Early Toxic Leukoencephalopathy after Methadone Overdose

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Introduction

Methadone is a synthetic opioid commonly used in the treatment of chronic pain, or as a maintenance substitute for opioid addiction, and is also a common street drug. Methadone is well absorbed from the gastrointestinal tract, resulting in a peak plasma level within 2 to 4 hours, with peak effect occurring within 2 hours. It has an average half-life of 25 hours and may be as long as 52 hours during long-term maintenance therapy.1

Since the first report of the leukoencephalopathy caused by heroin use, (“chasing the dragon”) from the Netherlands in 1982, there is increasing evidence of similar pathology caused by other opioids.2-3 Rare case reports describe development of delayed toxic leukoencephalopathy (TLE), occurring 1-3 weeks after methadone overdose. Furthermore, there are also three pediatric cases describing rapid development of cerebellar edema causing hydrocephalus and delayed damage to the white matter. We report an adolescent with acute toxic encephalopathy, following intentional methadone overdose. To the best of our knowledge, it is the first case of such acute presentation of TLE after synthetic opioid use.

Case report

A 16-year-old male with history of bipolar disorder, drug and alcohol abuse was found apneic and pale ten hours after ingestion of 150 mg of methadone. Cardiopulmonary resuscitation was initiated by his mother. Paramedics reported pinpoint pupils, strong peripheral pulses, slow respirations and oxygen saturation of 32% on room air. Bag and mask ventilation was initiated. Naloxone was administered with no response. On arrival to the emergency room, he was intubated for airway protection and placed on mechanical ventilation. A repeat dose of naloxone resulted in improved pupillary exam. Initial computed tomography (CT) of his brain was negative and he was transferred to the Pediatric Intensive Care Unit. He was started on a naloxone drip and extubated 24 hours post ingestion. Six hours after extubation, he was noted to have unequal pupils; A dose of mannitol was administered and emergent repeat CT scan was done with no new findings. His electroencephalogram showed diffuse slowing of background activity with mild intermittent frontal delta activity. Over the next few hours, he was also noted to have spastic quadriaparesis and left upper motor neuron facial palsy.

Magnetic Resonance Imaging of the brain obtained 64 hours post ingestion showed changes consistent with TLE (Figure 1,2,3 and 4).

80 hours post ingestion he was still disoriented. The patient was agitated at times with slurpped speech. His short-term memory was impaired while long-term was spared. Active movements were limited with decreased balance and truncal control. Over the next few days, his cognition improved and was close to baseline. He still had some weakness of left knee and hip, but was able to perform most activities of daily living independently. Two weeks after hospitalization, he was discharged home for subsequent outpatient rehabilitation and a substance abuse treatment program. His neurological exam had normalized at his 8 month follow-up visit.

Discussion

In this case report, we describe the clinical presentation and neuroimaging signs of acute TLE after intentional methadone overdose.

MRI revealed abnormal T2 signal and restricted diffusion in the deep cerebral hemispheric white matter with sparing of the cerebellum, consistent with acute TLE. The restricted diffusion of water is proposed to be secondary to spongiform degeneration of the white matter with vacuole formation between the myelin lamellae, leading to accumulation of restricted fluid. Sparing of the cortical grey matter, basal ganglia and watershed areas ruled out hypoxic-ischemic etiology. These findings are similar to cases of delayed onset TLE, previously described. The exact mechanism of TLE is yet to be elucidated. Of the 4 previously reported pediatric cases of delayed TLE, 1 patient died and 3 had complete recoveries based on their exams and imaging 1 year out.

Conclusions

1. Toxic encephalopathy should be considered after methadone overdose, especially with the occurrence of new neurological signs. Physicians should be aware of the neuroimaging signs of TLE.

2. Adequate oxygenation, ventilation, and hemodynamic support should be maintained in a patient after methadone overdose to reduce the occurrence of anaerobic metabolism, especially in brain cells.

3. More research is needed to investigate the role of naloxone in the prevention of the development of TLE.

References:


