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Mini Review

Carisoprodol Abuse a Re-emerging Issue: Perspective from Drug Rehabilitation in the UAE

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ABSTRACT

Toxicological monitoring at the National Rehabilitation Center (NRC) in the United Arab Emirates (UAE) for drug addiction prevention, treatment and rehabilitation of both inpatients and outpatients, has highlighted an increase in the use of carisoprodol and/or its metabolite, meprobamate. Due to their status as more historic drugs of abuse and reductions in their prescribing/marketing authorisation, neither substance is often included in routine drug screening. These data from routine analysis over a prolonged period therefore provide new and important information to support international concerns around a re-emergence of these substances as drugs of abuse. Furthermore, the toxicity risks of their reported abuse context with concomitant use of other central nervous system depressant drugs (such as benzodiazepines and opioids), demonstrate a need for toxicology laboratories and investigators to be aware of the potential involvement of carisoprodol and meprobamate in clinical and forensic casework. This article provides a toxicological perspective within a substance-using patient population in the Middle East to better inform global monitoring of drug abuse and advise professionals accordingly.

Keywords: Carisoprodol; Meprobamate; Drugs of abuse; Toxicology; UAE; Middle east

INTRODUCTION

For many years, as part of the clinical testing and medical laboratory services of the National Rehabilitation Center (NRC) in Abu Dhabi, the toxicology division undertakes analysis of patient urine samples (predominantly urine compared to blood). This includes the use of immunoassays with chromatographic and mass-spectral confirmation for drugs of abuse, prescription drugs and other substances [1,2]. This has allowed the detection of drugs within the substance-using patient population and monitoring of trends in those detections in order to provide an evidence-based assessment of drugs within the UAE area [3]. Within this, a trend over the last few years has been identified involving increased detections of carisoprodol (and/or its metabolite, meprobamate), suggesting an increase in its use amongst the patient population. Carisoprodol and meprobamate were first discussed as drugs of abuse around 30 years ago with some countries controlling the substances or re-considering market authorisation [4-9]. Following concerns around the issue of increasing misuse, carisoprodol was subject to pre-review a recent meeting of the Expert Committee on Drug Dependence at the World Health Organisation (WHO) [10]. With few published data (mainly from the USA), the following communication highlights the trend as well as reviewing carisoprodol abuse to inform substance professionals, laboratories and policy makers.

Carisoprodol, a muscle relaxant used to treat musculoskeletal pain, is increasingly recognized as a drug of abuse. Originally perceived as relatively safe, its potential for addiction and misuse has become more apparent. This issue is re-emerging globally and poses significant challenges for healthcare providers and drug rehabilitation centers, particularly in the UAE, where drug abuse patterns are evolving. Carisoprodol works by disrupting neuronal communication within the reticular formation and spinal cord, producing muscle relaxation and pain relief. However, its metabolite, meprobamate, has anxiolytic and sedative properties similar to barbiturates, contributing to its abuse potential. The drug's ability to produce euphoria and sedation makes it attractive for misuse, leading to dependency and severe withdrawal symptoms. While comprehensive data on Carisoprodol abuse in the UAE is limited, anecdotal evidence from rehabilitation centers indicates a rising trend. The UAE's strategic location

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and advanced transportation networks facilitate the smuggling of pharmaceuticals, contributing to increased availability and misuse of Carisoprodol. Additionally, societal pressures, stress, and the quest for quick pain relief are factors driving its abuse. The UAE maintains strict anti-drug laws, reflecting its zero-tolerance stance towards drug abuse. Possession, use, and trafficking of illegal substances are met with severe penalties, including lengthy prison sentences and heavy fines. However, recent policy shifts demonstrate a nuanced approach aimed at treating addiction as a health issue rather than solely a criminal one. In 2016, the UAE enacted a new law that emphasizes rehabilitation over punishment for first-time drug offenders. This legislation allows courts to mandate treatment and community service instead of jail time, provided the offense was not drug trafficking or a repeat violation.

LITERATURE REVIEW

NRC drug trends

The NRC undertakes toxicological analysis for routine diagnostic and clinical purposes for in-patient and especially out-patient admissions. This involves urine samples collected in an ethical and responsible manner from patients. Urine is preferable due to an extended window of detection compared to blood (generally 1-3 days depending on analytical sensitivity and may be longer for some drugs). Table 1 shows the results of toxicological analysis of patient urinary samples between January 2013 and October 2023. As described in a previous publication, the number of patients admitted to the NRC for treatment increased significantly from 2013 with the relative frequency of detection published [3]. Over the updated 10 year period shown in Table 1, a variety of different drugs/drug classes have been commonly encountered, in particular, amphetamines, opiates, tramadol, benzodiazepines and more recently, pregabalin. Within the carisoprodol and meprobamate findings across the 10 years, there were frequent detections between 2013 and 2016, followed by a decline to no cases in 2019 and 2020. The reasons for this are unclear but the subsequent increase in 2021, 2022 and now 2023 (representing the highest number of detections within the NRC trending history) have prompted this communication to the toxicological and wider community and support the concerns around recent increases in abuse. This is especially because carisoprodol and meprobamate are not commonly or routinely analysed for within drug screening, largely due to their chemical nature as well as their use and abuse being more historic. Therefore, if laboratories are not regularly analysing for the presence of carisoprodol or meprobamate, they will not be aware of either its involvement in a case (clinical, forensic or otherwise), nor determine how common such use may be within casework.

Table 1: Detections of drugs in patient urine samples, 2013-2023.

	Detections per year (total no. of positive samples)										
Drug/Class	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**	**2021**	**2022**	**2023***
Amphetamines	68	91	154	460	1330	2379	2594	2241	1771	1787	2264
Opiates	446	485	818	1169	943	968	1355	798	648	574	484
Tramadol	702	354	391	458	237	177	140	105	110	168	240
Cannabinoids	113	236	374	380	359	562	507	544	356	390	317
Benzodiazepines	293	238	361	552	675	977	1035	671	444	454	1065
Pregabalin	6	3	589	644	644	731	685	647	650	773	1156
Gabapentin	18	3	17	111	24	19	6	9	23	54	117
Antihistamines+Methorphans (Cough syrup)	144	255	459	830	406	524	462	277	356	198	37
Carisoprodol/Meprobamate (Metabolite)	160	133	131	191	84	32	0	0	19	59	187
Procyclidine	26	8	20	57	68	36	40	31	19	43	2
Trihexyphenidyl	5	3	2	18	6	1	0	0	0	0	0
Cocaine	1	1	8	1	7	6	5	3	4	4	11
Methadone	0	0	6	4	17	12	8	7	9	11	11
GHB(Gamma-Hydroxybutyrate)	0	0	0	0	1	12	94	61	67	59	1

Note: N/A=Analyte not included in analysis at that time. *Jan-Oct 2023.

Carisoprodol and meprobamate

Carisoprodol and its metabolite, meprobamate, have been prescription drugs for many decades, although their medical use has reduced over the years due to misuse and potential toxic effects outweighing therapeutic benefits [11-12]. When prescribed, carisoprodol is used for musculoskeletal conditions through its centrally acting muscle relaxation properties, although it's exact mechanism is not clear and may be related to its sedative effects. A typical dose is 250 to 350 mg given orally three or four times daily for up to 2 to 3 weeks, with a lower dose recommended for elderly patients. Drowsiness, dizziness, and headache are the most common adverse effects reported with carisoprodol and in overdose, seizures, stupor, coma, respiratory depression and rarely death may occur. Cases of abuse and dependence have been associated with high dose and long-term use of carisoprodol, with withdrawal symptoms after cessation of use. Meprobamate is important as many (if not all) of the effects of carisoprodol are likely associated with this metabolite and its central nervous system depressant activity through GABA-A receptors [13-16]. Meprobamate itself has been prescribed for short-term treatment and management of anxiety disorders and insomnia, with any muscle relaxant effects thought to be related to meprobamate-induced sedation. Prescribed dosage is somewhat similar to carisoprodol with an anxiolytic dose of 400 mg orally three or four times daily to a maximum of 2.4 gm daily, with lower doses in the elderly.

DISCUSSION

In a review of the legal status and patterns of abuse for these drugs, Fass JA [17], highlighted published case reports involving a relatively small number of patients whereby users consumed 12-30 tablets of carisoprodol per day either alone or along with tramadol, benzodiazepines and alcohol [17]. The combinational use of carisoprodol with benzodiazepines (e.g., alprazolam) and opioids (e.g., tramadol, hydrocodone and oxycodone) has been associated with "doctor shopping" and street terms such as the "Holy Trinity". "Las Vegas Cocktail" and "Houston Cocktail", particularly in the USA [18-20]. Toxicologically, the combined use of such central nervous system depressant drugs presents a risk of toxicity, including potentially fatal respiratory depression [21,22]. These combinations are also of interest within the NRC drug trends data given that whilst there has been an apparent decrease in opiate detections, there has been a recent increase in tramadol and especially benzodiazepines (Table 1). Further work is ongoing to determine the medical and rehabilitation circumstances and other drug detections within the patient population involving carisoprodol and meprobamate use.

Within case reports, effects of carisoprodol abuse included hallucinations, euphoria and irritability [17]. Furthermore, Gupta highlighted carisoprodol abuse in adolescence and described the sought-out effects of carisoprodol as being relaxation, giddiness and drowsiness [18]. With euphoria also being a desired effect, whilst usually consumed orally, snorting (insufflation) as a route of administration results in euphoric effects reportedly occurring much sooner [18].

CONCLUSION

Drug trend data within the drug rehabilitation patient population of the NRC in the UAE, have identified an increase in the frequency of carisoprodol use. This supports concerns in the literature and global drug control (especially as despite some local controls, carisoprodol or its metabolite, meprobamates are not internationally controlled) around its re-emergence as a drug of abuse. The context of use within an apparent poly-pharmacy setting also has toxicity risks that could be significant within a range of clinical and forensic casework, including drug driving and fatal and non-fatal intoxications. Given that carisoprodol and meprobamate are not typically included in modern routine drug screening (or even specific analysis), it is therefore important that toxicology laboratories and investigators are aware of the potential involvement of these drugs in casework and consider inclusion within analytical methods applied.

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COMPETING INTERESTS

The authors confirm there are no competing interests to declare and no funding was received.

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