Anesthesiology
59:559–560, 1983

Early Respiratory Depression with Epidural Narcotic and Intravenous Droperidol

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The possibility that severe respiratory depression can follow epidural narcotic administration is well documented. Little attention has been directed toward the possibility that concurrently administered nonnarcotic drugs might precipitate this complication. We describe a case of severe respiratory depression following the administration of epidural hydromorphone (Dilaudid®) and a small dose of droperidol.

REPORT OF A CASE

A 34-year-old, 170-cm, 61-kg, gravida 3, para 1, woman was scheduled for elective repeat cesarean section. She was healthy except for recurrent respiratory infections during the pregnancy, which had been accompanied by mild wheezing and had been treated with antibiotics, cough suppressants, and terbutaline. However, all therapy had been discontinued one month prior to delivery, and the patient was asymptomatic at the time of admission. Previous general and epidural anesthesia had been uneventful.

Epidural anesthesia for cesarean section was induced successfully with a test dose of 3 ml of 1% lidocaine with epinephrine, followed 4 min later by 18 ml 0.75% bupivacaine administered through the needle. An additional 6 ml bupivacaine was administered through the catheter to produce a T4 block, which gave excellent anesthesia for the entire procedure. Shortly after delivery of a healthy infant, the patient complained of nausea. This was treated initially with glycopyrrolate, 0.2 mg, iv, with no improvement, and then with droperidol, 1.25 mg, iv, with good effect.

The patient had agreed to participate in a study comparing morphine and hydromorphone administered epidurally for postcesarean analgesia. Thus, 10 min after the droperidol had been given, she received a 15-ml injection containing hydromorphone, 1.25 mg in saline. Respiratory and cardiovascular status remained stable throughout surgery, and she was transferred to the recovery room, awake and talking to her husband. In addition to receiving routine postoperative care, study patients are nursed in the head-up position and are monitored with an apnea alarm (Hewlett Packard Model 78202B) for 24 h.

Fifteen minutes after the epidural injection of hydromorphone (25 min after droperidol was administered) she became apneic during periods when she was resting quietly. She felt only slightly drowsy and ventilated normally when active and talking to her attendants. At other times she had no apparent urge to breathe, although she readily responded to the nurse's instructions to do so. Naloxone, 0.4 mg, was administered iv, without effect. During the next 45 min, naloxone, 3.2 mg, was given iv, with no increase in her ventilatory drive. She remained awake, but "tired," with good color and a respiratory rate determined solely by the nurse's encouragement to breathe. Blood–gas analysis was not performed, as ventilation was maintained at a satisfactory rate by her attendants and tidal volume appeared adequate. The anesthetic block was still at T4, and she complained of no sensation of dyspnea.

At this point it was thought that any narcotic depression of ventilation should have been reversed and that, in spite of the small dose, the droperidol might be responsible. Physostigmine, 1 mg, was administered iv and within 3 min, spontaneous ventilation at a rate of 22 breaths · min^{-1} resumed. The patient was tremulous and upset for a short period, but this soon resolved, and she had no further respiratory problems. The anesthetic block receded at the usual rate. Nausea and pruritis were troublesome between 4 and 6 h following anesthesia; they failed to respond to iv naloxone, but improved following diphenhydramine, 25 mg im. Analgesia remained excellent until 20 hours after the epidural narcotic injection, after which time oral analgesics were administered. The patient ambulated 7 h after delivery and felt well until discharged 4 days later.

DISCUSSION

Both early and delayed respiratory depression following epidural and intrathecal morphine have been reported.[1] Vascular absorption with systemic effect probably causes early depression; this is more common with the lipid-soluble narcotic meperidine.[2] Rostral spread within the neuraxis is said to be responsible for late depression,[3] which has occurred most frequently with morphine, a drug of low lipid solubility. We are not aware of reports of respiratory depression following epidural hydromorphone, although we now have encountered three cases of delayed hypoventilation when this agent was administered epidurally, either alone, or in conjunction with other narcotics. Respiratory depression in these cases occurred several hours after the initial injection and was reversed easily with naloxone. Hydromorphone is moderately lipid soluble, and the early onset of apnea in the patient currently described coincided with the time at which peak blood and cerebrospinal fluid levels of narcotic have been identified following epidural administration.[4] Naloxone is said to antagonize respiratory depression resulting from epidural opiates, while leaving analgesia intact, presumably because only low levels of the drug reach the spinal cord.[1] However, the large dose of naloxone

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Received from the Department of Anesthesia, Stanford University Medical Center, Stanford, California 94305. Accepted for publication May 2, 1983.

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Key words: Analgesics: hydromorphone. Anesthetic technique: epidural. Complications: respiratory depression.

administered in this case makes it extremely unlikely that the narcotic alone was responsible for the apnea.

Physostigmine, an anticholinergic agent, has been successful in reversing respiratory depression and sedation from a variety of nonnarcotic agents, including ketamine, phenothiazines, benzodiazepines, tricyclic antidepressants,[5] and droperidol.[6] Weinstock and associates[7] also administered physostigmine to patients treated with droperidol and morphine. They concluded that physostigmine had reversed the respiratory depressant and sedative effects of morphine, while leaving analgesia intact. They appeared to ignore the fact that all patients also had received 2.5 to 5 mg of droperidol to prevent nausea. The success of physostigmine in our patient suggests that the butyrophenone droperidol was partially or completely responsible for the respiratory depression. The mechanism by which physostigmine reverses the effects of droperidol is unknown. Physostigmine may act as a nonspecific central nervous system stimulant or it may reverse an imbalance in brain acetylcholine and dopamine activities caused by droperidol.[6] The duration of effect of physostigmine in this circumstance is about 60 min, and if depression recurrs additional doses may be necessary.

The respiratory effects of droperidol in doses ranging from 5 to 20 mg have been studied with, generally, minimal or no depression reported.[8–10] However, a recent study described wide individual variation in respiratory drive following droperidol, 0.3 mg/kg, with a marked (50%) decrease in ventilatory and occlusion pressure responses to CO_2 occurring in one subject.[10] Our patient, who received only 1.25 mg (0.02 mg/kg), may have been exceptionally sensitive to this effect of droperidol, although apnea has never been reported after such a low dose. The epidural narcotic and droperidol probably acted in a synergistic manner, although naloxone should have reversed the narcotic component. Alternatively, perhaps the deafferentation of sensory input from intercostal muscles due to the T4 block, combined with the absence of pain and the mental state of indifference sometimes caused by droperidol, may have resulted in loss of the urge to breathe.

This case demonstrates that respiratory depression in patients with epidural narcotic analgesia is not always reversible with naloxone. Ventilatory insufficiency may be due to administration of other drugs, either as an unrelated phenomenon or because of drug interactions. Droperidol, a potent antiemetic, might be used in the treatment of nausea following epidural narcotic administration. The phenothiazines, drugs with similar depressant potential, also have been used for treatment of the side effects of epidural narcotics. As prolonged respiratory depression has been demonstrated following epidural narcotics,[11,12] we strongly recommend that all patients treated with them be monitored continuously for the first 24 hours. Additionally, it may be prudent to initially treat nausea and itching with naloxone, before resorting to drugs with sedative properties. Finally, this report supports the contention that large doses of naloxone can be administered without interfering with the excellent analgesia afforded by epidural narcotics.

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