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Mini-Review

A 6-year review of drug trends in the United Arab Emirates from the perspective of the National Rehabilitation Center (NRC), Abu Dhabi

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ABSTRACT

The National Rehabilitation Center (NRC) is a national response centre in the United Arab Emirates (UAE) for drug addiction prevention, treatment and rehabilitation of both inpatients and outpatients. Medical care is supported by clinical laboratory services, including toxicology for the detection of drugs in patients' samples (primarily urine). The results of these tests have allowed the NRC to detect the drugs within the substance-using patient population and monitor trends in those detections in order to provide an evidence-based assessment of drugs within the UAE area applicable to the wider Middle East region. This article presents the outcomes of this over a 6-year extended period, between 2013 and 2018, representing 14247 samples confirmed positive for various types of drugs and substances. Across the 6 years, there has been a constant presence of amphetamines, opiates, tramadol, cannabis, benzodiazepines, pregabalin, gabapentin, antihistamines, methorphans, carisoprodol and ketamine found in patient samples. However, there have been changes in the relative frequency during this time, including an increase in amphetamines, a recent decrease in tramadol and frequent detection of cannabis, pregabalin, benzodiazepines and cough syrup constituents (antihistamines and methorphans). Furthermore, in the past few years there has been an increasing number of samples related to gamma-hydroxybutyrate (GHB) use. These data provide drug and drug trend information within a substance-using patient population in the UAE to assist in improving knowledge associated with global monitoring of drug abuse within the Middle East region that is often not sufficiently represented in such monitoring systems.

KEYWORDS: NRC, drugs of abuse, toxicology, UAE, Middle East.

INTRODUCTION

The National Rehabilitation Center (NRC) was launched in 2002 as a national response centre in the United Arab Emirates (UAE) for drug addiction prevention, treatment and rehabilitation. With an initial bed capacity of 10, increasing to the current capacity of nearly 100 beds (with future expansion to 200) along with laboratory and ancillary facilities, the NRC provides a wide scope of medical services to adolescent and adult patients. The integrated biopsychosocial patient treatment programmes are delivered by multi-disciplinary teams with a continuum of care from an outpatients department (ambulatory care) together with standard residential care (for detoxification, relapse prevention and motivational units). The cycle of treatment and rehabilitation is completed with intensive follow up and aftercare services. The clinical services employ evidence and practice-based interventions,

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tailored and personalized to patient requirements [1]. The NRC also has a strong training and research emphasis with global academic and other partnerships, including its surveillance department which is tasked with provision of data to advise policy and decision makers about changing trends of substance misuse [2, 3]. In recognition of the NRC's services and activities, in 2018, the World Health Organization (WHO) declared the NRC as a WHO Collaborative Center.

The prevalence of substance use disorders is considered low with associated high abstinence rates in the Middle East region compared with the West and some countries in the East [4, 5]. This is thought to be due to adherence to Islam in the region and the fact that the consumption of alcohol and/or illicit drugs is a crime [1].

As part of the clinical testing and medical laboratory services of the NRC (including clinical biochemistry, haematology, microbiology and serology), the toxicology division undertakes toxicological analysis of patient urine samples (predominantly urine compared to blood). This includes the use of point of care testing devices and immunoassays with subsequent chromatographic and mass-spectral confirmation for drugs of abuse, prescription drugs and other substances [3, 6]. The results of these tests have allowed the NRC to detect the drugs within the substance-using patient population and monitor trends in those detections in order to provide an evidence-based assessment of drugs within the UAE area. This article presents the outcomes of this over a 6-year extended period, between 2013 and 2018. The Middle East region is often not sufficiently represented in global drug abuse monitoring systems but due to the existence and work of the NRC in Abu Dhabi with associated published NRC data, this is changing.

MATERIALS AND METHODS

The NRC toxicology laboratory uses immunoassay, gas chromatography–mass spectrometry (GC/MS) and liquid chromatography–tandem mass spectrometry (LC-MS/MS) for the qualitative analysis of drugs with quantitative determination of some drugs as required, including buprenorphine and norbuprenorphine in serum and urine [3]. Procedures incorporate general drug screening as well as the analysis of opiates, new (and classical) psychoactive substances, benzodiazepines, barbiturates and GHB. Methods used were chosen on the basis of proven sensitivity, selectivity, specificity and reliability. The results and findings are based on the toxicological analysis of patient urinary samples between January 2013 and December 2018. Due to the extended window of detection of drugs in urine (generally 1-3 days depending on analytical sensitivity, longer for some drugs) compared to blood/serum/plasma, urine analysis provides a useful indicator of drug use outside of the acute admission time period [7].

The number of patients admitted to the NRC for treatment increased significantly between 2013 and 2018, with 545 admissions in 2013, 648 in 2014, 649 in 2015, 784 in 2016, 792 in 2017 and 1750 in 2018. In terms of new patients each year (which is important when monitoring drug trends as it is expanding the detectable patient population), there were 417 in 2013, 428 in 2014, 410 in 2015, 434 in 2016, 475 in 2017 and 502 in 2018. Finally, there were 4450 patient visits in 2013, 5625 in 2014, 8169 in 2015, 8054 in 2016, 10872 in 2017 and 11273 in 2018, resulting in a total of 43,448 patient visits, with over 90% of patients being male, less than 10% female. Urine samples were collected in an ethical and responsible manner from patients for routine diagnostic and clinical purposes across the various admissions and patient engagements, including urine collections on multiple occasions in some cases. Information as to the context of drug use and detections was available as part of the medical and drug history of the patients and within the treatment programme at the NRC. Drugs administered during medical care and the treatment programme are not reported.

RESULTS

Between January 2013 and December 2018, a total of 51170 patient urine specimens were analysed to determine the presence or absence of drugs. 36528 of these samples were available for analysis by GC/MS and LC-MS/MS. 14247 samples were confirmed positive for the various types of drugs and substances, within the range of screening performed and analytical sensitivity.

The absolute number and relative occurrence of urinary drug detections (listed as specific drugs or drug classes where appropriate) is shown in Table 1.

Table 1. Detections of drugs in patient urine samples, 2013-2018.

	Detections per year (total no. of positive samples) (% of total positive samples)					
DRUG/CLASS	**2013 (1171)**	**2014 (672)**	**2015 (1861)**	**2016 (2041)**	**2017 (3265)**	**2018 (5237)**
AMPHETAMINES	68 (6%)	91 (14%)	154 (8%)	460 (23%)	1330 (41%)	2379 (45%)
OPIATES	446 (38%)	485 (72%)	818 (44%)	1169 (57%)	943 (29%)	968 (18%)
TRAMADOL	702 (60%)	354 (53%)	391 (21%)	458 (22%)	237 (7%)	177 (3%)
CANNABINOIDS	113 (10%)	236 (35%)	374 (20%)	380 (19%)	359 (11%)	562 (11%)
BENZODIAZEPINES	293 (25%)	238 (35%)	361 (19%)	552 (27%)	675 (21%)	977 (19%)
PREGABALIN	6 (1%)	3 (<1%)	589 (32%)	644 (32%)	644 (20%)	731 (14%)
ANTIHISTAMINES + METHORPHANS (cough syrup)	144 (12%)	255 (38%)	459 (25%)	830 (41%)	406 (12%)	524 (10%)
CARISOPRODOL/MEPROBAMATE (metabolite)	160 (14%)	133 (20%)	131 (7%)	191 (9%)	84 (3%)	32 (1%)
GAPAPENTIN	18 (2%)	3 (<1%)	17 (1%)	111 (5%)	24 (1%)	19 (<1%)
PROCYCLIDINE	26 (2%)	8 (1%)	20 (1%)	57 (3%)	68 (2%)	36 (1%)
TRIHEXYPHENIDYL	5 (<1%)	3 (<1%)	2 (<1%)	18 (1%)	6 (<1%)	1 (<1%)
COCAINE	1 (<1%)	1 (<1%)	8 (<1%)	1 (<1%)	7 (<1%)	6 (<1%)
METHADONE	0 (<1%)	0 (<1%)	6 (<1%)	4 (<1%)	17 (1%)	12 (<1%)
METHYLPHENIDATE + ETHYLPHENIDATE	N/A	N/A	N/A	N/A	N/A	13 (<1%)
GHB	0 (<1%)	0 (<1%)	0 (<1%)	0 (<1%)	1 (<1%)	12 (<1%)

Note: N/A = analyte not included in analysis at that time.

The 3 most commonly encountered drugs/drug classes in 2013 were tramadol, opiates and benzodiazepines. In 2014 the top 3 were opiates, tramadol and "cough syrup" constituents, antihistamines & methorphans. In 2015, opiates were most prevalent, followed by pregabalin and antihistamines & methorphans. In 2016, opiates were again most prevalent, second was antihistamines & methorphans and third, pregabalin. In 2017, amphetamines were most prevalent, second was opiates and third, benzodiazepines. In 2018, amphetamines continued to be most prevalent, second was benzodiazepines and third, opiates. Furthermore, in the past few years there has been an increasing number of samples where GHB (gamma-hydroxybutyrate) has been detected as a result of GHB or GBL (gamma-butyrolactone) use.

Across the 6 years, specific drugs within each of the drug classes include amphetamines (amphetamine, methamphetamine and rarely MDMA: 3,4-methylenedioxymethylamphetamine), opiates (codeine, morphine and heroin markers), cannabinoids (delta-9-tetrahydrocannabinol (THC) metabolite, cannabidiol (CBD)), benzodiazepines (diazepam, clonazepam, alprazolam metabolites and rarely midazolam) and "cough syrup" constituents, antihistamines (diphenhydramine and rarely promethazine) and methorphans (dextromethorphan).

The data show an increase in the relative detection of amphetamines, accounting for 6% of all positive samples in 2013 to accounting for 45% in 2018. Conversely, a decrease in the relative detection of tramadol was noted accounting for 60% of all positive samples in 2013 to representing 3% of positive findings in 2018. For the other frequently detected drugs/classes, opiate, cannabinoid, benzodiazepine and carisoprodol detections peaked in 2014 but were regularly detected across the 6-year period. Whilst the gabapentinoids (pregabalin and gabapentin) were detected across all years, there was an increase from 2015 onwards with pregabalin being the most commonly found. Cough syrup constituents, antihistamines and methorphans, were frequently seen to be present in inpatient samples, peaking in 2016. Of the drugs/classes less frequently detected, procyclidine and trihexyphenidyl are used in the treatment of drug-induced Parkinson's symptoms or Parkinson's disease itself. Carisoprodol and its metabolite meprobamate (used medically for muscle relaxation), were detected across the 6-year period, peaking in 2014 but only represented 1% of positive samples in 2018. Unlike other regions such as Europe and the Americas, cocaine was rarely detected in patient samples between 2013 and 2018. Methadone (used in heroin treatment programmes) was also rarely detected over the 6-year study period and is reflective of the use of buprenorphine and naloxone in such treatment within the UAE instead of methadone. The stimulant drugs, methylphenidate (Ritalin® prescribed for Attention Deficit Hyperactivity Disorder) and ethylphenidate (a new psychoactive substance, "designer drug") were only recently included within the scope of laboratory screening but only accounted for less than 1% of positive samples in 2018.

DISCUSSION

A wide variety of drugs were detected in the patient samples between 2013 and 2018, providing evidence of drug use within the UAE, including many drugs also commonly abused in other regions in the world such as amphetamines, heroin, cannabis and benzodiazepines [1, 3]. Conversely, cocaine and MDMA were rarely detected. Of one of the most commonly detected drug classes, the absolute and relative detection of amphetamines (almost exclusively amphetamine and methamphetamine – "Crystal Meth") in patient samples is believed to be due to increased supply and availability to users, with lower prices for purchase.

In the vast majority of cases, poly drug use was observed with multiple drug detections in samples. This was exemplified with opiates such as codeine, morphine and heroin in addition to tramadol with the additional taking of cough syrup to potentiate the effects and supplement opiate/opioid availability. Similarly, pregabalin and gabapentin often feature within an opiate/opioid misuse context as well as benzodiazepine misuse [6, 8]. With regard to the latter, of some specific note was the detection of midazolam in some patient samples as a result of diversion of the medicine into the illicit drug use market. Tramadol was noted to be a particularly prevalent drug by the NRC at an early stage of drug surveillance and controls were put in place (including prescription-only status) in the UAE. This may be one of the reasons for the observed decrease in tramadol detections in patients. Another reason, based on NRC patient information, is a switch from tramadol to stimulants such as methamphetamine, which may also be related to the described changes in availability of tramadol and amphetamines. An additional analytical and patient observation was the presence of very low concentrations of tramadol comparable to amphetamine in some cases, with patients denying any tramadol use leading to the inference of an apparent adulteration of amphetamine with tramadol, however this cannot be confirmed. The use of stimulants such as amphetamines featured in patient information around poly drug use, with users looking to use drugs to calm the post-peak stimulant effects and to avoid negative adverse effects. This may be the reason for the detection of carisoprodol with additional patient mentions of the use of anti-Parkinson drugs (procyclidine and trihexyphenidyl) in the belief they potentiate the effects of post-stimulant "downers", tramadol, pregabalin and benzodiazepines.

The noted increase in the number of GHB/GBL detections in patient samples since 2017 is an important and concerning trend, especially given the substances were not previously known to be particularly present in the UAE region. This is contrary to many other regions in the world, especially

Europe, where GHB/GBL have long been drugs of abuse within a variety of settings from body building and as a euphoric "party drug" to an additional and current role in the "chemsex" phenomenon [9]. In the NRC patients, information has indicated GHB/GBL is used as an alternative to benzodiazepines and at parties with the additional belief that the drug is not widely detectable particularly by the police. Some important aspects should be noted, such as GHB is the detected compound whether GHB or GBL has been consumed, as GBL is converted to GHB in the body [10]. Furthermore, GHB is an endogenous compound naturally occurring the body at low concentrations and the detection time of GHB/GBL is typically 12 hours in urine (i.e. it takes 12 hours for a typical dose to reduce to endogenous concentrations) [10]. This has resulted in GHB/GBL not always being detected when there is an extended period of time elapsed between use and sampling for analysis. It is therefore somewhat interesting that GHB is detected in the rehabilitation patients attending the NRC but as patients have a propensity to consume drugs immediately before attending for cessation and rehabilitation, this explains the detectability in this patient population, especially as some of the patients are noted to be intoxicated exhibiting GHB-like sedative symptoms at the point of admission. Of final note is that within the first 6 months of 2019 (full year statistics not yet available), there were 42 detections of GHB in patient samples, which is a more than 3-fold increase compared to 2018. The detections of GHB and context of use will continue to be monitored as part of this surveillance.

A new development within the analytical service and surveillance relevant to the Middle East region has been the monitoring of theophylline, especially in conjunction with amphetamine as this can be an indicator of "Captagon" (fenethylline) use [11]. Chemically, fenethylline is amphetamine and theophylline combined in a single chemical molecular structure and acts as a pro-drug for both these drugs as fenethylline converts to these in the body when taken. It can be clandestinely manufactured and has been noted as a drug of abuse in various regions, including the Middle East [11, 12]. Consequently, monitoring for its use is important. However, analytically, it is amphetamine and theophylline that are detected in biological fluid following use and as these substances could also be present due to amphetamine and caffeine-containing products, respectively, this is a challenge. Nevertheless, analysis for the presence of these two compounds and relative concentrations (albeit the inherent problems arising from the interpretation of urinary drug concentrations) may provide a useful tool in assessing its presence in patient samples, coupled with the medical and drug history information available from NRC patients.

Future developments of the toxicology laboratory and drug monitoring will involve further evolution of testing to encompass a wider variety of new psychoactive substances (NPS), aside from the stimulants (e.g. cathinones, phenidates) currently covered to an extent. Whilst some initial exploratory testing regarding synthetic cannabinoids has been performed (with an indicated presence of UR-144 and JWH-030 in two patient urine samples), the constant evolution of synthetic cannabinoid chemistries, very low concentrations and the often-reduced availability of reference material for associated urinary metabolites makes this a challenging aspect of analytical toxicology. There is also a need to enhance testing for potent synthetic opioids such as illicit fentanyl and especially its analogues to investigate any prevalence within the region. This is in addition to the detection of NPS benzodiazepines (e.g. flualprazolam, flubromazolam, etc.), dissociatives (e.g. methoxetamine, phenidines and related compounds), "kratom" (mitragynine alkaloid) and hallucinogens (e.g. LSD and PCP derivatives) that have been reported globally [5]. The future utilisation of newer technologies such as high-resolution mass-spectrometry will assist in these endeavours.

CONCLUSIONS

Over the last 6 years there has been a constant presence of amphetamines, opiates, tramadol, cannabis, benzodiazepines, pregabalin & gabapentin, antihistamines & methorphans, carisoprodol and ketamine found in patient samples analysed at the National Rehabilitation Center in Abu Dhabi, United Arab Emirates. However, there have been changes in the relative frequency during this time. Trends of note are an increase in amphetamines, a recent decrease in tramadol and frequent detection of

cannabis, pregabalin, benzodiazepines and cough syrup constituents, antihistamines and methorphans. Potential reasons for these trends have been obtained through clinical contact with the patients as part of their treatment, for which the NRC is in a unique position. The recent increased detections of GHB also require on-going monitoring as well as developments of NPS detection. These data provide drug and drug trend information within a substance-using patient population in the United Arab Emirates to improve knowledge and assist in the global monitoring of drug abuse within the Middle East region.

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CONFLICT OF INTEREST STATEMENT

The authors have no declarations or conflicts of interest.

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