

Detection of synthetic cannabinoid intoxication in the Emergency Department: when routine toxicological tests are not enough

Detección de la intoxicación por cannabinoides sintéticos en Urgencias: cuando las pruebas toxicológicas rutinarias no bastan

FRANCESCO DAL SANTO*, ÁNGELA VELASCO**,***,****, LORENA DE LA FUENTE-TOMÁS**,***,****, LETICIA GONZÁLEZ-BLANCO*,**,***,****, JULIA RODRÍGUEZ-REVUELTA*,**,***.

* Servicio de Salud del Principado de Asturias (SESPA), Oviedo, España. ** Área de Psiquiatría, Universidad de Oviedo, Oviedo, España. *** Instituto de Investigación Sanitaria del Principado de Asturias (ISPA), Oviedo, España. **** Centro de Investigación Biomédica en Red de Salud Mental (CIBERSAM), Oviedo, España.

Synthetic cannabinoids (SC) are a heterogeneous group of substances with high affinity for cannabinoid receptors. They represent an emerging class of new drugs, the use of which has been expanding rapidly in recent years (Ford, Tai, Fantegrossi & Prather, 2017). Initially sold through specialized websites as legal alternatives to marijuana in the form of a mixture of herbs under the names “Spice” (Europe) or “K2” (USA), they have been subject to surveillance by the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) since 2008, when CS JWH-018 was shown to be present in these products (European Monitoring Centre for Drugs and Drug Addiction, 2017). The continuous modification and manipulation of these compounds by illegal laboratories has significantly accelerated the introduction of new molecules in the market (Ford et al., 2017): by December 2016, 169 SCs had been notified to the EMCDDA (European Monitoring Centre for Drugs and Drug Addiction, 2017), with progressively more potent substances being detected (Adams et al., 2017).

The increase in the use of illegal psychotropic substances, especially cannabis, among the youngest (Blasco-Fontecilla, 2018) and frequent maladaptive internet use in this population (Golpe, Gómez, Braña, Varela & Rial, 2017), could facilitate the acquisition and consumption of SC as early as adolescence: in the 2016 ESTUDES survey, 0.9% of students aged 14-18 years stated that they had tried “Spice” at least once in their lives (Plan Nacional sobre Drogas, 2016).

Synthetic cannabinoid products have higher affinity for the CB1 receptor than delta-9-THC: unlike cannabis herbal derivatives, which contain different molecules with variable psychoactive power (Casajuana Köguel, López-Pelayo, Balcells-Olivero, Colom & Gual, 2018), SCs act as pure receptor agonists (Ford et al., 2017). There is experimental evidence that SCs also act on non-cannabinoid receptors, such as the 5-HT_{2B} receptor or dopaminergic receptors. (Adams et al., 2017). In addition, SCs lack cannabidiol in their composition, which is found in herbal cannabis and is capable of exerting antipsychotic effects, thereby moderating the action of delta-9-THC (Rowley et al., 2017). These characteristics mean SCs have a greater psychoactive effect, as well as increasing the frequency and severity of side effects.

Psychiatric symptoms of intoxication can include anxiety, agitation, hallucinations, confusion, amnesia, paranoid delusions, bizarre behaviors, heteroaggressivity, and suicidal ideation. At the somatic level, they can cause tachycardia, hypertension, drowsiness, deterioration of the level of consciousness, vertigo, paresthesia, epileptic seizures, acute myocardial infarction and cerebrovascular accidents, even death in some cases (Tournebize, Gibaja & Kahn, 2017). The concomitant use of other substances is usually associated with greater clinical severity (Rowley et al., 2017).

Given the variety and nature of the substances available, procedures such as gas chromatography or mass spectrometry are required for their analytical determination, which makes SCs difficult to detect in routine clinical practice.

Received: December 2018; Accepted: January 2018.

Send correspondence to: Francesco Dal Santo. Departamento de Psiquiatría, Facultad de Medicina. Av. De Julián Clavería nº6, 3ª planta. CP: 33006. Oviedo, Asturias, España.
E-mail: frdalsanto@gmail.com.

Some cannabis users may opt for SCs to avoid testing positive (Rowley et al., 2017).

For this reason and given the nonspecific clinical manifestations in routine toxicological tests, symptoms of SC poisoning can be confused with other psychiatric or somatic pathologies.

Currently, there is an increase in people accessing emergency services due to SC poisoning (Tournebize et al., 2017). Cases of mass poisoning have been described: in New York, in July 2016, 33 people were treated during the notorious “zombie epidemic”, caused by exposure to CS AMB-FUBINACA (Adams et al., 2017). This set alarm bells ringing in the general population, the media and health professionals.

Previous studies have highlighted the fact that SC users have a risk up to 30 times greater of needing emergency room treatment for the effects of acute poisoning compared to users of natural cannabis (Winstock, Lynskey, Borschmann & Waldron, 2015). Most patients are usually treated with intravenous fluid therapy, sedatives and antiemetics, although measures such as sedation or intubation may be necessary as well as, in a quarter of all cases, hospitalization (Rowley et al., 2017).

In light of the above, we would like to stress the particular relevance at this time of training professionals involved in emergency care services with regard to these new psychoactive substances. The growing spread of these drugs, especially among the young population, implies the need for updated knowledge to help detect possible SC intoxication, establish a correct differential diagnosis and permit the prompt application of the most appropriate treatment. And we should not forget that, given the usually negative toxicological test results, careful observation of clinical manifestations remains the most effective tool at our disposal.

Conflicts of interests:

The authors of this article declare that there is no conflict of interest.

Bibliography

- Adams, A. J., Banister, S. D., Irizarry, L., Trecki, J., Schwartz, M. & Gerona, R. (2017). «Zombie» Outbreak Caused by the Synthetic Cannabinoid AMB-FUBINACA in New York. *The New England Journal of Medicine*, 376, 235-242. doi:10.1056/NEJMoa1610300.
- Blasco-Fontecilla, H. (2018). Postmodernity, addictive societies, cannabis and suicidal behaviour: Towards a brave new world? *Adicciones*, 30, 3-8. doi:10.20882/adicciones.1104.
- Casajuana Köguel, C., López-Pelayo, H., Balcells-Olivero, M. M., Colom, J. & Gual, A. (2018). Psychoactive constituents of cannabis and their clinical implications: a systematic review. *Adicciones*, 30, 140-151. doi:10.20882/adicciones.858.
- European Monitoring Centre for Drugs and Drug Addiction. (2017). Cannabinoides sintéticos en Europa. Retrieved at http://www.emcdda.europa.eu/topics/pods/synthetic-cannabinoids_es.
- Ford, B. M., Tai, S., Fantegrossi, W. E. & Prather, P. L. (2017). Synthetic Pot: Not Your Grandfather's Marijuana. *Trends in Pharmacological Sciences*, 38, 257-276. doi:10.1016/j.tips.2016.12.003.
- Golpe, S., Gómez, P., Braña, T., Varela, J. & Rial, A. (2017). The relationship between consumption of alcohol and other drugs and problematic Internet use among adolescents. *Adicciones*, 29, 268-277. doi:10.20882/adicciones.959.
- Plan Nacional sobre Drogas. (2016). Encuesta sobre uso de drogas en Enseñanzas Secundarias en España (ESTUDES) 2016. Retrieved at http://www.pnsd.mscbs.gob.es/profesionales/sistemasInformacion/sistemaInformacion/encuestas_ESTUDES.htm.
- Rowley, E., Benson, D., Tiffée, A., Hockensmith, A., Zeng, H., Jones, G. N. & Musso, M. W. (2017). Clinical and financial implications of emergency department visits for synthetic marijuana. *The American Journal of Emergency Medicine*, 35, 1506-1509. doi:10.1016/j.ajem.2017.04.044.
- Tournebize, J., Gibaja, V. & Kahn, J. P. (2017). Acute effects of synthetic cannabinoids: Update 2015. *Substance Abuse*, 38, 344-366. doi:10.1080/08897077.2016.1219438.
- Winstock, A., Lynskey, M., Borschmann, R. & Waldron, J. (2015). Risk of emergency medical treatment following consumption of cannabis or synthetic cannabinoids in a large global sample. *Journal of Psychopharmacology*, 29, 698-703. doi:10.1177/0269881115574493.