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Mephedrone (4-methylmethcathinone): What is new in our understanding of its use and toxicity

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ABSTRACT

Mephedrone (4-methylmethcathinone) is a synthetic cathinone that has been used as a recreational drug in Europe and elsewhere in the world since 2007. In addition to published scientific papers there are a number of different data sources available which provide information on the sources, availability and prevalence of use of mephedrone. Whilst there are no formal human studies to determine the acute toxicity of mephedrone, there is a range of different levels of data available which describe the acute toxicity of mephedrone. These include user Internet discussion fora, sub-population level surveys of user previous experiences of acute toxicity and individual case reports and case series of toxicity related to both self-reported and analytically confirmed mephedrone use. In this review article we describe how through the process of data triangulation using a combination of these different sources, it is possible to develop an understanding of the acute toxicity of mephedrone. This demonstrates that mephedrone has a pattern of acute toxicity that is similar to other stimulant drugs such as MDMA, amphetamine and cocaine.

1. Introduction

'Mephedrone', the synthetic cathinone 4-methylmethcathinone, has been available on the European recreational drug scene since 2007 (Dargan and Wood, 2010; Dargan et al., 2011). Although it was initially legally available throughout Europe, it was controlled as a Class B substance under the Misuse of Drugs Act, 1971 in the UK in April 2010 and in December 2010, The European Council adopted a decision on submitting mephedrone to control measures across the European Union (Council Decision, 2010). It was also controlled in 2011 under the Controlled Substances Act in the US (DEA, 2011). In this review article, we will provide a background to introduce what mephedrone is, and then discuss what is new in the prevalence of use of mephedrone and our understanding of the toxicity related to its use.

2. Background

2.1. What is mephedrone?

Mephedrone is usually purchased by/sold to users in powder form in small sealed plastic bags which are marked as 'not for human consumption' or 'research chemical' (Dargan and Wood, 2010; Dargan et al., 2011; Newcombe, 2009; Psychonaut 2009; Schifano et al., 2011). It is marketed under a number of brand names, including 'plant feeder', 'plant food' and 'bath salts', and of note in Europe it was more commonly sold as mephedrone or 'plant food', but in the US was more commonly sold as 'bath salts' (Dargan and Wood, 2010; Newcombe, 2009; Prosser and Nelson, 2012; Psychonaut, 2009; Schifano et al., 2011; Spiller et al., 2011). Despite these brand names, mephedrone has no proven use as a plant food or as a bath/cosmetic product. Although the majority of mephedrone is sold in powder form, it is available in tablet or encapsulated forms (Dargan et al., 2011). Use is predominately by nasal insufflation, although some users report that this is associated with significant unwanted nasal effects, and therefore some individuals may dissolve it in water/other drinks or swallow the powder wrapped in paper (known as 'bombing') (Dargan et al., 2011; Dargan and Wood, 2010; Measham et al., 2010).

2.2. Sources of mephedrone

Mephedrone has been reported to be available from street-level drug dealers, high-street retail outlets known as 'head shops' and the Internet (Dargan et al., 2011; Dargan and Wood, 2010; Dargan et al., 2010; Drugs

Abbreviations: ED, Emergency Department; EMCDDA, European Monitoring Centre for Drugs and Drug Addiction; EWS, Early Warning System; GC–MS, Gas-chromatography mass-spectrometry; LC–MSMS, Liquid chromatography with mass-spectrometry mass–spectrometry; MDMA, Methylenedioxymethamphetamine; NMR, Nuclear magnetic resonance; NPIS, National Poisons Information Service; UPLC–QTOF–MS, ultra performance liquid chromatography–quadrupole time of flight-mass spectrometry.

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Forum; EMCDDA, 2010; EMCDDA, 2011; Erowid; Measham et al., 2010; Newcombe, 2009). The European Monitoring Centre for Drugs and Drug Addiction, using their 'snapshot' Internet survey techniques, demonstrated that there was a significant increase in the number of Internet sites selling mephedrone between December 2009 and March 2010, when there were increasing reports of mephedrone use, and that the majority of these were UK based (Dargan and Wood, 2010; EMCDDA, 2010; EMCDDA, 2011; Hillebrand et al., 2010). They typically were mephedrone specific websites, and would ship mephedrone to any country on request. After the control of mephedrone in the UK in April 2010, not only was there a significant decrease in the number of internet sites selling mephedrone, the majority of sites were no longer UK based and a significant proportion had changed to selling other 'legal highs', which may in fact be mephedrone being sold covertly under different brand names (Brandt et al., 2010a, 2010b; Dargan and Wood, 2010). This puts the individual purchaser at risk of potential criminal conviction, since inadvertently they may be purchasing a substance that is controlled in the country where it is being supplied to.

Use of the internet to source mephedrone in the UK prior to its control appeared to be less common amongst younger aged users; it was felt that this was due to the limitation of appropriate banking facilities to purchase on line and/or a secure delivery address away from parents/guardians (Dargan et al., 2010). These users were more likely to source their mephedrone from street-level drug dealers or friends. There is some suggestion that there has been a shift to greater sourcing of mephedrone from street-level drug dealers amongst all users; for example in one survey of 150 individuals who had used mephedrone prior to the UK control, 95 (63%) had continued to use it after its control and the proportion who had sourced from street-level drug dealers increased from 41% to 57% (Dargan and Wood, 2010; Measham et al., 2011a; Winstock et al., 2010).

2.3. Analytical techniques to detect mephedrone

There are currently no 'field tests' for mephedrone and it does not give a colour reaction with the Marquis Field test (this is a spot field test used to detect MDMA, amphetamine and other structurally related drugs). Detection of mephedrone and its metabolites is possible using techniques that have been developed for gas-chromatography mass-spectrometry (GC–MS), liquid chromatography with mass spectrometry–mass spectrometry (LC-MSMS), ultra performance liquid chromatography–quadrupole time of flight-mass spectrometry (UPLC-QTOF-MS), microcrystalline identification and nuclear magnetic resonance (NMR) (Bell et al., 2011; Brandt et al., 2010a; Camilleri et al., 2010; Elie et al., 2012; Gibbons and Zloh, 2010; Jankovics et al., 2011; McDermott et al., 2011; Meyer et al., 2010; Power et al., 2011; Reitzel et al., 2011; Santali et al., 2011; Sørensen, 2011). However, it should be noted that some of these techniques do not distinguish between the different methyl-methcathinone isomers, although this is possible through the use of nuclear magnetic resonance spectroscopy (NMR), where these facilities are present (Gibbons and Zloh, 2010; Meyer et al., 2010).

Hair analysis has previously been used to detect chronic use of recreational drugs such as cocaine and amphetamine. This type of analytical technique has also been extrapolated to mephedrone (Martin et al., 2012; Petróczi et al., 2011; Shah et al., 2012). These studies have demonstrated that it is not only possible to detect mephedrone in hair samples, but also two of its metabolites — 4-methylephedrine and 4-methylnorephedrine. The concentration of mephedrone and its metabolites in hair appear to be in the pg/mg hair to ng/mg hair range, similar to that with other recreational drug incorporation.

3. Prevalence of use

Information on the prevalence of use is available from data on seizure at both border and local law enforcement level and population or subpopulation level surveys.

3.1. Border and law enforcement seizure data

Within the European Union, information on detection of drugs such as mephedrone is collated through the EMCDDA Early Warning System (EWS) (EWS, 2007). The first reported seizure of mephedrone was in 2007 in Finland of capsules containing mephedrone and in 2008 it was detected in the UK and other Scandinavian countries (Sweden, Norway and Denmark) (Dargan and Wood, 2010; Dargan et al., 2011; EMCDDA-Europol, 2010). By the end of 2010 it had been detected in 31 European and neighbouring countries, suggesting widespread availability throughout Europe.

3.2. Population and sub-population use prevalence data

Collection of population prevalence of use of mephedrone was not undertaken by any EU country until the British Crime Survey included questions relating to the use of mephedrone in the 2010/2011 survey (Home Office Statistical Bulletin, 2011). Overall the prevalence of use in 16–59 year olds in the last year was 1.4%, which was the same reported prevalence for ecstasy. However, the prevalence of use was higher in those aged 16–24 at 4.4%, compared to 0.6% in those aged 25–59 years; the prevalence of use in those aged 16–24 was the same as the reported prevalence of cocaine use in this age range.

There have been two surveys of school/university aged children (Dargan and Wood, 2010; Dargan et al., 2010; Dargan et al., 2011). In a survey of 1006 Scottish school and college/university students undertaken prior to the control of mephedrone in the UK, 205 (20.3%) reported that they had used mephedrone on at least one occasion previously (Dargan et al., 2010). Self-reported "occasional use", defined as on more than one occasion but not more than once a week, in this study increased with increasing age. Regular daily use was reported by 4.4% of those who had used mephedrone, with the highest daily use rates occurring in the younger aged individuals, particularly those under the age of 21. A subsequent survey of 154 pupils aged 14–15 in Northern Ireland in May 2010, after the control of mephedrone in the UK, reported that 40% of those interviewed had used mephedrone on at least one occasion in the past (Dargan and Wood, 2010).

There have been two studies undertaken in South London 'gay friendly' nightclubs, one in 2010 approximately three months after the UK control of mephedrone and one in 2011 over a year after mephedrone's control (Measham et al., 2011a; Wood et al., 2012). In the 2010 survey of 308 clubbers, 54% reported life-time use of mephedrone and 52% reported use within the last year (Measham et al., 2011a). There was continuing popularity of mephedrone in the 2011 survey, with 41% reported that at the time of the survey they had already taken mephedrone and/or were planning on taking mephedrone later that evening (34% had already taken it and 35% were planning to take it later) (Wood et al., 2012). Respondents were also asked to name their favourite drug in this survey; mephedrone was the most commonly reported favourite drug (20.4%) of those surveyed. A third convenience sample of 207 bargoers in the night-time economy of Lancaster, a town in Northern England, showed approximately 5% of those surveyed reported use of mephedrone in the last month (Measham et al., 2011b). This study reported that mephedrone was being added to existing drug repertoires, rather than displacing other established drugs.

The self-reported prevalence of mephedrone use in same-sex attracted adults in Sydney, Australia was lower than in the UK (Lea et al., 2011). In an online survey of 572 same-sex attracted men and women aged 18 to 25 years, who lived or regularly spent time in Sydney, life-time prevalence of mephedrone use was 4.0% of those surveyed; 2.1% had used in the preceding 6 months and 1.4% in the preceding month. In a study of 693 regular ecstasy users in Australia, 28% reported that they had previously used an emerging psychoactive substance in the last six months (Bruno et al., 2012). Mephedrone was the most commonly used emerging psychoactive substance,