Analysis of Deaths Related to Synthetic Cannabinoid (“Bonsai”) in Eskişehir, Turkey

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Abstract

Introduction, Objective; In literature, there are studies reporting that SC affects many systems such as cardiac, respiratory, urogenital, digestive system and cause death even in the first use. In this study, it is aimed to determine frequency of death resulting from use of SC and also the rate of forensic deaths in Eskişehir province.

Method: In this study, cases in which cause of death is related to the use of SC and which are included in forensic deaths that occurred between 1 January 2011 and 31 December 2016, are going to be included in this study. The rate of cases in which deaths result from SC to the rate of all forensic deaths is going to be detected. Also, demographic data of the cases such as age, gender, educational status, marital status, working status and residence are going to be examined.

Findings: Within 6 years-period the study includes, it was determined that 33 people died because of SC. In 2011, the first year that the study includes, the rate of deaths resulting from SC to forensic deaths was 0.3%, and this rate reached up to 3.1% in 2016. It was noted that SC named AM-2201 and JWH-018 (totally n=22, 66.7%) were mostly related to the death.

Discussion: In our study, it was observed that the deaths associated with SC increased until 2016. It is known that the use of other synthetic drugs or stimulants has increased in the last 2 years instead of SC. Hence, need for examination, equipment and experience required for identifying and reporting these synthetic substances will increase day by day.

Keywords; Synthetic cannabinoid, Death, Autopsy, Eskişehir, Turkey

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Eskişehir’de Sentetik Kannabinoid (Bonzai) Kullanımına Bağlı Ölümlerin Analizi

ÖZET
Giriş, Amaç; Literatürde sentetik kannabinoidlerin birçok sistemi etkilediği ve ilk kullanımda dahi ölüme neden olduğu bildiren çalışmalar mevcuttur. Bu çalışmada, ilimizde, sentetik kannabinoid kullanımlarına bağlı ölümlerin sıklığının belirlenmesi ve tüm adli nitelikli ölümlere oranının saptanması amaçlanmaktadır.

Gereç Yöntem; Bu çalışmada 1 Ocak 2011 ile 31 Aralık 2016 tarihleri arasındaki adli nitelikli ölümlerden ölüm nedeni sentetik kannabinoid kullanımlarına bağlı olan olgular çalışma kapsamına alınacaktır. Sentetik kannabinoid kullanımlarına bağlı ölümlerin, tüm adli nitelikli ölümlere oranı belirlenecektir. Ayrıca olguların yaş, cinsiyet, öğrenim durumu, medeni durum, aktif olarak çalışma hayatında olup olmadığı, yaşadığı yer gibi demografik verileri de incelenecektir.

Bulgular; Çalışmanın kapsadığı 6 yıllık dönemde SC nedeniyle toplam 33 kişinin öldüğü belirlenmiştir. Çalışmanın kapsadığı ilk yıl olan 2011’de, SC nedenli ölümlerin, tüm adli nitelikli ölümlere oranı, % 0,3 iken, 2016 yılında bu oran % 3,1’e yükselmiştir. Toplamba en sık AM-2201 ve JWH-018 isimli SC’lerin (toplamba, n=22, % 66,7) ölümle ilişkili olduğu belirlenmiştir.

Tartışma; Sentetik Kannabinoidlerin kullanılmadaki artış göz önünde bulundurulduğunda yakın zamanda en problemli uyuşturucu maddelerden biri olacağını ve sorun olmaya devam edeceği öngörülebilir. Çünkü kimyasal olarak yapılabilecek değişiklikler ve ortaya çıkabilecek olasılıklar çok fazladır.

Anahtar Kelimeler; Sentetik Kannabinoid, Ölüm; Otopsi, Eskişehir; Türkiye

INTRODUCTION
Main psychoactive component of cannabis sativa affecting central nervous system is Δ9-tetrahydrocannabinol (THC). Synthetic cannabinoid (SC), a subgroup of cannabinol, is among new psychoactive substances, which have been present in a huge amount in drug market in recent years. In these days, the use of new generation SC increases among young people and young adults (1,2).

SC started to be produced as an alternative to marijuana, and it has become available in the market since 2004. Substances involving SC are defined as “Spice” or “K2” in Europe and America. In Turkey, these substances are known as “Bonsai” or “Jamaica”. “Bonsai” occurred as “herbal mixture” and stated that this mixture wholly comprises of herbs. However, these mixtures contain SC, and SC shows its effects after using (3).

SC are generally used through cigarette (through pipe, cigarette or hookah), and they are also used through vaporization, orally or rectally (4,5). SC shows its effects by activating cannabinoid receptors in the body. There are two subgroups of cannabinoid receptors: CB1
cannabinoid receptor is mostly found in the brain. The CB2 receptor is more commonly found in the immune system. SC has full agonistic effect on CB1 cannabinoid receptor, thus it produces maximum effect even in low doses (6).

In these says, SC is applied on green-leafy herbs by being mixed with many chemicals, and put on the market illegally (2-11). Active ingredients within herbal preparations consistently change, therefore it is hard to detect them in toxicological examination (1,2,4). In literature, there are studies reporting that SC has negative effects on the brain, heart, lung, kidneys, immune system and they are associated with mental illnesses and they cause death even in the first use (12-22).

Forensic toxicology laboratories try to analyze many samples containing SC(s) that not been completed yet. European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) has established warnings groups that are within national units connecting to EMCDDA and named early warning system (EWS) to facilitate the struggle with new drugs. Denunciations that are reported to EMCDDA by means of these groups are shared with all countries, thus early precautions against drugs (23,24). New cannabinomimetic analogs are consistently submitted to the market to overcome the obstacles even though the use of Early Warning System (Turkey Monitoring Centre for Drugs and Drug Addiction) has increases in Turkey.

Deaths, that have been recently occurring in Turkey depending on the use of SC, appear in both printed media and visual media. However, when literature is considered, there is no study reporting frequency of deaths resulting from the use of SC. Studies are generally like case report or survey study.

Eskisehir province where the study was carried out, is in West Anatolia and is a university city where young people commonly lives. Its population is nearly 850.000. The socio-economic and cultural level of Eskisehir is above the national average. There are many social areas and facilities where young people can spend time.

This study is important because it will help to determine frequency of deaths resulting from the use of SC and to detect the rate of these deaths to the rate of forensic deaths. Also, it is also aimed to reveal factors associated with deaths resulting from the use of SC through demographic data and information of dead persons gained during legal investigation.
METHOD

Method research was started to study on 06.09.2017 with approval of Eskişehir Osmangazi University, Non-Interventional Clinic Research Ethics Board dated on 17.08.2017 and no. 45425468-32. Eskişehir Osmangazi University, Group B Scientific Research Project Fund supported this study.

In this study, cases in which cause of death is related to the use of SC and which are included in forensic deaths that occurred between 1 January 2011 and 31 December 2016, have been included in this study.

Also, demographic data of the cases such as age, gender, educational status, marital status, working status and residence have been examined. There is no laboratory in the province where the study was conducted. The samples are sent to the central laboratories of the Forensic Medicine Institute in Istanbul. There is no quantitative amount in the results. It has been reported whether SC was detected in the samples. In all cases, the cause of death is decided after autopsy and toxicological examination. All other causes of death are excluded. Exchange rate of deaths resulting from the use of SC that have occurred within the years has been researched. Data have been evaluated with SPSS 22 analysis program and have been analyzed.

FINDINGS

It was determined that totally 2125 deaths occurred in Eskişehir province within 6 years this study included and 33 of these deaths (1,6%) emerged due to the use of SC. It was noted that this rate reached up 0,3% on 2011 and it gradually increases and it became 3.1% (11/359) on 2016.

Table 1; Distribution of cases by all forensic deaths

| Years | All forensic deaths | SC deaths |
|-------|--------------------|-----------|
|       | n                  | %         |
| 2011  | 349                | 1         | 0,3       |
| 2012  | 335                | 2         | 0,6       |
| 2013  | 361                | 4         | 1,1       |
| 2014  | 354                | 6         | 1,7       |
| 2015  | 367                | 9         | 2,5       |
| 2016  | 359                | 11        | 3,1       |
Demographic data of cases are indicated in Table 2. It was determined that all cases were male, the youngest case was 16 years old and the oldest case was 44 years old, age average was $22 \pm 5.3$, and 9,1% (n=3) of cases was younger than 18 years, 72,7% (n=24) of cases lived in city center, 57,5% (n=19) of cases graduated from high school, 94% (n=31) of cases was single and 66,7% of cases did not work in a work actively.

**Table 2: Demographic data of cases**

| Age     | n  | %   |
|---------|----|-----|
| <18     | 3  | 9,1 |
| 19-25   | 23 | 69,7|
| >25     | 7  | 21,2|

| Gender   | n  | %   |
|----------|----|-----|
| Male     | 33 | 100,0|
| Female   | 0  | 0   |

| Place they live | n  | %   |
|-----------------|----|-----|
| City center     | 24 | 72,7|
| County, town    | 8  | 24,3|
| Village         | 1  | 3,0 |

| Educational status* | n  | %   |
|---------------------|----|-----|
| Primary school      | 5  | 15,2|
| Secondary school    | 8  | 24,3|
| High school         | 19 | 57,5|
| University          | 1  | 3,0 |

| Marital status    | n  | %   |
|-------------------|----|-----|
| Single            | 31 | 94,0|
| Married           | 1  | 3,0 |
| Widowed           | 1  | 3,0 |

| Work status        | n  | %   |
|--------------------|----|-----|
| Not working actively| 22 | 66,7|
| Student            | 3  | 9,1 |
| Worker             | 4  | 12,1|
| Officer            | 1  | 3,0 |
| Tradesmen          | 3  | 9,1 |

**Total**          | 33 | 100,0|

*The school that has been completed was evaluated.

Places where the bodies have been found are indicated in table 3. It was revealed that the cases have been mostly found inside of parked cars (n=14, 42,4%) .

During autopsies of cases, no finding belonging to traumatic lesion or forcing was detected in bodies of cases. Findings regarding autopsies of cases are stated in table 4. In totally 10 cases (30,3%), findings were noted in brain, heart and lung.
Distribution of SC detected in systemic toxicological analysis by years is shown in table 5. Totally, SC named as AM-2201 and JWH-018 are frequently related with deaths (totally n=22, 66.7%).

Methamphetamine was found in blood in 13 of cases in addition to SC, and ethanol was detected in rate of levels ranging from 34 mg/dl to 109 mg/dl in 6 cases.

**Table 3.** Distribution of places where the bodies have been found

| Places where the bodies have been found     | n  | %     |
|---------------------------------------------|----|-------|
| Inside of parked cars                       | 14 | 42.5  |
| At home                                     | 11 | 33.3  |
| In open fields                              | 6  | 18.2  |
| In restroom of entertainment center         | 1  | 3.0   |
| At workplace                                | 1  | 3.0   |
| **Total**                                   | 33 | 100.0 |

**Table 4.** Findings detected in autopsy

| Time of death        | n  | %     |
|----------------------|----|-------|
| 0 to 3 hours         | 6  | 18.2  |
| 3 to 12 hours        | 17 | 51.5  |
| 12 to 24 hours       | 10 | 30.3  |

**Traumatic finding in external examination**

| Not present | Present |       |
|-------------|---------|-------|
| 33          | 0       | 100.0 |

**Cerebral edema**

| Not present | Present |       |
|-------------|---------|-------|
| 30          | 3       | 90.9  |

**Pointer hemorrhages in cerebral parenchyma**

| Not present | Present |       |
|-------------|---------|-------|
| 28          | 5       | 84.8  |

**Atheroma plaques in coronary arteries**

| Not present | Present |       |
|-------------|---------|-------|
| 29          | 4       | 87.9  |

**Pointer hemorrhage in hearth, pleura and pericardium**

| Not present | Present |       |
|-------------|---------|-------|
| 26          | 7       | 78.8  |

**Cardiac hypertrophy**

| Not present | Present |       |
|-------------|---------|-------|
| 28          | 5       | 84.8  |

**Pulmonary edema**

| Not present | Present |       |
|-------------|---------|-------|
| 25          | 8       | 75.8  |

**Total**

|       |       |
|-------|-------|
| 33    | 100.0 |

**It was supported with histopathologic examination.**
Table 5. Distribution of detected SC by years

| SC             | Years | Total | n | % |
|----------------|-------|-------|---|---|
|                | 2011  | 2012  | 2013 | 2014 | 2015 | 2016 |   |   |
| AM-2201        | -     | -     | 2   | 1   | 3    | 5    | 11 | 33,3|
| XLR-11         | -     | -     | 1   | 2   | 1    | 4    | 9  | 12,1|
| 5-F-AKB-48     | -     | 1     | -   | 1   | 1    | 1    | 4  | 12,1|
| JWH-18         | 1     | 1     | 1   | 2   | 1    | 3    | 9  | 27,3|
| PB-22          | -     | -     | 1   | 2   | -    | -    | 3  | 9,1 |
| AM-2201-JWH-018| -     | -     | 1   | -   | 1    | 2    | 2  | 6,1 |
| **Total**      | **1** | **2** | **4** | **6** | **9** | **11** | **33** | **100,0** |

LIMITATION OF STUDY

In this study, psychological autopsy of cases, and environmental medical history (anamnesis) reports and social worker reports have not been present, all these situations as deficiency. It is also unknown how long these cases have been using SC. The study includes data from a city. This is a limitation for article. Multicenter studies should be conducted. There is no discussion regarding the quantitative concentrations of the detected SC.

DISCUSSION

The use of SC increased among young people until 2016 (11,18,24-26). In cross-sectional study in which 359 autopsy cases between 2011-2015 were evaluated in Tokyo, it was reported that 12 people (3,34%) died because of SC (26). In a study made in Trabzon in Turkey, it was reported that samples from 1571 cases were sent to forensic toxicology laboratory to be examined and SC was found in 58 (3,7%) of these cases (27). In 2011, the first year that the study includes, the rate of deaths resulting from SC to the forensic deaths was 0,3%, and this rate reached up to 3,1% in 2016. It was revealed that the deaths resulting from SC have been rising within the years in Eskisehir province. In Turkey, many multicentered studies must be performed regarding this topic.

It was noted that SCis more frequently taken by young adults (12,26). It was reported in a study made in Japan that people died because of SC were male (91,7%) and age average was 34,7 (26). In a study in which 16 cases which came to the emergency service due to effect of SC in İstanbul, Turkey were evaluated, it was stated that 15 of cases (93,8%) were male and age average was 15,4 (25). In a study in which Ergül and et al evaluated 6 cases which came to the emergency service due to the use of SC, it was reported that all cases were male (24). In given study, it was determined that all cases were male and age average was 22±5,3 and 9,1% (n=3)
of cases was under 18 years. It was noted that victims did not work actively in general and did not study at university. The situation that deaths most frequently occurred inside of parked cars made think that victims took SC alone and the deaths emerged suddenly.

It is clear that there is no specific autopsy finding and that autopsy can be identified through only toxicological examination. It was determined that preparation with AM-2201 active substance most frequently caused death in Eskişehir province (n=13, 39,4%). In a study made in forensic toxicology laboratory in Trabzon, it was recorded that SC was found in 58 cases and AM-2201 active substance was found in 27 (46,6%) of these cases (27). It was reported that 23 years old male person died suddenly in Arkansas in the USA and AM-2201 active substance was found in his body fluids during toxicological examination and this situation caused his death (28). AM-2201 is a SC known as it is used commonly around the world (28-31). It is thought that AM-2201 active substance is more common and the use of preparation with AM-2201 active ingredient is increasing in our country.

In literature, toxic effects of SC upon brain, heart, lung and kidneys are pointed out (1-27). In a study evaluating cases of deaths occurred due to SC in Japan, coronary stenosis has been reported in 3 of 12 cases (26). In presented study, in autopsies of 10 cases (30,3%), findings were observed in brain, heart and lung. Pointer hemorrhages in cerebral parenchyma were found in 5 cases (15,2%), cerebral edema was found in 3 cases (9,1%), coronary stenosis was found in 4 cases (12,1%), pulmonary edema was found in 8 cases (24,2%), cardiac hypertrophy was found in 5 cases (15,2%), pointer hemorrhages in heart, pleura and pericardium were found in 7 cases (21,2%).

In toxicological examinations in literature, it was stated that SC are present together with methamphetamine and ethanol (13,25,26,31). In a study, methamphetamine was found in body fluids in 13 of cases in addition to SC, and ethanol was detected in rate of levels ranging from 34 mg/dl to 109 mg/dl in 6 cases.

Because of commonly misuse of SC, further examinations are needed to identify pharmacology and toxicology of SC better and to make proper legal planning and arrangements.

Since data related to the common use of SC are less, execution of epidemiologic researches together with forensic-toxicological researches will be very beneficial for evaluating dimensions of problem.
Consequently, it can be predicted that SC will be one of the most problematic drugs soon and will continue to pose a problem when the increase in use of SC is considered. This is because there are many changes that will be made chemically and many possibilities that will occur. In our study, it was observed that the deaths associated with SC increased until 2016. It is known that the use of other synthetic drugs or stimulants has increased in the last 2 years instead of SC. Hence, need for examination, equipment and experience required for identifying and reporting these synthetic substances will increase day by day.

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