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ORIGINAL ARTICLE

New psychoactive substances in a drugged driving population: Preliminary results

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Summary Action against driving under the influence of drugs (DUID) often starts with an on-site immunological screening which is not yet developed for new psychoactive substances (NPS). Our aim was to determine the prevalence of NPS in drivers screened positive for a classical illicit drug. Blood samples ($n = 556$) were obtained between January—August 2015 in Belgium. The on-site Drugwipe 5S (Securetec) results and the subjects' signs of recent drug use were available. Classical illicit drugs were confirmed in blood via LC-MS/MS methods. NPS screening was performed using 2 methods: LC-HRMS and LC-MS/MS. Of the 256 samples yet analysed, NPS were detected in 13 samples (5%) including following substances (n): ketamine (5), methoxetamine (2), diphenidine (2), 5-MeO-DALT (1), 4-AcO-DiPT (1), methiopropamine (1), methedrone (1), α-PVP (1), a mix of 5-MAPB/5-EAPB (1), and AB FUBINACA (1). This preliminary study demonstrates a prevalence of 5%. However, this result should be confirmed and reassessed at the end of our study.

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Introduction

A challenging issue for drafting international and European drug policies is how to respond effectively to the increasing and dynamic new psychoactive substances (NPS) market. NPS, including synthetic cannabinoids, synthetic cathinones, phenethylamines, opioids, tryptamines, benzodiazepines and arylalkylamines are mainly sold in Internet Shops. For instance, 98 new substances were detected for the first time in the EU in 2015, bringing the number of new substances monitored by the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) to more than 560, of which 380 (70%) were detected in the last 5 years [1,2]. In this situation, one main challenge consists in the identification of NPS in biological samples (blood, urine, hair, oral fluid) in clinical and forensic cases, e.g., intoxications or driving under the influence of drugs (DUID).

Action against DUID often starts with an on-site immunological screening focusing on classical drug of abuse (DOA): i.e. cannabis, cocaine, amphetamine or heroin use. These rapid tests are not yet developed for NPS. Actually, in Belgium as well in France, roadside testing is performed in oral fluid using an on-site immunological screening for DOA: Drugwipe® 5S — Securetec. In the case of a positive result, a blood sample is subsequently collected for confirmation using liquid chromatography with tandem mass spectrometry detection (LC-MS/MS) [3].

The aim of this study is to determine the prevalence of NPS in drivers screened positive for classical illicit drugs.

Material and methods

Plasma samples were obtained between January and August 2015 in Belgium in 3 geographic areas (Bergen [Mons], Mechelen [Malines] and Turnhout [Turnhout]) mainly following unexpected roadside controls.

The on-site Drugwipe 5S (Securetec) results and the subjects' signs of impairment were available. After a dual (Brussels and Lille) confirmation step for usual drugs of abuse using liquid chromatography and tandem mass spectrometry detection (LC-MS/MS) in Multi Reaction Monitoring (MRM) mode methods [4—7], screening for NPS was performed using 2 previously reported methods [8,9]: (M1) liquid chromatography and high resolution mass spectrometry detection (LC-HRMS) with a Xevo-G2 QTOF-XS system (Waters, Manchester, UK), and (M2) an LC-MS/MS using a XEVO TQS system (Waters, Manchester, UK).

Briefly, for M1, 400 μL of sulfosalicylic acid (3%) was added to 100 μL of blood. After on-line extraction using OASIS® HLB (Waters), separation was performed on a Acquity™ UPLC HSS C_{18} column (Waters) and detection occurred in MS^e (ESI+) mode. Data processing was performed using ChromaLynx™, TargetLynx™, MassFragment™ and MetaboLynx™ associated softwares (Waters) using a homemade database of more than 1.400 substances including nearly 300 NPS or metabolites. For M2, 100 μL of blood sample was deproteinated (300 μL methanol), diluted (100 μL of ammonium formate/0.1% formic acid buffer), and analysed after separation by an Acquity™ UPLC BEH C_{18} column (Waters). Detection occurred in the MRM mode (ESI+) for 222 NPS or metabolites.

Results and discussion

Between January and August 2015, 556 collected blood samples were taken after positive roadside tests. To date, 256 have been analyzed. These 256 samples represent about 8% of all collected blood samples in Belgium after positive roadside testing over the period considered.

These samples were obtained from DUID controls (98%) or after minor accidents (2%). The Drugwipe 5S tests in oral fluid related to these samples were positive for THC (76%), cocaine (19%), amphetamine (16%) or MDMA (8%) either for one parameter or in combination.

NPS were detected in 13 of 256 samples (5%) including following substances (*n*): ketamine (5), methoxetamine (2), diphenidine (2), 5-MeO-DALT (1), 4-AcO-DiPT (1), methiopropamine (1), methedrone (1), α-PVP (1), a mix of 5-MAPB/5-EAPB (1), and AB FUBINACA (1). The results of theses 13 cases are presented in Table 1. Noteworthy are the facts that (i) all users are male and this is in coherence with previously published data reporting that the vast majority of 'legal-high' users were men [10], (ii) 6 of these 13 NPS positive cases (46% of positive cases) were obtained from a control nearby a festival site (the music festival of DOUR), and (iii) these 13 drivers admitted their classical drug use, detected with the on-site screening, but they did not mention their NPS use. This latter fact leads us to the question whether drug users always know what they are using or if it is due to a direct confrontation with a test result that they are willing to confirm there drug use.

Among the results, we want to focus on case #4 in which 5-MeO-DALT was detected in blood after a false-positive cocaine on-site screening in oral fluid (Fig. 1). There are no data in the literature about false positive result of cocaine immunoassay-based tests due to 5-MeO-DALT and, more broadly, tryptamine derivatives seem not detectable with common applied immunoassay-based techniques [11]. In order to investigate this case, we had performed an assay with a blank oral fluid specimen spiked with 5-MeO-DALT (1 g/L) using an *ad hoc* testing device (Drugwipe® 5S — Securetec) at our disposal: the obtained result was positive for cocaine. So, the possibility of positive result of an immunoassay-based test for cocaine due to the presence of 5-MeO-DALT in oral fluid should be considered, but requires further studies to be confirmed.

Lastly, in the challenging NPS area with an increasing and dynamic market, it is not possible to be sure that no NPS was missed by the used analytical techniques, even if the used LC-HRMS method exhibits acceptable analytical criteria for drug sample identification regarding to literature recommendations in this context [12,13].

It is difficult to assess the meaning and impact of the observed NPS prevalence (5%) in this drugged driving population. Indeed, it is challenging to compare these preliminary results to data found in the literature due to the differences in studied populations and applied analytical tools [14]. Nevertheless, the following data can be considered. In the EU, the NPS prevalence is estimated by the 2014 Flash Eurobarometer, a survey of over 13 000 young adults aged 15—24 in the EU Member States, which asked about their NPS use. Eight percent of respondents had used an NPS at least once, with 3% in the last year. The countries with the highest levels of use in the last year were in Ireland (9%),