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Prevalence of synthetic cannabinoids in blood samples from Norwegian drivers suspected of impaired driving during a seven weeks period

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ABSTRACT

From early year 2000 different herbal products containing synthetic cannabinoids (SC) have appeared on the drug market all over the world, and new substances are frequently introduced. The prevalence of SC use in different populations is however still mainly unknown, also in Norway. This information is difficult to obtain, but studies of drivers suspected of driving under the influence of drugs (DUID), might provide important information.

The aim of this study was to assess the prevalence of SC in drivers suspected of being under the influence of drugs in Norway, and investigate if SCs impair driving performance.

For two periods of three and four weeks all blood samples from drivers suspected of DUID in Norway were analyzed for the presence of 12 and 18 different SCs, respectively. A new ultra performance liquid chromatography tandem mass spectrometry method was developed.

A total of 726 cases were analyzed during our study period, and SCs were detected in 16 cases (2.2%) in total. The mean age of these drivers was 29.6 years. High concentrations of other psychoactive drugs were detected in all the blood samples where a SC was found. AM-2201 and JWH-018 were the most frequently detected SCs, each found in five cases. In addition RSC-4, JWH-122, JWH-081 and JWH-250 were detected. None of the drivers had reported using SCs prior to driving.

Despite the limited number of SCs investigated in this 7 week study period, a considerable percent of the cases were positive. Other psychoactive drugs of abuse were always found concomitant with the SCs, and the age of these drivers indicates that experienced drug users also ingest SCs. Since other drugs were found in all the samples, the psychomotor impairment caused by the SCs is difficult to estimate. Our study shows the importance of screening analyses of biological samples from different populations to assess the prevalence of drug use, since self-reporting might be encumbered with significant under-reporting.

1. Introduction

In the course of the past few years several types of synthetic cannabinoids (SC) have appeared on the drug marked word wide, as well as in Norway (Vardakou et al., 2010; Fattore and Fratta, 2011; Tuv et al., 2012). These compounds, known as e.g. "K2" and "Spice" are available on the Internet, often referred to as "legal highs" (Fattore and Fratta, 2011). To be able to keep up with the frequent appearance of new substances on the drug market, Norway has regulated groups of SCs under schedule 1 control (Slv, 2013) from February 14th 2013. Prior to this legislation, only eight SCs were registered as illicit drugs. The prevalence of use of these compounds in the drug abuser population is not known. It is in addition not known to what extent this population drives a car after intake of SCs and to what degree SCs impair driving skills and cause increased risk of traffic accidents.

Some studies have investigated the prevalence of SC use, both by surveys and analysing biological material. Winstock et al. investigated the population associated with the dance music scene in England, and 13% reported having used "Spice" (Winstock et al., 2011). Surveys conducted each year among households in England and Wales, revealed that the prevalence of Spice use was 0.4% among the age group 15–24 and 0.1% among the group 25–59 years (Smith and Flatley, 2011). The prevalence among college students from USA is reported to be 9% for use of "Spice and other smokable blends" (Hu et al., 2011b). Among athletes one study found SC in 2 out of 7500 urine samples tested (Moller et al., 2011) and in another study the prevalence of JWH-018, JWH-073 or any of their

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metabolites, were found to be 4.5%, when urine samples from 5956 athletes were tested (Heltsley et al., 2012).

SC receptor agonists are a large family of chemically distinct compounds functionally similar to delta-9-tetrahydrocannabinol (THC), the main psychoactive compound of cannabis, and bind to the same cannabinoid receptors in the brain and in peripheral organs (CB-1 and CB-2 receptors) and mimic the effects of cannabis (Showalter et al., 1996; Grotenhermen, 2003; Wintermeyer et al., 2010). THC is among the drugs most frequently detected in blood samples from suspected drugged drivers (Christophersen et al., 1990; Waller et al., 1997), and there is strong evidence from experimental studies that THC has significant effects on the cognitive and psychomotor tasks associated with driving (Ramaekers et al., 2000). Studies concerning injured and fatally injured drivers in Australia reported cannabis as present in 10.8% (Longo et al., 2000) and 13.5% (Drummer et al., 2003) of cases, respectively. The psychoactive effects of SC are perceived to be even stronger than cannabis (Griffifths et al., 2010). Symptoms of SC toxicity are similar to the euphoric and psychoactive effects of cannabis with additional sympathomimetic symptoms, including diaphoresis, agitation/panic attacks, anxiety and restlessness (Piggee, 2009; Banerji et al., 2010; Wells and Ott, 2011; Vearrier and Osterhoudt, 2010; Bebarta et al., 2012).

Little is known about the frequency of SC use among car drivers, and to which degree impaired driving is seen. Recently Musshoff et al. (Emcdda, 2010) published a series of seven cases of DUI with analytically confirmed ingestions of SCs. Based on analytical results and signs of impairment, they concluded that consumption of SCs can lead to impairment similar to typical performance deficits caused by cannabis use which are not compatible with safe driving. Particularly the centrally sedating effects and the impairment of fine motor skills are of concern, but awareness to further dangerous adverse reactions related to the ingestion of SCs is also needed.

The aim of this study was to assess the prevalence of SCs in DUID suspects in Norway, and compare findings of SC in blood samples with results from the clinical examination performed by a physician.

2. Materials and methods

At the Division of Forensic Medicine and drug abuse research at the Norwegian Institute of Public Health (NIPH), all blood samples collected from drivers suspected for drugged driving from the whole country, are analyzed. The Norwegian population consists of about five million inhabitants, and about 8.000 DUID cases are analyzed each year (Fhi, 2010).

About 3000 of these cases are analyzed only for ethanol, and about 5000 are screened for a broad selection of legal and illegal psychoactive drugs. SCs are, however, not included in this routine screening. Blood samples are usually drawn within 1–2 h after apprehension (Vindenes et al., 2013).

2.1. Samples

Whole blood samples were collected from Norwegian drivers apprehended for suspicion of driving under the influence of drugs (DUID). The samples were collected for two periods that lasted for three and four weeks; November 14th 2011 to December 2nd 2011 ($n = 297$), and March 26th 2012 to April 23th 2012 ($n = 429$).

Blood samples were collected in 5 mL glass BD Vacutainer evacuated tubes containing 20 mg sodium fluoride and 143 I.U. heparin (BD Diagnostics, Velliver Industrial Estate, Plymoth, UK).

2.2. Analysis

All samples were analyzed shortly after arrival at the institute for more than 40 different medicinal and psychoactive drugs in addition to the chosen SCs (Kristoffersen et al., 2006; Oiestad et al., 2011; Dahl et al., 2012).

During the first screening period 11 SCs were analyzed in all the blood samples sent to our Institute; JWH-018, JWH-073, JWH-081, JWH-122, JWH-200, JWH-210, JWH-250, AM-2201, RCS-4, JWH-019 and WIN 55,212-2. During the second period we included eight additional SCs; JWH-015, JWH-020, JWH-251, AM-694, RCS-4-C4, RCS-8, CP 47,497 and HU-210. These latter substances were not available in our laboratory during the first screening period.

The SC analyses were performed using an ultra-performance liquid chromatography–tandem mass spectrometer (UPLC–MS/MS) (Presley et al., 2013). Sample preparation (0.5 mL blood) was a liquid–liquid extraction with ethylacetate/heptane following evaporation to dryness. The dry residue was then reconstituted with 80 μL of ethanol. Chromatographic separation was achieved using an Acquity UPLC HSS T3 column (2.1 × 100, 1.8 μm). The mobile phase consisted of ammonium formate buffer pH = 3.1 (A) and methanol (B), with a gradient from 10% B to 90% B. Mass detection was performed by positive ion mode electrospray tandem mass spectrometry for all compounds. Within-day relative standard deviations varied from 4% to 17%, and day-to-day variations were in the range of 11–22%.

2.3. Clinical test of impairment (CTI)

In Norway drivers suspected of DUID are usually examined by a physician to assess drug impairment. The Norwegian Clinical Test of Impairment (CTI) consists of 25 tests and observations related to common signs of drug impairment, including 7 tests of alertness, cognitive function and vestibular function, four observations on eyes, two observations on signs on intravenous drug abuse, four tests of motor activity and coordination and eight observations concerning appearance. The CTI has been describes elsewhere (Bramness et al., 2003). Based on the results from the tests the physician makes a conclusion regarding the overall degree of impairment of the subject, using a four-step scale: not impaired, mildly impaired, moderately impaired or greatly impaired. In the cases where a CTI had been performed, we compared these results with the drug findings in the blood samples.

In relation to the CTI the driver is questioned by the physician about history of drug abuse prior to the driving. Both medicinal and recreational drug use is reported if the driver admits to such use, and also the ingested doses and time point for last intake of drug before apprehension.

2.4. Legal status of the SCs during the study period

During our study periods, only eight SCs were regulated under schedule 1 control; JWH-018, JWH-073, JWH-081, JWH-122, JWH-203, JWH-210, JWH-250 and AM-2201. All the other SCs were only regulated by medicines laws.

From February 14th 2013, groups of SCs are registered under schedule 1 control, to make it easier to keep up with the very fast changes in the drug market regarding the SCs.

3. Results

A total of 726 cases were analyzed during the seven weeks investigated, and 16 were SC positive. Eleven of these cases were a result of suspicion of DUID by the police, while four of the cases were collected as a result of traffic accidents and one case was collected as suspicion of drug use.