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Review

E-cigarettes—An unintended illicit drug delivery system

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ABSTRACT

Since the introduction of electronic cigarettes (e-cigarettes) in 2003, the technology has advanced allowing for greater user modifications, with users now able to control voltage, battery power, and constituents of the e-cigarette liquid. E-cigarettes have been the subject of a growing body of research with most research justifiably focused on the chemical makeup and risk analysis of chemicals, metals, and particulates found in e-cigarette liquids and vapor. Little research to date has focused on assessing the risks associated with the drug delivery unit itself and its potential for use as an illicit drug delivery system. In light of this, a range of illicit drugs was researched focusing on pharmacodynamics, usual method of administration, the dosage required for toxicity, toxic effects, and evidence of existing use in e-cigarettes in both literature and online illicit drug forums. A systematic literature search found evidence of current use of e-cigarettes to vape almost all illicit drug types analyzed. This presents both a potential population health risk and a management issue for clinicians. It also raises the issue of policing illicit drugs due to potential altered characteristic smells and storage within e-cigarette fluids. E-cigarettes are a viable illicit drug delivery system with evidence both inside and outside of the formal medical literature detailing their potential use for drug delivery of a wide range of illicit and legal drugs.

1. Introduction

The electronic cigarette (e-cigarette) first appeared in 2003 as an alternative to traditional tobacco cigarettes for nicotine delivery (Schraufnagel et al., 2014). Since its introduction, e-cigarette awareness and use has grown rapidly (Adkison et al., 2013; Schraufnagel et al., 2014) expanding into the global market with United States (U.S.) retail sales expected to approach $10 billion by 2017 (Besaratinia and Tommasi, 2017), and presenting a challenge for tobacco regulatory bodies and health departments (WHO, 2014). The past six years have seen a ten-fold increase in the number of adult smokers seeking to transition from smoking to vaping, with recent estimates showing more than 4 million Americans are using e-cigarette devices (Besaratinia and Tommasi, 2017). In 2014, e-cigarettes became a more common tobacco product among U.S. youth than traditional cigarettes (Eggers et al., 2017) and a survey of students in Wales, UK found that among year 11 students (aged 15–16) 37.3% had used an e-cigarette (ever) where only 26.5% had smoked a traditional cigarette (ever) showing the increased popularity of e-cigarettes among youth (Lacy et al., 2017). This has warranted an influx of research around both the technology and its delivery method.

Most studies to date have examined the chemical composition of e-cigarette vapor and liquid. This has included: nicotine delivery concentrations per puff (Czogala et al., 2014; Goniewicz et al., 2014; Pellegrino et al., 2012); e-cigarette liquid nicotine concentrations (Pisinger and Døssing, 2014); exhaled concentrations of propylene glycol (Pellegrino et al., 2012; Schober et al., 2014; Schripp et al., 2013) and its effects (Werley et al., 2011); glycerine vapor concentrations (Pellegrino et al., 2012) and its effects (Farsalinos and Polosa, 2014); acetone vapor concentrations (Schripp et al., 2013); formaldehyde vapor concentrations (Goniewicz et al., 2014, 2013; Schripp et al., 2013); nitrosonornicotine presence in vapor (Goniewicz et al., 2014; WHO, 2007); tobacco-specific nitrosamine presence in vapor (Farsalinos and Polosa, 2014; McAuley et al., 2012); metals in vapor (Goniewicz et al., 2014; Williams et al., 2013) and flavoring concentrations and toxicity (Bahl et al., 2012; Farsalinos et al., 2015; Khlystov and Samburova, 2016). Particulate matter (PM) levels have also been researched with studies showing that e-cigarettes produce PM_{10}, $PM_{2.5}$ and $PM_{1.0}$ (Pellegrino et al., 2012; Schober et al., 2014), though these levels are lower than traditional cigarettes (Czogala et al., 2014; Pellegrino et al., 2012) and differ depending on e-cigarette liquid brand and composition (Czogala et al., 2014; Schober et al., 2014). Common consensus is that e-cigarette users do not inhale the carcinogens contained in tars (Douglas et al., 2015), and the e-cigarette liquids

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are not heated to the point of combustion, therefore the health effects relating to the use of e-cigarettes are likely to be lower than for traditional cigarettes even though the long-term effects are largely unknown. There has also been a growing interest in the use of e-cigarettes as a tobacco smoking cessation device, with some studies showing promise for its use (Barbeau et al., 2013; Bullen et al., 2013), while others provide conflicting results (Orr and Asal, 2014) or suggest e-cigarettes may be a pathway to increased youth tobacco smoking (Dutra and Glantz, 2014; Leventhal et al., 2015). Despite this influx of research, some concerns have arisen. A serious concern addressed by a meta-analysis by Pisinger and Døssing is that of academic bias. They claimed that 34% of included authors on papers describing e-cigarette toxicity had a conflict of interest and that the majority of their included studies were either funded or supported to some degree by e-cigarette manufacturers (2014).

Another concern identified in the research is the lack of academic focus on the risk analysis of the e-cigarette drug delivery unit. Since the release of the first-generation e-cigarette, which was cigarette-shaped (Rom et al., 2015), three generations have followed. Second generation devices exhibited a change in style as well as introducing elements of larger rechargeable batteries and refillable e-cigarette fluid tanks (Dawkins et al., 2015). Third generation devices added the ability to modify the voltage provided to the atomizer to alter the atomizer temperature (Dawkins et al., 2015), generally up to 212 °C (Giroud et al., 2015), with consequent effects on the amount of vapor production. Further to this, third generation devices, with larger battery capacity and unit size, allowed the attachment of larger tanks allowing for greater e-cigarette liquid storage (Dawkins et al., 2015). These generational changes as well as the advanced user's ability to personally modify devices add a difficult to control variable when assessing the risk of the e-cigarette unit, especially considering the potential to deliver drugs of abuse.

Despite the growing catalog of research and studies surrounding e-cigarettes and the fact that inhalation has been noted as an increasingly common route of administration of illicit drugs due to the rapid onset of action, very little research has focused on possible alternative uses of e-cigarette technology (Bell and Nida, 2015). Since e-cigarettes have proved to be an effective nicotine drug delivery system (Schroeder and Hoffman, 2014), the question arises as to whether other illicit drugs are also able to be effectively delivered by e-cigarettes. Referring to the most commonly abused illicit drugs in Australia (AIHW, 2008) and around the world, the pharmacodynamics and pharmacokinetics of these drugs indicate the potential for the use of e-cigarette technology as a novel drug delivery system. The vaporization of cannabis had been proposed well before the first e-cigarette (Gieringer, 2001) with studies demonstrating that vaporization of medicinal cannabis produces plasma concentrations of Δ-9-tetrahydrocannabinol (Δ-9-THC) comparable to traditional cannabis combustion smoking (Abrams et al., 2007; Gieringer et al., 2004).

Due to the limited pool of literature on illicit drug delivery via e-cigarettes (Giroud et al., 2015), the question arises as to what other illicit drugs are being used via e-cigarette technology. In addition to summarizing the current literature relating to this topic, this paper, investigates the plausibility and risk of e-cigarette technology as a drug delivery system for illicit drugs. Drugs assessed include: cannabis, synthetic cannabinoids (SCs), synthetic cathinones, benzoylmethylecgonine (cocaine), gamma-hydroxybutyric acid (GHB), heroin, fentanyl, 3,4-methylenedioxyamphetamine (MDA), 3,4-methylenedioxymethamphetamine (MDMA), and methamphetamine. These drugs will be reviewed in terms of their known mechanisms of action, the dosage required for toxicity and toxic effects. Finally, the literature will be reviewed for evidence of e-cigarette use for each drug and where no evidence can be found illicit drug use internet forums will be accessed for preliminary evidence of possible usage.

The term 'vaping' is used both colloquially and in the literature to describe the through mouth inhalation of a vaporized product from a device that uses electrical power to heat the product to the point of vaporization. The product can refer to substances with desired inhalation effects such as nicotine dissolved in e-liquids (usually a mix of propylene glycol and glycerine); crushed plant material placed directly into the vaporizing device; concentrated extracts from plant materials in the form of thick waxes or oils either on their own or diluted in e-liquid; or substances directly dripped onto the hot coil to produce vapor. Vaping devices can be classified into two broad categories portable vaporizing devices, powered by batteries, or table-top vaporizers. For the purposes of this paper 'e-cigarettes' is used as a collective term for all types of portable vaporizing devices, not only those that resemble traditional cigarettes. 'Vaping' can refer to use of either e-cigarettes or table-top vaporizers or both unless specified.

2. Methods

2.1. Search strategy

A systematic search for the use of electronic cigarettes or other vaping devices to vape illicit drugs in the literature was conducted on 14 March 2018. The databases employed were ProQuest, Scopus, Web of Science and PubMed. The literature search was left deliberately broad to ensure all results involving the use of electronic cigarettes or other vaping devices to vape illicit drugs were captured. The search strategy employed for all databases was as follows: ab(cannabis OR THC OR cathinone OR alpha-PVP OR MDPV OR methylone OR mephedrone OR cocaine OR GHB OR "gamma-hydroxybutyric acid" OR heroin OR fentanyl OR oxycodone OR opioid OR MDA OR "3,4-methylenedioxyamphetamine" OR amphetamine OR methamphetamine OR MDMA OR "3,4-methylenedioxymethamphetamine" OR Molly OR ecstasy OR "synthetic cannabinoid" OR cannabinoid OR "bath salts" OR "legal high") AND (vapor OR vapor OR vaping OR vape OR e-cigarette OR "electronic cigarette" OR e-cig OR "e-cig" OR vaporizer OR vaporizer OR vaporizer) limited to English (abstract only). Illicit drug user forums were accessed in lieu of formal medical literature to assess evidence for the use of illicit drugs with e-cigarettes. Forum websites were searched using the same terms as the academic literature search, however, colloquial and street names were used in the search. The following websites were utilized: www.bluelight.org/vb/content/; https://drugs-forum.com/forum/index.php; https://www.reddit.com/r/Drugs/; https://www.quora.com; and https://www.erowid.org. Evidence of use was subjectively assessed via forum threads and user comments directly indicating either personal or known associate use.

2.2. Search selection

The initial database search identified 1603 papers, which once duplicates were removed left 1118 results (Fig. 1). Of those, 935 records were eliminated because of their irrelevance to the topic, and a further 145 were removed following full-text screening as they did not provide specific examples of the use of electronic-cigarette style devices to vape illicit drugs. The remaining 38 articles were used in the final analysis, articles relating to cannabis use in e-cigarettes are marked in the reference list with a *; articles relating to any other type of illicit drug use in e-cigarettes are marked with a ^.

3. Results

3.1. Cannabis

Cannabis (marijuana) is currently the most widely used illicit drug in the world (3.5% adults), with the highest rates of past year usage in Oceania (10.3%) (Gowing et al., 2015). It is usually administered orally or by inhalation (Grotenhermen, 2003; Pillay, 2013). The theory behind vaping cannabis is a reduction in inhalation of smoke-related toxins and carcinogens including tar, carbon monoxide and ammonia (Budney