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Frequency and structure of stimulant designer drug consumption among suspected drug users in Budapest and South-East Hungary in 2012–2013

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ABSTRACT

Identification of abuse and frequency patterns of stimulant designer drugs (SDDs) provides important information for their risk assessment and legislative control. In the present study urine and/or blood samples of suspected drug users in criminal cases were analysed by GC–MS for 38 SDDs, and for the most frequent illicit and psychoactive licit drugs in Hungary. Between July 2012 and June 2013, 2744 suspected drug users were sampled in Budapest and during 2012 and 2013, 774 persons were sampled in South-East Hungary (Csongrád County – neighbour the Romanian and Serbian borders). In Budapest 71.4% of cases, and in South-East Hungary 61% of cases were positive for at least one substance. Pentedrone was the most frequent SDD in both regions; however, the frequency distribution of the remaining drugs was highly diverse. SDDs were frequently present in combination with other drugs – generally with amphetamine or other stimulants, cannabis and/or benzodiazepines. The quarterly distribution of positive samples indicated remarkable seasonal changes in the frequency and pattern of consumption. Substances placed on the list of illicit drugs (mephedrone, 4-fluoro-amphetamine, MDPV, methylone, 4-MEC) showed a subsequent drop in frequency and were replaced by other SDDs (pentedrone, 3-MMC, methiopropamine, etc.). Newly identified compounds from seized materials were added to the list of new psychoactive substances (“Schedule C”). While the risk assessment of substances listed in Schedule C has to be performed within 2 years after scheduling, continuous monitoring of their presence and frequency among drug users is essential. In summary, our results suggest which substances should be dropped from the list of SDDs measured in biological samples; while the appearance of new substances from seized materials indicate the need for developing adequate standard analytical methods.

1. Introduction

Stimulant designer drugs (SDDs) in general are derivatives of “classical” amphetamines (amphetamine – AM, methamphetamine – MA, methylendioxy-amphetamine – MDA, methylendioxy-metamphetamine – MDMA and methylendioxy-ethylamphetamine – MDEA) and cathinone (β-keto-amphetamine) and have sympathomimetic stimulant effects. The “classical” amphetamines were present in the illicit market and classified as illicit drugs before 2008–2009, when SDDs began to spread worldwide. The motivation behind producing SDDs was to avoid legislative control by altering the chemical structure of illicit substances in a way that new compounds maintained the stimulant activity, but could not be detected by routine drug tests. These new products were sold on the streets and via online head shops as “bath salts” or “plant fertilizers” – indicating that they are “not for human consumption” – or as “legal high” [1].

Although, some designer drugs were previously available on the black market, e.g. fentanyl analogues [2–4] or synthetic cathinones closely related to pyrovalerone [5], their use escalated in 2009. The American Association of Poison Control Centers (AAPCC) reported 304 incidents of bath salts use in 2010, which increased to 6138 in 2011, and has remained high [6]. In 2009, the most widely abused cathinones in the US were MDPV (3,4-metylendioxy-pirovalerone)

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and methylone (β-keto-MDMA) while in the European countries it was mephedrone (4-methylmetcathinone) [7]. Since 2009, the Early Warning System has reported a steady increase in the number of forensic and criminal cases related to synthetic cathinones in Europe [8]. Between 2009 and 2010, the UK Poison Information Service received an increasing number of inquiries regarding synthetic cathinones [5]. The number of Google searches for the term "mephedrone" showed a 6–7-fold increase between July 2009 and March 2010 in the UK [9]. In 2009, a cross-sectional, self-reported online survey was performed in the UK with the participation of the readers of a leading dance/music magazine. A total of 947 (41.3%) of 2295 participants reported having used mephedrone [10]. In a 2010 survey, 205 (20.3%) of 1006 Scottish school and college/university students reported that they had used mephedrone on at least one occasion. A subsequent survey in Northern Ireland showed 40% of 14- to 15-year-old pupils admitted that they had tried mephedrone at least once [11]. Before 2012, the top 5 synthetic cathinones reported to UNODC were mephedrone, MDPV, methylone, 4-MEC and 4-FMC [12], with 4-FA (4-fluoro-amphetamine), 2C-I (2,5-dimethoxy-4-iodophenethylamine), and 4-FMA (4-fluoro-metamphetamine) being the most common phenylethylamines [13].

The toxic nature of these substances and their widespread use led to legal regulation. In the United States, methylone, MDPV, and mephedrone were added to Schedule 1 of the Controlled Substances Act in 2011. Consequently, their prevalence decreased by mid-2011 and pentedrone (α-methylamino-valerophenone) became the most prevalent SDD. In many European countries, when mephedrone became a controlled drug in 2010, naphyrone (naphtylpyrovalerone) appeared on the market first as a legal alternative followed by more than 30 other SDDs [14,15].

In Hungary, data on the spreading of SDDs have originated mainly from analysis of confiscated materials [16,17]. In 2009, mephedrone was seized only twice but in 2010 the number of mephedrone busts increased to 339. By mid-2010, the frequency of mephedrone seizure exceeded that of amphetamine [16]. In January 2011, mephedrone was classified as an illicit drug, which resulted in a considerable decrease in its use. The illicit market reacted quickly: within a few months MDPV, 4-MEC (4-methyl-etcathinon), and 4-FA (4-fuoroamphetamine) became the most common legal alternatives of mephedrone. After those were also added to the list of illicit drugs in January 2012, pentedrone became the most frequently abused SDD [17].

As confiscated materials include both goods that were intended for use and those for sale, distribution or transfer, their analysis gives only an approximate estimation of their abuse. More detailed information may be gained by analysis of biological samples derived from subpopulations of illicit drug users. These data represent real consumption of illicit drugs and psychoactive substances in the investigated population, allowing a more precise risk assessment of the new substances. Thus, our work aimed to investigate the pattern of SDD abuse among suspected drug users in 2012–2013, in Budapest and South-East Hungary.

2. Materials and methods

Altogether, 2744 subjects were sampled in Budapest between 1 July 2012 and 31 June 2013, and 774 in South-East Hungary (Csongrád County) between 1 January 2012 and 31 December 2013. Blood and urine samples were collected from subjects prosecuted for illicit and/or designer drug use. In the majority of cases only urine samples were taken but when impairment (to driving and violent criminal behaviour) was also suspected, blood or blood and urine samples were both provided for analysis. Only blood samples were available from 20 subjects in Budapest and 8 subjects in South-East Hungary. Both types of samples were prepared using a liquid-liquid extraction system and analysed directly by a gas chromatography–mass spectrometer (GC–MS) (Agilent GC: 6890N; MS: 5975B) without pre-screening. The conditions of sample preparation, GC–MS analysis, and validation criteria (linearity, intra- and inter-day precision, selectivity, stability and extraction recovery) are described in the final report of DRUID (Driving under the Influence of Drugs, Alcohol and Medicines) [18]. The method used for analysis fulfilled the following validation criteria for all substances: linearity: $R^2 \geq 0.98$, inter-and intra-day precision: bias and RSD <15%, selectivity: LOQ (limit of quantitation): matrix ratio ≥3 for target ions and ≥2 for qualifiers, stability: <20% degradation within 24 h.

The sample preparation and GC–MS analysis of the stimulant designer drugs were performed together with the "classical" amphetamines (AM, MA, MDA, MDMA, MDEA). The substances were selected for analysis according to their presence in confiscated goods in Hungary before 2014. The cut-off values and the starting date of detection for each substance are listed in Table 1. Statistical analysis was performed by the chi-square test or by Poisson regression analysis setting the probability level to $P < 0.05$.

3. Results

Altogether, 2744 persons out of 1.74 million inhabitants were sampled in Budapest during the 1-year investigation period (1 July 2012 to 30 June, 2013) and 774 people out of 418 000 inhabitants in Csongrád County (South-East Hungary) during the years 2012–2013. The percentage of positive samples was 71.4% in Budapest (1959 of 2744 persons) and 61.0% in South-East Hungary (472 of 744 persons). There was no significant difference in gender and age distribution between the two regions, among the samples or the positive cases (in Table 2 the distribution of positive cases is given). Two or more substances were detected in 50.1% (n = 982) of the cases in Budapest and in 40.7% (n = 192) of cases in South-East Hungary.

The prevalence pattern of "classical" illicit drugs (THC, classical amphetamines, morphine, and cocaine) was the same in both populations and was similar to previous years [17]. The frequency of cannabis consumption was not different in the two regions but amphetamine and MA use was higher in Budapest than in South-East Hungary. Heroin consumption could be proven in 21 cases in Budapest as the samples were also positive for 6-acetylmorphine (6AM) and not only for morphine and codeine. In South-East Hungary, 4 out of 18 morphine positive persons stated that they had consumed poppy seed tea. Ketamine consumption was only detected in Budapest (n = 7; Table 3).

The prevalence of medical opiates (codeine, methadone, and tramadol) was similar in the two populations. Among the investigated licit drugs, clonazepam was the most frequent in both groups followed by alprazolam. Diazepam and its metabolite nordiazepam were rare but present in both regions; midazolam and zolpidem were detected only in Budapest (Table 4).

The structure of stimulant designer drug abuse was similar in the two populations but some differences were observed. The frequency of designer drugs detected (>1% of positive cases) was pentedrone (34.7%), mephedrone (11.7%), 4-MA (5.31%), 3,4-DMMC (1.28%), and 3-MMC (0.97%) in Budapest. Due to the lower sample size in South-East Hungary only pentedrone (30.4%) and 3-MMC (5.07%) were present in significant number for ranking. The frequency of 4-MA (1.90%), mephedrone (1.69%), 2-MPA (1.69%), 4-FA (1.25%), and some other SDDs were too low for comparison between the two areas (Table 5). In the majority of positive cases, the stimulant designer drugs were present in