U.S. National Library of Medicine
National Center for Biotechnology Information

NLM Citation: LiverTox: Clinical and Research Information on Drug-Induced Liver Injury [Internet]. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases; 2012-. Phencyclidine. [Updated 2016 Apr 11].
Bookshelf URL: https://www.ncbi.nlm.nih.gov/books/

Phencyclidine

Updated: April 11, 2016.

OVERVIEW

Introduction

Phencyclidine is an illegal, hallucinogenic drug that was initially used as an anesthetic agent in the 1950s and early 1960s, but was then withdrawn in 1965 because of dissociative hallucinogenic effects that were often disturbing and sometimes severe and prolonged. The "out-of-body" intense psychological and behavioral effects of low doses of phencyclidine led to its abuse. In the late 1960s and 1970s, phencyclidine ("angel dust") became a widely used hallucinogenic drug. The effects were often extreme, marked by acute psychosis and aggressive and violent behaviors, and overdoses led to many emergency room visits and deaths from status epilepticus, hyperthermia, rhabdomyolysis and subsequent renal, respiratory and hepatic failure.

Background

Phencyclidine (fen sye' kli deen) is an arylcyclohexylamine anesthetic that acts as a noncompetitive inhibitor of N-methyl-d-aspartate (NMDA) receptors in the brain. Phencyclidine infusions rapidly produce anesthesia and a unique cataleptic state with profound analgesia, unresponsiveness and amnesia, but often with maintenance of muscle tone, involuntary movements, open eyes and spontaneous breathing. The effect is called dissociative anesthesia, which can be associated with vivid hallucinations, agitation and delirium during emergence. These psychological and behavioral effects can be very disturbing, arise several hours after the anesthesia and persist for days. Because of these effects, phencyclidine (Sernyl) was withdrawn from human use in 1965. Phencyclidine continued to be available as a veterinary anesthetic (Sernylan), but was withdrawn from that use in 1978 in attempts to control its illicit availability. These same dissociative effects led to the recreational abuse of phencyclidine and for a period in the late 1960s and 1970s, phencyclidine (commonly known as "angel dust") became a major drug of abuse. Phencyclidine taken by mouth or inhaled (smoked) in doses of 1 to 10 mg leads to rapid onset of euphoria and feelings of omnipotence, superhuman strength and social and sexual prowess. Use of phencyclidine chronically can be associated with severe violent and aggressive behavior and episodes of acute psychosis. Higher doses cause progressive confusion, disorientation, coma and seizures, and can lead to malignant hyperthermia, shock, rhabdomyolysis, renal failure and sudden death. In recent years, wider knowledge of its dangerous effects and the increasing limitation on its production have led to a decrease in the frequency (but not disappearance) of phencyclidine abuse. Attempts to modify the tertiary amine structure of phencyclidine to develop a safer and more useful anesthetic agent led to the development of ketamine, another anesthetic which has a similar mechanism of action as well as similar, although lesser, potential for abuse.

Hepatotoxicity

Phencyclidine is no longer used medically and its production is outlawed. Nevertheless, phencyclidine remains an agent of abuse, used for its hallucinogenic effects. At low doses, phencyclidine appears to have little effect on the liver. However, high doses of phencyclidine have been associated with malignant hyperthermia which can trigger acute hepatitis necrosis and liver failure. Patients generally present with seizures and coma followed by severe hyperthermia, rhabdomyolysis and renal failure. The liver injury arises 1 to 2 days after the overdose with marked, rapid elevations in serum ALT, AST and LDH, with minimal increases in alkaline phosphatase and delayed rises in bilirubin (Case 1). Coma arises early along with prolongation of the prothrombin time, hyperammonemia and metabolic acidosis. The abnormalities resolve almost as rapidly as they develop and with suitable life support, survival is not uncommon (Case 1). The clinical syndrome is that of acute hepatic necrosis and resembles the acute liver injury that occurs with heat shock, severe hypoxia and hepatic ischemia. Liver biopsy shows severe centrilobular necrosis with mild inflammation.

Likelihood score: C[HD] (probable cause of clinically apparent acute liver injury but only when given in high doses).

Mechanism of Injury

The mechanism of acute liver injury by phencyclidine is probably hyperthermia, hypoxia and hypotension, and the clinical course and outcome resembles that associated with shock or severe hypoxia.

Outcome and Management

Clinically apparent hepatobiliary injury associated with phencyclidine arises in the context of malignant hyperthermia, rhabdomyolysis and shock, usually the result of overdose which may be unintended and caused by the lack of reliability and control of drug concentration and purity in sources of this illicit agent. With adequate life support, recovery is generally rapid and complete.

Drug Class: Agents of Abuse; Anesthetics, General (withdrawn from market)

See also: Ketamine

CASE REPORT

Case 1. Hyperthermia followed by acute liver failure from phencyclidine overdose.

[Modified from case 3 in: Armen R, Kanel G, Reynolds T. Phencyclidine-induced malignant hyperthermia causing submassive liver necrosis. Am J Med 1984; 77: 167-72. PubMed Citation]

A 25 year old man was arrested for bizarre behavior believed to be due to phencyclidine intoxication and developed severe agitation and hallucinations a few hours later. He was taken to a County hospital and found to have severe hyperthermia [108.4°F], tachycardia [160/min] and tachypnea [44/min]. He underwent intubation and mechanical ventilation and was treated with a cooling blanket and acetaminophen. His temperature fell but he remained in coma. Phencyclidine was detected in a gastric aspirate. Liver tests, which had been normal on admission, rose by day 2 to 3, with bilirubin rising from 0.7 to 22.5 mg/dL, ALT from 30 to above 9,000 U/L, and prothrombin index falling from 95% to 5% (Table). He remained in coma for 10 days, underwent emergency abdominal surgery on day 21 for a perforated duodenal ulcer, but then improved and was able to leave the hospital after 37 days. In follow up at 50 days, symptoms had resolved and all liver tests were normal or near normal.

Key Points

Medication:	Phencyclidine (unknown amount)
Pattern:	Hepatocellular
Severity:	4+ (jaundice, hospitalization, coagulopathy)
Latency:	1-2 days
Recovery:	Almost complete within 2 months
Other medications:	None mentioned

Laboratory Values

Days After Starting/ Stopping	ALT (U/L)	Prothrombin Index (%)	CPK (U/L)	LDH (U/L)	Bilirubin (mg/dL)	Other
1	29	95%	512	577	0.7	Admission, creatinine 1.9
2	>9,000	5%	5,880	2,850	15.1	Intubation
3	4,420	22%	1,208	518	22.5	
7	505	69%	1,057	620	7.7	
21	152	87%	382	417	2.0	Emergency surgery
50	79	103%	28	411	0.8	Outpatient visit
Normal Values		**<40**	**>80%**	**<200**	**<300**	**<1.2**

Comment

A young man was arrested for bizarre behavior suspected to be due to phencyclidine intoxication and became increasingly agitated, which led to hospital admission where he was found to have malignant hyperthermia. He promptly went into coma and required mechanical ventilation. The following day he was found to have severe hepatic injury as well. While serum bilirubin climbed from normal to 22.5 mg/dL within two days, other features of the liver injury began to improve rapidly. He developed an acute abdomen requiring emergency surgery for a perforated duodenal ulcer after 3 weeks in the hospital. A liver biopsy taken during surgery showed confluent centrizonal necrosis and cell dropout with minimal inflammation and no fibrosis, consistent with the clinical course of acute hepatic necrosis. Thus, the liver injury linked to phencyclidine overdose is more likely due to the hyperthermia caused by the drug rather than its direct toxic effect on hepatocytes.

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Phencyclidine – Generic, Sernyl®

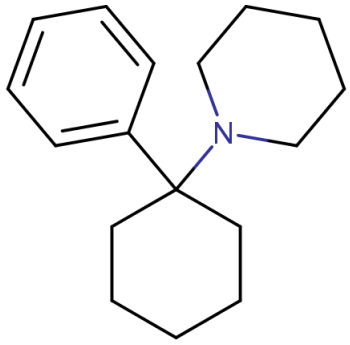
DRUG CLASS

Agents of Abuse

COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Phencyclidine	77-10-1	C17-H25-N	

ANNOTATED BIBLIOGRAPHY

References updated: 11 April 2016

Zimmerman HJ. Anesthetic agents. In, Zimmerman, HJ. Hepatotoxicity: the adverse effects of drugs and other chemicals on the liver. 2nd ed. Philadelphia: Lippincott, 1999: pp. 457-82.

(Expert review of hepatotoxicity of anesthetic agents published in 1999, mentions that phencyclidine can cause hyperthermia, rhabdomyolysis, renal and liver failure accompanied by severe, centrizonal [zone 3] hepatic necrosis resembling injury that occurs with heatstroke).

Kenna JG. Mechanism, pathology, and clinical presentation of hepatoxicity of anesthetic agents. In, Kaplowitz N, DeLeve LD, eds. Drug-induced liver disease. 3rd ed. Amsterdam: Elsevier, 2013: pp 403-22.

(Review of liver injury from anesthetic agents; does not discuss phencyclidine).

Patel PM, Patel HH, Roth DM. Ketamine. General anesthetics and therapeutic gases. In, Brunton LL, Chabner BA, Knollman BC, eds. Goodman & Gilman's the pharmacological basis of therapeutics. 12th ed. New York: McGraw-Hill, 2011, pp. 538-9.

(Textbook of pharmacology and therapeutics).

Noguchi TT, Nakamura GR. Phencyclidine-related deaths in Los Angeles County, 1976. J Forensic Sci 1978; 23: 503-7. PubMed PMID: 744979.

(Description of 5 fatal cases of phencyclidine overdose and 11 other deaths in which phencyclidine was contributory, often with a history of acute psychosis, several dying in drowning incidents).

Thompson TN. Malignant hyperthermia from PCP. J Clin Psychiatry 1979; 40: 327. *(31 year old man developed malignant hyperthermia [106.7* ^{o} PubMed PMID: 457624.

F] 6 hours after ingesting phencyclidine with coma, seizures and subsequent renal failure requiring a 25 day hospitalization; no mention of ALT levels or liver injury).

McCarron MM, Schulze BW, Thompson GA, Conder MC, Goetz WA. Acute phencyclidine intoxication: incidence of clinical findings in 1,000 cases. Ann Emerg Med 1981; 10: 237-42. PubMed PMID: 7224271.

(Among 1000 episodes of phencyclidine intoxication seen at a Los Angeles medical center, median age was 23 years [range 13-65 years], 88% were men; 57% had nystagmus, 57% hypertension, 37% acute brain syndrome, 11% unconscious, 35% violent behavior, 34% agitated, 19% hallucinating, 3.5% no behavioral changes, 30% tachycardia, 2.6% hyperthermia; among those tested, CPK was elevated in 70% and ALT in 50%, but none had accompanying bilirubin elevations).

Barton CH, Sterling ML, Vaziri ND. Phencyclidine intoxication: clinical experience in 27 cases confirmed by urine assay. Ann Emerg Med 1981; 10: 243-6. PubMed PMID: 7224272.

(Among 107 patients with phencyclidine intoxication, 27 were confirmed by urine testing including 20 men and 7 women, ages 17 to 30 years, often with hypertension, tachycardia and tachypnea, abnormal behavior [23: 85%], nystagmus [24: 89%], hospitalization [6: 22%], rhabdomyolysis [3: 11%] and renal failure [2: 7%], but no patient died).

Aniline O, Pitts FN Jr. Phencyclidine (PCP): a review and perspectives. Crit Rev Toxicol 1982; 10: 145-77. PubMed PMID: 7044685.

(Review of the clinical features and consequences of phencyclidine abuse, described as an "epidemic in urban North America").

Armen R, Kanel G, Reynolds T. Phencyclidine-induced malignant hyperthermia causing submassive liver necrosis. Am J Med 1984; 77: 167-72. PubMed PMID: 6741977.

(Three young men with acute, severe phencyclidine intoxication, ages 21 to 32 years, were arrested for bizarre behavior and developed hyperthermia followed in 24 to 72 hours by acute liver and renal failure [bilirubin peak to 8.0 to 22.5 mg/dL, ALT >9000 U/L, Alk P not given, prothrombin index 5% to 22%], all ultimately recovering in 1-2 weeks: Case 1).

Patel R, Connor G. A review of thirty cases of rhabdomyolysis-associated acute renal failure among phencyclidine users. J Toxicol Clin Toxicol 1985-1986; 23: 547-56. PubMed PMID: 3831378.

(Description of 15 cases of rhabdomyolysis and renal failure after phencyclidine use seen at a Los Angeles hospital between 1979-84, and review of 15 cases from the literature including 28 males, 21 blacks, ages 17 to 46 years, 19 developing oliguria, 16 dialyzed, creatinine 2.3-18 mg/dL, 94% with myoglobin in urine and 3 dying of sepsis, status epilepticus and pulmonary embolism; no mention of ALT levels or liver injury).

Riordan SM, Williams R. Liver disease due to illicit substance use. Addict Biol 1998; 3: 47-53. PubMed PMID: 26736079.

(Review of the hepatotoxicity of illicit substances of abuse including amphetamines, MDMA [ecstasy], cocaine, heroin, LSD, and phencyclidine which, with overdoses, has been associated with hyperthermia induced acute hepatic necrosis).

Jentsch JD, Roth RH. The neuropsychopharmacology of phencyclidine: from NMDA receptor hypofunction to the dopamine hypothesis of schizophrenia. Neuropsychopharmacology 1999; 20: 201-25. PubMed PMID: 10063482.

(Review of the neurologic basis of phencyclidine effects and the possible role of glutamate neurotransmission through NMDA receptors in the pathogenesis of schizophrenia).

Mozayani A. Phencyclidine - Effects on Human Performance and Behavior. Forensic Sci Rev 2003; 15: 61-74. PubMed PMID: 26256594.

(Review of the chemistry, pharmacology, and mechanism of action of phencyclidine as well as the clinical features and management of intoxication).

Mozayani A, Schrode P, Carter J, Danielson TJ. A multiple drug fatality involving MK-801 (dizocilpine), a mimic of phencyclidine. Forensic Sci Int 2003; 133: 113-7. PubMed PMID: 12742697.

(45 year old man was found dead with an empty bottle of dizocilpine, an anticonvulsant and NMDA receptor antagonist similar to phencyclidine, autopsy did not show liver injury).

Carls KA, Ruehter VL. An evaluation of phencyclidine (PCP) psychosis: a retrospective analysis at a state facility. Am J Drug Alcohol Abuse 2006; 32: 673-8. PubMed PMID: 17127556.

(Among 20 patients with acute psychosis due to phencyclidine, the average hospitalization was for 4.1 [range 1-9] days compared to 13.6 [range 3-41] days for "functional" psychosis).

Bey T, Patel A. Phencyclidine intoxication and adverse effects: a clinical and pharmacological review of an illicit drug. Cal J Emerg Med 2007; 8: 9-14. PubMed PMID: 20440387.

(Review of the pharmacology, clinical effects, complications and management of phencyclidine intoxication and overdose).

deRoux SJ, Sgarlato A, Marker E. Phencyclidine: a 5-year retrospective review from the New York City Medical Examiner's Office. J Forensic Sci 2011; 56: 656-9. PubMed PMID: 21291469.

(Among 138 cases examined by the New York City Medical Examiner between 2003 and 2008 that tested positive for blood phencyclidine, 80 were considered violent deaths, but drug levels varied greatly suggesting that co-morbid conditions and mixed drug intoxications accounted for many of the deaths; no mention of liver failure).

Lodge D, Mercier MS. Ketamine and phencyclidine: the good, the bad and the unexpected. Br J Pharmacol 2015; 172: 4254-76. PubMed PMID: 26075331.

(History of the development of phencyclidine and its congener ketamine initially as anesthetic agents, but when found to cause dissociative states and hallucinations used as drugs of abuse. The identification of these anesthetics as antagonists of NDMA receptors in the CNS led to the hypothesis that schizophrenia was due to abnormalities of this glutamatergic neurotransmission pathways).