Variation in the pattern of synthetic cannabinoid use by a female patient during 2018

Variación en el patrón de consumo de cannabinoides sintéticos de una paciente a lo largo de 2018

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The use of synthetic cannabinoids (SCs) is, nowadays, an important social concern. A quick search on the literature shows how these compounds have been related to numerous intoxication cases (Adams et al., 2017; Kusano et al., 2018). The Spanish Early Warning System (SEAT) has notified the detection of seven new SCs since 2014 (Observatorio Español de las Drogas y las Adicciones, 2017). In addition, several SC have been reported in herbal blends acquired in Spanish shops (Ibáñez et al., 2013). However, detecting SC use through urine analysis cannot be carried out directly since these substances are rapidly and completely metabolized, making it necessary to detect their main metabolites (Scheidweiler, Jarvis & Huestis, 2015).

This study is a follow-up of an SC user attending an Addictive Behaviour Unit (ABU) in Valencia (Spain). We analysed the patient's urine samples, as well as the herbs and cigarettes which we took from her. Herbs sold in the smart shop in which the patient was thought to have been buying were also analysed. The change observed in the pattern of use was linked to the prohibition of certain cannabinoids in Spain (Ministerio de Sanidad Consumo y Bienestar Social, 2018).

Urine and herbal samples were collected in the ABUs participating in the study, following the protocol approved by the local ethics committee (Ref: DGNRI6 14-24-10). The urine and herbs seized from the patient were collected at the ABU which was treating her, while the second ABU impounded herbs and cigarettes from other patients. Additionally, herbs were bought at a well-known smart shop in the town where the patient lives. The analysis of herbs and urine was carried out following the methodology described in the literature (Fabregat-Safont et al., 2017; Ibáñez et al., 2013).

The analyses were performed by high performance liquid chromatography-high resolution mass spectrometry. An Acquity I-Class liquid chromatograph (Waters, Mildford, MA, USA) was coupled to a Vion IMS Qtof system (Waters, Manchester, UK) using electrospray ionization.

When the patient went to the ABU, she was a 17-year-old adolescent who had been adopted aged 6 from an East European country. Parental pressure compelled her to visit the ABU, where she sought counselling regarding cannabis use because she lacked any awareness of the problem. She has been receiving continuous child psychiatry treatment since the age of 11 for behavioural disorders and mild mental retardation. She does not have a good relationship with her parents, who, moreover, are not very effective in handling the patient. She has displayed self-harm behaviours and has been in trouble with the Child Prosecution Office, without further consequences. She has dropped out of school.

In interviews conducted before the summer, the patient admitted to consuming a certain herb called *Hardcore* (Figure 1A). The analysis of this product allowed the identification of three SCs, belonging to the same family: XLR-11, UR-144 and, at lower concentration level, the chlorinated N-pentyl analogue of UR-144. Once the product's compo-

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sition was known, the patient's urine was analysed, looking for the metabolites described for XLR-11 and UR-144 (Jang et al., 2016). The main metabolite of XRL-11 (N-pentanoic acid) was detected in two of the three urine samples collected from the patient during the first half of 2018.

Figure 1. Samples of use analysed. **A** *Hardcore* herb containing XLR-11 and UR-144. **B, C** Herbs seized in the ABUs containing 5F-ADB. **D** Cigarette seized at the ABU containing 5F-ADB. **E** *Matador* herb containing 5F-ADB.

However, in the urine collected after the summer, no metabolite of XLR-11 was found. Thus, either the subject had stopped using SCs, or her pattern of use had changed. A quick search of Spanish legislation revealed that XLR-11 had been banned, as published in the Boletín Oficial del Estado (Official State Gazette) on July 12, 2018 (Ministerio de Sanidad Consumo y Bienestar Social, 2018). It seemed logical to think that the subject had changed her consumption habits, although it was unknown which substance she might be smoking at that time. Weeks later, various herb samples were seized (Figure 1B), and the analyses revealed a dangerous new SC known as 5F-ADB or 5F-MDMB-PINACA. A high level of potency is attributed to this compound (Banister et al., 2016) and it has been linked to various deaths (Hasegawa et al., 2015; Kusano et al., 2018).

Once this new SC was identified, urine samples were reprocessed searching for the three metabolites described for 5F-ADB (Kusano et al., 2018). In two of the six samples collected after the summer, the three main metabolites of 5F-ADB were detected. The results obtained suggest that the prohibition of XLR-11 prompted manufacturers and/or sellers of new psychoactive substances to replace this product for one that was not legislated.

A few weeks later, a third herb (Figure 1C) and a cigarette (Figure 1D) were taken from two subjects treated in the second participating ABU. In addition, a new herbal blend available at the local smart shop was purchased (*Matador*, Figure 1E). We found 5F-ADB in all these samples, suggesting that this substance started being used frequently in Valencia after the summer.

Our work illustrates how the prohibition of SCs can alter their patterns of use. These results suggest that trends in the use of SCs depend largely on current legislation, so when a cannabinoid is banned, it disappears from the market and is replaced by a new compound, which quickly reaches the streets.

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Conflicts of interest

The authors declare no conflicts of interest.

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