Complications Related to Sexualized Drug Use: What Can We Learn From Literature?

Hélène Donnadieu-Rigole1,2, Hélène Peyrière2,3, Amine Benyamina4,5 and Laurent Karila4,5,6*

1 Addictions Department, Saint Eloi Hospital, University Hospital of Montpellier, Montpellier, France, 2 INSERM U 1058, Pathogenesis and Control of Chronic Infections (PCCI), Montpellier, France, 3 Addictovigilance Center, Department of Medical Pharmacology and Toxicology, University Hospital of Montpellier, Montpellier, France, 4 Centre d’Enseignement, de Recherche et de Traitement des Addictions, Hôpital Universitaire Paul-Brousse (APHP), Villejuif, France, 5 Paris-Saclay University, Saint-Aubin, France, 6 Unité de Recherche PSYCOMADD, Villejuif, France

Chemsex is described as the use of specific psychoactive substances (PS) during sexual activity to sustain, enhance, disinhibit or facilitate the sexual experience. It preferentially concerns men who have sex with men (MSM). They use new synthetic substances like cathinones, methamphetamines, gamma-butyrolactone/gamma-hydroxybutyrate (GBL/GHB), ketamine, and cocaine. The prevalence of chemsex varies from 3 to 31% during lifetime. The Internet has participated significantly in the evolution of sexual behaviors, both in terms of sexual dating and the availability of new synthetic substances. The advent of geolocation applications contributed to the development of chemsex. The literature describes many complications linked to these sexual practices; the main clinical effects related to cathinones consumption were psychiatric symptoms; agitation, hallucinations, anxiety, suicidal ideation, paranoia, and confusion. Regular GBL/GHB consumption alter cognitive functions, particularly memory and emotion management. Use of these drugs in party and play is dramatically associated with high-risk sexual behaviors. The prevalence of hepatitis B, hepatitis C syphilis, and HIV is higher in men who use methamphetamine and Viagra and/or who declared they practiced slamming, chemsex, and fisting. Other sexually transmitted infections (STIs) such as gonorrhea have increased with methamphetamine and GHB/GBL use. Actually, the care of individuals who practice Chemsex in a problematic way is currently not codified, but the use of integrative and specific interventions is necessary.

Keywords: psychoactive substances, sexual behaviors, cathinones, sexualized drug use, GBL/GHB

INTRODUCTION

Drug use in a sexual context has been described since antiquity in order to improve sexual performance or to promote desinhibition. In this review we specifically studied the recent phenomenon of “chemsex” secondary to geolocation applications and new designer substances, which has increased exponentially since the 2000s. Numerous substances are linked to sex

Abbreviations: PS, psychoactive substances; BBV, bloodborne viruses; STI, sexually transmitted infections; MSM, men who have sex with men; EDDs, erectile disorder drugs.
use and they are associated with different populations and sexual behaviors. Alcohol, cannabis and MDMA (methylene-dioxymethamphetamine) are more commonly used in heterosexual practices (Law et al., 2019), whereas men who have sex with men (MSM) use cathinones, methamphetamine, gamma-butyrolactone/gamma-hydroxybutyrate (GBL/GHB), ketamine, and cocaine. This behavior is referred to “chemsex” (formerly “sexualized drug use”). Chemsex is described as the use of specific psychoactive substances (PS) during sexual activity to sustain, enhance, disinhibit, or facilitate the sexual experience. (Giorgetti et al., 2017). The Internet has participated significantly in the evolution of sexual behaviors, both in terms of sexual dating and the availability of new synthetic substances. Chemsex is associated with a high risk of contraction of sexually transmitted infection (STI) and bloodborne viruses (BBV). The care of individuals who practice Chemsex in a problematic way is currently not codified. The objective of this review was to describe complications related to drug use in a sexual context in order to adapt specific care.

METHODS

A review of the literature was conducted using PubMed. The search was carried out per theme using the keywords reported in Table 1.

These keywords were used alone or in association with the keyword “chemsex.” The Table 1 shows the number of articles identified for each keyword and in association from 2000 to 2020. This technique has allowed to find many articles with keyword alone and/or association with the main keyword “chemsex.” We have selected those that seemed more relevant for this review about complications related to drug use (Figure 1). Original animal articles have been excluded.

PREVALENCE

Currently, the prevalence of chemsex is difficult to estimate because its definition varies between countries (Schmidt et al., 2016). It varies from 3 to 31% during lifetime and from 0.4 to 16.3% the last month. The frequency of chemsex depending on the city of residence and countries studied, and the taking into account or not of HIV-positive individuals (Elliot et al., 2017), the use of dating applications and the type of PS used (Maxwell et al., 2019).

Slamming is the term used for intravenous injection of these PS during party and play. In Australia, the prevalence of slamming is 10% in MSM, and in England it was found to be 16% in an MSM population diagnosed with Shigella flexneri 3a infection (Gilbart et al., 2015). Slamming is more common in MSM and women who have sex with women (WSW) than in libertine heterosexuals practicing chemsex (Heinsbroek et al., 2018). These differences in prevalence show how interesting it would be to define the practice of chemsex in an international way: target population, drugs used, and exclusion criteria.

SEX MEETING APPLICATIONS

The practice of combining sex and PS has increased steadily with the development of mobile applications. The advent of geolocation applications in 1990 transformed the way gay and bisexual men meet (Grov et al., 2014) and contributed to the development of chemsex. These new applications allow to meet one or more partners very quickly in their surroundings and to express their sexual desires, and their preferences in the practice of chemsex. Sex meeting applications made it possible for “clubbers” and “sexers” to meet. These 2 populations did not have the same sexual practices. “Sexers” had harder practices and used drugs, which have since become widespread amongst MSM.

At least 40% of MSM and 68% of the youngest individuals (Garofalo et al., 2007) find their partners using the Internet. Finding a sex partner on Internet or using a mobile application increases condomless anal intercourse and the risk of HIV transmission (Lewnard and Berrang-Ford, 2014; Whitfield et al., 2017). Sociologists are worried about the disappearance of non-virtual meeting places associated with the development of phone applications and describe the increase of solitude felt by homosexuals (Renninger, 2018).

DESIGNER SUBSTANCES AND ERECTILE DISORDER DRUGS (EDDS)

New designer substances appeared in the early 2000s and participated in the development of chemsex. New synthetic substances are detailed in the Figure 2 and in the Table 2. The main complications are described in Table 3. Most of these studies come from emergency or intensive care.

Synthetic Cathinones

The most used PS are synthetic cathinones, the leader of which being mephedrone or 4 MMC (4-methylmethcathinone). Their development was inspired by the Khat plant (Catha edulis) that is considered as a natural amphetamine and is used in certain countries of East Africa and the Arabian Peninsula (Kalix, 1990). These new designer substances are sold as bath salts “not for human consumption” to circumvent

TABLE 1 | Keywords (from 2000 to 2020).

| Themes       | Keywords          | Alone/Association |
|--------------|-------------------|-------------------|
| Sexual behavior | Chemsex | 228               |
|              | Slamming         | 52/9              |
| Drugs        | Cathinones       | 766/17            |
|              | Mephedrone       | 830/77            |
|              | Methamphetamine | 335/123           |
|              | GHB              | 1704/34           |
|              | GBL              | 456/23            |
|              | GBL/GHB          | 10/3              |
|              | Ketamine         | 13 711/76         |
|              | Erectile designer drugs (Sildenafil, Tadalafil, and Vardenafil) | 2859/14 |
| Applications | Sex meeting application | 122/22 |
the legislation (Coppola and Mondola, 2012). They belong to the phenylethylamine family (Petit et al., 2013) and are psychostimulants with an amphetamine- or cocaine-like effect. They generate agitation, euphoria, and empathy in users and increase libido and sexual performance.

These PS have a strong addictogenic effect with dependence levels of 30% according to DSM-IV criteria (Dargan et al., 2011; Winstock et al., 2011). The main acute complications are cardiac, psychiatric, and neurological, and they can be fatal (Busardo et al., 2015; Ezaki et al., 2016; Sande, 2016; Kronstrand et al., 2018; Riley et al., 2019; Table 3).

Blood levels in cases of lethal intoxication are higher than in cases of non-lethal poisoning, and lethal situations arise from the combining of several drugs (Papaseit et al., 2017). These substances have been classified as narcotics in Europe since 2010 (Forsyth, 2012) and it is currently illegal to purchase or possess them, but they are usually obtained on the Internet or directly during party and play. Cathinones take the form of a white powder or small crystals. They are taken orally, by snorting, intrarectally (boobump), or by injection (slamming).

In the study of Spiller et al. (2011) the main clinical effects (>10%) related to cathinones consumption were agitation (82%), combative violent behavior (57%), tachycardia (56%), hallucinations (40%), paranoia (36%), confusion (34%), myoclonus (19%), hypertension (17%), chest pain (17%), and mydriasis (13%).
TABLE 2 | New designer drugs and their expected effects.

| Drugs name | Common names | Expected effects | Way of administration |
|------------|--------------|------------------|-----------------------|
| Cathinones | MDPV         | Psychostimulants | Orally                |
|            | 4-MMC        | amphetamine-like | Sniff                 |
|            | Mephedrone   | euphoria         | Intraurally           |
|            | 4-MEC        | increase libido  | Sniff                 |
| Methamphetamine | Meth | Powerful psychostimulant | Orally               |
|            | Crystal Ice  | euphoria         | Sniff                 |
| GBL/GHB    | "G"          | Relaxation       | Sniff                 |
| Ketamine   | "Ke"         | Psychostimulant  | Sniff                 |

In another series, main complications of cathinones related to chemsex were psychotic symptoms, agitation, anxiety, suicidal ideation, or suicide attempt (Batisse et al., 2014). More recently, severe psychiatric symptoms have been observed with ephylone, a recent available synthetic cathinones, in a context of chemsex (Serre et al., 2019).

Excited delirium has been reported with the use of synthetic cathinones, with a challenging combination of paranoia, confusion, severe agitation, and violent behavior (Diestelmann et al., 2018; Schmoll et al., 2018). The presentation of these patients has been frequently complicated by evidence of skeletal muscle damage, dehydration, renal dysfunction, and hyperthermia that may lead to multiorgan failure and death. The precise pathophysiology underlying the syndrome of excited delirium is incompletely understood. However, the role of the central dopamine dysregulation, inducing a thermoregulation dysfunction has been suggested (Penders et al., 2012).

Cathinones are often combined with other illicit PS such as methamphetamine (Maxwell et al., 2019), GBL/GHB (Bourne et al., 2015; Edmundson et al., 2018), ketamine, and cocaine (Melendez-Torres et al., 2018b).

**Methamphetamine**

Methamphetamine (crystal meth), like cocaine and amphetamines, inhibits the reuptake of monoamine transporters and stimulate the release of dopamine, noradrenaline, adrenaline, and serotonin (Liechti, 2015). Crystal is characterized by its stronger psychostimulant effects and its immense addictogenic potential. Use of this dangerous substance is mainly described in the United States and the United Kingdom (Degenhardt et al., 2010) with prevalence ranging from 27% (lifetime use) to 7% (recent use) (Benotsch et al., 2012). Methamphetamine can be swallowed, smoked injected or intrarectally administrated. Methamphetamine has been linked to a lot of cardiac, psychiatric, neuropsychological and dental effects (Table 3).

TABLE 3 | Drugs and their main complications (without STI and BBV).

| Drugs          | Main risks                                                                 | Treatment                          | Studies                        | Number of subjects |
|----------------|---------------------------------------------------------------------------|------------------------------------|--------------------------------|--------------------|
| Cathinones     | Psychiatric: panic attack, feeling of persecution, depression, confusion, | Psychiatric hospitalization         | Batisse et al., 2014           | 21 subjects        |
|                | Hallucinations, suicide attempt or suicidal ideation, severe agitation,   | Symptomatic treatment              | Spiller et al., 2011           | 236 subjects       |
|                | or violence                                                                |                                    | Sande, 2016                    | 249 subjects       |
|                | Cardiac: hypertension, tachycardia, and chest pain                         | Symptomatic treatment              | Schmoll et al., 2018           | 96 subjects        |
|                | Cardiac ischemia                                                           |                                    | Diestelmann et al., 2018       | 50 subjects        |
|                | Dependence                                                                |                                    |                                |                    |
|                | Sympathomimetic syndrome and rhabdomyolysis                                | Intensive care                      | Ezaki et al., 2016             | 61 autopsy cases   |
| Methamphetamine| Cardiac: methamphetamine-associated caridiomopathy, heart rhythm         | Blockage of the renin–angiotensin   | O’Connor et al., 2015          | 102 subjects       |
|                | disturbance, acute coronary syndromes, pulmonary arterial hypertension,   | system                             | Froberg et al., 2015           | 23 subjects        |
|                | and hypertension                                                           |                                    | Umebach et al., 2016           | 8 subjects         |
|                | Psychiatric: depression, confusion, acute psychosis and psychiatric        | Antipsychotic medications          | Neeki et al., 2018             | 449 subjects       |
|                | symptoms, and anxiety disorder                                            |                                    |                                |                    |
|                | Neuropsychological effects: alteration of executive function, episodic     |                                    |                                |                    |
|                | memory, psychomotor functions, and complex information processing speed,   |                                    |                                |                    |
|                | and dependence                                                             | N-acetyl-cysteine                   | McKetin et al., 2013           | 278 subjects       |
|                | Dental and periodontal disease                                            |                                    |                                |                    |
| GBL/GHB        | Coma, presentation to a emergency department, and neurological              | Intensive care                      | Scott et al., 2007             | Meta-analysis (18  |
|                | complications                                                              |                                    |                                | studies)           |
|                | Dependence                                                                | Backofen                           |                                | 180 subjects       |

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Gamma-hydroxybutyrate/Gamma-butyrolactone

Gamma-hydroxybutyrate is a central nervous system depressant that has a double stimulant and sedative effect (Raposo Pereira et al., 2019b). GBL, which is cheaper, is taken orally in liquid form and transformed into GHB (Busardo et al., 2018).

Gamma-butyrolactone/gamma-hydroxybutyrate is most often mixed with another drink. The sought-after effects are relaxation, disinhibition, increased desire and sensuality, and easier penetration. The main acute risk is overdose with significant sleepiness and hypothermia that can lead to coma and death.

An increase in the number of deaths in London related to GHB use was observed between 2011 and 2015 with 61 reported deaths, while a 119% increase in deaths between 2014 and 2015 was observed versus 25% for cocaine (Hockenhull et al., 2017). Regular GBL/GHB consumption and repeated comas alter cognitive functions, particularly memory (Raposo Pereira et al., 2018) and emotion management (Raposo Pereira et al., 2019a; Table 3). GBL/GHB dependence can be established using physical and psychological criteria with consumption outside of sexual intercourse.

Ketamine, Cocaine, and Speed

Ketamine, an anesthetic used in human or veterinary medicine, is a phencyclidine (PCP) derivative that blocks non-competitively the glutamate N-methyl-D-aspartate (NMDA) receptor (Corazza et al., 2013). It is used as a psychoactive substance in sexual sessions for its euphoric effects. It can cause hallucinations at higher doses. Urologic complications are described with ketamine. Cases of bladder dysfunction have been reported in the literature, mainly ulcerative cystitis. Cases of hydronephrosis have also been reported. Symptoms described by users are frequency and urgency of urination, dysuria, urge incontinence, and occasionally painful hematuria (Morgan and Curran, 2012).

Cocaine and speed are still used in a sexual context but less frequently since the advent of the new designer drugs (Busardo et al., 2019).

Erectile Dysfunction Agents

Non-psychoactive substances such as erectile dysfunction agents (sildenafil, tadalafil, and vardenafil) are used to facilitate or enhance sexual performances. These drugs are diverted from their medical use to counterbalance the negative effects of psychoactive drugs and to prolong the duration of sexual intercourse (Giorgetti et al., 2017). Combining all these drugs is associated with high cardiac toxicity (Bracchi et al., 2015).

STI AND BBV

In addition to the complications already described, the major risks are related to the sexual behaviors of the users, and the injection of drugs that increases the risk of spreading BBV and STI.

Use of illicit and licit drugs in party and play is dramatically associated with high-risk sexual behaviors. Use of methamphetamine is strongly associated with condomless anal intercourse (Fisher et al., 2011), multiple sex partners (Melendez-Torres et al., 2018a), sex marathons, and sex with HIV-positive MSM (Benotsch et al., 2012; Bui et al., 2018). The prevalence of hepatitis B, syphilis (Rana et al., 2019), and HIV is higher in men who use methamphetamine and Viagra which is associated with serodiscordant unprotected sexual intercourse (Spindler et al., 2007). Hepatitis C seroprevalence is higher in HIV-positive MSM who declared they practiced slamming, chemsex, and fisting (Vaux et al., 2019). Other STIs such as gonorrhea have increased with methamphetamine and GHB/GBL use (Kohli et al., 2019) and there has been a worldwide increase in all STIs among MSM that is linked to chemsex and Internet, which facilitates high-risk sexual behaviors (Soriano and Romero, 2018).

PREVENTION AND INTERVENTION

Phone applications would be ideal to promote messages in terms of sexual health, STI and prevention of addictions. Some applications have started to emit HIV prevention messages (Chan et al., 2016). Medina et al. (2019) explained that future HIV prevention approach should pass through dating applications. Moreover another study showed that interventions that facilitate condom negotiation could exist in future applications (Tang et al., 2016).

Providing care to individuals suffering from the problematic practice of chemsex is complex; there are no explicit recommendations on specific drugs that could be used for withdrawal or regulation and the care must simultaneously take into account pharmacological, addictological, and psychological and sexual aspects. The use of integrative and specific interventions is necessary. Different types of therapy are tested as cognitive behavior therapy, contingency management, and gay-specific cognitive behavior therapy (GCBT). These therapies are used with or without medications for withdrawal or maintaining abstinence. GCBT integrated elements from standard cognitive behavior therapy with cultural and social elements of chemsex users. Reback has proved the efficiency of this therapy in methampetamines users in the United States (Reback and Shoptaw, 2014). CBT and motivation interview improve adherence to HIV medication in gay and bisexual men (Parson et al., 2018).

For GBL/GHB withdrawal, the most used drugs are benzodiazepines, neuroleptics, and sometimes barbiturates (Cappetta and Murnion, 2019). Serious complications may occur with these, including hallucinations, delusions, and epileptic fits (Liao et al., 2018; Neu, 2019). Baclofen has been tested for the long-term maintenance of GBL/GHB abstinence, but randomized studies are required before specific recommendations can be issued (Beurmanjer et al., 2018).

Drugs such as atypical antidepressants (mirtazapine) or naltrexone have been tested to reduce sexual risk-taking and methamphetamine use (Knight et al., 2019).

Fighting against the transmission of infections requires preventive interventions and harm reduction including condom
are confronted with medical, psychiatric, and sexual risks. Some sociology, infectious medicine, addiction, and sexology. Its users

CONCLUSION

such as sexual health centers need to be opened to break down sexual health need to be increased and new community spaces to be developed.

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distribution and needle exchange programs. These practices need to be developed.

Special attention should be paid to MSM with problematic chemsex behavior so they may have access to the best possible post-exposure prophylaxis (PEP) and pre-exposure prophylaxis (PrEP) (Hammoud et al., 2018; Sewell et al., 2019).

Actions focusing on prevention, addiction management and sexual health need to be increased and new community spaces such as sexual health centers need to be opened to break down barriers and help alleviate the shame of chemsex drug users (Giorgetti et al., 2017; Sewell et al., 2018).

Chemsex is a complex issue. The behavior is at the crossroads of sociology, infectious medicine, addiction, and sexology. Its users are confronted with medical, psychiatric, and sexual risks. Some users engage in chemsex seeking sexual disinhibition, others in order to embrace their sexual preferences, and others still for the effects of the drugs.

The phenomenon can be a claim of part of the MSM population that wants to have unbridled sex with protection against HIV. There is still enormous stigma and shame associated with HIV infection and being homosexual (Dubov et al., 2018). With chemsex, caregivers are confronted with a continuum between normal and pathological sexual and drug use behaviors. The care to be provided to chemsex users must be validated by large sample studies. CGBT and LGBT-specific-e-therapy (Lucassen et al., 2018) are interesting ways to facilitate prevention and access to care for problematic chemsex users.

AUTHOR CONTRIBUTIONS

HD-R and HP reviewed the literature and wrote the manuscript. LK and AB revised the manuscript. All authors contributed equally to this manuscript.
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