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CASE REPORT

Monoamine Oxidase Inhibitor Poisoning Resulting from Internet Misinformation on Illicit Substances

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ABSTRACT

The Internet may represent a new mechanism by which adolescents initiate the use of illicit substances. The existence of multiple partisan websites providing misinformation regarding the safety of these substances may lead to an increase in unsafe behavior among this age group. Adverse outcomes related to Internet-based drug information are rarely identified. We report a case of an adolescent whose use of the Internet to obtain drug information led to severe poisoning from the combination of a monoamine oxidase inhibitor, harmaline, and a hallucinogenic tryptamine, 5-methoxydimethyltryptamine (5-MeO-DMT).

Key Words: Internet; Monoamine oxidase inhibitor; 5-MeO-DMT; Harmaline.

INTRODUCTION

The Internet is a medium that may increase the dispersal of illicit drug information among vulnerable populations such as adolescents and young adults. The availability of such information may lead to an increase in unsafe activities among certain demographic groups. Adverse outcomes related to Internet-based drug information are rarely identified (1,2). We report a case of an adolescent whose use of the Internet led to experimentation with illicit substances, an increase in drug use, and poisoning from a naturally occurring monoamine oxidase inhibitor, harmaline.

CASE REPORT

A 17-year-old male college student was introduced to Web sites that describe illicit drugs, their doses, modes of administration, as well as intended effects. Although he reported occasional marijuana and MDMA (methylenedioxymethamphetamine, or ''ecstasy'') use

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while in high school, he denied additional drug use during that time period. As a college freshman he discovered testimonials from various Internet Web sites vividly describing personal experiences with other types of illicit substances. Based on these personal accounts he began experimenting with hallucinogens according to Internet dose recommendations. Initially he used drugs such as dimethyltryptamine (DMT) only on weekends but progressed to daily hallucinogen use. After several months, he wanted to expand the breadth of his experience with hallucinogens and began using 5-methoxydimethyltryptamine (5-MeO-DMT). He enjoyed the intensity of the hallucinations produced by smoking the drug but found the extremely short duration of action undesirable. He learned from an Internet drug library (www.erowid.org) that extracts of naturally occurring monoamine oxidase inhibitors (MAOIs) could dramatically prolong as well as enhance 5-MeO-DMT effects. He therefore purchased Syrian rue seeds online and followed instructions on the Erowid site to produce an extract that contained the naturally occurring MAOI harmaline.

On the morning of the presentation he was found on his freshman dorm room floor by classmates. His friends called 911 and revealed to EMS providers that at 4 a.m. he had ingested extract from three Syrian rue seeds, smoked 10 mg of 5-MeO-DMT, and snorted an additional 15-20 mg of 5-MeO-DMT. Paramedics described him as ''extremely combative, hallucinating,'' and unable to answer questions. Vital signs were unobtainable due to severe agitation. His pupils were dilated; his skin was diaphoretic. He experienced one bout of emesis en route to the hospital.

Triage vitals in the emergency department revealed an axillary temperature of 105.2°F, HR 186 bpm—sinus on the monitor, BP 136/66, and RR 24. Four-point restraints were required to prevent injury to himself and staff. Lorazepam was administered intravenously to a total dose of 2.5 mg with good effect. His heart rate decreased to 130 bpm and his agitation waned. Shortly after chemical sedation, his general appearance was that of a moderately anxious thin male with multiple abrasions on his arms and chest from his struggle with paramedics. He was disoriented to time and place. Heart, lung, and abdominal exams were unremarkable. The pupils were 4 mm and reactive. His skin was hot and moist. Laboratory data was significant for elevation of the WBC to 26.9 TH/mm^3, BUN 20 mg/dL, and Cr. 1.7 mg/dL. Initial CK was 350 U/L.

Subsequently he was transferred via helicopter to a regional toxicology treatment center for further management. That afternoon in the ICU his mental status was somnolent, but arousable. His temperature decreased to 100°F. His heart rate slowed to 60 bpm followed by hypotension to 80/35 mmHg. In addition to autonomic lability, he developed rhabdomyolysis with a peak CK of 26,219 U/L and mild elevation of transaminases: ALT 167 U/L, AST 415 U/L. After 24h his mental status returned to normal and his vital signs were stable. With intravenous hydration his renal function normalized and rhabdomyolysis resolved. He confirmed the initial story of taking Syrian rue seeds and 5-MeO-DMT. GC/MS analysis of urine confirmed the presence of both harmaline and harmine. HPLC suggested possible caffeine.

DISCUSSION

The Internet

The Internet occupies an increasingly important position in American lives. Data from the Internet is fundamentally different than that from other media such as books, magazines, radio, and television in that the Internet is a global system enabling instantaneous exchange of knowledge among participants (3). Systems such as instant messaging and chat groups make the medium interactive. Therefore, users can obtain specific information from others online instantaneously (4). With the Internet available in schools, colleges, public libraries, and homes, access to the vast quantity of information on the Web has unprecedented convenience (4,5). As an example of wide availability, McDonald's recently announced a plan to provide 60 min of Internet access in certain restaurant locations with the purchase of a ''combo meal'' (6).

While Internet usage across all age groups of the American population is increasing, some of the Internet's most frequent users are adolescents and young adults (7). Rates of Internet usage appear to be comparable across socioeconomic strata, with adolescents from wealthy educated families using the Internet as frequently as their less fortunate peers (7). The World Wide Web may function as a virtual peer group, with online acquaintances replacing real-world peers. A recent widely publicized death from a drug overdose captured on a Webcam provides a disturbing example of this peer interaction. In that case, others in the chat room encouraged the victim to continue taking more and more drugs until he died (8).

The Internet may represent a new mechanism by which adolescents initiate the use of illicit substances.

Moreover, information from the Internet may affect the progression of substance abuse. The theory of ''gateway drugs'' proposes that experimentation with one substance, such as marijuana, leads to progressively expanding drug experimentation and use. With some online drug encyclopedias introducing over 200 psychoactive substances, Web users may initiate use of whatever drug is most appealing. Web-based drug information may therefore obviate the theory of gateway drugs by promoting initiation of atypical or unexpected substances.

Demand for information regarding illicit drugs has led to several Web sites devoted to the topic (9–11). Both ''partisan'' Web sites and ''antidrug'' Web sites exist. However, using common search engines to find information about drugs routes users to far more ''partisan'' Web sites (12). Virtual libraries describing drugs are especially appealing to adolescents and young adults. One online drug library, ''Erowid,'' receives more than 180,000 visits per day and describes over 200 psychoactive substances (13). Many of these partisan Web sites detail the variety of drugs in existence, how to use them, obtain them, and avoid legal restrictions (9,11). Unfortunately, most partisan Web sites provide misinformation on illicit drugs and furthermore suggest practices that may be harmful if followed by their readers (12). Data found on drug Web sites are often presented in a medical format, with specific pharmacokinetic information on duration to maximum effect and enzyme metabolism. Unfortunately, the risks of illicit substance use are often minimized. One recent study identified that every partisan site made potentially harmful recommendations for the management of the adverse effects of illicit drugs (12). In fact, some adverse events related to illicit drug use are directly linked to information from partisan internet Web sites (1,2,14,15). Drug libraries such as www.erowid.org and www.lycaeum.org offer some warnings to its readers regarding potential toxicity, but then suggest that sometimes risks are worth taking. These sites, which provide detailed descriptions for home synthesis of illicit drugs, appear to condone drug use despite occasional disclaimers. Much of the information is referenced in a scientific fashion to provide a sense of believability. However, many of the references are of personal experiences by ''scientists'' in the field. As an example, the Erowid site provides reference to papers published by a ''purveyor of natural products'' who has no stated educational degree. In these publications he provides an account of self-experiments for dosing the psychedelic tryptamines DMT and 5-MeO-DMT in combination with harmaline (16,17). Our patient drew his knowledge of tryptamines from this format.

Monoamine Oxidase Inhibitors and Tryptamines

Syrian rue (*Peganum harmala*) is a perennial from the Middle East and North Africa. Its seeds contain several alkaloids including harmaline, harmine, and tetrahydroharmine (18). Harmine and harmaline, members of the beta-carboline chemical class, are both potent reversible inhibitors of the enzyme monoamine oxidase (MAO) (19–21). The compound 5-MeO-DMT is a psychedelic tryptamine derived from a variety of South American plants. The compound is a potent hallucinogen when administered parenterally; however, MAO degrades 5-MeO-DMT to an inactive metabolite following oral dosing. One indigenous practice in Amazonian regions involves the ingestion of the beverage *Ayahuasca*, also known as *yajé, caapi, lagé, hoasca*, or *daime* in shamanic rituals (18,22). Formal analysis of samples of this beverage demonstrate the presence of DMT, harmine, harmaline, and tetrahydroharmine (18). Beta-carbolines—harmaline, harmine, and tetrahydroharmine—inhibit the MAO enzyme, thus preventing degradation of the hallucinogen DMT. As a result, users could potentially achieve an increase in both hallucinogenic effect as well as duration of action.

The combination of a MAOI with another centrally active serotonergic agent such as 5-MeO-DMT poses significant preventable health risks from either MAOI poisoning or serotonin syndrome. Monoamine oxidase inhibitor toxicity is initially characterized by hyperthermia, tachycardia, and agitated delirium; these findings arise from excess sympathomimetic tone secondary to inhibited enzymatic degradation of catecholamine neurotransmitters. Rhabdomyolysis occurs as a consequence of increased muscle activity. Widely fluctuating vital signs and depression of mental status occur as catecholamine stores are consumed. The period during which recovery occurs—typically several days in duration—coincides with restored synthesis of sympathomimetic neurotransmitters. Except for hypertension, which is seen in severe cases, this patient demonstrated all aspects of MAOI poisoning.

Alternatively, this patient may have developed serotonin syndrome, which arises in the setting of excess stimulation of 5-HT_{1A} receptors in the central nervous system. First described in patients who were given MAOI to enhance the activity of agents with serotonergic activity, serotonin syndrome is characterized

by mental status changes, hyperreflexia, tremor, and increased muscular tone leading to hyperthermia. Serotonin syndrome is managed by withdrawal of causative serotonergic agents and is usually brief in duration. The time course of this patient's illness was inconsistent with ultra-short-acting serotonergic agents and makes this entity less likely.

Although no deaths have been reported from *Ayahuasca* or other tryptamine/MAOI combinations, the risks of serotonin syndrome or MAOI poisoning are present (23). Some Web sites make reference to this and provide a list of serotonergic medications and tyramine containing foods to avoid (9). Despite such warnings, the vivid experiences described on partisan Web sites may encourage potential drug users to engage in risky behavior. The combination of harmaline and harmine with the serotonergic agent 5-MeO-DMT may have resulted in the hyperthermia, tachycardia, agitation, and rhabdomyolysis seen in this case. Interestingly, our patient stated that based on his knowledge of drugs obtained on the World Wide Web he ''would have been just fine if they'd left [him] alone.''

SUMMARY

Drug libraries on the internet are ubiquitous, easily accessible, and littered with misinformation (9,12). A disturbing trend of adverse events stemming from Internet-based drug information has emerged (1,2,14,15). Many of the drugs discussed in these forums are unfamiliar to physicians. Most of the drugs discussed on the partisan Web sites are not detectable on routine laboratory analysis. Therefore, clinicians must be aware of these alternate drug information sources used by patients in order to accurately predict and diagnose toxicity.

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