Case Report

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Two Fatal Cases Involving Synthetic Cannabinoid, 5F-AKB-48

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ABSTRACT

The usage of new psychoactive substance (NPS), particularly synthetic cannabinoids (SCs), has blasted at extraordinary pace in recent years universally. A quite number of these drugs has more toxic consequence than Δ 9 -tetrahydrocannabinol (THC). Due to their enhanced strength and uncontrolled dose, these drugs might cause critical clinical consequences. The toxicological finding of SCs from two postmortem cases in Scotland with suspected intake of SCs, is presented in this research. Liquid chromatography-tandem mass spectrometry (LC–MS/MS) was used to analyze the samples after a basic liquid extraction. A total of twenty SCs were included in this method; 5F- AKB-48 was positive in both cases. Although there is inadequate evidence to link blood 5F-AKB- 48 concentration to effect in additional to the lack of other rational interpretations, the drugs should be counted as the causative case of death based on history and circumstances, as well as toxicological data. Consequently, SCs appear to be more toxic than cannabis because of their increased potency and dose, which might result to overdose and catastrophic clinical effects. Under specific conditions, the acute toxic effects may contribute to death.

Keywords: Cause of Death; Postmortem; Synthetic Cannabinoids; 5F-AKB-48; Toxicology

Abbreviations: AKB-48: 1-Pentyl-N-Tricyclo [3.3.1.13,7] Dec-1-yl-1H-Indazole-3-Carboxamide; 5F-AKB-48: N-((3s,5s,7s)-Adamantan-1-yl)-1-(5-Fluoropentyl)-1H-Indazole-3-Carboxamide; 5F-AKB-48 (N-4 OH Pentyl):1-(5-Fluoro-4-Hydroxypentyl)-N-Tricyclo[3.3.1.13,7]Dec-1-yl-1H-Indazole-3-Carboxamide;NPS: psychoactive substance; SCs: Particularly Synthetic Cannabinoids; THC: Tetrahydrocannabinol; DRD: Drug-Related Deaths; MPA: Methylthienylpropamine

Introduction

SCs are a significant group of structurally various chemical compounds, and they were developed in the 1990s to obtain the medical value of THC. However, SCs became as a concern in the beginning of 2000 [1]. They are generally sold in powder form or coted on herbal materials under a range of labels, such as, “Spice” and “K2”. SCs act on specific receptors (CB1 and/or CB2) and simulate the effects of THC [2]. The amount and variety of spice products has expanded since 2009, and the list of SCs appears to be growing on a daily basis [3]. AKB-48 was discovered in herbal smoking combination in Japan in 2012 [4]. 5F-AKB-48 is made up of an indazole ring with a fluorophenyl chain at R1 and a carboxamide linkage connecting it to an adamantly group. One of the main metabolites of 5F-AKB- 48 is 5F-AKB-48 (N-4 OH pentyl) [5]. Deaths that can be attributed directly to drug usage and that typically occur soon after drug use are known as drug-related deaths (DRD) [6]. Several deaths and major side effects have been linked to SCs, each SC requires greater evaluation. On older generations of SCs, some pharmacologic and pharmacokinetic data is available. Newer drugs, on the other hand, frequently have vague receptor- binding affinity and selectivity, which could lead to surprisingly sever toxicity [7].

There are various cases of SC-related deaths have recently been documented in publications, whether on their own or in concurrence with other drugs [8,9]. When SCs are documented in the case history,

they are increasingly tested in postmortem cases. In other cases, SCs aren't clearly implicated in the case history, therefore toxicology is the only option to confirm a SC-caused death. The purpose of this study was to learn more about how SCs contribute to deaths. Clinical research involving human participants was approved by the University of Glasgow's College of Medical, Veterinary, and Life Sciences Ethics Committee. They reviewed the proposed study and found no moral problems with it.

Case History

Case 1

A man aged 26 had a history of drug abuse of heroin and cannabis is the victim in this case. He was given a prescription for merhadone. After some time, he started to dabble with legal highs, which led to bizarre behaviors. He attended the emergency room reporting hallucinations and reported he had been using cannabis, «Purple G Punch" and «Dark Obsession. His condition deteriorated rapidly the next day and he passed away. Only a blood sample (preserved) was available to study his case.

Case 2

The victim is a man aged 34 year-old with mood disorders including bipolar and schizophrenia who had used cannabis frequently in the past. His doctor put him on risperidone and citalopram. His parents were concerned about his consumption of "Diesel" branded SCs. He was discovered lying on his back in the living room by the police, ostensibly dead, next to him were cigarette papers, overflowing ashtrays and trace of substantial quantity of green herbal goods.

Experimental

As part of the DRD-related medical-legal cases filed to the University of Glasgow, 4 samples of blood and urine, that were collected at postmortem, were examined for a panel of SCs using LC– MS/MS. Samples of two postmortem cases were suspected consumption of NPS.

Results and Discussion

In case 1, the concentration of 5F-AKB-48 in the blood was1 ng/mL. Blood can show a user's impairment level and is useful for establishing their most recent drug use. The relationship between 5F-AKB-48 level in the blood and potentially catastrophic effects is yet unknown. As a result, it become more difficult to analyze toxicological evidence in order to determine the exact extent to which factor contributed to death. However, the results of this case indicate that 5F-AKB-48 as the cause of death. Blood concentrations of 5F-AKB-48 in four cases of Driving Under the Influence of Drugs ranged from 0.9 to 6.5 ng/mL, as determined by Solo and colleagues [10].

In case 2, toxicology confirmed the presence of alcohol in preserved blood and urine at 11 and 17 mg/dl, respectively. Blood tests revealed concentrations of 0.62 ng/mL citalopram and 0.36 ng/mL methylthienylpropamine (MPA) (unpreserved). While the 5F-AKB-48 (N-4 OH pentyl) content in the urine sample was measured at 18 ng/mL. Urine can be used as a source for toxicological examination, proving the existence of a drug history. However, determining the potency of a drug based on a sample of urine is notoriously difficult. Notably, the quantity of drug use or impairment at the time of urine collection cannot be accurately determined based on drug concentrations observed in urine. In spite of this, positive outcomes and signs are attainable. For instance, if the results are positive, it may be because the targeted drug(s) are present; these findings may be related to the patient's background and symptoms. Regular drug users will predictably have increasing drug concentrations in their urine [11].

Both cases involved poly-drug use. There are several confusing and astonishing elements in the explanations of the postmortem toxicology results, including individual variation, the lack of data examining the effects of postmortem restructuring, and the dearth of information regarding the lethal dose of the drug and in cases in where the victim had also taken other substances (poly-drug). Individual differences in pharmacogenetics and drug use behavior, such as frequency and dosage, can affect how long a drug stays in the body and its concentration, which in turn can lead to a wide range of fatality rates [12]. In the time between a person's death and when their samples are taken, drug concentrations might shift, a phenomenon known as redistribution [13].

The toxicity of SCs appears to be worse than that of natural cannabis, that could be because of the higher effectiveness and may also to the existence of various cannabinoids in the smoked incense and the complications of appropriate dosing [14]. Illegal industrialization of spice items may lead to the presence of impurities, contaminants, or variability in SC, which may have varying degrees of effect depending on the batch [7]. There are no obvious symptoms which indicate a single exposure to SCs in a person with no history of SC-product use [15], That could lead to death-cause misreporting.

Conclusion

The relationship between 5F-AKB-48 and deaths appears to be extremely problematic due to the fact that the dangerous concentration of 5F-AKB-48 in blood is unclear, particularly in the presence of other chemicals known as "poly-drugs". Due to the rapid global spread of SCs, data on the dangerous and/or deadly amount of these chemicals must be updated whenever a new SC is discovered.

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Conflict of Interest

Nill.

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