

IMPLICATIONS OF RESEARCH FOR TREATMENT: **KETAMINE**

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Ketamine, a derivative of phencyclidine hydrochloride, is an anesthetic that has been approved for human and animal use, both in trauma and emergency surgery as well as in veterinary medicine. The drug's potential for abuse has been recognized since the early 1970s. Ketamine on the street is also known as Special K, Vitamin K, K, kit-kat, keets, super acid, super k, and jet [1]. Ketamine users try to achieve or "fall into" a "k-hole," which is described as physical immobilization and social detachment lasting up to an hour. It is characterized by a distorted sense of space, such as a small room appearing the size of a football field, and an indistinct awareness of time, such as a few minutes seeming like an hour. As the body slows and disengages from time and space, the mind turns to experiential realms such as spiritual journeys, interactions with famous or fictitious persons, and hallucinatory visions. The k-hole ends rather abruptly but can be quickly reentered following another dose of ketamine [2].

LATEST RESEARCH FINDINGS

Ketamine is a Schedule III controlled substance and is available in powder and tablet forms as well as an injectable formulation. It is difficult to manufacture and most users acquire it through diversion of the prescription product or theft from veterinary supplies. It is usually inhaled, although it can also be injected. Ketamine users will often take several sequential doses of the drug in order to maintain psychotropic effects over time. Elimination half-life is approximately two hours. Anesthesia doses are 2 to 10 mg/kg while recreational doses can range between 50-100 mg [3].

Adverse Effects

Eighty percent of patients who came to Drug Abuse Warning Network emergency rooms in 2002 with a mention of ketamine use also were using other drugs: alcohol (29%), heroin (24%), marijuana (19%), cocaine (13%), MDMA (12%),

methamphetamine (7%), amphetamines (4%), LSD (3%), and GHB (3%). The motives for use of ketamine were psychic effects (68%), suicide (16%), or other/unknown (16%). The reason for going to the emergency department was overdose (47%), unexpected reaction (28%), chronic effects (11%), or seeking detoxification (9%) [4].

Cognitive/Psychiatric Associations

Frequent users often take ketamine in a pattern of cyclical binges similar to cocaine or amphetamine dependence. Tolerance builds rapidly and can be very high. Users can become psychologically dependent, with craving and a high tolerance, but there is little documented evidence of a physical withdrawal syndrome [5], although the literature does contain case reports [6]. At high doses, ketamine can cause delirium, amnesia, impaired motor function, high blood pressure, depression, and potentially fatal respiratory problems. Low dose effects are described as "mild, dreamy, floaty, and

slightly outside their bodies.” Higher doses produce hallucinogenic “trippy” effects that make one seem far away from one’s body, and reaching the “K-hole” is described as being a near-death experience that can be frightening or “spiritually significant,” according to websites. Flashbacks can recur days or weeks after use [7].

In recreational users, ketamine appears to induce acute and severe impairments of working, episodic, and semantic memory as well as psychotogenic and dissociative effects [8]. These effects could reflect chronic or residual effects of taking the drug or pre-existing differences in ketamine users [9], but they also suggest that repeated use of ketamine produces chronic impairments to episodic memory, findings which have worrying implications for the burgeoning population of ketamine abusers [10].

A survey of individuals in Sydney who had ever used ketamine found they were a well-educated older group of party drug users who used ketamine while dancing. Many users had experienced significant negative effects such that some had either reduced their dose or stopped use altogether. Users reported regularly experiencing an inability to speak, blurred vision, lack of coordination, and increased body temperatures. However, these symptoms were seen by the users as positive effects of the drug which encouraged, rather than discouraged, experimentation among regular party drug users [11].

While ketamine is typically inhaled, a study of young ketamine injectors in New York City found intramuscular injecting more common than intravenous injection. Multiple injections within a single episode were common, and bottles of ketamine were shared. Most use was not in club or rave settings but in a street or park, as injecting ketamine often created an experience that did not require a specialized setting such as a rave. Ketamine injectors represent an emerging, though often hidden, population of injection drug users who are at high risk both because of their injecting practices and their homelessness, drug dealing, and sex work [2].

The survey of gay and bisexual men in San

Francisco who attended circuit parties found that among those who reported a drug overuse incident in the past year, 45% said ketamine was the drug most often involved. In the most recent circuit party weekend, among those who had used three or more drugs, 58% had used ketamine [12]. In addition, a study of gay and bisexual males attending circuit parties in three cities found over 60% had used ketamine at parties in the past year and the relationship with unsafe sexual behavior was significantly associated with frequent use of ketamine [13].

An HIV-specific issue is that adherence to antiretroviral regimens is a primary concern and the hallucinogenic effects of ketamine may affect drug-taking behavior and cardiovascular effects of the drug may be deleterious among patients with underlying heart disease or lipid abnormalities [14].

Recreational exposure to subanaesthetic doses of ketamine is likely to induce wide-ranging compromise of cognitive function ranging from mnemonic to attentional to motor domains. Even if such acute compromise of function was short lasting, it might produce significant secondary and tertiary health risks ranging from disruption of the ability to operate a motor vehicle to poor decisions regarding risky sexual behavior, which may be of particular importance for ketamine-using subpopulations [15].

Long-term cognitive or neuropsychiatric effects have not been sufficiently studied in ketamine users [7]. Earlier studies found that chronic abuse of ketamine may be associated with persisting impairment of memory and other cognitive function in humans, although it may not affect attentional processes or spatial memory but may interfere only selectively with cognition [15]. As with other “club drugs,” drug-challenge investigations of the effects of ketamine in humans are limited by ethical concerns.

A study of compulsive ketamine use found it acutely impaired response inhibition and had related biphasic effects on the subjective reinforcing effects of the drug. It altered glutamatergic transmission, which may underlie the continued compulsive abuse

of ketamine. There was no residual cognitive affects following a single dose of ketamine, but it did increase schizophrenic-like and dissociative symptoms [16].

TREATMENT IMPLICATIONS

In 2004, 7 clients with a primary, secondary, or tertiary problem with ketamine were admitted to programs funded by the Texas Department of State Health Services. Average age was 17.7 years, all were male, 57% were White and 43% were Hispanic. All had been referred from the criminal justice system and 43% had a history of injecting drug use. Other drugs used with ketamine included marijuana, hallucinogens, cocaine, and ecstasy.

No antidote exists for ketamine overdose; management is supportive care with special attention to cardiac and respiratory functions [17]. Two ketamine-dependent patients who presented to psychiatric services in Singapore had psychedelic and psychotic effects that were dose-related and included multimodal hallucinatory experiences, a sense of slowing, paranoid ideation and enhancement of sexual, musical, and sensory enjoyment. The psychotic symptoms resolved

quickly with symptom-targeted treatment, but breaking the ongoing compulsion to use seemed more difficult [18].

After detoxification, one treatment protocol recommended following the model used for cocaine and amphetamine dependence, with abstinence from all drugs from day one. As with stimulant dependence, the therapist should avoid confrontation, as the likelihood of the person dropping out of treatment was very high. Relapse prevention involved discovering what situations and triggers occur before taking the steps which lead to relapse so alternative responses could be developed [6]. Additional studies are needed to better understand the extent of ketamine abuse and dependence and to identify symptoms of withdrawal and effective treatments [7].

TOXICOLOGY

Ketamine is not detected in routine drug screens, and clinicians should be aware that immunoassays for PCP may cross react with ketamine assays [18]. High-performance liquid chromatography is required to reliably detect ketamine [19].

GLOSSARY

antiretrovirals—substances used to kill or inhibit the multiplication of retroviruses such as HIV; antiretroviral drugs attack HIV, which is a retrovirus.

biphasic—having two phases.

circuit parties—multi-event weekends that cater to gay and bisexual men and can be a venue for use of drugs and alcohol.

dependence—a pattern of substance misuse characterized by a combination of factors, such as withdrawal, tolerance, cravings, out-of-control use, and use despite negative effects.

depression—a mood disorder characterized by poor appetite or overeating, sleeplessness or hypersomnia, low energy or fatigue, low self-esteem, feelings of hopelessness, and difficulty concentrating or making decisions.

disseminated intravascular coagulation—a complex and controversial systemic thrombohemorrhagic disorder involving the generation of intravascular fibrin and the consumption of procoagulants and platelets. It is seen with a number of well-defined clinical situations, including sepsis and major trauma.

dissociative—of, relating to, or tending to produce dissociation, such as the dissociative phenomena associated with schizophrenia.

executive functioning—associated with mental operations such as planning, working memory, and initiation and self-regulation of goal-directed behavior.

glutamatergic transmission—transmission of glutamate, the main excitatory neurotransmitter in mammals.

hypertension—high blood pressure.

k-hole—described as a “desired” state of physical immobilization and social detachment lasting up to an hour caused by abuse of ketamine.

mnemonic—assisting or intended to assist memory.

psychosis—a thought disorder in which reality is grossly distorted. Symptoms can include seeing, hearing, smelling, or tasting things that are not there; paranoia; delusions. Psychosis can occur as a result of brain injury or disease, and is seen particularly in schizophrenia and bipolar disorders.

psychotogen—a chemical agent (as a drug) that induces a psychotic state.

rave—an all-night dance party.

schizophrenia—a severe mental illnesses whose symptoms may include loss of personality (flat affect), agitation, catatonia, confusion, psychosis, unusual behavior, and withdrawal. The illness begins in early adulthood in many cases.

verbal fluency letter generation—a classic neuropsychological test of language production which involves subjects generating and articulating a word in response to a cue the Verbal Fluency Task. As an example, in the letter category, participants are asked to produce as many words as possible beginning with a specified letter in one minute.

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