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Case Report

Case Report of Intrathecal Morphine Overdose: A Successful Management

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Abstract

Background: This article presents a case of intrathecal morphine overdose resulting from a human error in drug dilution. This study aims to underscore the importance of accurate dilution procedures for preventing such incidents and highlights the need for enhanced safety measures in medical practices.

Case presentation: The patient was a 53-year-old African woman, experienced adverse effects, following the administration of the incorrectly diluted morphine, including nausea, vomiting, and somnolence, Timely intervention with naloxone successfully reversed the overdose, emphasizing its crucial role as an antidote in managing such complications.

Conclusion: This case underscores the importance of precision in drug dilution processes to prevent intrathecal morphine overdose. The successful resolution of the disease with naloxone highlights the importance of swift intervention.

Keywords: Morphine; Overdose; Intrathecal; Naloxone

Introduction

Intrathecal morphine administration has been recognized as an effective method for postoperative pain management since 1979. This administration technique enables morphine to remain in the cerebrospinal fluid for an extended period, owing to its hydrophilic properties. As a result, the analgesic effect can last up to 36 hours. However, it is important to note that this approach carries the risk of potentially delayed respiratory depression [1].

Studies have shown that the incidence of respiratory depression following the intrathecal administration of morphine at doses less than 1 mg varies between 0.5% and 3.0%. Notably, this variance can be partly attributed to the diversity in defining respiratory depression [1].

Occasional instances of intrathecal morphine overdose have been reported, but most of these cases involve patients who have been chronically exposed to these medications and have developed tolerance. However, only a few documented cases in the literature have described the perioperative course of an intrathecal opioid overdose [2].

In our report, we provide a detailed account of the successful management of an intrathecal morphine overdose during spinal anesthesia.

Case presentation

The patient was a 53-year-old African woman with no medical history. Approximately four months ago, the patient noticed a

painless, mobile, and hard mass of approximately 4 cm in her left knee. Recently, she experienced an acute onset of knee locking in semiflexion, restricting both extension and flexion and causing severe pain, redness, and swelling. As a result, she presented to the orthopedic department seeking consultation.

MRI was performed and showed intra-articular tissue formation that initially suggested a tissue hemangioma. Additionally, grade 4 chondropathy was observed in the femoro-patellar compartment.

In view of the MRI findings, a biopsy was indicated and planned to be performed via arthroscopy.

Preanesthetic evaluation: Cardiovascular examination revealed exercise tolerance greater than 4 METs (metabolic equivalents). Her blood pressure was 125/67, her heart rate was 76, and she had no effort angina.

Respiratory examination revealed eupnea, no signs of respiratory distress, normal auscultation, and 99% saturation in ambient air. Neurological examination revealed consciousness, good orientation in time and space, and no sensory-motor deficits. Anesthetic-focused examination revealed the following: good general condition, good venous access, good mouth opening, thyro-mental distance greater than 65 mm, Mallampati grade 1, supple neck, and a positive Allen test. Electrocardiogram revealed a regular sinus rhythm, a left heart axis, and no repolarization or conduction disturbances.

The patient was classified as ASA1, who's clinical and paraclinical examinations were unremarkable.

Patients who were eligible for surgery under spinal anesthesia were eligible for inclusion. The patient was admitted to the operating room and placed on the operating table. Monitoring included ECG, noninvasive blood pressure, and pulse oximetry.

A peripheral intravenous line of 18 gauges was taken. Equipment for spinal anesthesia was prepared, as was the intubation equipment and emergency drugs. Spinal puncture was performed via the midline approach at the L2-L3 interspace with the patient in the sitting position. The patient received 12.5 mg of hyperbaric bupivacaine, 25 µg of fentanyl, and 100 µg of morphine. The patient remained stable during the procedure and conscious, well-oriented, and eupneic, with a respiratory rate of 17 cycles per minute, a blood pressure of 123/67, and a heart rate of 76 bpm.

After surgery, we noticed that an error occurred during the dilution of morphine; instead of the intended 100 µg dose, the patient accidentally received 1000 µg. Clinical examination revealed a conscious patient with no drowsiness, eupnea, a respiratory rate (RR) of 16 cycles/minute, and oxygen saturation (SpO2) of 99% in ambient air who was hemodynamically stable. Due to this error, the patient was admitted to the intensive care unit (ICU) for continuous monitoring. The patient was started on an infusion pump using naloxone at a dose of 0.4 mg/h to counteract the effects of the high dose of morphine. Her level of consciousness and ventilatory mechanics were closely monitored for a duration of 48 hours.

During her stay in the ICU, she experienced controlled episodes of nausea and vomiting after 4 hours, and the patient received metoclopramide, which was associated with a positive outcome and drowsiness after 9 hours. Her FOUR score was 14/16 with her eyelids closed but open to loud voice, (the full outline of unresponsiveness (FOUR) score was used to assess and monitor her level of consciousness). However, the patient was placed under a high-concentration mask as a precautionary measure, and her oxygen saturation level remained stable at 99%, as did her respiratory rate at 16-18 cycles/minute. There was no need for noninvasive ventilation or intubation.

After 48 hours of monitoring and a total dose of naloxone (9.6 mg) for 24 hours, the patient's condition improved, and she was discharged from the ICU. She was subsequently transferred to the orthopedic ward for further management and care.

Discussion

Morphine is a potent opioid used as an analgesic for many years, whether administered orally, intravenously, subcutaneously, epidurally, or intrathecally. Morphine is used for its central analgesic effects; however, it can lead to life-threatening side effects. Excessive doses of morphine can cause nausea and vomiting, urinary retention, respiratory depression, pulmonary edema, hypothermia, high blood pressure, myoclonic seizures, drowsiness, coma, and even death [3,4].

In our patient's case, the accidental intrathecal administration of 1 mg of morphine was due to a single dilution instead of a double dilution of 10 mg/1 ml morphine. The nurse inadvertently diluted the 10 mg/ml morphine in a 10 ml syringe, resulting in a dilution of 1 mg/ml. A second dilution of 1 mg of morphine in a 10 ml syringe was necessary to achieve a dilution of 100 µg/1 ml, but unfortunately, this was not performed. However, the anesthesiologist had to verify the dilution.

The accidental administration of a high dose of morphine has been reported, especially in patients with malfunctioning pumps controlling analgesia, during epidural anesthesia, or during spinal anesthesia [2].

Our patient experienced nausea and vomiting 4 hours after the injection, followed by drowsiness 9 hours later, without any respiratory depression or the need for mechanical ventilation.

A literature review indicated that somnolence and respiratory depression were the most frequently reported symptoms. The onset of somnolence and respiratory depression typically occurs within a range of 2 to 24 hours after injection. The dose of morphine associated with adverse events varied. Doses less than 900 µg of morphine were found to cause respiratory depression, but respiratory depression became life-threatening only when morphine was administered with potentiating medication. Life-threatening adverse events involving doses greater than 1000 µg of morphine were observed [1].

Midazolam [5,6] and lorazepam [7] potentiate the effect of morphine and can be life-threatening. In the literature, one case in which 100 µg of morphine was administered along with 3 mg of intravenous midazolam was reported, where the use of flumazenil resolved respiratory depression [5]. Additionally, another case

involved the administration of 100 µg of morphine along with metoclopramide and granisetron, resulting in Cheyne Stokes respiration that was not attributed solely to morphine, as it was not resolved by naloxone [6,8]. This highlights that the life-threatening effects of morphine are related to its potentiating effects.

Opioids can lead to myoclonic seizures of varying severity depending on the route of administration. Intravenous administration of morphine can induce myoclonus, which can be resolved by naloxone, as demonstrated by Bowdle and Rook. Similarly, myoclonus following intravenous administration of sufentanil can be resolved with a dose of 40 µg of naloxone [9]. However, myoclonus secondary to intrathecal administration does not respond to naloxone. This can be explained by mediation through nonopioid receptors. Scott B Groudine demonstrated that myoclonus following an accidental intrathecal administration of 250 mg of morphine did not respond to naloxone [10].

Sandouk et al. [11] identified morphine-3-glucuronide and morphine-6-glucuronide as metabolites produced in the brain and may be involved in the cerebral toxicity of morphine. Therapeutic management involves antagonizing morphine with naloxone and providing symptomatic treatment for various complications.

However, treatment with relatively low-dose naloxone has been shown to effectively antagonize the adverse effects of morphine while preserving its analgesic effects [12,13]. The analgesic effects of morphine persist, while respiratory depression and somnolence can be reversed by neuraxial administration of naloxone [14]. This phenomenon can be attributed to the highest concentration of morphine being localized around the injection site, specifically the substantia gelatinosa in the lumbar region [15]. Therefore, a higher concentration of naloxone may be required to counteract this localized effect than a lower concentration of morphine in the respiratory center. Based on these differential effects, one approach could be the routine administration of continuous naloxone to prevent respiratory depression while maintaining analgesia [16,17]. However, further research is needed to explore the optimal dose, effectiveness and potential side effects of this strategy.

Naloxone should be administered early, as soon as the overdose is discovered and before symptoms appear, and should be administered continuously via the infusion pump at small doses, avoiding the need for a loading dose to prevent the adverse effects of naloxone resulting from a rapid increase in sympathetic tone, such as potentially life-threatening hypertension that can lead to hemorrhagic strokes, pulmonary edema, cardiac rhythm disturbances, and re-emergence of pain [18].

In our patient, naloxone was started at the infusion pump at a dose of 0.4 mg/h 3 hours after the intrathecal administration of morphine, which likely mitigated the adverse effects of morphine overdose and the detrimental effects of a high dose of naloxone.

Opioid-induced respiratory depression can lead to hypoxemia, which is characterized by decreased alveolar pO2 due to hypercapnia, as explained by Dalton's law. Hypoxemia can be reversed by a small increase in FiO2, if there is no increase in the Alveolo-arterial gradient. To prevent the hypoxic effects of respiratory depression, we recommend routinely administering 3 L/min of supplemental oxygen following the use of intrathecal morphine. Additionally, clinicians should investigate and treat the underlying cause of respiratory depression and hypoxemia if present [1].

Our patient was placed on 5 L/min of oxygen and did not experience respiratory depression, with an oxygen saturation level of 99%. Finally, in the case of a massive dose of intrathecal morphine, it is possible to consider drainage of cerebrospinal fluid (CSF) through aspiration or irrigation to eliminate the morphine [10]. and replacement of CSF by saline [19], which helps improve respiratory depression and prevents the direct neurotoxicity of morphine, which is responsible for myoclonus that does not respond to naloxone [3].

Table 1: Summary of the discussion and comparisons between the different case reports.

Author	Morphine dose	Indication	Morphine overdose immediate treatment	Complications			Evolution
				type	Installation time	treatment	
I. Hmadate	1000 ug	Spinal anesthesia	Naloxone: 0,4 mg/h	-Nausea and vomiting	4 hours	-Metoclopramide	Favorable
			Total dose: 9,6 mg/24 h	-Drowsiness			
					9 hours	-Naloxone	
A. Borgeat 20	3 mg	Analgesia: extradural catheter	-	Generalized tonico-clonic seizure with loss of consciousness	6 hours	Phenobarbital	-
Scott. B10	250 mg	continuous intrathecal pump analgesia	-Naloxone: 100 µg/h	-Myoclonic activity	90 min	-Thiopental	Favorable
			-Drainage of cerebrospinal fluid: C1-C2 interspace catheter with infusion of 900 ml of warmed Ringer Lactate and lumbar drainage through 2 lumbar needles of cerebrospinal fluid	-Agitation, Dyspnea		-Intubation	
				-High blood pressure		-Labetalol, hydralazine, stop Naloxone infusion	

M.cannesson2	25 mg	Spinal-epidural block	Naloxone: 80 µg/h after a loading dose of 0,4 mg	-Somnolence	3 hours	-Naloxone 200 µg/h,	
				-Bradypnea (Respiratory rate =8cycles per minute)		-Metoclopramide	Favorable
				-Nausea	24 hours		
Kent Sauter21	450 mg	Analgesia: intraspinal catheter with subcutaneous infusion device	-Naloxone: 8 mg	-Hyperventilation	-	-Intubation	Favorable
			-Naloxone: 20 mg/h for 20 hours and then 15 mg/h for another 20 hours (Total dose 884 mg in 4 days)	-Hypertension		-Nitroprusside	
			-Drainage of cerebrospinal fluid: 12 ml immediately then 10 ml/h (Total 560 ml in 2 days)	-Myoclonic seizure		-Phenytoin, Phenobarbital	
				-Frontal parenchymal and subarachnoid hemorrhage			
H. Dworzak 5	0,1 mg +3 mg of midazolam	Intrathecal analgesia	Naloxone: >6 mg	-Severe respiratory depression	3,5 hours	Flumazenil	Favorable
				-Somnolence			

Conclusion

In conclusion, this study sheds light on the potential risks associated with human errors in morphine dilution, which can lead to an intrathecal overdose and adverse effects such as nausea, vomiting, and somnolence. The successful reversal of the overdose with naloxone underscores its crucial role as an antidote in such situations [20,21]. Moving forward, implementing stringent quality control measures, standardized dilution protocols, and enhanced training for healthcare professionals are essential steps to prevent similar incidents. Heightened awareness and continuous education can contribute to a safer healthcare environment, minimize the occurrence of medication-related errors and improve patient outcomes.

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Conflict of Interest

No conflict of interest.

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