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Case Report

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Severe Neurological Sequelae after a Recreational Dose of LSD

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Abstract

A young man with an unremarkable medical history suffered a seizure with subsequent cardiorespiratory arrest and severe neurological sequelae after ingesting a blotter. Analysis of a similar blotter and a serum sample obtained 3 h after the event detected lysergic acid diethylamide (LSD) at an amount of 300 μg in the blotter and at a concentration of 4.0 ng/mL (12.4 nmol/L) in the serum. No other drugs were present in concentrations which may confer significant effects. In addition, no individual traits which would make the patient particularly susceptible to adverse LSD effects have subsequently been identified. This suggests that LSD may confer toxic effects in previously healthy individuals.

Introduction

Since the discovery of the mind-altering properties of lysergic acid diethylamide-25 (LSD) in 1943, the drug has at various times been evaluated as a model compound for inducing psychosis; as a therapeutic option in psychological, psychiatric and other ailments; and for recreational use. LSD is most frequently encountered as an illicit drug of abuse. LSD seizures by Norwegian police accounted for 1% of all drug seizures in 2019 and amounted to ∼13,000 user doses (1). The propensity of LSD to cause adverse events is a matter of controversy. In a recent review article, Nichols and Grob (2) advocated that LSD is nontoxic and medically safe when administered in standard doses (50–200 μg). They discussed what they call the unfortunate misidentification of lethal LSD toxicity in five cases which, in their opinion, most likely were due to massive overdoses, the restraining of agitated subjects or—in one case—hyperthermia most likely caused by a drug other than LSD.

Herein, we report a tragic outcome in a previously healthy young man exposed to what was assumed to be a safe dose of LSD in a recreational setting.

Clinical Summary

The patient was a man in his late teens with no history of illicit drug use and an unremarkable medical history. In particular, there were no epileptic fits, other types of seizures or cardiac arrhythmias in the patient's or in his family history. At a gathering, he and several of his friends each consumed a blotter from a presumed identical batch of what was believed to be LSD. They initially experienced what later was described as typical LSD effects before the patient suddenly fell to the floor with a tonic spastic seizure with occasional shallow breaths followed by oral frothing, retching, vomiting, aspiration and cyanosis. Emergency medical personnel arrived 25 min after the start of symptoms and found the patient in cardiorespiratory

arrest. He was intubated and received cardiopulmonary resuscitation therapy. Upon arrival at the emergency department, he had a supraventricular tachycardia with lactic acidosis suggesting severe cerebral hypoxia. This was subsequently confirmed by magnetic resonance imaging and electroencephalography. Electrocardiography rapidly normalized, and no signs of long QT syndrome or any other cardiac abnormalities were detected at any time. None of the others who ingested similar blotters reported any unfortunate experiences. Almost 1 year later, the patient is still in rehabilitation with severe cerebral sequelae.

Methods

Serum and urine samples obtained 3 h after the onset of symptoms and two blotters, reportedly identical to the blotters ingested at the gathering, were subjected to a comprehensive drug analysis. Both blotters weighed ∼23 mg. One was cut into small pieces and dissolved and diluted in methanol. The solute was injected on an Agilent 1290 Infinity liquid chromatograph coupled to an Agilent 6540 quadropol time-of-flight mass spectrometer (LC–QTOF-MS).

The acquired MS-MS spectra showed that the blotter contained LSD and smaller amounts of the primary LSD metabolite 2-oxo-3-hydroxy-lysergic acid diethylamide (2-oxo-3-OH-LSD), *N,N*-dimethyltryptamine (DMT), methamphetamine, amphetamine and 3,4-methylenedioxymethamphetamine (MDMA). To confirm the results from QTOF analysis, we developed quantitative methods for LSD, 2-oxo-3-OH-LSD and DMT on ultraperformance liquid chromatography (UPLC)–MS-MS (Waters, Acquity UPLC, Xevo TQ-S) instrumentation in serum, urine and blotter extract. For quantification of amphetamine, methamphetamine and MDMA, accredited routine UPLC–MS-MS methods were used. In addition, LC-QTOF-MS indicated the presence of lidocaine, metoprolol, fentanyl, norfentanyl and rocuronium in the serum. These findings reflect treatment given during resuscitation and were not further quantified.

For the LSD method, LSD was acquired from Chiron, Norway; 2-oxo-3-OH-LSD from Chiron and Sigma-Aldrich, Norway; and the internal standard (IS; deuterated 2-oxo-3-OH-LSD) from Chem-Support, Norway. One-hundred microliters of serum/urine/blotter extract was mixed with 40 μL of the IS (50 μg/L) prior to precipitation with 400 μL acetonitrile. Ten microliters of the supernatant was injected into the UPLC–MS-MS system. Chromatographic separation was achieved using a Waters Acquity UPLC BEHC18 column (1.7 μm, 2.1 × 50 mm) and gradient elution starting with 80% ammonium formate (5 mmol/L, pH 10.1) (A) and 20% methanol (B) which was kept for the first 2 min. From 2.0 to 2.5 min, the mobile phase was altered with a linear gradient to 90% B and then altered back to 80% A within 1 min, resulting in a total run time of 3.5 min. The flowrate was 0.5 mL/min. For detection and quantification of LSD, electrospray ionization in positive mode and the *m/z* 324 > 223 and *m/z* 324 > 207 transitions were used. For 2-oxo-3-OH-LSD, the *m/z* 356 > 222 and *m/z* 356 > 313 transitions (*m/z* 359 > 222 for the IS) were used. The retention times for LSD, 2-oxo-3-OH-LSD and IS were 1.52, 1.19 and 1.21 min, respectively. The standard curves were spiked with LSD and 2-oxo-3-OH-LSD to concentrations of 0, 1, 5, 10, 50, 100, 500 and 1,000 ng/mL and were linear ($R^2 > 0.999$). The method's limit of quantitation (LOQ)/limit of detection (LOD) corresponds to the lowest concentration evaluated, that is, 1 ng/mL.

For the DMT method, DMT and the IS (deuterated ethylone) were acquired from Chiron and Sigma-Aldrich, respectively. One-hundred microliters of serum/urine/blotter extract was mixed with 25 μL ethylone-d_5 (1 μg/mL) prior to precipitation with 375 μL acetonitrile. One-half microliter of the supernatant was injected into the UPLC–MS-MS system. Chromatographic separation was achieved using a Waters Acquity UPLC BEHC18 column (1.7 μm, 2.1 × 50 mm) and gradient elution starting with 98% H_2O with 0.1% formic acid (A) and 2% methanol (B) which was kept for the first 0.7 min. From 0.7 to 1.9 min, the mobile phase was altered with a linear gradient to 80% B, then for the next 0.2 min to 98% B and subsequently back to 98% A, resulting in a total run time of 2.2 min. The flowrate was 0.5 mL/min. For detection and quantification of DMT in positive ionization mode, the *m/z* 189 > 58 and *m/z* 189 > 144 (*m/z* 227 > 179 for ethylone-d_5) transitions were used. The retention times for DMT and IS were 1.15 and 1.22 min, respectively. The standard curves were spiked with DMT to concentrations of 0, 1, 10, 100, 500 and 1000 ng/mL and were all linear ($R^2 > 0.999$). The method's LOQ/LOD was 1 ng/mL.

Discussion

The indole alkaloid DMT is not orally active due to rapid degradation by monoamine oxidase (MAO) and is administered with MAO inhibitors when taken by the oral route in recreational settings. When given intravenously, doses in the 0.1–0.4 mg/kg range produce psychedelic effects (3). The DMT content in the analyzed blotter is several orders of magnitude below this level. Likewise, amphetamine and methamphetamine are usually taken in repeated doses of ≥50 mg when used recreationally (4), doses much higher than encountered in the analyzed blotter. MDMA is usually administered as tablets containing 50–150 mg of the compound, with the average user ingesting ∼three tablets per session (5). These doses also exceed the very low level of MDMA in the analyzed blotter by several orders of magnitude. Thus, the contents of DMT, amphetamines and MDMA in the blotter are of no pharmacological or toxicological significance for the present case and most likely reflect contamination of illicitly produced LSD through inadequate cleaning procedures of production equipment or similar negligence. The insignificant role played by these moieties is corroborated by the fact that they were not detected in more than trace amounts (amphethamine in urine) in any of the biological samples (Table I).

In the most recent comprehensive investigation of LSD pharmacokinetics, oral LSD doses of 100 and 200 μg were administered to 24 and 16 subjects, respectively. Maximum plasma concentrations of 1.3 (1.2–1.9) and 3.1 (2.6–4.0) ng/mL were measured after ∼1.5 h. The plasma half-life of LSD in this series was 2.6 (2.2–3.4) h (6). To our knowledge, direct measurements of LSD plasma concentrations after administration of 300 μg doses to humans in experimental settings have not been undertaken. The LSD concentration in the plasma sample obtained 3 h after the patient's sudden loss of consciousness in the present case is not at odds with an assumed dose of 300 μg of the drug.

Seizures are a recognized and potentially serious complication of recreational drug abuse. In a study examining the factors associated with seizures after exposure to such drugs in a collaborative effort involving 32 emergency departments in 21 European countries, there were 4.2% with reported seizures (7). Reviewing the clinical outcome after 3554 exposures to LSD over a 17-year period in US hospitals, Leonard et al. (8) reported 144 instances (4.05%) of seizures of different types. Laboratory confirmation of LSD intake was not available in this dataset, but it demonstrates an association between presumed LSD intake and onset of seizures. In addition, we

Table I. Analytical Findings in a Blotter, Serum and Urine[a]

Analyte	Content in blotter (μg)	Concentration in serum (ng/mL)	Concentration in serum (nmol/L)	Concentration in urine (ng/mL)	Concentration in urine (nmol/L)
LSD	300	4.0	12.4	1.3	4.0
2-Oxo-3-OH-LSD	1.6	<1	<3	5.9	16.6
DMT	0.38	ND	ND	ND	ND
Amphetamine	456	ND	ND	TA	TA
Metamphetamine	0.077	ND	ND	ND	ND
MDMA	0.096	ND	ND	ND	ND

[a]The biological samples were obtained 3 h after the onset of the patient's seizure. Abbreviations: LSD, lysergic acid diethylamide; 2-oxo-3-OH-LSD, 2-oxo-3-hydroxy-lysergic acid diethylamide; DMT, *N*,*N*-dimethyltryptamine; MDMA, methylenedioxymethamphetamine; ND, not detected; TA, trace amounts.

have retrieved a few other published case reports (9–11) that document seizures after ingestion of LSD or other hallucinogens. Notably, in these cases, no neurological sequelae were reported.

We consider the present case to be an LSD-induced seizure with ensuing aspiration of stomach content resulting in asphyxia and cerebral injury with serious sequelae. Importantly, we have not identified any individual traits or vulnerabilities which would make the patient particularly susceptible to such tragic consequences. In our view, this case suggests that the assumption of LSD as 'nontoxic and medically safe' (2) may be erroneous.

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