Too Much Medication, Too Little Monitoring

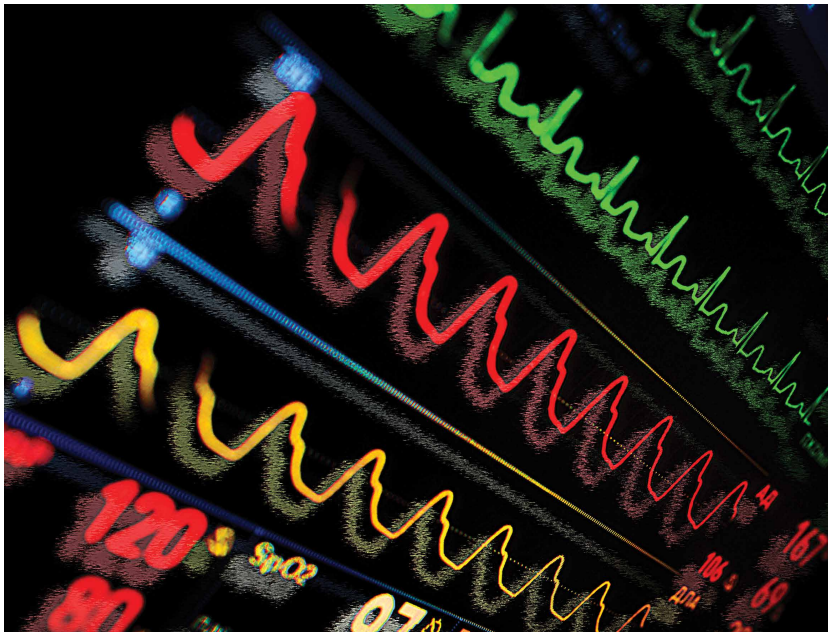
A 58-year-old man presented to the ED via emergency medical services (EMS) for evaluation of severe low-back pain. The patient said the pain started abruptly, approximately 1 hour earlier when he was picking up a 50-lb television set. He stated that the pain was so severe that he was unable to move and was forced to lie down on the floor. Although the patient noted that he had a history of a "bad back," he said he never required surgery and never experienced an episode this severe. The patient denied any radiation of pain or lower extremity numbness or weakness. He denied any chest pain or abdominal pain. His medical history was significant for obstructive sleep apnea and hypertension for which he was taking hydrochlorothiazide. Regarding his social history, he denied any tobacco or alcohol use.

Upon presentation, the patient was found to be in extreme discomfort, rating his pain as an "11" on a scale of 0 to 10. His vital signs were heart rate (HR), 110 beats/minute; blood pressure (BP), 154/91 mm Hg; respiratory rate, 20 breaths/minute; and temperature, 98.6°F. Oxygen (O_2) saturation was 98% on room air.

When the emergency physician (EP) entered the examination room, the patient was in bed, resting on his side and moaning from the pain. The head, eyes, ears, nose, and throat, cardiac, and lung examinations were all normal. The patient's abdomen was soft and nontender and without guarding, rebound, or palpable mass. When the EP examined the patient's back, there was no midline tenderness over the thoracic and lumbar spine. The patient did, however, exhibit bilateral paraspinal lumbar muscle tenderness to palpation and muscle spasm. After much prompting, he demonstrated 5/5 motor strength in his lower extremities bilaterally. The dorsalis pedis and posterior tibial pulses were 2+ and symmetrical.

To treat the patient's severe pain, the EP had a saline lock placed and ordered intravenous (IV) hydromorphone 1 mg, ondansetron 4 mg, and diazepam 5 mg. No laboratory or imaging studies were ordered. Ninety minutes after receiving the analgesics, the patient continued to complain of severe pain without any improvement, and the EP ordered another two rounds of IV hydromorphone 1 mg and diazepam 5 mg. The EP did not return to check up on the patient, but rather relied solely on updates from the patient's nurse.

Despite the additional doses of hydromorphone and diazepam, the patient continued to complain of severe pain, and the EP ordered IV hydromorphone 2 mg and diazepam 10 mg. Shortly after the patient received this third round of analgesics, his wife arrived at the ED asking to see her husband. When she entered his room, the patient was unresponsive. A code was called and the patient was found to be in asystole. Despite aggressive resuscitative efforts that included intubation, cardiopulmonary resuscitation, and advanced cardiac life support medications, the patient did not recover.



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The patient's wife sued the EP, the ED nurse, and the hospital for failure to appropriately monitor her husband while he received multiple doses of analgesic and sedative agents. The plaintiff argued that the patient's death was caused by a cardiac arrest occurring secondary to a respiratory arrest, and that the respiratory arrest was secondary to the medications he was given in the

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ED. The defendants denied the allegations. A $2 million settlement was reached prior to trial.

Discussion

This was clearly a preventable death. Emergency physicians treat pain daily and should be knowledgeable about and experienced in managing acute pain. When evaluating and treating a patient's pain, the EP must select the appropriate medication. Though we often talk about a tiered approach to pain in the ED, most of us would agree that opioids, usually via IV, are the first choice for managing severe pain.

In addition to prescribing the appropriate analgesics, the EP must identify which patients are at risk of opioid complications. This patient was at risk for opioid-induced respiratory depression based on his age (ie, >55 years old) and history of obstructive sleep apnea. These two risk factors, along with pre-existing chronic obstructive pulmonary disease, anatomic oral or airway abnormalities, and comorbidities (eg, renal or hepatic impairment), place patients at high risk for opioid-associated complications.[1] Patients with any of these conditions must be closely monitored and, based on their response to the prescribed analgesia, the EP may need to decrease the analgesic dosage and increase dosage intervals. In addition to close monitoring, reversal agents such as naloxone should be readily available in case of respiratory depression.

The problem in this case was not the selection of hydromorphone as the initial analgesic agent. Hydromorphone is frequently used safely in the ED to treat severe pain associated with conditions such as sickle cell vaso-occlusive pain crisis, renal colic, and long-bone fracture. Issues arise when hydromorphone is combined with a benzodiazepine (in this case, diazepam), which by itself causes sedation and anxiolysis. Central nervous system (CNS) depression may be additive and occur when benzodiazepines are used concomitantly with drugs that also cause CNS depression (eg, opioids).[1] This combination can lead to excessive sedation, resulting in partial airway obstruction and hypoxia.[1] For example, in an investigation by Bailey et al,[2] in human volunteers, neither hypoxemia nor apnea was evident after administration of .05 mg/kg of IV midazolam. In patients who received 2 mcg/kg of IV fentanyl alone, hypoxemia occurred in 50%, but apnea did not occur in any of the patients studied. However, when the same doses of these drugs were administered together, 92% of participants exhibited hypoxemia and 50% became apneic.[2]

When a combination of an opioid and benzodiazepine are given over frequent intervals, the clinician crosses over from treating pain to performing procedural sedation and analgesia—whether he intended to or not. As such, the patient in this case required proper monitoring, including cardiac monitoring and pulse oximetry; he also should have been placed on supplemental O_2. Ideally, the patient would have benefited from end-tidal carbon dioxide ($ETCO_2$), monitoring, if available. This is a noninvasive measurement of the partial pressure of CO_2 in exhaled breath. Hypoventilation from respiratory depression results in an increase in $ETCO_2$, and hyperventilation results in a decreased $ETCO_2$. While pulse oximetry is excellent at monitoring O_2 saturation, it is ineffective in the early detection of respiratory depression, hypoventilation, and apnea. The hypercarbia precedes the hypoxemia—by as much as 60 seconds (range 5-240 seconds), according to a study by Deitch et al.[3]

Finally, rather than relying solely on the reports from the nurse, the EP should have personally reassessed the patient at some point. Nursing updates are extremely helpful, but when ordering repeated doses of IV opioids and benzodiazepines, the EP should personally reassess the patient.

References

1. Jarzyna D, Jungquist CR, Pasero C, et al. American Society for Pain Management Nursing guidelines on monitoring for opioid induced sedation and respiratory depression. *Pain Manag Nurs.* 2011;12(3):118-145.e10.
2. Bailey PL, Pace NL, Ashburn MA, Moll JW, East KA, Stanley TH. Frequent hypoxemia and apnea after sedation with midazolam and fentanyl. *Anesthesia.* 1990;73(5):826-830.
3. Deitch K, Miner J, Chudnofsky CR, Dominici P, Latta D. Does end-tidal CO2 monitoring during emergency department procedural sedation and analgesia with propofol decrease the incidence of hypoxic events? A randomized, controlled trial. *Ann Emerg Med.* 2010;55(3):258-264.

Hot Red Knee

A 64-year-old man presented to the ED with a chief complaint of right knee pain, which he stated began approximately 2 days earlier. He denied any injury or trauma or a recent history of fever, chills, or other joint complaints. He described the pain as constant, worse with weight bearing, and becoming progressively more painful. The patient had a history of gout; however, previous attacks had only affected his great toes and elbows. His medical history was also significant for hypertension, for which he was taking lisinopril and hydrochlorothiazide. He admitted to moderate

alcohol consumption but denied tobacco use.

On physical examination, the patient appeared uncomfortable due to the knee pain. All of his vital signs were normal. A focused examination of the affected knee revealed a small effusion, diffuse tenderness to palpation, mild erythema, and slight increased warmth. The patient exhibited pain with flexion and extension of the right knee. The right ankle examination and right dorsalis pedis pulse and posterior tibial pulse were all normal. No laboratory or imaging studies were obtained.

Based on the patient's history and physical examination, the EP believed the patient's symptoms were due to an episode of gout. He prescribed oral colchicine, allopurinol, and acetaminophen/hydrocodone; he also advised the patient to apply warm compresses to the affected area and limit his activity. He discharged the patient home with instructions to follow up with his primary care physician.

Two days after discharge, the patient returned to the same ED via EMS. On this presentation, he was febrile, with a temperature of 102.6°F; a HR of 120 beats/minute; and a BP of 92/50 mm Hg. He also had altered mental status. The patient's right knee appeared more swollen, and he would not flex it due to the severe pain. The EP was concerned for sepsis, and ordered blood cultures, a complete blood count, basic metabolic profile, and lactic acid evaluation. The patient was administered 2 L normal saline IV and broad-spectrum antibiotics. Despite the addition of vasopressors, he continued to deteriorate; he ultimately went into cardiac arrest and died.

The patient's family sued the EP from the initial ED visit for failure to diagnose the right knee pain and swelling as septic arthritis (SA). The plaintiff's attorney argued that this failure to diagnosis directly caused the patient's sepsis and death. The EP argued that the patient's history and physical examination were consistent with an acute gout attack, that there was no evidence of infection in the right knee, and that this was not the cause of the patient's death. At trial, the jury returned a verdict in favor of the defense.

Discussion

Gout is caused by the precipitation of uric acid crystals into a joint. Attacks are usually monoarticular as opposed to polyarticular. The presence of hyperuricemia is variable; some patients have high serum uric acid levels and never experience gout, while other patients have normal serum uric acid levels and experience gout attacks. The condition is more common in men than in women. There are multiple risk factors for the development of gout, including obesity, hypertension, chronic kidney disease, regular excessive consumption of alcohol, taking diuretics, and consuming foods high in fructose corn syrup.[1] The joints most often affected are the great toe and knee. Patients with gout typically complain of pain, swelling, redness, and increased warmth in the affected area.

Unfortunately, the clinical presentation of an acute gout attack and SA are indistinguishable.[2] Risk factors for SA include IV drug abuse, diabetes mellitus, having a prosthetic joint, immunosuppression, and human immunodeficiency virus infection. The only reliable way to distinguish between gout and SA requires arthrocentesis with microscopic examination of the synovial fluid for bacteria, crystals, white blood cell (WBC) count, and culture.[2]

It is critical not to miss SA because it is associated with significant morbidity and a mortality rate of 11%.[2] To further complicate the diagnosis, some patients can experience SA in the setting of an acute gout attack. In a study of all joint aspirations with crystals (both uric acid and calcium pyrophosphate), there was a 5.2% incidence of concomitant infection.[2] Similarly, in patients with confirmed SA, crystals were present 21% of the time.[2]

A gram stain of the synovial fluid is highly specific, but only positive in 59% of cases of SA. Therefore, a negative gram stain does not exclude the diagnosis. Similarly, the presence of crystals does not exclude a coexisting joint infection. If there is high clinical suspicion for SA or an elevated synovial WBC, the patient should be presumed to have SA and treated as such until cultures prove otherwise.

It is unclear if this patient had SA. However, an EP is taking a risk in diagnosing an acute gout attack based solely on a patient's history and physical examination. The EP should always be mindful that gout and SA can present with the identical signs and symptoms, and can present concomitantly.

References

1. Becker MA. Gout (beyond the basics). UpToDate.com. Available at http://www.uptodate.com/contents/gout-beyond-the-basics. Updated January 21, 2016. Accessed April 12, 2016.
2. Papanicolas LE, Hakendorf P, Gordon DL. Concomitant septic arthritis in crystal monoarthritis. *J Rheumotal.* 2012;39(1):157-160.