**Title:** **Sphincter of Oddi Dysfunction Induced by Ketamine: A Case Report**

**Abstract**

Ketamine is commonly abused as a recreational drug worldwide due to its ability to induce euphoria-like effects. Ketamine abuse is associated with many hepatobiliary side effects ranging from cholestasis to biliary sepsis and death.Here we present a case of a young 29-year female with upper abdominal pain due to sphincter of Oddi dysfunction (SOD) resulting from chronic use of ketamine.Sphincter of Oddi dysfunction can result in obstruction or dysfunction of the bile and pancreatic ducts. Ketamine induces SOD by activation of the muscarinic receptors in the sphincter of Oddi.Detail history of substance abuse is crucial for early identification of ketamine-induced SOD. Early identification and treatment of this rare condition can prevent permanent injury to the liver and pancreas.

**Keywords:** drug abuse, biliary diseases, sphincter of oddi dysfunction, low-dose ketamine

**Introduction**

Ketamine is used as a recreational drug (street ketamine) due to its ability to induce euphoria and a trance-like state. Street ketamine can be inhaled, swallowed, or injected. It is abused in many parts of the world1. Even though the dose used for recreational purposes is 15-20 % lower than that used for anesthesia, its side effect and death are increasing due to its recreational use for a prolonged duration2. In the United States, more than 2.3 million teens and adults used ketamine in their lifetime2.

Although the effects of ketamine on the urinary bladder have been widely reported, its effects on the bile duct and its management have not been extensively studied3. We report a rare case of the sphincter of Oddi dysfunction in a young female who presented to the hospital with abdominal pain.

**Case Presentation**

A 29-year-old female with a history of recreational ketamine use for the past eight years presented to the emergency department with right upper quadrant abdominal pain associated with nausea and non-bilious, non-bloody vomiting. At the presentation, her vitals were stable. Physical examination was unremarkable except for the tenderness in the right upper quadrant, without guarding or rebound tenderness. Lab studies revealed an Alkaline Phosphatase (ALP) of 116 U/L. Chest X-ray did not show any cardiopulmonary pathology. Electrocardiogram showed a normal sinus rhythm. Ultrasound of the abdomen revealed a prominent common bile duct (CBD) without gallbladder pathology. Computed Tomography (CT) of the abdomen and pelvis showed dilatation of the CBD measuring up to 9 mm. She was admitted to the hospital for the workup of CBD dilation and pain management. During hospitalization, her pain was managed adequately with analgesics; however, her liver enzymes continued to increase (Table 1).

Table 1: Progression of liver enzymes during hospitalization

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Liver Function Test | On the day of hospitalization | Day 1 | Day 2 | Day 3 | Day 4 |
| Total Bilirubin (mg/dl) | 0.2 | 0.2 | 0.2 | 0.3 | 0.2 |
| Direct Bilirubin (mg/dl) | 0 | 0 | 0 | 0 | 0 |
| Aspartate Aminotransferase (U/L) | 16 | 148 | 168 | 91 | 489 |
| Alkaline Phosphatase (U/L) | 116 | 139 | 165 | 173 | 241 |
| Alanine Aminotransferase (U/L) | 18 | 113 | 151 | 520 | 520 |

An inpatient gastroenterology consultation was done, and a decision was made to perform an Endoscopic retrograde cholangiopancreatography (ERCP), given her symptoms of right upper quadrant pain, ketamine abuse, the elevation of liver enzymes, and dilatation of the CBD without obstructive pathology. ERCP revealed the dilatation of CBD and Type 1 SOD (Figure 1). Sphincterotomy was performed (Figure 2) and post-sphincterotomy fluoroscopy was done which suggested reduced CBD dilatation. This resulted in subsequent symptom resolution and eventual discharge with outpatient gastroenterology follow-up. The patient was happy with the treatment provided.

 

Figure 1 Figure 2

Figure 1: ERCP showing obstructive cholangiogram.

Figure 2: during sphincterotomy

**Discussion**

Sphincter of Oddi dysfunction (SOD) is a condition characterized by abnormal muscular valve function regulating the flow of bile and pancreatic juice into the duodenum. SOD can result in obstruction or dysfunction of the bile and pancreatic ducts, leading to symptoms including abdominal pain, nausea, vomiting, and diarrhea. The prevalence of SOD is estimated to be 1.5% in the general population and up to 29% in patients with chronic abdominal pain4.

Ketamine is a dissociative anesthetic drug used for pain management and sedation. Ketamine has a short half-life, undergoes extensive first-pass metabolism in the liver, and is primarily excreted through urine and bile5. Although some studies have shown that ketamine can induce the contraction of the sphincter, leading to obstruction of the bile and pancreatic ducts, more studies are still required to confirm this6,7. The mechanism by which ketamine induces SOD is not fully understood, but it is thought to involve the activation of the muscarinic receptors in the sphincter of Oddi. It has been shown to enhance the release of acetylcholine, a neurotransmitter that activates the muscarinic receptors in the sphincter. This increases the tone and contraction of the sphincter, which can obstruct the bile and pancreatic ducts6,8. This can result in elevated liver enzymes, jaundice, and pancreatitis.

The diagnosis of SOD due to ketamine abuse is based on the patient's history of ketamine use, symptoms of biliary or pancreatic dysfunction, and imaging studies such as magnetic resonance cholangiopancreatography (MRCP) or endoscopic retrograde cholangiopancreatography (ERCP). MRCP can detect any structural abnormalities in the bile and pancreatic ducts, while ERCP can measure the sphincter's pressure and diagnose SOD8,9. The treatment of SOD due to ketamine abuse includes cessation of ketamine use and using medications to relax the sphincter, such as nitrates, calcium channel blockers, and anticholinergics. Endoscopic sphincterotomy, a procedure that involves cutting the sphincter, can also relieve the obstruction of the bile and pancreatic ducts9.

In conclusion, SOD due to ketamine abuse is a serious medical condition that can lead to biliary and pancreatic dysfunction. It is essential to identify the condition early to prevent complications such as pancreatitis and hepatic damage. Treatment involves cessation of ketamine use and the use of medications or endoscopic sphincterotomy to relieve the obstruction of the bile and pancreatic ducts.

**Conclusion**

Ketamine is commonly abused among teens and adults worldwide. Ketamine-induced sphincter dysfunction can be life-threatening if an early diagnosis is not made. Physicians should be aware of this rare finding in patients with acute abdominal pain. Early diagnosis and management can prevent further hepatic and pancreatic injury.

**Declaration of Competing Interest**

None.

**Provenance and peer review**

Not commissioned, externally peer reviewed.

**Consent**

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

**References**

1. Lankenau SE, Sanders B, Bloom JJ, Hathazi D. Towards an Explanation of Subjective Ketamine Experiences among Young Injection Drug Users. *Addiction Research & Theory*. 2008;16(3):273-287. doi:10.1080/16066350801983749

2. Liu Y, Lin D, Wu B, Zhou W. Ketamine abuse potential and use disorder. *Brain Res Bull*. 2016;126:68-73. doi:10.1016/j.brainresbull.2016.05.016

3. Srirangam S, Mercer J. Ketamine bladder syndrome: an important differential diagnosis when assessing a patient with persistent lower urinary tract symptoms. *Case Reports*. 2012;2012(sep26 1):bcr2012006447-bcr2012006447. doi:10.1136/bcr-2012-006447

4. Bistritz L. Sphincter of Oddi dysfunction: Managing the patient with chronic biliary pain. *World J Gastroenterol*. 2006;12(24):3793. doi:10.3748/wjg.v12.i24.3793

5. Dinis-Oliveira RJ. Metabolism and metabolomics of ketamine: a toxicological approach. *Forensic Sci Res*. 2017;2(1):2-10. doi:10.1080/20961790.2017.1285219

6. AL-Nowfal A, Al-Abed Y. Chronic biliary colic associated with ketamine abuse. *Int Med Case Rep J*. Published online June 2016:135. doi:10.2147/IMCRJ.S100648

7. Varadarajulu S, Wilcox CM. Prospective Evaluation of Ketamine On Sphincter of Oddi Motility. *Gastrointest Endosc*. 2006;63(5):AB281. doi:10.1016/j.gie.2006.03.726

8. Nyirenda TJ, Shirazi-Nejad A, Soliman AS. Persistent Ketamine-Induced Cholangiopathy: An Approach to Management. *Cureus*. Published online November 21, 2020. doi:10.7759/cureus.11611

9. Afghani E, Lo SK, Covington PS, Cash BD, Pandol SJ. Sphincter of Oddi Function and Risk Factors for Dysfunction. *Front Nutr*. 2017;4. doi:10.3389/fnut.2017.00001