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Assessment of types of synthetic cannabinoids in narcotic cases assessed by the Council of Forensic Medicine between 2011–2015, Ankara, Turkey

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ABSTRACT

Synthetic cannabinoids mimic the effects of cannabis and are the largest and fastest growing class of newly appearing designer drugs. Reports have revealed that various types of synthetic cannabinoids are mixed with herbal substances. The present study investigated the herbal substance cases involving synthetic cannabinoids in Ankara and nearby cities in Turkey. Data were collected from the reports of synthetic cannabinoids that were analyzed between January 01, 2011 and December 31, 2015 in the Ankara Narcotic Department of the Council of Forensic Medicine at the request of the judicial authorities. In all, 4610 narcotic reports were obtained and reviewed. Among these narcotic reports during the period, 370 reports (8%) were related to synthetic cannabinoids. 28 synthetic cannabinoid compounds could be identified in herbals: 5-F-AB-PINACA, 5-F-AKB-48, 5-F-NNEI, 5-F-PB-22, AB-CHMINACA, AB-FUBINACA, AB-PINACA, ADB-CHMINACA, ADB-FUBINACA, AKB-48, AM-2201, EAM-2201, JWH-018, JWH-022, JWH-031, JWH-122, JWH-201, JWH-210, JWH-250, JWH-251, JWH-307, MAM-2201, NM-2201, PB-22, RCS-4, THJ-2201, UR-144, XLR-11. The amount of herbals was 30.72 g, 329.22 g, 665.89 g, 4844.7 g, and 5684.3 g in 2011, 2012, 2013, 2014, and 2015, respectively. Generally, herbals contained more than one synthetic cannabinoids. ADB-FUBINACA was the most common synthetic cannabinoid among the herbals determined in this study, which was 3132.43 g, excepting multi-synthetic cannabinoid herbals. The amount and diversity of synthetic cannabinoid compounds have increased dramatically between 2011 and 2015.

1. Introduction

Synthetic cannabinoids are molecules that mimic Δ^9-THC; they are produced under laboratory conditions to elaborately enhance their cannabinoid effects, in addition to evaluating their medical potential; they are used clinically for their pharmacological properties. In recent years, synthetic cannabinoids are increasingly abused both in Turkey and worldwide, albeit their addictive properties, and are popular among drug addicts as strong psychoactive drugs, marketed in Turkey under the name of "Bonsai". Synthetic cannabinoids are substances developed to benefit from the therapeutic properties of the endocannabinoid system. However, since early 2000s, synthetic cannabinoids have been dried after synthesizing in laboratories and sold as an alternative to cannabis by spraying on dried plants. SCs are known as "Bonsai and Jamaica" in Turkey, as "Spice" in Europe and as "K2" in the USA.

Synthetic cannabinoid products can be found in the form of an herb mixture containing one or more cannabinoid compounds or in the form of a pill [1,2]. Although synthetic cannabinoids are usually smoked (cigars, cigarettes, e-cigarettes or waterpipes) [3], there are reports on their consumption through vaporizing, by an oral route, or by rectal administration [4]. The dose used of these compounds in herbal products was found to vary in different studies. Lindigkeit et al. [5] reported that the range of the concentrations in 9 different brands was between 3–11 mg/g for CP-47,497-C8 and 6–23 mg/g for JWH-073. In another similar study, it was reported that the dose range of synthetic cannabinoid in 46 herbal products was 1–17 mg/g for CP-47,497-C8 and 2–36 mg/g for JWH-018 [6].

These products especially attract the attention of teenagers because of their cannabis-like effects, easy accessibility through

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the Internet, and the lack of reliable and quantitative toxicological detection methods [1,7]. The first compounds detected with the forensic analysis of botanical materials were JWH-018, JWH-073, and CP 47,497 [8]. In spite of all kind of efforts to control sales, number of new compounds continue to arise worldwide and many compounds are not yet illicit or detectable.

Although psychoactive effects of synthetic cannabinoids are like those of Δ^9-THC, the duration of their effects may vary. Their half-lives are usually longer than that of Δ^9-THC, and their toxic effects last longer. For example, it was reported that the activity of JWH-018 continues for 1 to 2 h, and the activity of CP-47,497-C8 continues for 5–6 h. This can affect addicts' preferences and the effects of their use [9].

Cannabinoids can attach to one of the cannabinoid (CB) receptors known to be endogenous compounds in human cells, such as Type 1 (CB1) and Type 2 (CB2) receptors. The CB1 receptor is mainly located in the brain and spine and is typically responsible for the physiological effect of cannabis and partially responsible for its psychotropic effect. The CB2 receptor is mainly located in the spleen and immune cells and is responsible for the immunomodulator effect. Synthetic cannabinoids typically have a full agonist effect on the CB1 receptors, and thus, have a maximal effect even at low doses [10]. As in the case of JWH-200, the affinity of synthetic cannabinoids to the CB1 receptors may resemble that of Δ^9-THC [11], or as in the case of AM2389, it can be 105-fold higher than that of Δ^9-THC [12].

There are case reports on cardiovascular problems and psychological disorders occurring after use, especially due to synthetic cannabinoid use at high doses. Cerebral hemorrhage, hypertension, cardiac arrests, convulsion, hallucinations, and paranoia can be listed among the clinical symptoms, which can even lead to death [13,14].

The first capture of a synthetic cannabinoid (JWH-018), which is not produced in Turkey and was illegally imported into the country by the police departments was on May 2010. Although limited in number, there are reports of toxicity and death resulting from synthetic cannabinoid use, in addition to the reports on other compounds among the increasing diversity of synthetic cannabinoids in Turkey [15]. The results of the present study, in which the role and frequency of synthetic cannabinoid use in judicial cases as an indicator of their increasing use were investigated, will provide information on the prevalence of synthetic cannabinoid use in Turkey.

2. Materials and methods

2.1. Sampling of herbals

The herbals containing the synthetic cannabinoid that were seized by the police from the user or the dealer were first analyzed by gas chromatography-mass spectrometry (GC–MS) and determined to contain synthetic cannabinoid or not. Narcotics reports were generated for products containing synthetic cannabinoid. In all, 4610 narcotic reports obtained and reviewed between January 01, 2011 and December 31, 2015 in the Ankara Narcotic Department of the Council of Forensic Medicine at the request of the judicial authorities were retrospectively reviewed for synthetic cannabinoids. Among these narcotic reports during the period, reports were evaluated related with synthetic cannabinoids, and those about classical marijuana use were not included. It has been determined that 1.1% (n = 49) products investigated contain cannabis together with synthetic cannabinoids. This study was performed by permission of the Presidency of Scientific Board of Council of Forensic Medicine.

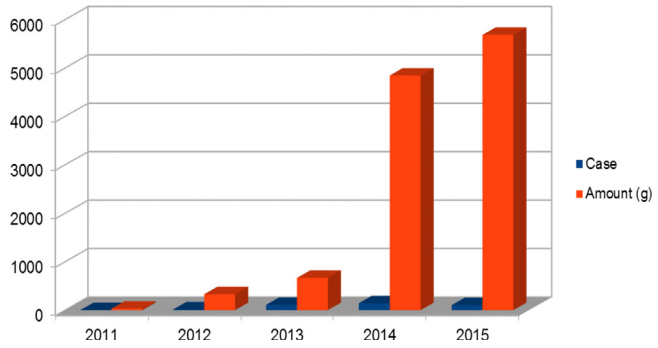

Fig. 1. Synthetic cannabinoid containing cases and herbal product amounts by years.

2.2. Sample preparation and gas chromatography–mass spectrometry parameters

The presence of synthetic cannabinoids in the herbals was determined by the method reported by Rossi et al. [16]. with the help of GC–MS system. The herbal samples were dissolved in methanol to injection into the GC–MS system. For chemical characterization of the synthetic cannabinoids at unit mass resolution, a GC–MS system consisting of a Thermo Trace 1310 gas chromatograph coupled to a Thermo ISQ LT mass spectrometer was used. Chromatographic separation of the analytes was achieved by split injection (1:5) of 1 μL on a DB-5MS capillary column (30 m; 0.25 mm; film thickness 0.25 μm; Agilent, Waldbronn, Germany). The following temperature program was used: 80 °C (2 min), 10 °C/min–130 °C (2 min), 20 °C/min–310 °C (25 min). The following MS settings were applied: ionization energy 70 eV, ion source temperature 280 °C and interface temperature 290 °C. SWGDRUG Mass Spectral Library and Cayman Spectral Library were used [17,18]. Only synthetic cannabinoids identification in herbals was determined by the GC–MS method, synthetic cannabinoids quantification was not performed.

3. Results and discussion

During this 5-year study, 4610 narcotics cases were reported and 370 (8%) of total cases involved synthetic cannabinoids. In herbal products, 28 different synthetic cannabinoid compounds were determined (5-F-AB-PINACA, 5-F-AKB-48, 5-F-NNEI, 5-F-PB-22, AB-CHMINACA, AB-FUBINACA, AB-PINACA, ADB-CHMINACA, ADB-FUBINACA, AKB-48, AM-2201, EAM-2201, JWH-018, JWH-022, JWH-031, JWH-122, JWH-201, JWH-210, JWH-250, JWH-251, JWH-307, MAM-2201, NM-2201, PB-22, RCS-4, THJ-2201, UR-144, XLR-11).

The amounts of herbal products in 2011, 2012, 2013, 2014, and 2015 were 30.72 g, 329.22 g, 665.89 g, 4844.681 g, and 5684.336 g, respectively; the number of cases in these years was 3, 16, 114, 142, and 101, respectively. Synthetic cannabinoid containing herbal product amounts significantly increased over the years (Fig. 1).

Herbal products usually contain more than one synthetic cannabinoid compounds. The synthetic cannabinoid contents of herbal products with the highest synthetic cannabinoid ratios are given in detail in Fig. 2, between 2011 and 2015 by amount; the remaining amounts were categorized as "other" and their synthetic cannabinoid ratios were given in total. Among all synthetic cannabinoids, at 27.11% (3132.399 g), ADB-FUBINACA had the highest ratio, followed by AM-2201, at 19.63% (2267.485 g), and ADB-FUBINACA + AM-2201, at 9.85% (1138.519 g). Table 1 shows in detail the synthetic cannabinoid types herbal products contain. The chemical structures and mass spectras for the 28 synthetic