ABSTRACT

Background: The majority of published data on the clinical toxicity of 3,4-methylenedioxymethamphetamine (MDMA) consists mainly of isolated case reports. We performed the following study to record systematically our experience with MDMA toxicity.

Methods: Our poison center database was retrospectively searched for the years 1993 to 1999 inclusive. Patient demographics, coingestants, and symptoms were recorded. Outcome was scored according to AAPCC criteria. The annual incidences of MDMA cases were compared using linear regression and calculation of a Pearson’s correlation coefficient.

Results: There were 191 cases reported during this 7-year period. 123 males and 66 females were exposed; the gender of 2 patients is unknown. The median age was 22 years (IQ25-75 = 18-25 yrs). 52 cases (27%) experienced moderate to major toxicity, including 1 death due to hyperthermia. 139 cases (73%) experienced minor or no toxicity. The most commonly reported symptoms were tachycardia (22%), agitation (19%), and nausea and vomiting (12%). Hyperthermia and hyponatremia, the most serious complications of MDMA use, were reported in 7 patients and 3 patients, respectively. Urinary retention was reported in 4 patients, 3 of whom also reported concurrent ketamine use. Coingestants included cocaine, ethanol, heroin, marijuana, phencyclidine, and psilocybin-containing mushrooms. Beginning in 1997, ketamine and GHB were newly reported as common coingestants. MDMA reports increased with time (r = 0.88, p < 0.05).

Conclusion: Increasing MDMA exposures in our region occurred predominately in a young population, of whom nearly a third met AAPCC criteria for moderate to severe effects. Although hyperthermia and hyponatremia occurred infrequently, we advocate rapid initial screening for these potentially devastating complications, while providing appropriate supportive care.

INTRODUCTION

MDMA, 3,4-methylenedioxymethamphetamine, or “Ecstasy” has been a popular drug of abuse for two decades. Beginning in Europe and the United Kingdom, use of the drug has spread to the United States and many other countries over the last few years. Use of MDMA is most popularly associated with young people who participate in underground rave parties where dancing to modern music is an all night experience.

Although users desire the drug’s effects that include euphoria and an intense feeling of closeness to other people, many adverse reactions have been reported that vary from minor to quite severe. Consistently reported minor adverse reactions include tachycardia, hypertension, bruxism, muscle tension, nausea, diaphoresis, headache (1), and urinary retention(2). Other more serious complications that have been reported are serotonin syndrome (3), parkinsonism (4), hypoglycemia (5), hepatitis (6), renal failure (7), and intracranial hemorrhage (8). By far the most commonly reported severe complications of MDMA use are syndrome of inappropriate antidiuretic hormone (SIADH) (9,10) and hyperthermia (11-15). The majority of these data are reported in case reports and case series while no large report documents any information on trends or populations at large. One study randomly asked college students about MDMA use and found nearly 40% had...
tried the drug at least once (16). We examined data reported to our poison center over seven years to provide more information regarding the use and consequences of MDMA.

METHODS

We retrospectively searched the database at the New York City Poison Control Center from 1993 to 1999 inclusive for data on patients who reportedly used "ecstasy." The database was searched for the terms "ecstasy," "XTC," and "MDMA." We also searched for all words ending in "...tasy" to attempt to find cases where the subject drug was misspelled. "Ecstasy" was searched for as either the primary or secondary drug used as entered in the database. There was no available method to exclude cases of "liquid ecstasy" or "herbal ecstasy" if the drug "ecstasy" was the only drug entered into the database. Patient demographics, coingestants, and symptoms were recorded. Symptoms were recorded as either present or absent on the poison center data form regarding hyperthermia/fever, altered mental status, electrolyte abnormalities, etc. Only a few cases recorded data quantitatively. Outcome was scored according to AAPCC criteria (17). The annual incidences of MDMA cases were compared using linear regression and calculation of a Pearson’s correlation coefficient.

RESULTS

In the seven years that were investigated, there were 191 cases reported where MDMA was recorded as either the primary or secondary drug used. Male patients numbered 123, females were 66, and the gender of 2 patients remains unknown. Patients ranged in age from a reported 2 years old to 45 years old where the mean age was 22.4 years (IQ25-75 = 18-25 years old). The number of cases reported each year generally trended upward over time. The Pearson’s correlation coefficient was calculated to be 0.88 (p<0.5)

The reported symptoms ranged widely. Mild symptoms included agitation, hypertension, tachycardia, nausea and vomiting, and hallucinations. Nine patients had generalized seizures. Three patients were found to have electrolyte abnormalities including hyponatremia. Seven patients were found to be hyperthermic.

Of 191 patients, 52 (27%) were reported to have moderate to severe toxicity according to AAPCC criteria. One patient expired due to complications resulting from hyperthermia.

Figure 1  Number of MDMA Calls

![Number of MDMA Calls graph]

A graph representing the number of MDMA calls to the NYC Poison Center by year.
Coingestants used included heroin, cocaine, marijuana, psilocybin containing mushrooms, phencyclidine, LSD, and amphetamines, although there was no pattern of use among these drugs. In 1997, ketamine and gamma-hydroxybutarate (GHB) began to be reported as MDMA coingestants. Ethanol was also reported as a coingestant with greater frequency since 1997.

DISCUSSION

MDMA, also known as Adam, E, X, XTC, bean, roll, and ecstasy was first synthesized in 1912 and was "rediscovered" by Alexander Shulgin in 1965. In the late 1970's and 1980's, MDMA was used as a non-FDA approved adjunct medication for psychotherapy in an attempt to allow patients greater closeness and enhanced communication during therapy sessions (3,18-22). Today, although MDMA has been classified as schedule 1, it is estimated by the media that annually hundreds of thousands of doses are used illegally, and millions of tablets have been confiscated by law enforcement agencies (23). Most commonly, young people use MDMA as they "roll" at underground rave parties where dancing to modern music often lasts all night.

MDMA is popularly considered an entheogen, which is a neologism deriving from Greek roots meaning becoming divine within. The word entheogen attempts to describe states of shamanic and ecstatic possession induced by ingestion of mind-altering drugs. It is the desire for euphoria, intense closeness, and a general feeling that all is right in the world that makes the drug so popular.

As a synthetic analogue of methamphetamine, MDMA is taken orally in doses that generally range from 75mg to 125mg costing $25 to $50 per dose. The effects tend to last 3-5 hours per dose. As an amphetamine, MDMA causes catecholamine release, which accounts in part for the tachycardia and hypertension that accompanies its use. MDMA also causes massive release of serotonin (21), which may play a role in the user's emotional response to the drug, as well as the generation of hyperthermia (24,25). Experimentally, MDMA selectively damages central serotonergic neurons in nonhuman primates (26-29) as well as inhibits monoamine oxidase (MAO) A and B (30).

![Diagram of amphetamine and its structural analogue.](image)

Figure 2 – Diagrams of amphetamine and its structural analogue.
Clinically the most significant, relatively common adverse reactions to MDMA use include hyperthermia, with or without the presence of the serotonin syndrome (3,22), and hyponatremia in the setting of inappropriate antidiuretic hormone secretion (SIADH). Patients with hyperthermia have been reported with body temperatures as high as 43° C (109.4° F) (11-15,31-34) and generally include a history of prolonged, vigorous exercise. The complications of hyperthermia include hepatic failure, disseminated intravascular coagulopathy (DIC), rhabdomyolysis, renal failure, cerebral edema, and death. However, the association between use of MDMA and hyperthermia may not be so straightforward (14,35).

Hyponatremia and the syndrome of inappropriate antidiuretic hormone (SIADH) release are also reported following MDMA use (9,10,36). MDMA releases antidiuretic hormone (ADH) in human volunteers (37), which combined with a loss of solute during exercise and the intake of free water, have decreased serum sodium levels and caused seizures.

Poison center data should always be interpreted cautiously. These cases were gathered passively and case information was supplied via telephone calls by poison center staff. Detailed data on these cases varies from sparse to near complete, where the most seriously ill patients were followed most closely. None of the patients reported in this series were reported to have MDMA levels verified in the blood.

Conclusion

This study represents the largest collection of cases of MDMA use to date. Although these cases were gathered passively from poison center data, they strongly support the idea that most users of MDMA are young and that the number of users who become ill is growing. We support a rapid screening process for the potentially devastating complications of MDMA use, including the measurement of a core body temperature and serum sodium level, while providing appropriate supportive care.

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