

# Severe neurological symptoms following synthetic cannabinoid intoxication

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## ABSTRACT

Synthetic cannabinoids are becoming increasingly popular as substances of abuse. However, in the Netherlands synthetic cannabinoid intoxications are rare. We report a 16-year-old male who became deeply comatose and was admitted to the intensive care unit for invasive mechanical ventilation after abuse of an initially unknown drug. Routine toxicology screening with an immunoassay only detected tetrahydrocannabinol, but additional tests with liquid chromatography mass spectrometry revealed synthetic cannabinoid use. This case underlines the challenging diagnosis of synthetic cannabinoid intoxications and the severe complications they can produce.

## KEYWORDS

Synthetic cannabinoids, intoxication, coma, drugs of abuse, LC-MS/MS

## INTRODUCTION

Synthetic cannabinoids are becoming increasingly popular as drugs of abuse, mainly in Europe and the United States.<sup>1</sup> As a result, patients are presenting to emergency departments with unwanted effects of these drugs. Synthetic cannabinoids are sold in colourful packages under various names, including 'spice', 'K2', 'crazy monkey' and 'chill out'. Synthetic cannabinoids are a chemically very diverse class of drugs and structurally different from tetrahydrocannabinol in natural cannabis, but all substances were designed to act as agonists of cannabinoid receptors (CB1 and CB2). This explains their

### What was known on this topic?

Although on the rise globally, synthetic cannabinoid intoxications are extremely rare in the Netherlands. Symptoms can be similar to cannabis. However, depending on the exact substance more serious neurological and cardiovascular complications may occur.

### What does this add?

Neurological symptoms of synthetic cannabinoid intoxications can be as serious as a comatose state with absence of some brain stem reflexes. Because of their low prevalence and the fact that synthetic cannabinoid intoxications are not detected in most urine toxicology screenings, their diagnosis in a clinical setting can be challenging.

psychoactive effects.<sup>1</sup> Although intoxications with synthetic cannabinoids are globally on the rise, they are still a very rare phenomenon in the Netherlands.<sup>2</sup> This case report describes a patient with very severe neurological symptoms after synthetic cannabinoid intoxication and explains why these intoxications can be very difficult to diagnose.

## CASE REPORT

A 16-year-old male with no medical history presented to our emergency department. The patient had lost consciousness after smoking cannabis and subsequently a drug called 'Bonsai'. On arrival to the emergency department physical examination revealed a Glasgow Coma Score of E1M1V1, dilated pupils, unresponsive to light and absence of some of the other brainstem reflexes.

Vital signs on presentation were normal except for mild tachycardia (100 beats/minute). ECG and laboratory examination showed no abnormalities. Because of persisting lack of consciousness the patient was intubated and invasive mechanical ventilation was started. A CT scan and CT angiography of the brain showed no pathological abnormalities.

A urine sample, which was obtained at admission, was positive for tetrahydrocannabinol but negative for amphetamines, barbiturates, benzodiazepines, cocaine, methadone, opioids and tricyclic antidepressants in our immunoassay testing kit. Ethanol and gamma-hydroxybutyric acid were measured in the serum, but could not be detected.

On the ICU we attempted to stop sedation. However, the patient became very agitated, so he was kept sedated overnight. The next morning sedation was successfully stopped and the patient was extubated and discharged home in good clinical condition.

After discharge, a toxicology screening of the patient's serum was obtained by liquid chromatography mass spectrometry (LC-MS/MS). The target screening method was based on the method described by Jaenicke et al.<sup>3</sup> and consisted of 32 synthetic cannabinoids. Based on the retention time and mass spectra, the presence of O-2545, a synthetic cannabinoid, was confirmed.

## DISCUSSION

Synthetic cannabinoids were originally developed as potential therapeutics.<sup>4</sup> However, since the early 2000s several synthetic cannabinoids are sold online and in smart shops as legal alternatives for cannabis. In American surveys amongst selective groups (students, club visitors) both life-time and past year intake of synthetic cannabinoid was reported to be around 6-8%.<sup>5,7</sup> In the Netherlands, synthetic cannabinoid use appears to be very rare.<sup>2</sup> This may be related to the availability of high-quality cannabis without legal consequences for possession. Because of the low prevalence of synthetic cannabinoids in the Netherlands, hospital admissions due to intoxications are very rare.

In this case, testing urine for the most common drugs of abuse only revealed tetrahydrocannabinol, which was consistent with the anamnesis as the patient had smoked cannabis. However, it was unlikely that tetrahydrocannabinol produced these severe neurological symptoms, so this was not helpful for the diagnosis. A quick online search on 'Bonsai'<sup>8</sup> pointed to a possible intoxication with the benzodiazepine phenazepam. However, neither the negative benzodiazepine screening in urine nor the clinical state of the patient seemed to support this hypothesis. Furthermore, phenazepam is usually taken

orally instead of being smoked. Only after additional searching of the literature did we define the working diagnosis as synthetic cannabinoid intoxication, which was confirmed after discharge by LC-MS/MS. This underlines the diagnostic difficulties that arise because synthetic cannabinoids are not detected by the commonly used kits for screening on drugs of abuse. Fortunately, definite confirmation of synthetic cannabinoids by LC-MS/MS is usually not necessary because their use is clear from the anamnesis and treatment is aspecific and mostly supportive.

After acute synthetic cannabinoid intoxication psychoactive symptoms, such as agitation, restlessness, confusion, anxiety and psychosis, are common.<sup>9</sup> Patients usually display physical signs that also occur with cannabis intoxication, including dilated pupils, red conjunctivae, nausea, slurred speech and sweating. Cardiovascular symptoms, such as hypertension, tachycardia and chest pain, may also be present and rarely synthetic cannabinoid intoxications can lead to myocardial infarction, kidney injury or death. Laboratory tests and electrocardiogram are generally normal and in many cases urine toxicology screens are negative for drugs other than tetrahydrocannabinol, which is often used on the same occasion. Importantly, synthetic cannabinoid use is not ruled out by negative drug screening for tetrahydrocannabinol nor confirmed by a positive tetrahydrocannabinol result.

Treatment of synthetic cannabinoid intoxication is usually supportive and determined by the order and magnitude of symptoms.<sup>10</sup> Agitation and confusion can often be managed with reassurance and avoidance of stimulation, while benzodiazepines can be administered for more serious symptoms such as psychosis. Rarely, prolonged sedation or intubation can be necessary to prevent end-organ damage or rhabdomyolysis. Mild intoxications typically last less than eight hours.<sup>11</sup> However, clinical effects and the duration and degree of toxicity depend on the specific compound used.

In conclusion, synthetic cannabinoid intoxications are on the rise in Europe and the United States. Although they are still very rare in the Netherlands, it is quite possible that Dutch emergency departments will be increasingly confronted with synthetic cannabinoid intoxications. Symptoms can be of greater magnitude and duration compared with cannabis intoxication. This patient presented with severe neurological symptoms including absence of some brain stem reflexes. Mechanical ventilation was necessary. Diagnosis of a synthetic cannabinoid intoxication can be challenging because it is not revealed by most urine drugs of abuse kits. Confirmation is possible with LC-MS/MS, but this technique is costly and is not readily available in most cases.

## DISCLOSURES

All authors declare no conflict of interest. No funding or financial support was received.

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