O56

The role of analytical pharmacotoxicology in adressing the main functions of the National Early Warning System on NPS

Simona Pichini[1,*], Silvia Graziano[1], Maria Rosaria Varì[2], Manuela Pellegrini[2], Emilia Marchei[2], Maria Concetta Rotolo[2], Paolo Berretta[2], Anastasio Tini[3], Annagiulia Di Trana[4], Francesco Busardò[4]

[1] *National centre on addiction and doping, ISS, Rome, Italy*
[2] *Ncad, ISS, Rome, Italy*
[3] *Sapienza university, Rome, Italy*
[4] *Università politecnica delle Marche, Ancona, Italy*
[*] *Corresponding author.*
E-mail address: simona.pichini@iss.it (S. Pichini)

Aim In compliance with the European Council Decision 2005/387/JHA, the Italian AntiDrug Policies Department designated the National Center for Addiction and Doping of the Istituto Superiore di Sanità (ISS) to organize and manage the National Early Warning System (NEWS) on New Psychoactive Substances (NPS) to promote a rapid exchange of information on NPS within Italy and between Italy and the EU. The analytical pharmacotoxicology Unit of the Center supports NEWS with screening and confirmation of NPS presence in conventional and non-conventional biological matrices from acute and fatal intoxication cases. Furthermore, yearly, pure standards of new NPS are tested and provided to Laboratories from collaborative centres and proficiency testing on NPS in oral fluid and hair are organized.
Method Different analytical technologies, including high-sensitivity gas chromatography-mass spectrometry (GC-MS) and tandem mass spectrometry (GC-MS-MS), liquid chromatography-tandem mass spctrometry (LC-MS-MS) and ultra-high-performance liquid chromatography-high-resolution mass spectrometry (UHPLC-HRMS) are used for a screening and confirmation analysis of classic drugs, prescription medicines and new psychoactive substances in and their metabolites in blood, plasma, urine, hair and oral fluid from intoxication cases and clinical trials. Sample preparation involves both liquid-liquid or solid phase extraction. Dilute and shoot methodology is also applied.
Results During 2021 and first months of 2022, around 80 different psychoactive substances, including new synthetic opioids and/or metabolites were identified in urine from 296 spanish patients with a history of opioid use disorder; 12 classic drugs and NPS were detected in hair from 300 mexican pregnant women; cocaine, THC, heroin, methadone, ketamine and mephedrone and metabolites were determined in urine from 76 italian prisoners; JWH-122 and JWH-210, UR-144 were quantified in oral fluid from consumers and finally some cases of intoxications with fentanyl, norfentanyl and analogs were also disclosed. Furthermore, two exercises of Proficiency testing for NPS in oral fluid and hair were organized. Samples from both matrices were prepared in cooperation with Comedical (Trento, Italy). For the 2021 round classic drugs together with 5-fluoro CUMYL-PeGACLONE, 5-fluoro MDMB-PICA, AB-FUBINACA,5F-ADB, Ethylone, Euthylone, Furanylfentanyl, Ocfentanyl, Isobutyryl fentanyl, Fentanyl and Isotonitazene were included. For the 2022 round, classic drugs plus 5-MMPA, Methoxpropamine, Brorphine, Butonitazene, Etodesnitazene, Flunitazene, 4-fluoro MDMB-BUTICA, 5-fluoro CUMYL—PICA, 5-fluoro EDMB-PICA, 3-Methylmethcathinone, ADB-4en-PINACA, MDMB-4en-PICA were comprises. About 20 different pharmacotoxicological national laboratories participated in the exercised with very variable quali-quantitative results.
Conclusion Although the NPS phenomenon is not uniform, it is well known as a global problem, concerning all the region of the world. Due to the mutating nature of the phenomenon, we believe that investments in toxicological and forensic analytical data sources are strongly needed. Differently from the past when psychotropic drugs occupied the fingers of two hands, in the 21th century, more than 1000 NPS have been identified. Not all of them found the same diffusion in the illicit market, but many of them are temporary adulterant of substitute of controlled compounds or finally fake drugs. The values of accurate and immediately available toxicological and forensic data are crucial to the implementation of national and international early warning system on NPS. Indeed, the drug related severe intoxications and fatalities are seldom associated with the consumption of one substance alone. Drug consumption patterns are often characterized by polyconsumption of both classical drugs and NPS and laboratories supporting emergency rooms, forensic toxicologies and police forces must be enabled to identify the substance/s causing the acute or chronic intoxication or a fatality.
Disclosure of interest The authors declare that they have no competing interest.

https://doi.org/10.1016/j.toxac.2022.06.063

O57

A method for the sensitive targeted screening of synthetic cannabinoids and opioids in whole blood by LC-QTOF with simultaneous suspect screening using HighResNPS.com

Stephen Trobbiani[1,*], Peter Stockham[1], Chris Kostakis[2]

[1] *Toxicology, Forensic science sa, Adelaide, Australia*
[2] *Toxicology, Forensic science sa, Adelaide, Aruba*
[*] *Corresponding author.*
E-mail address: stephen.trobbiani@sa.gov.au (S. Trobbiani)

Aim To develop and validate a qualitative screening method capable of detecting the low concentrations found in cases of synthetic cannabinoid and opioid consumption using a targeted scope, while simultaneously performing efficient suspect screening against a much larger database. Screening for synthetic cannabinoids and opioids in blood samples remains challenging due to the large number of substances available and the constantly changing market, as well as the low limits of detection required for some compounds. Many laboratories employ LC-QQQ when screening for these compound classes due to the ubiquity and sensitivity of those instruments but LC-HRMS instruments are similarly able to detect a large number of pre-defined analytes with high sensitivity and specificity, as well as acquiring full scan data which enables both suspect screening and retrospective screening if required.
Method Analytes were extracted from 0.5 mL of whole blood using alkaline liquid-liquid extraction and data were acquired using data dependent acquisition on an Agilent 6545 QTOF. 28 opioids and 23 cannabinoids were validated for limit of detection, recovery, matrix effects, selectivity, extract stability and carryover. Data processing occurred in two stages; first a targeted screen was performed using an in-house database containing retention times (RT), accurate masses and MS/MS spectra for the validated compounds plus an additional 16 opioids and 34 cannabinoids (101 total compounds). Suspect screening was then performed using a database downloaded from the crowdsourced NPS data website HighResNPS.com which contains mass, consensus MS/MS spectra and laboratory specific predicted retention times for over 1400 compounds. The suspect screening workflow was assessed by determining the accuracy of the retention time prediction and MS/MS library matching against consensus spectra. For this workflow, qualifying parameters for initial presumptive identification included mass accuracy of ±4mDa, MS/MS match score greater than 20 and retention time difference to predicted RT of ±2 min. In practice, results of this suspect screen would be verified following purchase of authentic reference material for comparison. The method was applied to 66 forensic cases where synthetic cannabinoid or opioid screening was requested by the client or their use was suspected due to case information.