Clinical Reports

The reversal of epidural morphine induced somnolence with physostigmine

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Two case reports are presented of patients with post-thoracotomy pain treated with epidural morphine who developed somnolence several hours after the procedure. Physostigmine, 1 mg IV successfully reversed the somnolence without any effect on analgesia.

Key words

ANAESTHETIC TECHNIQUES: epidural; ANALGESICS: morphine; COMPLICATIONS: somnolence; ANTAGONISTS, MISCELLANEOUS: physostigmine.

Physostigmine has been shown to reverse somnolence[1] and respiratory depression[2] due to intravenously administered morphine. In a case report of somnolence and respiratory depression following an inadvertent overdose of intrathecal morphine, physostigmine had no effect on somnolence.[3] We have observed two cases of somnolence in patients receiving epidural morphine and in each case the somnolence was successfully reversed with physostigmine.

Case report #1

The patient, a 73-year-old, 70 kg man, was scheduled for a right upper lobe lobectomy. The patient received no premedication and an epidural catheter was placed at the L_{2-3} interspace preoperatively. A 3 ml test dose of two per cent carbonated lidocaine was injected followed by 7 ml of two per cent carbonated lidocaine. Following the epidural injection, the patient had a level of analgesia at the T-4 dermatone. Thirty minutes later, anaesthesia was induced with sodium thiopentone, 300 mg IV. Pancuronium 7 mg IV was given to facilitate intubation. The patient was then intubated with a large left Robertshaw double-lumen tube. Anaesthesia was maintained with nitrous oxide, oxygen and enflurane. The patient was given 5 mg of preservative free morphine in 20 ml of normal saline shortly after induction of anaesthesia. The patient received 10 mg of hydralazine to control hypertension intraoperatively. No other drugs were given intraoperatively. Neuromuscular blockade was reversed at the end of the anaesthetic with neostigmine 2.5 mg IV and atropine 1.2 mg IV. The patient was extubated and taken to the recovery room. Thirty minutes after the termination of anaesthesia, and 5½ hours after the first dose of epidural morphine, the patient complained of pain and was given 5 mg of preservative-free morphine in 20 ml of normal saline via the epidural catheter. Ninety minutes after the second dose the patient was noted to be responsive to verbal commands, but was disoriented and did not initiate conversation. His respiratory rate was 16 and arterial blood gases with an FiO_2 of 0.40 by face mask, were : pH 7.32, PO_2-102, PCO_2-39. Physostigmine, 1 mg IV was administered. Within five minutes, he became very alert and responsive. The patient had no further problems and did not require any pain medications for the next 24 hours.

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Case report #2

The patient, a 72-year-old 85 kg man, was scheduled for a wedge resection of the right lung. An epidural catheter was placed at L_{2-3} preoperatively. A 3 ml test dose of two per cent carbonated lidocaine was given followed by 7 ml of two per cent carbonated lidocaine. The patient had a level of analgesia at the T-6 dermatome. Anaesthesia was induced 30 minutes later with sodium thiopentone 350 mg IV and succinylcholine 100 mg IV was given to facilitate intubation. The patient was intubated with a 9.0 mm endotracheal tube and anaesthesia was maintained with nitrous oxide, oxygen and enflurane. Further muscle relaxation was provided by d-tubocurarine. Shortly after induction, 5 mg of preservative-free morphine in 20 ml of normal saline was administered via the epidural catheter. No other drugs were given intraoperatively. Neuromuscular blockage was reversed upon completion of surgery with neostigmine 2.5 mg IV and atropine 1.2 mg IV. The patient was extubated and taken to the recovery room. Immediately upon reaching the recovery room and 90 minutes after the first dose of epidural morphine, he required a second dose of 5 mg of epidural morphine in 20 ml of normal saline. Five hours later in the intensive care unit, the patient started complaining of pain and 5 mg of morphine in 20 ml of normal saline was given through the epidural catheter. Eight hours postoperatively, the patient was responsive to painful stimulation but not to verbal commands. His respiratory rate was 16 and arterial blood gases on an FiO_2 of 0.35 by face mask were pH 7.32, PO_2-79, PCO_2-49. The elevation of the PCO_2 indicated some degree of respiratory depression. However, because of the associated somnolence it was elected to treat the patient with 1 mg of physostigmine IV. The patient responded within five minutes and became oriented and responsive. However, the arterial PCO_2 repeated one hour after physostigmine was still 50 mmHg in spite of the patient's continued ability to co-operate with nursing and physiotherapy staff. Three hours after the physostigmine the patient had again become drowsy but responded appropriately when aroused verbally. The arterial blood gases three hours after physostigmine on an FiO_2 of 0.35 by face mask were pH 7.25, PO_2-86, PCO_2-56. No further epidural morphine, or other analgesia was given over the next 24 hours. Six hours after the physostigmine the arterial PCO_2 was 46 mmHg and the patient was no longer somnolent.

Discussion

The two patients were part of a double-blind study comparing epidural and parenteral morphine in patients undergoing thoracotomies.[4] Immediately following induction, patients received 20 ml of normal saline epidurally and 0.05–0.07 $mg \cdot kg^{-1}$ morphine intravenously or 5 mg of preservative free morphine in 20 ml saline epidurally and 0.05–0.07 $ml \cdot kg^{-1}$ normal saline intravenously. Every time the patients had pain postoperatively they were given one of the above two regimes. When the two patients described above demonstrated somnolence it was not known whether they had received epidural or parenteral morphine. It was decided within the framework of the study to administer 1 mg of physostigmine to any somnolent patient. It was hypothesized that physostigmine probably would have little effect on the analgesia resulting from epidural morphine, since it is known to have no effect after intravenous morphine.[1] Physostigmine was used rather than naloxone because there was no significant respiratory depression in one patient, and moderate respiratory depression in the other patient. Although naloxone is said to antagonize respiratory depression resulting from epidural opiates and leave analgesia intact,[5] we have had disappointing results when naloxone was given to patients who developed side effects from epidural morphine. Small doses of naloxone (50–100 μg) given IV reversed severe pruritis from epidural morphine but also tended to reverse analgesia. Other investigators have found similar results.[6] Physostigmine has not been demonstrated to reverse respiratory depression caused by epidural narcotics, but it has been successful in reversing respiratory depression following the combined use of epidural narcotics and droperidol.[7]

The cause of somnolence from epidural morphine is likely due to the rostral spread of morphine[8] in the cerebrospinal fluid to receptors in the thalamus, limbic system and possibly to the cortical receptors as well.[10] There has been one reported failure of physostigmine to reverse morphine induced somnolence. In this case, a massive overdose of intrathecal morphine had been given.[3] It is not surprising that

a continuous naloxone infusion was required, since it was also required in a case of massive overdose of epidural morphine.[9]

Physostigmine appears to be effective in reversing somnolence induced by epidural morphine although it has no effect on respiratory depression as shown in patient number two. It probably should be used before naloxone, especially when there are no signs of respiratory depression.

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Résumé

On rapporte ici l'observation de deux patients qui ont présenté une somnolence marquée plusieurs heures après l'administration de morphine par voie péridurale qu'on employait comme analgésie post-thoracotomie. La physostigmine à 1 mg IV a corrigé cette somnolence sans modifier les effets analgésiques.