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Title Page

Title

SODAS : Surveillance of Drugs of Abuse Study

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Abstract

Objective Novel Psychoactive Substance (NPS) as a form of recreational drug use has become increasingly popular. There is a paucity of information with regards the prevalence and clinical sequelae of these drugs. The aim of this study was to detect NPS in patients presenting to the Emergency Department (ED) with suspected toxicological ingestion.

Methods The prospective study was performed in a large Emergency Department (ED) in the UK. During a three month period eighty patients were identified by clinicians as having potentially ingested a toxicological agent. Urine sample were analysed using liquid chromatography-high resolution mass spectrometry and basic clinical data was gathered.

Results 80 patients with a history of illicit or recreational drug consumption had urine screenings performed. 49% (39) of patients undergoing a screen had more than one illicit substance detected. 20% (16) of patients tested positive for at least one NPS.

Conclusions

Almost half of patients presenting had ingestion of multiple substances which correlated poorly with self reporting of patients. Developing enhanced strategies to monitor evolving drug trends is crucial to the ability of clinicians to deliver care to this challenging group of patients.

Introduction

Attendances in Emergency Departments (ED) due to the sequela of the effects of drugs of abuse creates a significant burden (1-3). Drug abuse became regarded as an epidemic problem with the rise of heroin in the 1960s (4). Recreational drug use is more prevalent amongst young adults and is associated with significant short term and long term health implications (5, 6). Novel Psychoactive Substances (NPS) is generic term used to describe substances produced to mimic the effects of traditional illicit drugs. These psychoactives are newly available and while not prohibited, pose a public health threat comparable with traditional illicit substances (7).

There has been a steady rise in the number of synthetic and plant-based psychoactive substances, with an exponential growth in the production and distribution of such drugs (8-10). The unknown safety profile, active ingredients and quantity increase the risk of overdose and serious clinical consequences (11, 12). There remains inconsistent sampling and reporting of attendances to the ED following ingestion of NPS and of the clinical manifestations (13).

Proliferation of NPS abuse has been facilitated by inconsistent legislation allowing uncontrolled access to substances. The ability to evade detection by standard toxicological screens allied with easy availability in shops and on the internet, has made these drugs increasingly attractive recreational substances (14). Developing analytical profiling of agents and reference standards is an area of considerable ongoing work (15, 16).

Surveillance of drug abuse patterns is crucial to developing strategies to direct both clinical and community based interventions (17). Creating a detailed understanding of current trends is challenging in the face of constantly evolving habits (18,19) While population surveys provide useful information, the illicit nature of drug abuse and the reliability of respondents is problematic (20, 21).

The clinical challenge is to safely treat patients who have ingested unknown substances which is achieved by responding to the toxidrome on presentation(22). The paucity of analytical confirmation of hazardous substances prevents clinicians from effectively managing these patients (23). Identification of these novel substances enables tracking of use, effects from ingestion of these novel drugs and also the changing patterns of abuse (24, 25). Co-ingestion of synergistic or antagonistic substances can lead to diagnostic and treatment challenges (26).

Prior to this surveillance study, urine samples were sent for analysis using a commercially available testing kit for traditional substances of abuse (Alere, San Diego Inc CA). It was increasingly recognised that this screen did not encompass the range of substances that were self-reported or corresponded to the toxidrome of the patient (21). Evolution of drug behaviours within the local population had extended beyond the testing capabilities of the ED and local laboratory provision.

Methods

Patients and Sampling

This was a single center prospective observational study. Glasgow Royal Infirmary is a large inner city ED with approximately 86,000 attendances each year. During a 3 month period (01/05/14 to 29/07/14), data was collected on all patients who attended the department whom treating clinicians identified by history or clinical suspicion as attending due to ingestion of novel psychoactive substance for which a urine sample was collected. Patients were excluded if they were under 16.

Data was collected using a standardised proforma. Patient's data was anonymised and linked to presentation by a unique code number. Urine samples were stored in additive free containers in a laboratory refrigerator until testing within a week of collection. Data analysis was performed using Excel (Microsoft 2011)

Urine samples were extracted using a simple liquid-liquid procedure with MTBE and TRIS buffer and analysed using liquid chromatography-high resolution mass spectrometry (LC/HR-MS). A Bruker MicrOTOF-Q with an Agilent 1260 Infinity HPLC was used for analysis. Identification was achieved by matching retention time, mass (4 decimal places) and isotope pattern.

Ethics

Ethics was sought and granted from NHS GG&C Ethics as a service evaluation. Consent was waived for the study as this was considered a service development study as urine samples are sent for a toxicology screen as a standard of care.

Results

80 patients with suspected ingestion of recreational drugs presenting in the ED had urine screenings performed. For the purposes of the study, a NPS was defined as a drug acting on the central nervous system, out-with those traditionally recognised as recreational drugs. The additional NPS tested for were: methoxetamine, etizolam, methylenedioxyaminoindane (MDAI), piperazines (including TFMPP), paramethoxyamphetamine (PMA), and any cathinones. Case histories were not available for 5 patients, so therefore demographic data is not available.

The range of drugs detected, and respective frequencies are shown in Table 1. There was a male predominance; 54 males (aged 17 to 55) compared to 21 females (aged 16 to 47). The source of referral for patients was: ambulance 49% (37); self-referral 19% (14) and police 32% (24). 36% (27) patients required admission, with the remaining 64% (48) discharged direct from the ED. 20% (16) of patients tested positive for at least one NPS.

The total number of non-prescribed drugs detected in patients is reported in Figure 1 49% (39) of the 80 patients undergoing a screen had more than one illicit substance detected.

Only five patients reported consumption of a NPS; the results of their screenings is shown in Table 2.

Table 3 lists the patients who tested positive for NPS agents and their reported ingestions. 11 patients were unable to give a history of ingestion due to their medical condition on arrival.

Discussion

The study reports the urine screening results of those patients who reported drug consumption for recreational purposes, or who presented with a clinical toxidrome suggestive of acute drug intoxication. The main objective was the detection of NPS in patients presenting to EDs; in our study 16 patients had NPS agents detected, of which only 5 patients reported consumption of these drugs. It is unclear whether there was deliberate misreporting by patients or if patients were not aware they had ingested an NPS.

A selection of NPS agents were detected, predominantly the ecstasy (MDMA) “mimics,” such as PMA/PMMA, MDAI, and TFMPP; only one patient gave a history of ecstasy consumption and tested positive for one of these compounds. From the NPS detected, only MDAI and etizolam are not currently regulated by the Misuse of Drugs Act in the UK. Only five patients reported taking a NPS (referred to as a “legal high” in their own terms); one patient tested positive for PMA, the rest were negative for NPS, this may, however, have been a synthetic cannabinoid agent which was not tested for in this study.

Of interest was the detection of amitriptyline and mirtazapine within our patient population; all the amitriptyline detected was present with patients also testing positive for methadone, diazepam, and other illicit substances. Only one patient

reported the ingestion of amitriptyline, none reported the use of mirtazapine; abuse of amitriptyline by patients on methadone substitution therapy has been recognised since 1978 (1), however the non-prescription use of mirtazapine has not been reported in the literature.

Etizolam, a thienodiazepine, is not currently regulated in the UK; as with amitriptyline, it was only detected in patients who tested positive for other illicit drugs. No patients reported the intentional consumption of etizolam and only two patients reported a history of consumption of benzodiazepines out of the seven who tested positive for the drug.

Limitations

Our study had several limitations. First, it was performed at a single institution and limited to patients whom individual clinicians had identified as having ingested a toxicological agent. Retrospective review of triage notes did not reveal any clearly missed patients but relied upon individual clinician's identification and subsequent inclusion in the study. Synthetic cannabinoids were not included in this study but will be included in future studies. Due to lack of reference standards some novel agents may not have been identified. There is the potential for degradation of metabolites and no quantitative work was performed on the analytes. In addition, 24 who were enrolled in the study had negative samples for which there a number of explanations. The patient had not ingested the substance; we did not test for the analyte, error during storage/sampling or the patient was incorrectly enrolled.

Future

The purpose of this study was to evaluate the current toxicology screening against the potential range of substances ingested presenting in a large city ED. Sharing of the findings within the ED and other agencies raised the awareness of these varied and potentially hazardous substances. Development of point of care testing to enable rapid identification during presentation would aid treatment and risk stratification. Incorporating testing for NPS in post mortems and development of new standards for testing may facilitate greater recognition of the contribution of these substances in forensic cases and inform future drug surveillance and regulation strategies.

Conclusions

Only a small percentage of samples tested positive for NPS. Most samples were positive for more commonly encountered drugs of abuse. It is important to understand the range of drugs that are affecting our local population. The extent of poly-ingestion has significant implications for management of these patients within the ED. The poor correlation between reporting and detection emphasises the need for clinicians to have a high degree of suspicion and treat the presenting toxicological syndrome. This may, of course, represent a lack of knowledge by patients about the substances they are ingesting. The combination of both illicit drugs, newer drugs of variable legal status and those previously unconsidered drugs represents a substantial challenge to the treating physician. By identifying the individual drugs and trends that are prevalent, we can direct resources into understanding their effects and implications on this challenging group of patients.

References:

1. Binks S, Hoskins R, Salmon D, Bengler J. Prevalence and healthcare burden of illegal drug use among emergency department patients. *Emergency medicine journal*. 2005;22(12):872-3.
2. French MT, McGearry KA, Chitwood DD, McCoy CB. Chronic illicit drug use, health services utilization and the cost of medical care. *Social Science & Medicine*. 2000;50(12):1703-13.
3. Vitale S, Mheen Dvd. Illicit drug use and injuries: a review of emergency room studies. *Drug and alcohol dependence*. 2006;82(1):1-9.
4. Kozel NJ, Adams EH. Epidemiology of drug abuse: an overview. *Science(Washington)*. 1986;334(4779):970-4.
5. Addiction. EMCfDaD. Annual report on the state of the drugs problem in Europe. 2009.
6. Elliott S, Evans J. A 3-year review of new psychoactive substances in casework. *Forensic science international*. 2014;243:55-60.
7. Stephenson G, Richardson A. New Psychoactive Substances in England: A review of the evidence. In: Science HO, editor. London: Crime and Policing Analysis Unit; 2014.
8. Board INC, Centre UNVI, Austria. International Narcotics Control Board: 2013 Annual Report. 2013.
9. Helander A, Beck O, Hägerkvist R, Hultén P. Identification of novel psychoactive drug use in Sweden based on laboratory analysis-initial experiences from the STRIDA project. *Scandinavian Journal of Clinical & Laboratory Investigation*. 2013;73(5):400-6.

10. Mounteney J, Griffiths P. Increasing complexity in European drug use: Highlights from the EMCDDA's 2014 European drug report. *Drugs: education, prevention and policy*. 2014(0):1-2.
11. Kronstrand R, Roman M, Thelander G, Eriksson A. Unintentional fatal intoxications with mitragynine and O-desmethyltramadol from the herbal blend Krypton. *Journal of analytical toxicology*. 2011;35(4):242-7.
12. Baron M, Elie M, Elie L. An analysis of legal highs—do they contain what it says on the tin? *Drug testing and analysis*. 2011;3(9):576-81.
13. Heyerdahl F, Hovda KE, Giraudon I, Yates C, Dines AM, Sedefov R, et al. Current European data collection on emergency department presentations with acute recreational drug toxicity: Gaps and national variations. *Clinical Toxicology*. 2014;52(10):1005-12.
14. Prosser JM, Nelson LS. The toxicology of bath salts: a review of synthetic cathinones. *Journal of Medical Toxicology*. 2012;8(1):33-42.
15. Elie MP, Elie LE, Baron MG. Keeping pace with NPS releases: fast GC - MS screening of legal high products. *Drug testing and analysis*. 2013;5(5):281-90.
16. Ayres TC, Bond JW. A chemical analysis examining the pharmacology of novel psychoactive substances freely available over the internet and their impact on public (ill) health. *Legal highs or illegal highs? BMJ open*. 2012;2(4).
17. Winstock AR, Barratt MJ. The 12 - month prevalence and nature of adverse experiences resulting in emergency medical presentations associated with the use of synthetic cannabinoid products. *Human Psychopharmacology: Clinical and Experimental*. 2013;28(4):390-3.
18. Hondebrink L, Nugteren-van Lonkhuyzen JJ, Van Der Gouwe D, Brunt TM. Monitoring new psychoactive substances (NPS) in the Netherlands: Data from the drug market and the Poisons Information Center. *Drug and alcohol dependence*. 2014.
19. Khey DN, Stogner J, Miller BL. Emerging Drug Trade and Use: Manufacturing, Marketing, and Understanding Novel Highs. *Emerging Trends in Drug Use and Distribution*: Springer; 2014. p. 33-51.

20. Brookoff D, Campbell EA, Shaw LM. The underreporting of cocaine-related trauma: drug abuse warning network reports vs hospital toxicology tests. *American Journal of Public Health*. 1993;83(3):369-71.
21. Macdonald S, Cherpitel CJ, Stockwell T, Martin G, Ishiguro S, Vallance K, et al. Concordance of self-reported drug use and saliva drug tests in a sample of emergency department patients. *Journal of Substance Use*. 2014;19(1-2):147-51.
22. Hill SL, Thomas SH. Clinical toxicology of newer recreational drugs. *Clinical toxicology*. 2011;49(8):705-19.
23. Green AR, Nutt DJ. Pharmacology should be at the centre of all preclinical and clinical studies on new psychoactive substances (recreational drugs). *Journal of Psychopharmacology*. 2014:0269881114528593.
24. Spiller HA, Ryan ML, Weston RG, Jansen J. Clinical experience with and analytical confirmation of “bath salts” and “legal highs”(synthetic cathinones) in the United States. *Clinical Toxicology*. 2011;49(6):499-505.
25. Archer J, Dargan P, Lee H, Hudson S, Wood D. Trend analysis of anonymised pooled urine from portable street urinals in central London identifies variation in the use of novel psychoactive substances. *Clinical Toxicology*. 2014;52(3):160-5.
26. Zuba D, Byrska B. Prevalence and co - existence of active components of ‘legal highs’ . *Drug testing and analysis*. 2013;5(6):420-9.

Figure Legend

Figure 1. Number of Drugs