

## Aspiration Pneumonitis Caused by Delayed Respiratory Depression Following Intrathecal Morphine Administration

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Opioid analgesia is the primary pharmacologic intervention for managing pain. However, opioids can cause various adverse effects including pruritus, nausea, constipation, and sedation. Respiratory depression is the most fatal side effect. Therefore, cautious monitoring of respiratory status must be done after opioid administration. Here, we report a patient who suffered from respiratory depression with deep sedation and aspiration pneumonitis after intrathecal morphine administration. (Korean J Pain 2012; 25: 126-129)

### Key Words:

intrathecal, morphine, pneumonitis.

Implantable intrathecal morphine pumps have been increasingly used in patients with intractable chronic pain [1,2]. Prior to making the decision to implant an ITMP, a trial administration of intrathecal morphine should be done to estimate the effective dose and to determine any untoward side effects from the morphine. Side effects from intrathecal morphine administration may include pruritus, nausea, vomiting, constipation, fluid retention, sexual dysfunction, urinary retention, and respiratory depression [3]. Respiratory depression is the most fatal side effect of intrathecal morphine. Therefore, patients receiving intrathecal morphine should be monitored closely. Here, we report a case of respiratory depression with deep sedation after trial administration of intrathecal morphine.

### CASE REPORT

A 46-year-old man with chronic bilateral hip and leg pain was referred to our clinic. He was previously injured with a left sacral fracture and sacro-iliac joint separation from falling down in a building, and since then, he had been suffering from a tingling sensation and lancinating pain bilaterally in the hip and both legs. The intensity of the pain using the visual analogue scale (VAS) from 0 to 10 mm was 8 mm. Initial neurologic examination of the patient showed motor weakness of the lower extremities (grade III/I) and moderate sensory weakness of the lower extremities. His electromyography and nerve conduction velocity findings suggested left lumbosacral plexopathy

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and right chronic L5–S1 radiculopathy.

He had been treated with acetaminophen/tramadol tablet 3 times a day, imipramine 25 mg 3 times a day, divalproate 500 mg twice a day, and pregabalin 75 mg twice a day orally. He had received a lumbar sympathetic ganglion block; however, his pain did not improve. Pethidine HCl 75 mg was administered intravenously 4 or 5 times a day. Despite the oral medications, his pain intensity was high (VAS 4–8 mm).

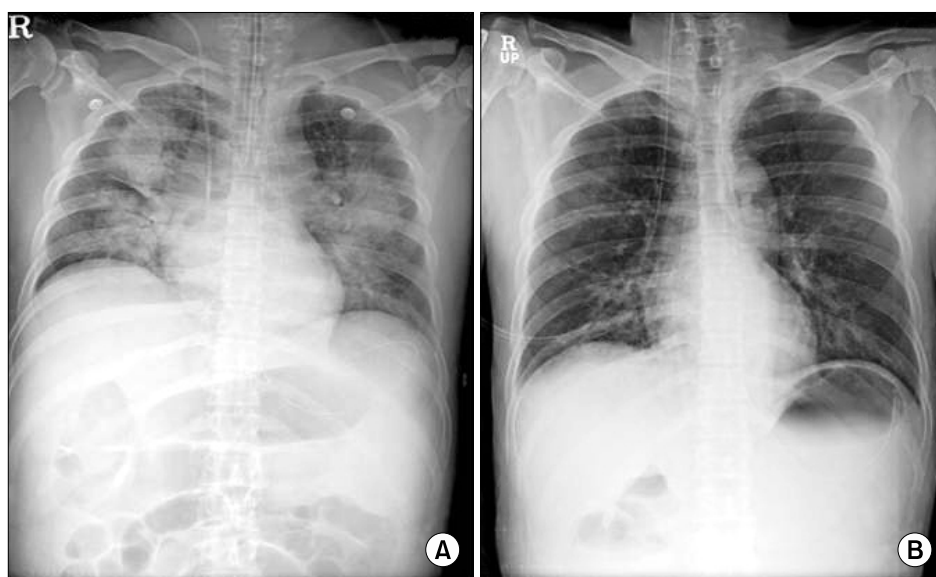
He underwent a patient-controlled continuous epidural morphine infusion since his pain was responsive to injections of opioids. Satisfactory catheter placement was confirmed by epidurogram and the reservoir bag contained preservative free morphine at a concentration of 0.28 mg/ml. The pump was programmed to deliver a basal rate of 0.5 ml/h, with an on-demand bolus dose of 4.0 ml, and a lock out interval of 30 minutes. He did not experience any significant adverse events and reported about 20% pain reduction. There was no further improvement in pain intensity despite increasing the basal rate up to 1.0 ml/h.

In order to control his pain, we considered neuromodulation. Spinal cord stimulation was expected to be difficult because of previous spinal surgery; therefore, implantation of an intrathecal morphine pump was selected after discussing it with the patient. Epidural PCA was stopped and he was placed in a lateral decubitus position on a table. His skin was prepared for needle insertion using an iodine-based antiseptic solution. A 25-gauge 10 cm spinal needle was inserted in the L4–5 interspinous space and

advanced to obtain a spontaneous flow of cerebrospinal fluid (CSF). After confirming the CSF free flow through the needle, 0.3 mg of morphine sulfate (BC World, Korea) was administered intrathecally. The dose of the intrathecal morphine was one tenth of the epidurally administered morphine in a half day.

One hour after morphine injection, he reported about 60% pain reduction and his respiratory rate was 17/min. However, his pain recurred 8 hours after the morphine injection with a VAS of 7. Tramadol 50 mg was injected because of severe pain 15 hours after intrathecal morphine injection. Epidural PCA was restarted. His family reported that he could communicate with others but he had dysarthria and drowsiness. Twenty-one hours after intrathecal morphine injection, he did not respond to painful stimulation. Epidural PCA was stopped.

Twenty-five hours after morphine injection, the patient was found to be unresponsive by his family members with a respiratory rate of 15/min, a blood pressure of 88/54 mmHg, and pulse oximetry showing oxygen saturation at about 69–71%. An oxygen mask with a reservoir bag was placed on him and he was transferred to the intensive care unit. Naloxone 0.4 mg was administered intravenously, but his mental state did not improve. His chest radiograph revealed newly developed multifocal patchy consolidation in the left upper and lower lung zones (Fig. 1A). We assessed that he developed aspiration pneumonia due to the morphine-induced deep sedation. Conservative therapy for aspiration pneumonia like antibiotic therapy



**Fig. 1.** Chest X-ray of the patient showing multifocal patchy consolidation consistent with aspiration pneumonia (A) and the decreased extent of pulmonary opacification in both central lung areas 3 days after initiation of the treatment (B).

and ventilation care was done. Three days after the event, the blood gas was within normal range and was mentally alert so extubation was done. His chest radiograph also improved (Fig. 1B). He was discharged with his previous medication and his VAS score was 7.

## DISCUSSION

The side effects with opioid administration may include pruritus, nausea, vomiting, constipation, fluid retention, sexual dysfunction, urinary retention, sedation and respiratory depression [3]. Advanced sedation and respiratory depression is the most fatal side effect of opioid administration. Opioid-related adverse effects were associated with significantly increased length of stays and hospitalization costs [4]. Sedation is a common adverse effect of opioids, particularly at the start and generally during the first 24 hours of opioid therapy and with increases in opioid doses [5]. Sedation generally precedes significant respiratory depression [6]. Opioid-induced sedation occurs on a continuum ranging from full consciousness to complete loss of consciousness and respiratory arrest [7]. Intrathecal opioid induced respiratory depression is divided into 2 types: early respiratory depression which occurs within 2 hours of injection of the opioid and delayed respiratory depression which occurs more than 2 hours after opioid administration [3]. Early respiratory depression due to intrathecal morphine administration has never been reported. In contrast, all reports of clinically relevant delayed respiratory depression have involved the administration of morphine, either intrathecally or epidurally [8]. Delayed respiratory depression usually occurs 6–12 hours following intrathecal or epidural morphine administration [9]. This patient showed dysarthria which is a kind of opioid intoxication 15 hours after morphine injection, and after that, he looked sleepy. Approximately 15 to 21 hours after the morphine injection, he suffered from respiratory depression with deep sedation. In this case, respiratory depression associated with an opioid occurred relatively late.

This patient was injected with tramadol after administration of the morphine since he still suffered from severe pain. Respiratory depression is not clinically significant in normal doses of tramadol; however, the concomitant administration of intrathecal morphine and tramadol may increase the risk of opioid-induced respiratory depression. The concomitant administration of neuraxial opioids and

parenteral opioids, sedatives, hypnotics, or magnesium requires increased monitoring (e.g., intensity, duration, or additional methods of monitoring) [10]. Careful monitoring was lacking in this case.

Unintended deep sedation from opioids is often a sign that the patient may be at higher risk for respiratory depression [11], suggesting a need for increased frequency of assessment of the sedation levels and respiratory status. The patient exhibited a drowsy state for several hours after the morphine injection; however, the frequency for assessing the respiratory status did not increase. In addition, the respiratory rate was only monitored for the assessment of respiration. All patients receiving neuraxial opioids should be monitored for adequate ventilation (e.g., respiratory rate, depth of respiration), oxygenation (e.g., pulse oximetry when appropriate), and level of consciousness [10].

Despite the opioid-induced sedation and undetected respiratory depression, there are no universally accepted guidelines to direct effective and safe assessment and monitoring practices. As a result, there are considerable variations in monitoring practices. The American society of anesthesiologist recommended practice guidelines for the management of respiratory depression associated with neuraxial opioid administration in 2009 [10]. The guideline emphasizes that the anesthesiologist should conduct a focused history and physical examination before administering neuraxial opioids. Particular attention should be directed toward signs, symptoms, or a history of sleep apnea, coexisting diseases or conditions (e.g., diabetes, obesity), current medications (including preoperative opioids), and adverse effects after opioid administration. The guideline also recommends that monitoring should be performed at least once per hour for the first 12 h after administration, followed by monitoring at least once every 2 h for the next 12 h and after 24 h, frequency of monitoring should be dictated by the patient's overall clinical condition and concurrent medications. Supplemental oxygen should be administered to patients with altered levels of consciousness, respiratory depression, or hypoxemia and continued until the patient is alert and no respiratory depression or hypoxemia is present.

In conclusion, respiratory depression with deep sedation is a rare but fatal complication of opioid administration. Therefore, the clinician should watch out for this complication and assess respiratory status carefully.

## REFERENCES

1. Lee SJ, Nam SK, Kim JH, Kim HJ, Lee SC, Kim YC. Implantation of an intrathecal drug Administration system: a report of two cases. *Korean J Pain* 2009; 22: 68–73.
2. Rhee SM, Choi EJ, Lee PB, Nahm FS. Catheter obstruction of intrathecal drug administration system –a case report–. *Korean J Pain* 2012; 25: 47–51.
3. Chaney MA. Side effects of intrathecal and epidural opioids. *Can J Anaesth* 1995; 42: 891–903.
4. Oderda GM, Said Q, Evans RS, Stoddard GJ, Lloyd J, Jackson K, et al. Opioid-related adverse drug events in surgical hospitalizations: impact on costs and length of stay. *Ann Pharmacother* 2007; 41: 400–6.
5. Jarzyna D, Jungquist CR, Pasero C, Willens JS, Nisbet A, Oakes L, et al. American Society for Pain Management Nursing guidelines on monitoring for opioid-induced sedation and respiratory depression. *Pain Manag Nurs* 2011; 12: 118–45.e10.
6. Abou Hammoud H, Simon N, Urien S, Riou B, Lechat P, Aubrun F. Intravenous morphine titration in immediate post-operative pain management: population kinetic-pharmacodynamic and logistic regression analysis. *Pain* 2009; 144: 139–46.
7. Young-McCaughan S, Miaskowski C. Definition of and mechanism for opioid-induced sedation. *Pain Manag Nurs* 2001; 2: 84–97.
8. Gustafsson LL, Schildt B, Jacobsen K. Adverse effects of extradural and intrathecal opiates: report of a nationwide survey in Sweden. *Br J Anaesth* 1982; 54: 479–86.
9. Ruan X, Couch JP, Liu H, Shah RV, Wang F, Chiravuri S. Respiratory failure following delayed intrathecal morphine pump refill: a valuable, but costly lesson. *Pain Physician* 2010; 13: 337–41.
10. American Society of Anesthesiologists Task Force on Neuraxial Opioids, Horlocker TT, Burton AW, Connis RT, Hughes SC, Nickinovich DG, et al. Practice guidelines for the prevention, detection, and management of respiratory depression associated with neuraxial opioid administration. *Anesthesiology* 2009; 110: 218–30.
11. Taylor S, Voytovich AE, Kozol RA. Has the pendulum swung too far in postoperative pain control? *Am J Surg* 2003; 186: 472–5.