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'Designer drugs'

Recognizing and managing their toxic effects

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Preview

"Adam," "Eve," "ecstasy," "China white." Illicit street drugs such as these are called designer drugs because they are designed to elicit certain effects and to bypass legal classification. Unfortunately, use and abuse of such substances can lead to serious medical problems and even death. Drs Sternbach and Varon describe the best-known compounds and discuss clinical characteristics and management of designer drug intoxication.

"Designer drugs" are substances intended for recreational use that have been modified from legitimate pharmaceutical agents to circumvent legal restrictions.[1] They are created by underground chemists who make slight alterations in the molecular structure of existing drugs. The drugs often have substantially greater potency than their parent compounds. Illicit production of designer drugs is relatively easy and inexpensive. During the 1970s, analogues of phencyclidine, methaqualone, and mescaline were popular drugs of abuse.[1] During the past decade, a number of new analogues have been produced. Use of such substances is increasing and constitutes a substantial health threat.

Currently, the most prominent designer drugs are analogues of meperidine, fentanyl, mescaline, and methamphetamine. The common designer drugs and their chemical designations are listed in table 1. As is often the case with drugs of abuse, a number of colorful street names have been used to identify these compounds (table 2).[2]

Synthetic opioids

Two types of synthetic opioids—derivatives of meperidine and of fentanyl—have become popular designer drugs because of their heroinlike effects on users.

MEPERIDINE DERIVATIVES—The classic designer drugs were based on the opiate meperidine (Demerol) hydrochloride.[3] Meperidine derivatives are sometimes called "designer heroin," although that is a misnomer because meperidine is actually the parent compound. In fact, heroin itself was initially produced in 1898 through the acetylation of morphine, which makes morphine the original opioid designer drug.

A compound marketed as "new heroin" and "synthetic heroin" was initially sold by drug dealers in San Jose, California, in 1982. The active substances were eventually identified as MPPP (1-methyl-4-phenyl-4-propionoxypiperidine) and MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine), both meperidine analogues.[4] MPPP is popular among drug dealers because when it is injected, it produces a euphoria similar to that produced by heroin.

MPPP and MPTP initially came to the attention of the medical community because irreversible Parkinson's disease developed in some users.[5] The effects were found to be caused by MPTP, which subsequently was shown to produce neuronal enzyme inactivation in the substantia nigra.[6] If the synthesis of MPPP from meperidine is not performed carefully, significant amounts of MPTP are produced. The parkinsonian syndrome results in increased muscular tone, difficulty in moving and speaking, drooling, and cogwheel rigidity of the upper extremities. Postural tremor in such patients characteristically involves the proximal muscles and is more pronounced than the typical involuntary rest tremor occur-

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The difference between a dose of "China white" that produces euphoria and a dose that leads to respiratory depression and death is slight.

Table 1. Chemical names of common 'designer drugs'

Meperidine derivatives
MPPP (1-methyl-4-phenyl-4-propionoxypiperidine)
MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine)

Fentanyl derivatives
α-Methyl-fentanyl
3-Methyl-fentanyl

Mescaline-methamphetamine derivatives
MDMA (3,4-methylenedioxymethamphetamine)
MDA (3,4-methylenedioxyamphetamine)
MDEA (3,4-methylenedioxyethamphetamine)

Table 2. Street names of common 'designer drugs'

α-Methyl-fentanyl
"China white"

MDMA
"Ecstasy"
"XTC"
"Adam"
"M & M"
"Hug drug"

MDA
"Love drug"

MDEA
"Eve"

ring in idiopathic parkinsonism.[7,8]

FENTANYL DERIVATIVES—Fentanyl (Sublimaze) is a synthetic opioid used extensively as an analgesic and tranquilizing agent in surgical procedures. It was introduced for clinical use in 1968. Its chemical structure is quite different from that of morphine. It has a short duration of action and a potency about 80 times that of morphine.[9] Illicit production of potent fentanyl derivatives began in the early 1980s.

The best-known fentanyl derivative is "China white" (α-methyl-fentanyl), which initially appeared in Orange County, California, in 1979. It was sold to heroin addicts because it duplicated the euphoria of heroin and resembled heroin from Asia in appearance. In fact, however, α-methyl-fentanyl is about 1,000 times more potent than heroin.[1] The difference between a dose that produces euphoria and one that leads to respiratory depression and death is slight.[10] Consequently, fatal overdoses of "China white" were soon reported.[9] Acute narcotic overdose syndrome was the typical cause of death. However, urine toxicologic testing was negative for opioids, because the amount of fentanyl used was minute and most toxicology laboratories did not test for fentanyl type substances.

Fentanyl derivatives are most commonly taken intravenously, although they can be smoked or snorted. The degree of euphoria achieved depends on the dose and the route of administration.

Since the identification of α-methyl-fentanyl, a number of similar analogues have been discovered in street drug samples (eg, "Mexican brown," "Persian

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With use of MDMA, or "ecstasy," acute psychiatric disturbances, including panic, anxiety, and paranoid thinking, may occur.

white").[4] Some are more potent than "China white." It has been estimated that 20% of heroin addicts in California are abusing fentanyl analogues.[1,4] More than 100 deaths have been attributed to synthetic fentanyl.[11]

Mescaline-methamphetamine analogues

Mescaline-methamphetamine analogues were initially synthesized in the early 1900s. They recently have been rediscovered and produced as street drugs.

MDMA—MDMA (3,4-methylenedioxymethamphetamine), best known as "ecstasy" or "Adam" on the street, is structurally similar to methamphetamine and mescaline. Consequently, it stimulates the central nervous system and produces hallucinogenic effects. MDMA was first synthesized in 1914 and was developed as an appetite suppressant, though it was never marketed as such.[12]

MDMA first appeared as a drug of abuse in 1972, but it was not widely used until the 1980s.[9] A number of deaths have been linked to its abuse. The cause of these deaths is uncertain, but it has been postulated that MDMA induced fatal cardiac dysrhythmias, hyperthermia with seizures, or intracranial hemorrhage in its victims.[2,13]

MDMA is typically taken orally. In its purest form, it is a white powder that can be packaged in clear gelatin capsules.[14]

MDMA is popular because it produces positive changes in state of mind, which have been variously described as elevated mood, increased self-esteem, and increased sense of intimacy with others.[12] However, because MDMA is closely related to the amphetamines, it may cause acute psychiatric disturbances, including panic, anxiety, and paranoid thinking.[4] Chronic abuse may produce a paranoid psychosis clinically indistinguishable from schizophrenia.[14] In the animal model, MDMA produces neurologic damage, selectively destroying cerebral nerve cell endings that release serotonin.[15] MDMA has also been reported to cause tachycardia, jaw clenching, nystagmus, ataxia, tremor, and hallucinations.[12] Acute intoxication with MDMA may produce life-threatening dysrhythmias, hypertension, hyperthermia, and seizures.[14]

MDA—MDA (3,4-methylenedioxyamphetamine) was initially synthesized in 1920.[16] Proposed uses reflected the anorectic, antitussive, and tranquilizing activities of the drug. Extensive abuse was not reported until the late 1960s.[17]

MDA and its metabolites release norepinephrine and block norepinephrine reuptake. Its mild euphoric and intoxicating effects earned it the street name "love drug." Ingestion of MDA produces a heightened need for interpersonal relationships. Those under the influence of the drug have an increased desire to be with and talk to people. Effects occur within 30 to 60 minutes of ingestion and last 6 to 10 hours.[17]

Signs and symptoms of MDA toxicity resemble those of amphetamine intoxication (hyperactivity, mydriasis, hyperthermia, tachycardia, hypertension, seizures). Several deaths have been attributed to MDA overdose, including one in a patient whose clinical presentation resembled that of severe amphetamine intoxication, which subsequently led to rhabdomyolysis, adult respiratory distress syndrome, and disseminated intravascular coagulation.[18]

MDEA—Following the designation of MDMA as a Schedule I controlled substance by the Drug Enforcement Administration, MDEA (3,4-methylenedioxyethamphetamine), which is known on the street as "Eve,"

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Ingestion of MDA, or the "love drug," produces a heightened need for interpersonal relationships.

appeared on the market as an analogue. The effects of MDEA are similar to those of MDMA. Deaths associated with MDEA have been reported, though cause could not definitely be attributed to the drug.[13] As with other deaths related to designer drug use, such deaths are rarely witnessed, often occur outside the hospital setting, and may take place in the presence of underlying physical illness or suicidal feelings.

Clinical presentation and management

The most dramatic effect of the synthetic opioids is acute overdose, which resembles narcotic overdose. Pupillary constriction, respiratory depression, and diminished level of consciousness are characteristic. Management is similar to that of narcotic overdose. Ventilatory support is required, and the opioid antagonist naloxone hydrochloride (Narcan) is administered. Because many designer opioids have markedly greater potency than natural opioids or heroin, the doses of naloxone required are likely to be higher than those used in treating standard narcotic overdose. An initial dose of 4 mg has been recommended.[4] Some patients may require continuous naloxone infusion.

Because MPPP is more potent than heroin on a comparable weight basis, overdoses with MPPP are particularly likely.[3] The effects produced by fentanyl and its analogues are intense but short-lived. The most dangerous acute effect is respiratory depression, which reaches its maximum 5 to 10 minutes after administration and resolves within 30 minutes.[14] Massive pulmonary edema has also been reported.[7]

The parkinsonian syndrome produced by MPTP can be managed with standard medications, such as levodopa and carbidopa (Sinemet).[8] However, because the syndrome is irreversible, symptoms recur if the patient discontinues the medication.

The acute psychiatric disturbances produced by the mescaline-methamphetamine analogues (panic, anxiety, paranoia) should be managed by "talking down" the patient and providing a comfortable, low-stimulus environment. Severe agitation can be controlled with haloperidol (Haldol) or benzodiazepines.[4,14] Hyperpyrexia should be treated with cooling blankets or ice baths. Hypertension may be treated with an alpha blocker such as phentolamine (Regitine), an alpha and beta blocker such as labetalol hydrochloride (Normodyne, Trandate), or a vasodilator such as nitroprusside sodium (Nipride, Nitropress).[14]

Some authorities have proposed the use of chlorpromazine hydrochloride (Thorazine) as an antidote for acute MDMA toxicity.[14] In the canine model, intravenous administration of chlorpromazine (10 mg/kg) was found to hasten restoration of normal hemodynamics and temperature.[19] Renal clearance of MDMA may be enhanced by acidifying the urine with oral ascorbic acid or ammonium chloride. However, acidification may increase the risk of renal tubular damage secondary to myoglobinuria.

Extent of the problem

The production and sale of designer drugs has been estimated to be a billion-dollar industry.[11] *Esquire* magazine, in a recent assessment of trends of the 1990s, identified "ecstasy" as the "new sincerity drug" of choice (replacing cocaine of the previous decade), because "it kills irony" (March 1991, pp 141-6).

A number of factors combine to make the dissemination and use of designer drugs a particular public health menace. Many of these substances can be produced

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Designer drugs are often more potent and less expensive than their parent compounds, so incentives for illicit production are substantial.

with relative ease, with minimal cost, and without the need for extensive or specialized knowledge of chemistry. Because synthetic counterparts are often more potent and less expensive than their parent compounds, the incentives for illicit production are substantial. Although the initial reports of designer drug abuse emanated from California, use of these substances has subsequently been reported nationally and worldwide.

An attendant problem is the relative difficulty of legally controlling designer drugs. New drugs have initially escaped control and classification because they have not been structurally identical to controlled substances. A number of designer drugs became controlled substances after their potential for abuse was recognized. However, once a drug's use is restricted by the Drug Enforcement Administration, a minor modification of its molecule may produce a new compound that is not regulated. Consequently, there is the potential for production of an almost infinite variety of designer compounds. This possibility has brought about a call for the regulation of entire classes of pharmaceutical compounds, rather than just single agents.

Conclusion

"Designer drugs" add a worrisome new dimension to the drug abuse epidemic. Use and abuse of these illicit substances will likely continue in the coming years. Physicians who are familiar with designer drugs and their adverse effects will be well equipped to recognize designer drug intoxication and treat its attendant toxic effects. PGM

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Accuracy of the references is the responsibility of the authors.

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