Methadone-Induced Strabismus and Loss of Consciousness in a First-Time User: A Rare Case Report

Amin Karimzadeh Kiskani[1], Masoomeh Varzandeh[2], Aryan Mohamadi Nezhad[2], Samaneh Jahangiri[2], Mana Khazaeli[1], Reza Ghaderi[2], and Sara Shafieipour[1]

[1]Kerman University of Medical Sciences
[2]Kerman University of Medical Sciences Faculty of Medicine

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Introduction

Methadone, a synthetic opioid agonist, has been widely used for the treatment of opioid dependence and chronic pain management for several decades (1). Methadone maintenance treatment (MMT) has proven to be an effective strategy in reducing illicit opioid use, improving patient outcomes, and decreasing the risk of HIV transmission among individuals with opioid use disorders (2). However, despite its therapeutic benefits, methadone can cause significant adverse effects, particularly in opioid-naive individuals or those who consume it recreationally (3).

Methadone overdose can lead to severe respiratory depression, cardiac arrhythmias, and death (4). The risk of overdose is particularly high in individuals who are not tolerant to opioids, as they may be more sensitive to the drug's effects (5). In addition to its well-known respiratory and cardiovascular side effects, methadone can also cause rare neurological and ocular manifestations, such as strabismus (6).

Strabismus, a misalignment of the eyes, can occur due to various etiologies, including congenital factors, nerve palsies, and pharmacological agents (7). Opioid-induced strabismus is an uncommon but documented consequence of opioid toxicity, with most cases reported in the context of heroin use (8). The exact mechanism underlying opioid-induced strabismus remains unclear, but it is thought to involve the drug's effects on the central nervous system and the oculomotor nerve (9).

In this case report, we present a rare instance of methadone-induced loss of consciousness and subsequent strabismus in a patient who consumed methadone for the first time. This case underscores the importance of recognizing the potential dangers associated with methadone use, especially in opioid-naive individuals, and the need for healthcare providers to be aware of the uncommon ocular manifestations of opioid toxicity. Prompt identification and appropriate management of methadone overdose and its associated complications can prevent long-term morbidity and mortality (10).

Case report

A 21-year-old female with no significant past medical history was brought to the emergency department of a tertiary hospital by her brother due to altered mental status. The brother reported that the patient had consumed 5 methadone pills prior to becoming unconscious. He denied any history of methadone use, alcohol abuse, or other substance abuse. The patient had no known medication allergies, and her medication history was unremarkable.

Upon arrival to the emergency department, the patient was unconscious and unresponsive to verbal or painful stimuli. Her vital signs were as follows: blood pressure 90/60 mmHg, pulse rate 60 beats per minute, oxygen saturation 90% on room air, respiratory rate 12 breaths per minute, and a corrected axillary body

temperature of 37.2°C. The patient was immediately placed on supplemental oxygen via a non-rebreather mask at 10 L/min.

Physical examination revealed an ill-appearing young female without signs of toxicity, cyanosis, or respiratory distress. Her skin was warm and dry, with no evidence of needle tracks or other signs of intravenous drug use. The patient's head was normocephalic and atraumatic, with no signs of external injury. Her pupils were equal, round, and pinpoint, measuring 1 mm in diameter, but they were reactive to light. The patient's oral mucosa was moist, and her dentition was intact. No signs of oral trauma or foreign bodies were observed.

Chest examination revealed a symmetrical chest wall with no deformities or signs of trauma. The patient's lungs were clear to auscultation bilaterally, with no wheezes, crackles, or rhonchi. There were no signs of accessory muscle use or increased work of breathing. Cardiac examination revealed a regular rate and rhythm, with no murmurs, gallops, or rubs. The patient's abdomen was soft, non-distended, and non-tender, with no organomegaly or palpable masses. Bowel sounds were present and normal in all quadrants.

Neurological examination showed the patient to be unresponsive to verbal or painful stimuli, with a Glasgow Coma Scale score of 3 (E1, V1, M1). Her muscle tone was flaccid, and deep tendon reflexes were diminished throughout. No signs of focal neurological deficits or meningeal irritation were observed.

The patient's extremities were warm and well-perfused, with no signs of cyanosis, edema, or trauma. Capillary refill time was less than 2 seconds in all extremities.

Based on the patient's clinical presentation and the reported history of methadone ingestion, a preliminary diagnosis of methadone toxicity was established. Initial management included the administration of intravenous naloxone, an opioid receptor antagonist, until the patient regained consciousness. Upon awakening, the patient was immediately commenced on intravenous fluid resuscitation, and naloxone was administered intravenously at a dose of 0.4 mg to reverse the effects of methadone toxicity. The patient's airway was secured with endotracheal intubation due to her decreased level of consciousness and risk of aspiration.

Blood samples were collected for a comprehensive metabolic panel, complete blood count, arterial blood gas and toxicology screening. The patient was then admitted to the intensive care unit for close monitoring and further management of the methadone poisoning. The laboratory results are summarized in table 1.

Table 1. Summarized laboratory results.

Laboratory exam	Result	Unit
Complete Blood Count (CBC)		
White blood cell	9.5	x 10^3/µL (cells/microliter)
Hemoglobin	14.4	g/dL (grams/deciliter)
Platelets	230	x 10^3/µL (cells/microliter)
Coagulation Profile		
Prothrombin Time (PT)	12.2	seconds
Partial Thromboplastin Time (PTT)	24	seconds
International Normalized Ratio (INR)	1	unitless ratio
Blood Chemistry		
Blood Sugar (BS)	150	mg/dL (milligrams/deciliter)
Blood Urea Nitrogen (BUN)	23	mg/dL
Serum Creatinine	0.9	mg/dL
Aspartate Aminotransferase (AST)	21	U/L (units/liter)
Alanine Aminotransferase (ALT)	10	U/L
Alkaline Phosphatase (ALP)	167	U/L
Total Bilirubin (Bili T)	1	mg/dL
Direct Bilirubin (Bili D)	0.3	mg/dL
Creatine Phosphokinase (CPK)	112	U/L

Laboratory exam	Result	Unit
Sodium (Na)	143	mEq/L (milliequivalents/L)
Potassium (K)	4.2	mEq/L
Arterial Blood Gas (ABG)		
pH	7.36	unitless
Partial Pressure of Carbon Dioxide (PCO_2)	60.4	mmHg (millimeters of mercury)
Bicarbonate (HCO_3)	33.6	mEq/L
Partial Pressure of Oxygen (PO_2)	76.1	mmHg
Base Excess (BE)	8.2	mEq/L
Toxicology		
Methadone	Positive	ng/mL
Morphine	Negative	ng/mL
Fentanyl	Negative	ng/mL
Benzodiazepines	Negative	ng/mL
Amphetamine	Negative	ng/mL
Methamphetamine	Negative	ng/mL
Ethanol	Negative	mg/dL
Barbiturates	Negative	ng/mL
Tricyclic Antidepressants (TCA)	Negative	ng/mL

Twelve hours following admission, the patient reported a new onset of diplopia. Upon examination, a notable divergence of the right eye was observed, with the left iris deviating towards the temporal canthus, indicative of lateral strabismus (Figure 1).

Considering this neurological finding, a comprehensive neurological consultation was promptly requested to further assess the patient's condition.

As part of the neurological evaluation, a non-contrast computed tomography (CT) scan of the brain was ordered to rule out any intracranial pathology that could potentially be contributing to the patient's strabismus. The CT scan would provide valuable information regarding the structural integrity of the brain, including any evidence of methadone-induced neurotoxicity, cerebral edema, or other abnormalities that may have developed secondary to the methadone overdose.

Upon further evaluation of the patient's neurological status, a comprehensive eye examination was performed to assess the extent and nature of the strabismus and to rule out any other ocular abnormalities related to the methadone poisoning. The patient's visual acuity was measured at 20/25 in the right eye (OD) and 20/30 in the left eye (OS). The pupillary examination revealed pupils that were equal in size and reactive to light bilaterally, with no evidence of a relative afferent pupillary defect (RAPD).

Extraocular motility testing demonstrated a full range of motion in all directions of gaze in the left eye. However, the right eye exhibited a restricted adduction, with a full range of motion in all other directions. A 30-prism diopter right exotropia was noted in primary gaze, consistent with the patient's reported symptom of diplopia. Confrontation visual fields were full to finger counting in all quadrants bilaterally.

Slit-lamp examination of the anterior segment was unremarkable, with normal lids, lashes, conjunctiva,

sclera, cornea, anterior chamber, iris, and lens in both eyes. Intraocular pressure was measured at 14 mmHg in the right eye and 15 mmHg in the left eye, both within normal limits.

A dilated fundus examination was performed to assess the posterior segment of the eye. The vitreous was clear bilaterally, and the optic nerves appeared normal with sharp margins and no signs of edema. The cup-to-disc ratio was 0.3 in both eyes. The macula exhibited a normal foveal reflex without any signs of edema, and the vasculature was of normal caliber with no evidence of occlusion or hemorrhage. The peripheral retina was flat and intact in both eyes.

The comprehensive eye examination confirmed the presence of a significant left exotropia, measuring 30 prism diopters, which was consistent with the patient's reported diplopia. The restricted adduction in the left eye further supported the diagnosis of lateral strabismus.

The emergence of strabismus in the context of methadone poisoning is a relatively uncommon neurological manifestation. However, it is crucial to thoroughly investigate any neurological signs or symptoms in patients presenting with opioid toxicity, as they may be indicative of more severe central nervous system dysfunction. By promptly recognizing and evaluating the patient's strabismus, the medical team aimed to identify any underlying neurological complications and provide appropriate management to prevent further deterioration and ensure the best possible outcome for the patient.

The patient's methadone toxicity was managed with intravenous naloxone and supportive care, including mechanical ventilation. The patient's altered mental status and respiratory depression resolved with treatment on hospital day 3.

The patient's strabismus was managed conservatively with observation and serial ophthalmological examinations. Over the course of her hospital stay, the right exotropia gradually improved, with a residual deviation of 10 prism diopters at the time of discharge on hospital day 7. The patient was advised to follow up with ophthalmology as an outpatient for further monitoring and management of her residual strabismus.

Discussion

Methadone, a long-acting synthetic opioid agonist, is widely used in the management of opioid dependence and chronic pain (3). While methadone has proven to be an effective treatment option, it is associated with a range of adverse effects, particularly in individuals who are opioid-naive or have a low tolerance to opioids (5). Methadone toxicity can manifest as respiratory depression, cardiac arrhythmias, and, in rare cases, neurological complications such as strabismus (4). The case presented here highlights a rare instance of methadone-induced strabismus and loss of consciousness in a first-time user. The patient, a 21-year-old female with no prior history of opioid use, consumed 5 methadone pills and subsequently developed altered mental status and respiratory depression. Upon regaining consciousness following naloxone administration, the patient reported diplopia and was found to have a significant right exotropia, consistent with lateral strabismus. The exact mechanism underlying methadone-induced strabismus remains unclear, but it is thought to involve the drug's effects on the central nervous system and the oculomotor nerve (9). Methadone, like other opioids, binds to and activates mu-opioid receptors in the brain, leading to a range of pharmacological effects, including analgesia, sedation, and respiratory depression (11, 12). In the case of strabismus, it is hypothesized that methadone may exert a direct effect on the oculomotor nerve or its nuclei, resulting in a disruption of the normal balance of extraocular muscle tone and alignment (7, 13).

The development of strabismus in the context of methadone toxicity warrants a thorough neurological evaluation to rule out any underlying intracranial pathology or neurotoxicity (10). In the present case, a non-contrast CT scan of the brain was performed, which did not reveal any significant abnormalities. However, it is important to note that the absence of radiographic findings does not preclude the presence of methadone-induced neurotoxicity, as subtle changes may not be detectable on imaging (10, 14).

The management of methadone-induced strabismus primarily involves the treatment of the underlying opioid toxicity. Naloxone, an opioid receptor antagonist, is the mainstay of treatment for methadone overdose (6). In this case, the patient's altered mental status and respiratory depression were successfully reversed with the

administration of naloxone. Supportive care, including intravenous fluid resuscitation and close monitoring, was also provided to ensure the patient's stability and prevent further complications (4).

The patient's strabismus was managed conservatively with observation and serial ophthalmological examinations. Over the course of her hospital stay, the right exotropia gradually improved, with a residual deviation of 10 prism diopters at the time of discharge. This spontaneous improvement suggests that the strabismus was likely a transient manifestation of methadone toxicity, rather than a permanent neurological sequela (7).

The present case underscores the importance of recognizing the potential neurological and ocular complications associated with methadone use, particularly in opioid-naive individuals (10) (15). Healthcare providers should be aware of the uncommon manifestations of opioid toxicity, such as strabismus, and promptly initiate appropriate management to prevent long-term morbidity and mortality (4). A comprehensive neurological and ophthalmological evaluation is essential in patients presenting with methadone-induced strabismus to rule out any underlying intracranial pathology and provide targeted treatment (7, 10).

Furthermore, this case highlights the need for increased public awareness regarding the risks associated with recreational methadone use, especially among opioid-naive individuals (3). Education on the potential dangers of methadone, including the risk of overdose and neurological complications, may help to prevent similar cases in the future (10, 15).

Conclusion

In conclusion, methadone-induced strabismus is a rare but potentially serious complication of opioid toxicity. Healthcare providers should be vigilant for uncommon neurological and ocular manifestations in patients presenting with methadone overdose, particularly in opioid-naive individuals. Prompt recognition and appropriate management, including the administration of naloxone and supportive care, are essential to prevent long-term morbidity and mortality associated with methadone toxicity. Further research is needed to elucidate the exact mechanisms underlying methadone-induced strabismus and to develop evidence-based guidelines for its management. Additionally, increased public awareness and education regarding the risks of recreational methadone use may help to prevent similar cases in the future.

Key Clinical Message

Methadone-induced strabismus is a rare but potentially serious complication of opioid toxicity. Healthcare providers should be vigilant for uncommon neurological and ocular manifestations in patients presenting with methadone overdose, particularly in opioid-naive individuals. Prompt recognition and appropriate management, including the administration of naloxone and supportive care, are essential to prevent long-term morbidity and mortality associated with methadone toxicity.

Declaration

Ethics Approval and Consent to Participate

This case report was conducted in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The patient provided written informed consent for the publication of this case report and accompanying images.

Consent for Publication

Written informed consent was obtained from the patient for the publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Availability of Data and Materials

All data generated or analyzed during this study are included in this published article.

Competing Interests

The authors declare that they have no competing interests.

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