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A matter of life and death: substance-caused and substance-related fatalities in Ibiza in 2015

Running title: substance-caused and substance-related fatalities in Ibiza

Keywords: Novel psychoactive substances; alcohol; cocaine; fatalities; drug-related deaths.

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Abstract

Objectives and methods. In the framework of the EU-funded project “EU-Madness”, we collected and analysed all the reports of fatalities directly or indirectly related to **substances of abuse** registered in Ibiza from January to September 2015, in order to analyse the characteristics of the sample, the identified substances and the nature of deaths associated with their consumption.

Results. A significant increase of **substance**-caused deaths with respect to the previous four years has been highlighted. Most of the subjects were young males, more than half were not Spanish. Males prevailed also among the victims of traffic accidents and suicides. The most commonly involved substances included MDMA, alcohol, cocaine, THC, opiates and prescription drugs. **Con-**

clusions. Although the use of NPS is rapidly increasing in Europe, according to the results from our sample, alcohol and well-known stimulants (MDMA and cocaine) are **still** the substances of abuse mainly involved in the cases of **substance**-caused and **substance**-related fatalities. The significant increase of fatalities in Ibiza in the last 5 years is an issue that must be taken into account and should be better investigated, as other theories besides NPS increased diffusion should be proposed, and therefore targeted prevention strategies should be designed.

Introduction

Illicit **substance** use is well known as an important contributor to the global burden of diseases; indeed, the extent of problem drug use in specific clinical settings such as psychiatric or emergency units is not limited to subjects with substance use disorders (SUD) or dependence, but it also includes occasional recreational drug users (Degenhardt et al., 2013). The physical and psychopathological risks of non-habitual **substance** consumption are frequently underestimated, and substance-related fatalities often involve first-time or sporadic clients. Moreover, in recent times, in addition to “classic” substances of abuse, Novel Psychoactive Substances (NPS) have emerged, determining a further health issue of growing importance. There is currently an increasing body of clinical evidence to demonstrate the potential acute and chronic health harms associated with the use of NPS, but often very little is known by both consumers and health care professionals (Martinotti et al., 2015; Simonato et al., 2013). A number of NPS has been directly or indirectly associated with serious adverse effects and fatalities: 2-DPMP and D2PM, two synthetic stimulants belonging to the class of piperidines, have shown both neuropsychiatric and cardiovascular toxicity, and they have been involved in three deaths in August 2010 (Corkery et al., 2012). Misuse of gamma hydroxybutyrate (GHB) and gamma butyrolactone (GBL) has been implicated in more than 150 fatalities in the UK from 1995 to 2013 (Corkery et al., 2015), and more recently, stimulants mixes and synthetic cannabinoids have emerged as potentially life-threatening (Santacroce et al., 2014). NPS-related deaths have been investigated mainly in the UK (Chiappini et al., 2015; Loi et al., 2015; Corkery et al., 2011), but in this context, poly-substance use and behavioural risk taking seem to be particularly widespread in the Balearic Islands nightlife scene. Indeed, Majorca, Menorca, Ibiza and Formentera are among the most popular tourist destinations in the whole of Europe: such an international and representative nightlife resort appears as a crucial key setting to address substance-related health problems and fatalities. Previous research projects conducted in the Islands have addressed substance use and risky behaviours undertaken by young tourists and foreign casual workers (Bellis et al., 2009; Kelly et al., 2014),

highlighting that **substance misuse** and sexual risk taking are widespread between both categories. The growth in international travel associated with nightlife, the additional risks posed by clubbing in an unfamiliar country, the threats of new and often unknown psychoactive substances and the changes in **substance** use and risk-taking amongst people visiting an international resort mean that both interventions, and basic health and safety measures are now required on an international basis (Bellis et al., 2002; Bellis et al., 2000).

In the framework of the EU-funded project “EU-Madness”, our goal was to focus on the records of all **psychoactive substance**-involving fatalities registered in Ibiza from January to September 2015, in order to analyse the characteristics of the sample, the identified substances and the nature of deaths associated with their consumption.

Methods

With the cooperation of the team of the Forensic Medicine Unit of Ibiza, coordinated by dr. Sancho Jaraiz, all the reports of fatalities directly related to drugs in 2015 were collected and tabulated in a dedicated database. A further addition regarded the collection of all the reports of fatalities that might involve **psychoactive substance** such as suicides and traffic accidents, for the same timeframe. When possible, comparison with data from 2011 to 2014 was performed. All reports included analysis of body samples (blood, urine, vitreous humour, bile) for both classic and novel substances of abuse. Sampled tissues were sent for specific analysis to the National Institute of Toxicology and Forensic Sciences in Barcelona. **Headspace-gas chromatography (GC) with flame ionisation detection (FID) was used to detect the presence of ethanol in the specimens. To assess the consumption of psychoactive substances and/or prescription drugs, GC was combined to mass spectrometry (MS) (GC-MS).**

Results

From January to the end of September 2015, 12 fatalities directly related to **substance misuse** have been registered in Ibiza, which represents a significant increase with respect to the previous four years (three fatalities in 2014, four in 2013, five in 2012, and just one in 2011). 9 out of 12 subjects were males (75%); mean age was 30.5 years, with the youngest deceased being two females, both 18 years old Britons (50% of the deceased subjects were British). Most of the victims (58.3%) were found dead in a hotel, while 25% died in his/hers own house, 8.3% in somebody else's house, and the same percentage was pronounced dead in the local hospital. Four subjects (33%) had a previous history of alcohol and **substance** abuse and/or psychiatric disorders (both in the mood spectrum). Most common causes of death were acute pulmonary oedema/haemorrhage, acute respiratory failure and multi-organ failure; one patient (8.3%) suffered multiple traumas due to precipitation from height while intoxicated. A number of the collected samples of blood, bile, urine and vitreous humour still have to be analysed: the cases for which definitive results were already available (**9 out of 12 - 75%**) **involved alcohol (6 cases - 66% of the currently available analyses), cocaine (5 cases, 55%), 3,4-Methylenedioxymethamphetamine - MDMA (4 cases - 44%), opiates (methadone, morphine and codeine, 3 cases, 33%) and a number of prescription drugs (3 cases, 33%, in which it has been evidenced a combination of trazodone, pregabalin, clonazepam, alprazolam, mirtazapine, corticosteroids and macrolide antibiotics, plus one case in which was detected phenytoin)**. MDMA and alcohol were found in the vitreous humour of the one subject whose death was traumatic (ascertained cause: traumatic cardiac rupture, multiple trauma due to precipitation from a height). A synthesis of the results is provided in Table 1.

- Insert Table 1 about here-

From January to the end of September 2015, seven traffic accident-related fatalities were registered in Ibiza. Six out of seven deceased (85.7%) were males; the only female was an 81-year-old Spanish woman, victim of an intoxicated driver. More than half of the deceased were Spanish (4

out of seven, 57%), while the remaining were foreigners (from Philippines, Belgium and Morocco). In three cases (41.8%) the deceased was an intoxicated driver (alcohol, or alcohol and cocaine); in three other cases, the driver was intoxicated (cocaine and delta-9-tetrahydrocannabinol [THC]; alcohol, THC and amphetamines; alcohol and THC) but the victim was **substance-free** (see Table 2 for a summary).

- Insert Table 2 about here-

From January to the end of September 2015, nine suicides were registered in Ibiza. Six out of nine victims were males (66.6%), mean age was 42.6 years old. Six again were Spanish, while the others were two Britons and a French. Five subjects had a previous history of psychiatric disorders (mostly depression and anxiety disorders); three were in treatment with antidepressants and benzodiazepines. Cocaine was implicated in two of the suicides, but it was not the cause of death (one was hanging and the other jumping from height – see Table 3 for a summary).

-Insert Table 3 about here-

Discussion and conclusions

According to the results from our sample, alcohol and stimulants (MDMA and cocaine) are the substances of abuse mainly involved in the cases of **substance-caused** and **substance-related** fatalities. A **substance-caused** fatality may be defined as a death in which the direct toxic effects of the **psychochoactive** caused or contributed to the death, while a **substance-related** fatality is a death in which the **substance of abuse** was demonstrated in the blood, but did not directly cause death (e.g., polytrauma for accidental precipitation). Again, alcohol is present in almost the totality of traffic accident-related deaths, followed by cocaine, THC and MDMA, and it is also one of the few substances detected in suicides, together with cocaine and prescription drugs. Alcohol is still

the most commonly abused psychoactive substance: according to the 2014 Global Drug Survey (GDS), which involved around 80,000 subjects in 18 countries, 90.8% of the interviewees had used alcohol in the 12 months before the survey (The Global Drug Survey, 2014). A recent **epidemiological** research on more than 1,000 Italian young adults aged 18-26 highlighted that 80.5% of the sample habitually consumed alcoholic drinks, and almost 20% drank 5 or more units of alcohol per time (a unit of alcohol corresponds to a drink containing 12 grams of ethanol) more than once a week (Lupi et al., 2015). Moreover, a relevant subgroup (66.5%) admitted a binge-drinking pattern of alcohol consumption, with consistent psychophysical consequences (loss of control and consciousness, aggressive behaviour, hospitalisation, sexual disinhibition, need for prescription drugs after intoxication). Similar figures have been presented by the World Health Organization in its Information System on Alcohol and Health (World Health Organization, 2011), while the ESPAD survey, which is focused on a younger population (15- and 16-year-old students from 36 European countries), evidenced a prevalence of alcohol consumption of 79% in the year before the survey, with a significant increase over the years for “heavy episodic drinking” (from a mean average of 29% in 1995 to 38% in 2011) (European School Survey Project on Alcohol and Other Drugs, 2012). Deaths related to alcohol intoxication occur most frequently if a large quantity of ethanol is ingested in a short timespan: this makes binge drinking and heavy episodic drinking extremely dangerous from a public health point of view. Data from the Vital Signs report of the US Center for Disease Control and Prevention (CDC) underline that there are more than 2,200 alcohol poisoning deaths in the US each year, with an average of 6 per day (Center for Disease Control and Prevention, 2015). Alcohol is frequently consumed together with other drugs: according to the gateway theory, it may also be considered as a “first step” before moving to different or harder substances. In the US, 69.9% of heavy alcohol users aged 12 to 17 are also illicit drug users. This is over 13 times higher than non-alcohol users, where 5.2% use illegal substances (National Institute for Drug Abuse, 2009). Poly-substance misuse may represent a notable increase in the risk of severe health consequences, including of course death. Alcohol may be associated with stimulants, or other central nervous system (CNS) depressors, and the pharmacological, toxicological and

psychopathological effects due to interactions among substances may be unpredictable and fatal in vulnerable individuals (Martinotti et al., 2009). Stimulants such as cocaine and MDMA, which are often reported in our sample, also account for a remarkable number of fatalities. With respect to Europe, cocaine use has the highest prevalence among young adults (15-34) in the UK (4.2%) and in Spain (3.3%); amphetamines figures appear to be lower, with the highest percentage of use in Estonia (2.5%), Germany (1.8%), and again UK (1.5%) and Spain (1.2%) (European Monitoring Centre for Drugs and Drug Addiction, 2015). Although use trends are increasing, data regarding the hazards of stimulants are limited. Cocaine appears to have played a determinant role in 1% to 15% of drug-related deaths in countries that were able to differentiate between drug types determining fatalities (European Monitoring Centre for Drugs and Drug Addiction, 2005). According to a study revising cocaine and crack-cocaine deaths in the UK from January 1990 to December 2004, these substances were involved in a total of 1022 deaths, with a peak of 185 fatalities in 2004. Alcohol, either alone or in combination with other substances, was found in 21% of the cases. Cocaethylene, the ethyl ester of benzoylecgonine, is formed in vivo by liver esterases when cocaine and ethanol coexist in the blood (Dean et al., 2001). Both ethanol and cocaethylene reduce mean cocaine clearance by 47% and 26%, respectively (Parker et al., 1996). Cocaine effects are therefore prolonged, and this may facilitate its role in poly-drug combination deaths. Cocaine consumption is also peculiarly high among clubbers: a recent British research found that young people (age 16–29) who visit nightclubs are more than twice as likely to use cocaine as non-club goers (e.g. last month use in 2005/6, 4.2% in club-goers vs. 1.6% in non-club goers) (Roe & Man, 2006). Amphetamines, on the other hand, belong to the chemical class of phenethylamines; they tend to be stimulants and/or hallucinogens and have some entactogenic properties, and in higher doses, they may induce euphoria, stronger feelings of self-esteem, but can also increase blood pressure, raise body temperature (hyperthermia), increase heart rate, and lead to acute brain damage (starting with memory loss) or even death due to stroke or cardiac arrest (Parrott & Lasky, 1998). MDMA has a strong connection with dance music culture, as it became the most popular drug in the mid-1980s in acid house parties and raves. Light shows, intense colours and high-pitch music

are in fact better appreciated due to the increased sensitivity and the pupil dilation caused by MDMA: Ibiza and its renowned discos represent therefore the ideal setting for ecstasy experimenting. According to Bellis et al., while visiting Ibiza, 7.2% of British tourists try MDMA for the first time, with similar percentages amongst Spanish (8.6%) but not Germans (1.8%) or those visiting Majorca (0.8, 1.5 and 1.2%, respectively) (Bellis et al., 2009). In the meantime, most individuals visiting Ibiza were already illicit drugs users in their home country, with nearly the totality of the subjects continuing to consume psychoactive substances in Ibiza. The “holiday” use of most drugs in the island appears to differ from the “home” pattern of consumption for the binge behaviour, with many individuals using drugs 5 or more nights per week (Bellis et al., 2003). Data from the UK np-SAD database (National Programme on Substance Abuse Deaths) covering the years 1997-2007 reported 832 amphetamine/metamphetamine-related fatalities and 605 MDMA-related fatalities. In comparison with amphetamine/metamphetamine victims, the MDMA ones were more likely to be younger, less likely to be known as drug users and to have a suicidal intent (Schifano et al., 2010): these data match with our results as well, as MDMA was never identified in suicide victims but it was prevalent among young victims of accidental drug-caused fatalities. Although the use of NPS is rapidly increasing in Europe, with report of relevant psychopathological consequences and fatalities, the use of alcohol, cocaine and “first generation” psychedelics still represent the main substances implicated in both direct and indirect deaths. The significant growth of drug-involving fatalities in Ibiza in the last 5 years is an issue that must be taken into account and should be better investigated. Indeed, if this trend is not determined by the direct use of the novel and highly toxic drugs, other theories should be proposed: 1) is there a wider “base” of substance misusers, with the subsequent exposition of more subjects which may be at higher risk for predisposing factors? (Duysen et al., 2008); 2) may the combination of different lifestyles and behaviours, such as polyabuse patterns, binge drinking, drunkorexia, intense physical activities during rave parties, be implicated? (Lupi et al., 2015; Martinotti et al., 2009); 3) are there chances that the research and exploration of the limits proposed online by psychonauts may be

becoming a trend in real life as well? All the above-mentioned considerations should be investigated in further studies together with a careful monitoring of critic “hotspots” of substance misuse, in order to design better and targeted prevention strategies.

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TABLES

Table 1. Drug-related and drug-caused fatalities 2015

Date of death	Sex	Age	Nationality	Place of death	Previous psychiatric or substance abuse history	Ascertained cause of death	Detected substances
02/06	M	26	UK	H	-	Polytrauma	Alcohol/MDMA
08/06	M	31	UK	H	Substance abuse	Shock; gastric haemorrhage	MDMA/cocaine/ alcohol/codeine
12/06	F	24	GER	H	Substance abuse	Acute resp failure; SNC depression	Cocaine/ methadone
15/06	M	21	UK	H	-	Asphyxia	-

19/06	M	36	SPA	Hou	-	Pulm acute oedema	Alcohol/cocaine /morphine/mCP P/Prescription drugs (pregabalin, alprazolam, clonazepam, levomepromazine, mirtazapine, trazodone)
19/06	M	40	SPA	Fr Hou	-	Pulm haemorrhage	Alcohol/morphine/prescription drugs (pregabalin, alprazolam, clonazepam, levomepromazine, mirtazapine)
23/06	M	33	SPA	Hou	-	Acute resp failure	Alcohol/cocaine
06/07	M	41	Other	H	-	Acute resp failure	-
21/07	M	23	UK	H	-	Multi-organ failure	Alcohol/MDMA/cocaine
28/07	M	55	SPA	Hou	Bipolar/alcohol and cocaine	Pulm oedema	Cocaine/Phenyt oin
23/09	F	18	UK	Hosp	Depression	Multi-organ failure	MDMA
29/09	F	18	UK	H	-	Still unknown	- (broken plastic bag with white powder found in the stomach)

Legend. H=hotel; Hou= house; FrHou = Friends' house; Hosp= hospital

Table 2. Traffic-related fatalities 2015

Date of death	Sex	Age	Nationality	Driver/victim	Detected substances (in driver)
23/02	M	38	Belgian	D	Alcohol/cocaine
14/04	F	81	SPA	V	Alcohol/THC
04/05	M	37	Moroccan	V	Alcohol/THC/MDMA
20/05	M	48	Filipino	V	Cocaine/THC
28/07	M	27	SPA	D	Alcohol
31/08	M	23	SPA	D	Alcohol
22/09	M	51	SPA	D	-

Table 3. Suicides 2015

Date of death	Sex	Age	Nationality	Previous psychiatric or substance abuse history	Ascertained cause of death	Detected substances
10/01	F	46	FRA	Major Depressive Disorder	Multi-trauma (precipitation)	Cocaine/Prescription drug (antidepressant)
12/01	M	65	SPA	Insomnia	Acute trauma; acute resp insuff (gunshot wound)	-
23/02	M	29	SPA	Substance abuse	Asphyxia (hanging)	-
31/03	M	32	SPA	-	Asphyxia (hanging)	-
06/05	M	51	SPA	-	Anoxia (hanging)	-

16/05	M	34	SPA	Major Depressive Disorder	Anoxia (incomplete hanging)	-
10/06	F	28	UK	Personality Disorder/substance abuse	Anoxia (incomplete hanging)	Cocaine/alcohol
13/07	F	51	SPA	Previous suicide attempt	Multi-trauma (precipitation)	-
13/07	M	48	UK	-	Neurogenic shock (stabbing)	-