the induction agent thiopental, halothane, and nitrous oxide[7,9]. Further, a strong dose of a local anesthetic agent administered epidurally supposedly affects the respiratory muscles, although it has not been found to increase the Pa_{CO_2}[10,11] or to impair the ventilatory response to CO_2[12,13].

Despite these limitations of our test protocols, the respiratory depression that we saw develop in our cervical groups given morphine or fentanyl is considered a rele-

vant finding with respect to the effect of an opioid in the cervical region, since no respiratory depression was observed in our cervical group given saline or in the lumbar group given morphine.

The present study also has demonstrated that the onset time of a respiratory depression occurred at 90 min after our cervical group received an epidural administration of morphine. Previous studies have shown that the respiratory response to CO_2 is depressed 5 to 8 hrs after morphine is administered epidurally in the lumbar region[1,2]. The difference in the onset time of a respiratory depression between a cervical and a lumbar epidural injection of morphine is considered to be related to the distance involved for the rostral spread of the morphine within the CSF[5,7,14,15]. In an clinical report that indicates a slower, rosral spread, the peak morphine concentration in the CSF, collected at the 7th cervical vertebrae, was found to occur at 120 min after the lumbar epidural injection[16].

In our study, the respiratory depression following the cervical administration of fentanyl occurred earlier than the depression that followed the cervical administration of morphine. The earlier onset of respiratory depression following the cervical administration of fentanyl is largely thought to be due to its lipophilicity and the faster dural penetration of fentanyl[7,16,17], although the paravertebral route also has been speculated to play a role[18].

In conclusion, the onset of a respiratory depression occurred 30 min after the injection of the fentanyl and 90 min after the injection of the morphine. Thus, although a cervical, epidural injection of an opioid is an excellent technique to relieve post-operative pain, further studies, including testing of the ventilatory response to CO_2 in volunteers, must be undertaken in order to use this technique more safely for the postoperative management of pain.

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