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Case Report

Meperidine-Induced Reversible Retrograde Amnesia

Ozlem Guneysel, MD; Ozge Onur, MD; Serkan Eroglu, MD; and Arzu Denizbasi, MD

Department of Emergency Medicine, Marmara University School of Medicine, Istanbul, Turkey

ABSTRACT

INTRODUCTION: Meperidine is a synthetic opioid analog that is frequently prescribed for acute pain management. Normeperidine, the only active metabolite of meperidine, is neurotoxic and can cause significant central nervous system adverse events.

CASE SUMMARY: A 29-year-old woman (height, 170 cm; weight, 85 kg) presented to Marmara University Hospital Emergency Department, Istanbul, Turkey, complaining of low back pain she described as "stabbing." Physical examination revealed impaired lower-extremity mobility and normal vital-sign findings. There was no evidence of foot drop, head or other trauma, and systemic physical examination was unremarkable. Other common causes (eg, pyelonephritis, nephrolithiasis, pancreatitis, trauma) of lower back pain were excluded. To achieve analgesia, meperidine 80 mg was administered intravenously in 100 mL of isotonic saline solution for 20 minutes. Within 20 minutes, analgesia was achieved, but the patient developed retrograde amnesia, becoming disoriented to time, location, and persons. Her speech slowed and perceptional changes developed. After the onset of amnesia, a complete physical examination was conducted. It failed to reveal focal neurologic deficit, and laboratory (sodium, potassium, magnesium, phosphorus, serum creatinine, blood urea nitrogen, albumin, bilirubin, hemoglobin, and platelet count) and subsequent vital-sign findings (blood pressure, 150/100 mm Hg; heart rate, 100 beats per minute; respiratory rate, 18 breaths per minute; body temperature, 37°C; and pulse oximetry, 99%) were within the normal range. Noncontrast computed tomography did not reveal any abnormality. Initially, the patient's condition was attributed to medication error due to incorrect dosage or infusion rate. Despite a review of medication logs, equipment, and the vital-sign record, the etiology for the phenomenon could not be identified. Meperidine was discontinued and oxygen and intravenous isotonic saline solution were initiated as supportive treatment. Three hours after meperidine administration was discontinued, the amnesia and disorientation spontaneously resolved.

CONCLUSION: Meperidine was probably associated with reversible amnesia in this healthy patient after a single therapeutic dose. (*Curr Ther Res Clin Exp.* 2008;69: 159–163) © 2008 Excerpta Medica Inc.

KEY WORDS: meperidine, amnesia, opioid analgesic, central nervous system toxicity.

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INTRODUCTION

Meperidine is a synthetic opioid analog that is frequently prescribed for acute pain management. Its narcotic analgesic effects are qualitatively similar to those of morphine. The most prominent of these involve the central nervous system and organs composed of smooth muscle.[1] The principal actions of therapeutic value are analgesia and sedation.[1] Compared with morphine, meperidine has a reported slightly faster onset of action (10–60 vs 20–60 minutes), a shorter duration of action (2.5–3.5 vs 4–5 hours), and shorter $t_{1/2}$ (2.5–4 vs 4–5 hours).[2] However, meperidine has the narrowest therapeutic index of all the opioids.[2] Acting predominantly as a μ-receptor agonist, meperidine produces its analgesic effects similar to that of morphine. In addition, meperidine has many of the same adverse events (AEs) as morphine, including respiratory depression, sedation, and constipation.[2] Meperidine is most often administered parenterally. It is metabolized by the liver into 2 metabolites: meperidinic acid (inactive) and normeperidine (active), which are excreted renally.[3]

Meperidine has been reported to be associated with neurotoxicity, a potentially severe AE that is due to the accumulation of the metabolite normeperidine.[4] It is difficult to predict which individuals will experience neurotoxic effects and how severe the reaction will be.[4] Normeperidine-mediated neurotoxicities (eg, nervousness, agitation, hyperreflexia, myoclonus, tremors, seizures, delirium, hallucinations, reversible parkinsonism)[5] are more likely to occur with higher doses, extended treatment,[6] or renal impairment. However, some of these symptoms can occur in healthy patients after a single dose.[7]

Retrograde amnesia is defined as a clinical condition in which an individual is unable to recall events that occurred prior to the onset of memory loss.[8] In its pure form, it typically results from injury to regions of the brain that are closely associated with episodic and/or declarative memory. Amnesia has several root causes, most of which are traceable to brain injury related to physical trauma, disease, infection, drug or alcohol abuse, or reduced blood flow to the brain (vascular insufficiency).[8]

The aim of this article was to report a case of reversible retrograde amnesia in a healthy patient who was administered IV meperidine for low back pain.

CASE SUMMARY

A 29-year-old woman (height, 170 cm; weight, 85 kg) presented to Marmara University Hospital's Emergency Department, Istanbul, Turkey, complaining of low back pain she described as "stabbing." Physical examination revealed impaired lower extremity mobility and normal vital-sign findings (blood pressure, 130/85 mm Hg; heart rate, 90 beats per minute (bpm); respiratory rate, 18 breaths per minute; body temperature 37.2°C; and pulse oximetry [SpO_2], 99 mm Hg). There was no evidence of foot drop, head or other trauma, and systemic physical examination was unremarkable. Other common causes (eg, pyelonephritis, nephrolithiasis, pancreatitis, trauma) of lower back pain were excluded.

Muscle spasm was identified in the lumbar region. The patient's medical history revealed a lumbar disc hernia that had been diagnosed 2 years prior and medical treatment was recommended. The patient's family medical history was unremarkable, and she was not receiving any medication. According to the patient, she had no known allergies and had not ingested any alcohol.

To achieve analgesia at a fast onset of action, meperidine (Pethidine®, Antigen Pharmaceuticals Ltd., Tipperary, Ireland) 80 mg was administered intravenously in 100 mL of isotonic saline solution for 20 minutes. Within 20 minutes, analgesia was achieved, but the patient developed retrograde amnesia, becoming disoriented to time, location, and persons. Her speech slowed and perceptional changes developed. She did not know the date, her location, or why she was present, nor could she identify her husband. Although we did not test the patient's memory prior to the administration of meperidine, she had been responding well in terms of answering questions and speaking coherently. After the onset of amnesia, a complete physical examination was conducted. The subsequent physical examination failed to reveal focal neurologic deficit, and laboratory (sodium, potassium, magnesium, phosphorus, serum creatinine, blood urea nitrogen, albumin, bilirubin, hemoglobin, and platelet count) and subsequent vital-sign findings (blood pressure, 150/100 mm Hg; heart rate, 100 bpm; respiratory rate, 18 breaths per minute; body temperature, 37°C; and SpO_2, 99%) were within the normal range. Noncontrast computed tomography did not reveal any abnormality.

Initially, her condition was attributed to medication error due to incorrect dosage or infusion rate. Medication logs were confirmed, equipment rechecked, and the vital-sign record was reviewed. However, the etiology for the phenomenon could not be identified. The patient was questioned again regarding use of medications, including opiates and herbal products; all were denied. The patient's responses were confirmed by her husband.

Meperidine was discontinued and oxygen and intravenous isotonic saline solution were initiated as supportive treatment. A neurologic consultation was performed, and the neurologist recommended monitoring the patient in the emergency department. Three hours after meperidine administration was discontinued, amnesia and disorientation spontaneously resolved. The patient's condition was therefore attributed to meperidine. The patient was observed for >4 hours and was then discharged.

DISCUSSION

According to the World Health Organization[9] an *adverse drug reaction* is "a noxious, unintended response to a drug that occurs at doses normally used in humans for prophylaxis, diagnosis, or therapy or for modification of physiologic function."[9]

Our patient developed retrograde amnesia after meperidine administration. The duration of amnesia (3 hours) and the half-life of meperidine (2.5–4 hours) were consistent. Normeperidine is primarily eliminated renally, and the half-life (15–30 hours) is 5 to 10 times longer than that of meperidine, depending on renal function. We could not identify any other explanation for amnesia in our patient. Risks for neurotoxicity include high, frequent doses (>150 mg TID or QID),[10] coadministration of agents that may induce seizures or lower the seizure threshold, and renal dysfunction.[1] In our patient, there was no reported use of other medications and all hepatic and renal functions were within the normal range.

Meperidine is not recommended as a first-line opioid analgesic.[5,6,11] The drug is lipophilic, and it has a more rapid onset and shorter duration of analgesia (usually 2.5–3.5 hours) than other short-acting opioids. This feature might be overlooked when

it is prescribed at a 4- to 6-hour dosing interval, which results in uncontrolled pain before the next dose is due.[5,11] Meperidine is believed to be effective in the management of pain due to pancreatitis, biliary and renal colic, back injury, and migraine. No studies have found that meperidine is more effective than morphine.[12]

To identify instances of AEs associated with meperidine, we performed a literature search in MEDLINE for relevant English-language publications from 1990 to June 2007 using key terms *meperidine*, *amnesia*, *opioid analgesic*, and *central nervous system toxicity*. We did not identify any reports of AEs associated with meperidine and amnesia. We also reviewed the US Food and Drug Administration's (FDA) prescribing information and the FDA's Adverse Event Reporting System[1] from January 1990 through June 2007. We also contacted the company that distributes meperidine (Filiz Ilac, Ltd., Ankara, Turkey). They indicated that they were not aware of any evidence suggesting an association between meperidine and amnesia. The incident was reported to the Turkish Ministry of Health[13] (Ankara, Turkey).

The Naranjo Adverse Drug Reaction probability scale[14] was used as an objective measure of causality. A score of 6 indicated that meperidine was the probable cause of amnesia in this patient.

CONCLUSION

Meperidine was probably associated with reversible retrograde amnesia in this healthy patient after a single therapeutic dose.

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ADDRESS CORRESPONDENCE TO: Ozlem Guneysel, MD, Department of Emergency Medicine, Marmara University Hospital, Tophanelioglu C Yurtacan S No 13/15 Altunizade, 81190 Istanbul, Turkey. E-mail: guneysel@gmail.com