CASE REPORT
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Dystonic Reaction After Ketamine Abuse

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A 20-year-old man developed an acute dystonic reaction following the self-administration of ketamine. The episode resolved upon treatment with diphenhydramine. Dystonia is an unusual toxic effect of ketamine abuse; potential mechanisms for its occurrence in this instance are discussed. [Felser JM, Orban DJ: Dystonic reaction after ketamine abuse. Ann Emerg Med 11:673-675, December 1982.]

INTRODUCTION

Ketamine, an intravenous general anesthetic chemically related to phencyclidine, has recently gained attention because of its abuse potential, especially on the West Coast.[1] We report a case of drug-induced dystonia that occurred after the self-administration of ketamine. Dystonia is an unusual adverse effect of ketamine, and mechanisms possibly responsible in this instance are discussed.

CASE REPORT

A 20-year-old man self-administered 0.5 cc of ketamine intravenously. Syringes, needles, and ketamine were obtained from a nearby veterinary hospital. No other drugs were concomitantly administered, and the patient had used ketamine before. Ten hours later, the patient presented to the UCLA Emergency Medicine Center after noting five episodes of sustained abnormal tongue and neck movements that interfered with speech. The last of these began one hour prior to arrival. At no time was generalized motor activity or loss of consciousness noted. The patient denied history of previous neurologic abnormalities.

Physical examination revealed an anxious but healthy-appearing man who was afebrile with stable vital signs including temperature, 37 C; blood pressure, 140/90 mm Hg; pulse, 86; and a respiratory rate of 18. Neurologic exam revealed equal and reactive pupils at 5 mm. The tongue was protruded and deviated to the left side and the neck was held in extension while deviated to the left. The patient was unable to speak, yet he was alert and able to communicate in writing. Deep tendon reflexes were 2+ and symmetric throughout; plantar responses were flexor bilaterally.

Serum chemistry studies included sodium, 140; potassium, 4.4; chloride, 107; bicarbonate, 24; glucose, 108; BUN, 22; and calcium, 9.5. Urinalysis was unremarkable. A dystonic reaction was diagnosed and diphenhydramine 50 mg was administered intravenously, resulting in complete resolution of the episode within three minutes. No recurrence of dystonia occurred during four hours of observation. The patient was completely asymptomatic for one month following the episode, after which he was lost to follow-up.

DISCUSSION

Ketamine was introduced as an anesthetic agent in the late 1960s after its predecessor, phencyclidine, was not approved for human use.[2] Both compounds are arylcyclohexylamines (Figure 1). Ketamine's original code name was CI-581 and it is currently marketed under the names Ketalar®, Ketaject®,

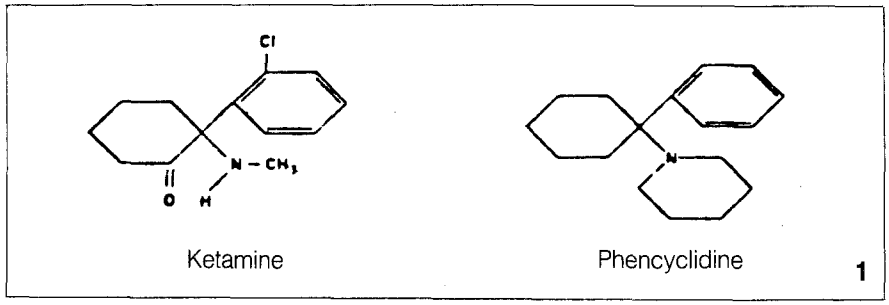

Fig. 1. *Structure of ketamine and phencyclidine.*

Solutions	Powders
K	Green
Kay	Purple
Jet	Mauve
Super Acid	Special LA Coke
1980 Acid	Super C
	K

2

Fig. 2. *Street names for ketamine (from Siegel[4]).*

and Ketavet®. Initially, the drug was greeted enthusiastically because it produces analgesia without cardiovascular depression and loss of protective reflexes. In addition, it is administered intravenously. However, because of central nervous system (CNS) toxicity, ketamine is currently reserved only for special situations, such as diagnostic procedures in children and during head and neck surgery.[3]

The most notable adverse effects of ketamine involve emergence reactions characterized by confusional states, hallucinations, vivid dreaming, and delusions. These reactions occur in approximately 12% of the patients.[1]

Abuse of ketamine has become popular. This practice was first noted on the West Coast in 1971.[4] Ketamine abuse in other countries has also been reported, as has abuse among physicians.[5] Most instances of ketamine self-administration involve abuse or experimental use. Only rarely is intensive or compulsive drug use noted.[4] In these settings, ketamine is administered intranasally, intramuscularly, intravenously, and by inhalation.[4] Several of the street names for ketamine (Figure 2) refer to its green crystalline appearance or the dark red color of Vitamin B-12 with which it is often admixed in the belief that this minimizes adverse reactions.

In addition to psychoactive effects, neurotoxic effects of ketamine have also been described (Table). The most serious involve convulsions;[6] these occur to a greater degree with phencyclidine.[6]

The dystonic reaction seen in our patient is distinctly unusual. Extrapyramidal disorders occur as a side effect of many drugs, especially phenothiazines and butyrophenones;[7] other agents such as tricyclic antidepressants, L-DOPA, antihistamines, anticonvulsants,[8] and metoclopramide[9] have also been implicated.[8] Reversible extrapyramidal effects that occur early in the course of drug treatment are classified in three categories:[10] drug-induced dystonia (DID), drug-induced Parkinsonism (DIP), and akathisia. Late-appearing neurologic sequelae (tardive dyskinesias) are associated with prolonged drug administration.[10]

Acute dystonic reactions are characterized by abnormal and prolonged muscle spasms that commonly involve the tongue, face, neck, and back.[11] Dystonia occurs in various CNS disorders as well as in idiopathic torsion dystonia (ITD), a familial disease in which dystonia is the predominant feature.[12] In contrast to DIP, which is more frequent in elderly individuals or those with antecedent CNS disease,[13] DID usually occurs in young, otherwise healthy patients. The maximum risk of developing DID occurs during the first week of treatment,[7] especially several hours after a dose when rapid diminution of blood levels is occurring.[14] The most common reactions seen in a large series of DID patients were buccolingual and torticollic abnormalities.[15] Our patient's episode of DID is consistent with all the above associations.

The factor common to all drugs that characteristically produce DID is blockade of dopaminergic receptors.[7] Such blockade has been used for years to explain the pathophysiology of DIP by analogy to idiopathic Parkinson's disease, in which degeneration of dopaminergic nigrostriatal pathways occurs.[11] In both idiopathic and drug-induced Parkinsonism, reduced central dopaminergic activity is believed to result in an imbalance between dopaminergic and cholinergic systems whereby a relative increase in cholinergic activity ensues. The benefit of anticholinergics like benztropine in both Parkinsonian conditions is consistent with this mechanism.[11]

However, several observations suggest that DID and DIP result from different pathophysiologic mechanisms. Forms of treatment other than anticholinergics are useful in DID and

include other CNS stimulants and depressants, drugs that are ineffective in DIP.[7] In addition, DID occurs early in the course of therapy, whereas DIP characteristically occurs after several weeks of treatment.[13] Finally, the neuroanatomical model that best explains the interaction of dopaminergic and cholinergic neurons in the basal ganglia correlates increased cholinergic activity with Parkinsonian akinesia, whereas dystonia represents a hyperkinetic state.[16]

Although DID may result from dopaminergic blockade, dopaminergic/cholinergic imbalance may not be responsible. A recent review[13] suggests that DID may result from dopaminergic/noradrenergic imbalance in the basal ganglia by analogy to ITD, because elevated levels of dopamine beta-hydroxylase (DBH) have been found in patients with ITD. DBH is the enzyme responsible for conversion of dopamine to norepinephrine and its levels in plasma are reflective of noradrenergic activity.[17] It is postulated that ITD and DID result from increased noradrenergic activity relative to dopamine.

Ketamine is not a drug that results in dopaminergic blockade or depletion, yet it may have produced dystonia in our case because of its potential to enhance central noradrenergic activity. Some experimental studies[18] have suggested that influence on noradrenergic transmission may underlie the actions of ketamine and its congener, phencyclidine. Ketamine has been shown to inhibit uptake of tritiated norepinephrine in rat cortical synaptosomes.[19] Miletich and colleagues[20] also showed that ketamine inhibits re-uptake of norepinephrine in the rat heart. Since neurotransmission at noradrenergic synapses is terminated mainly by re-uptake, blockade of this mechanism would result in increased central noradrenergic activity. Thus ketamine has the potential to produce dystonia on the basis of enhanced noradrenergic activity rather than dopaminergic blockade.

It remains unexplained why our patient developed DID following ketamine abuse. Episodes of DID can precede the development of ITD, and non-affected relatives of patients with ITD have a higher incidence of DID.[21] Our patient's family did not have a history of neurologic disease at the time of the episode.

TABLE. *Neurotoxic effects of ketamine (from Siegel[4])*

Effect	%
Ataxia	100
Slurring of speech	70
Dizziness	61
Mental confusion	35
Blurred vision	17
Anxiety	13
Insomnia	13
Decreased sexual motivation	9
Seizures	4

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