

# Psychosis and Severe Rhabdomyolysis Associated with Synthetic Cannabinoid Use: A Case Report

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## Abstract

**Background:** Synthetic cannabinoid (SC) or “spice” refers to a variety of herbal/chemical mixtures, which mimic the effects of marijuana. They are generally marked as “herbal incense” and best known by the brand names of “K2,” “spice,” “aroma,” “Mr. Nice Guy” and “dream.” Little data are available on the psychopathological and physical effects of SC. **Case Description:** We reported on a 23-year-old man without prior psychiatric history who developed acute psychosis and severe rhabdomyolysis (creatinine phosphokinase [CPK]: 44,300 UI/L) associated with “Mr. Nice Guy” consumption. To our knowledge, this is the first case report of severe rhabdomyolysis associated with SC use in the U.S. **Conclusions:** Physicians should be aware of the possibility of new-onset psychotic symptoms and rhabdomyolysis in patients that use SC.

**Key Words:** Synthetic Cannabinoids (SC), Psychosis, Rhabdomyolysis, Spice, Creatine Phosphokinase (CPK)

## Introduction

Synthetic cannabinoids (SC) are marked as “herbal incense” and refer to a series of products that are advertised and sold legally in some states in the U.S. (1). They are best known by the brand names of “K2,” “spice,” “aroma,” “Mr. Nice Guy” and “dream” (2-4). In March 2011, the U.S. Drug Enforcement Administration (DEA) temporarily placed five synthetic chemicals—JWH-018; JWH-073; JWH-200; CP-47, 497; and, cannabicyclohexanol—into Schedule I of the Controlled Substances Act. These substances produce

drug-like effects that resemble those resulting from tetrahydrocannabinol, a cannabinoid and the primary psychoactive ingredient in marijuana, but have different chemical structures. They are used to coat herbal blends, which are then sold under the names of “K2,” “spice,” “Mr. Nice Guy” and others. Under the DEA ruling, punishment for the possession or sale of these chemicals is the same as those for marijuana (5).

Delta (9)-tetrahydrocannabinol (THC) is responsible for most of the characteristic psychoactive effects of cannabis. However, its acid metabolite THC-COOH, the non-psychoactive cannabidiol (CBD), several cannabinoid analogues and newly discovered modulators of the endogenous cannabinoid system are also promising candidates for clinical research and therapeutic uses. Cannabinoids exert many effects through activation of G-protein-coupled cannabinoid receptors in the brain and peripheral tissues. Additionally, there is evidence for nonreceptor-dependent mechanisms. Previous research indicated that CBD attenuated THC’s

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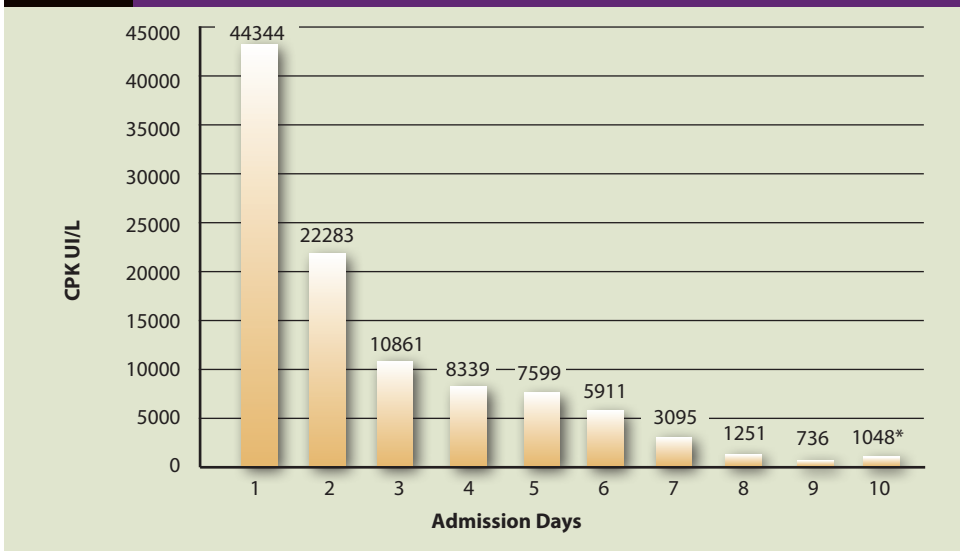
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**Figure 1** Creatine Phosphokinase (CPK) Levels



\*Patient received intramuscular medications and was placed in restraints.

pharmacodynamic effects, but the mechanism of interaction is unidentified. CBD may have anti-anxiety effects and lessen the psychoactive effects of THC. Of relevance, SC lacks CBD component; therefore, its psychoactive effects are actually unopposed (6).

Psychotic relapses following the use of SC have been reported in the literature. Intoxication with SC is associated with acute psychosis, worsening of previously stable psychotic disorders, and the ability to trigger a chronic (long-term) psychotic disorder among vulnerable individuals (3, 4, 8, 10, 12).

Alcohol, cocaine and other drugs are thought to produce conditions leading to muscle destruction from compression and ischemia caused by extreme exercise, catatonic states, and muscular hyperactivity, causing rhabdomyolysis (7). This condition is characterized for laboratory data indicating elevated creatine phosphokinase (CPK, normal values are between 60 and 400 UI/L).

We report on a 23-year-old Hispanic man who developed acute psychosis and severe rhabdomyolysis (CPK: 44,300 UI/L) after “Mr. Nice Guy” consumption.

### Case Report

Mr. V is a 23-year-old male with no known psychiatric or medical history who was brought to the medical emergency room due to altered mental status and severe agitation. The patient was reportedly banging his head on the ground and hitting himself while working as a waiter. Upon arrival to the hospital, the patient was agitated, disoriented to person, place and time, but no disturbance of conscious-

ness was noted. His mood was angry; his affect was irritable, labile and inappropriate. The patient was visibly psychotic as evidenced by persecutory delusions. According to emergency room records the patient was “discussing that people are evil.” He did not appear to be responding to internal stimuli. He denied suicidal or homicidal ideations or plans. His insight, judgment and impulse control were severely impaired.

Physical evaluation, including the neurologic exam, was unremarkable except for heart rate of 152 beats per minute as well as ecchymosis in the right arm. Abnormalities in the laboratory workup revealed CPK: 44,344 UI/L; anion gap: 27 (normal: 8–16); osmolality: 297 mOsm/kg (normal: 285–295); WBC: 20 x10E3/uL (normal: 4–10.5); glucose: 164 mg/dl (normal: 65–100); AST: 670 units/L (normal: 3–44); and, ALT: 316 units/L (normal: 0–40). The urine drug test was positive for cannabinoids only; results for phencyclidine (PCP) and methylenedioxypyrovalerone (MDPV) or “bath salts” were negative. CT scan of the brain and EEG were unremarkable. At the time of admission, the patient was treated aggressively with intravenous fluids and lorazepam in order to prevent renal failure and to control episodes of agitation, respectively.

Collateral information was obtained. As per mother, Mr. V had been behaving erratically for four days prior to admission. She reported that the patient had a dispute with his best friend regarding a car that his friend was selling to the patient. He thought that his “friend was in a cult and was the devil.” She stated that after the dispute he drove off and immediately wrecked his car but was uninjured. She stated that for the past four days the patient has not been sleeping

or bathing, and has at times been sleeping in his car and has recently been accusing her of being the devil. The patient's mother reported that Mr. V started using marijuana in his early teens but never behaved like this before. Family history was pertinent for a maternal uncle with schizophrenia.

On Day 2 of admission, the patient remained very suspicious, to the point of thinking that the normal saline drip was a "poisonous substance." He adamantly denied any recent substance use and reported a remote history of marijuana use, with last use "weeks ago." He denied the use of other illicit drugs such as cocaine, opiates, PCP, "spice" or "bath salts." At this time, intravenous lorazepam every six hours as needed for agitation was continued, but antipsychotics were not started due to the possibility of slowing down the resolution of rhabdomyolysis.

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During the course of hospitalization the patient was superficially cooperative, guarded and demanding. The patient was hypervigilant of the surroundings, scanned name tags and endorsed delusions of the "devil controlling things around me." In addition, the patient continued displaying episodes of agitation and aggression. The patient attempted to escape on more than one occasion, requiring physical and chemical restraints. Given the aggressive nature of the patient's behavior, intramuscular chlorpromazine as needed was added to the lorazepam treatment regimen. CPK levels were monitored on a daily basis (see Figure 1).

On Day 9 of admission, the patient was transferred to the Psychiatric Adult Intensive Unit after being medically cleared. On Day 10 of admission, the patient tried to escape from the unit and had to be placed on four-point restraints. The patient was started on haloperidol 10 mg TID, valproic acid 500 mg QAM/1,000 mg QPM and lorazepam 2 mg TID. On Day 13 of admission, the patient became less suspicious and his degree of paranoia decreased to the point that he was visible on the unit and he started socializing with peers. The patient reported that six months ago he had begun using sporadically an SC sold under the brand name of "Mr. Nice Guy" as a substitute for cannabis. Later, he admitted that he was using it almost daily two weeks before the admission to the hospital. On Day 15 of admission, a complete resolution of symptoms was achieved, the patient was pleasant, cooperative and no evidence of psychosis was elicited. Therefore, he was deemed stable for discharge.

## Discussion

To our knowledge, a few cases reported new onset of psychosis after the use of SC but no cases of rhabdomyolysis with a CPK of 44,300 UI/L have been reported. Five case reports described patients with new onset of psychosis following the use of SC compounds (1, 3, 8, 18, 19). There are some anecdotal reports that suggest that smoked inhalation of SC marketed as "natural herbal incense mixtures" have overlapping effects when they are smoked with marijuana, such as anxiety, tachycardia and psychosis. However, systematic evaluation of the new generation of SC agonist (e.g., JWH-018)-related psychoactive effects and side effects are lacking (20, 21). A recent article showed that synthetic cannabinoid intoxication is associated with acute psychosis, worsening of previously stable psychotic disorders, and also may have the ability to trigger a chronic psychotic disorder among vulnerable individuals with known psychiatric history (1). In our case, the patient was previously healthy and even though he had an uncle with schizophrenia, his prior use of marijuana never precipitated a psychotic break until he started using "Mr. Nice Guy."

The patient experienced a prolonged psychotic episode with periods of extreme agitation that lasted more than ten days after his last use of "Mr. Nice Guy." A possible explanation is the chronic and recent heavy use of "Mr. Nice Guy." However, it is important to consider that the patient was not medicated with antipsychotics for the first three days due to the risk of worsening of rhabdomyolysis secondary to a possible acute dystonic reaction or severe rigidity. Furthermore, when antipsychotics were started, chlorpromazine was given at low doses and in "as needed" fashion.

A naturalistic study found that patients with drug-induced psychosis show greater symptom improvement than patients with schizophrenia when given similar doses of quetiapine for two weeks (15). Our patient responded to a six-day course of high doses of haloperidol (30 mg/day), valproic acid (1,500 mg/day) and lorazepam (6 mg/day) to control psychosis, irritability and agitation. To our knowledge there are no controlled studies that support high antipsychotic dosing in substance-induced psychosis.

Multiple causes of rhabdomyolysis have been described in the literature such as: muscle injury after trauma, limb ischemia, extreme physical exertion or prolonged stasis. Other causes include: infections, autoimmune disorders, catatonia, use of restraints, alcohol abuse and neuroleptic administration; however, the incidence is not well known in psychiatric patients (7). Two case reports described the association between rhabdomyolysis and mania (16). More extensive data show the relationship between cocaine intoxication and rhabdomyolysis (17). However, there is not enough

literature that proves the relationship between rhabdomyolysis and the use of SC. Our patient presented with four days of insomnia, erratic behavior and hyperactivity, which can lead to excessive physical exertion and muscle injury; two of the most common causes of rhabdomyolysis. In our case, all available history points toward rhabdomyolysis secondary to psychomotor agitation from SC-associated psychosis. However, the possibility that SC can cause rhabdomyolysis throughout other mechanisms such as direct muscle ischemia, central hyperthermia or electrolyte serum abnormalities requires further study. On the other hand, CPK values decreased over time as the patient was getting intravenous hydration while on the medical floor. On Day 10 of admission, there was a small increment of the CPK (see Figure 1) because the patient was placed in restraints and received intramuscular medications due to agitation while in the psychiatric unit. Since the tendency of the CPK was to go down, no further follow-up was made in the hospital. However, CPK values would normalize in the following days and a recommendation to follow CPK with internal medicine was made.

A limitation in this case report is the inability to confirm the synthetic cannabinoid metabolite in urine since the sample was never tested for JWH-018 metabolites. However, the sample was negative for cocaine, MDPV and PCP which can cause rhabdomyolysis and psychosis. On the other hand, it is important to mention that the possibility of contamination with an unknown substance or a new combination with “Mr. Nice Guy” could not be ruled out.

Physicians should be aware of the possibility of new-onset psychotic symptoms and rhabdomyolysis in patients that use synthetic cannabinoids.

### Conflict of Interest

None.

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