Indian Journal of Health, Sexuality & Culture
Volume (7), Issue (1), June 2021
ISSN 2581-575X
https://www.iisb.org./

Review Article

Sexual function and its relationship with cannabis, tobacco, benzodiazepine and amphetamine-type stimulants use

Ajay Kumar[1], Sangha Mitra Godi[2], Arti Yadav[3]

[1]Assistant Professor, Department of Psychiatry, All India Institute of Medical Sciences, Raipur, Chhattisgarh, India
[2]Senior Resident, Department of Psychiatry, All India Institute of Medical Sciences, Raipur, Chhattisgarh, India
[3]Senior Resident, Department of Psychiatry, Institute of Mental Health and Hospital, Agra, Uttar Pradesh, India

Date of Submission :
15 May 2021
Date of Acceptance :
19 May 2021

Keywords: Sexual function, Cannabis, Cocaine, Club-drugs, Amphetamine-type stimulants

Abstract

Substance use interacts with biopsychosocial factors in an intricate manner affecting the sexual function of an individual. Therefore, we attempted to discuss the impact of substance use on sexual function, focusing on cannabis, tobacco, Benzodiazepines (BZDs), cocaine, amphetamine, and amphetamine-type stimulant (ATSs), and club drug.

Introduction

Our understanding has evolved about sexual health. In 1975, World Health Organisation (WHO) narrated sexual health as "the integration of the somatic, intellectual, emotional and social aspects of sexual being in ways that are positively enriching and that enhance personality, communication and love"(WHO, 1975). Subsequently, in 2006, WHO proposed a more inclusive definition, i.e., "Sexual health is a state of physical, emotional, mental and social well-being related to sexuality; it is not merely the absence of disease, dysfunction or infirmity" (WHO, 2006). The significance of sexual health is considered to be imperative to general health and has been recognized as an "important public health concern" as early as two decades ago (Laumann et al., 1999).

Sexual function is a tenant of sexual health, linked to the performance of a sexual act by an individual. A normal sexual function results from normal sexual desire, arousal, orgasm, and ejaculation and is greatly influenced by several physicals, psychological, interpersonal, cultural, social, and gender factors (Briken et al., 2020; Hatzimouratidis and Hatzichristou, 2007; Lewis et al., 2004). Thus, any deviation in any of these domains can result in sexual dysfunction. In addition, sexual dysfunction leads to significant psychosocial stress, which adversely affects the quality of life of an individual (Wagner et al., 2000).

Substance use disorder (SUD), licit or illicit, is suggested to interact with various biopsychosocial factors in a complex way and affect the sexual function of an individual. SUD may worsen pre-existing sexual dysfunction, precipitated or maintained it

Corresponding author: Ajay Kumar
Email: ajaypgimer2016@gmail.com
How to cite article: Kumar, A., Godi, S., Yadav, A. (2021). Sexual function and its relationship with cannabis, tobacco, benzodiazepine and amphetamine-type stimulants use. Indian Journal of Health, Sexuality & Culture, 7(1), 26-34.
DOI: 10.5281/zenodo.5151810

(Del Río et al., 2015; Ghadigaonkar and Murthy, 2019; Johnson et al., 2004). The secondary sexual dysfunction due to chronic substance use often appears from previously normal sexual functioning. Substances most involved are alcohol, tobacco, cannabis, opioids, followed by amphetamines, cocaine, inhalants, sedatives, etc. However, this review focussed on sexual function concerning substance use other than alcohol and opioids, i.e., cannabis, tobacco, BZDs, ATS and club drugs, etc.

Cannabis use and sexual function

Just like many other countries, in India, the entheogenic use of cannabis has been well accepted. In Atharva Veda, Cannabis sativa is outline das one of the five sacred plants that reduce anxiety and fear (Abel, 1982). It isthe most consumed illicit substance, with 2.5% of the global population (approximately 147 million) using cannabis (Cohen et al., 2019). Around 13.1 million people reported as cannabis dependent in 2010 (Degenhardt et al., 2017).

In India, according to the recent national survey on the magnitude of substance use, 2.8% of the population of 10-75 years of age (3.1 crore individuals) uses cannabis in any form (Ambekar A et al, 2019). Following Alcohol, Cannabis is the next commonly used substance in India, used illegally as charas, hashish, etc., and legally available as bhang in some states.

Cannabis has a reputation as an aphrodisiac historically, the numbers of research also verifying its positive effect on sexual functions. Marijuana smoking shown to have increased sexual desire, increase sexual frequency, sexual satisfaction, and improves orgasm (Dawley et al., 1979; Koff, 1974; Sun and Eisenberg, 2017). The aphrodisiac effect of cannabis possibly explained by its property of loosening inhibition, enhance sensate focus, increased sense of enjoyment (hedonism), slow perception of time, which perceived as prolonged pleasure, and its reputation as a sexual enhancer (placebo effect) (Ashton, 2001; Halikas et al., 1982; Jarvik ME, 1976). At the same time, long-term use of cannabis is linked to a range of sexual problems too. A study from Australia shown a significant association between the frequency of cannabis use and the numbers of sexual partners in both genders (Smith et al., 2010). A recent meta-analysis also reported that cannabis users had a two-fold higher risk of developing erectile dysfunction compared to controls (Pizzol et al., 2019). The chronic use of cannabis also affects semen quality; a 30% reduction is shown in sperm concentration if cannabis is used more than once per week (Gundersen et al., 2015).

The growing evidence suggests that tetrahydrocannabinol (THC) interacts with the overall endocannabinoid system (ECS) throughout the body.The central nervous system mainly has CB1 receptors, while the peripheral system primarily has CB2 receptors and some CB1 receptors. Centrally, CB1 receptors are concentrated in the hippocampus, hypothalamus, cerebral cortex, amygdala, and cerebellum. These receptors are also present in vital organs for sexual hormones and fertility in humans, i.e., the adrenal gland and ovaries (Lynn et al., 2020).

Tobacco use and sexual function

WHO reported that the global trend of tobacco use reflects one-third of the world population of 15 years and above were users of some form of tobacco (WHO, 2019). In addition, 28.6% (266.8 million)of 15 years and above age group uses tobacco globally (Global Adult Tobacco Survey, GATS 2, 2018). Tobacco use, smoke or smokeless, known to have a range of deleterious effects

on sexual health cause harm to sexual health (Harte and Meston, 2008; Olsen J, Rachootin P, Schiødt AV, 1983; Sansone et al., 2018; Sharma et al., 2016). More than 4700 chemicals have been identified in cigarette smoke, including cadmium, arsenic, and lead implicated in male fertility (Borgerding and Klus, 2005; Jurasovi et al., 2004). Chronic smoking and compromised lungs result in hypoxia, impairing spermatogenesis (Gabrielsen and Tanrikut, 2016). Furthermore, several micro-toxins affect the mitochondrial function and chromatin structure of human sperm, reducing its fertilization capacity (Sharma et al., 2016). Smoking reduces sperm count and motility, causing infertility (Sansone et al., 2018; Sharma et al., 2016). Smoking is one of the independent risk factors for erectile dysfunction due to its strong vasoconstrictor effect (Chew et al., 2009; Harte, 2014). Cigarette smoke and its components reduce neuronal nitric-oxide synthase activity in penile tissue. Nicotine also reduces other vasoactive substances such as endothelium-derived relaxing factors, perhaps results in erectile dysfunction (Demady et al., 2003).

Smoking prevalent among women too, about 30% of women of reproductive age smoke (Penzias et al., 2018). Studies on the effects of smoking on female sexual function (FSD) arevery few. An epidemiological study recognized the implication of smoking on FSD as early as 1983 (Olsen, 1983). The subsequent report suggests that just like male sexual dysfunction, smoking is an independent risk factor for FSD (Choi et al., 2015). Moreover, the severity of FSD is correlated with the amount of smoking, i.e., pack-year (Choi et al., 2015). Contrary to this, another study found that smoking status associated with increased sexual desire, while nicotine dependence correlated with lower sexual desire and increased sexual problems (Costa and Peres, 2015).

Benzodiazepine uses and sexual function

BZDs are the most prescribed psychotropic agents by physicians and psychiatrists in clinical practice as an add-on medication. The effect of benzodiazepine on sexual function are scarcely documented. Only limited studies, including retrospective / prospective sand a few case reports, found benzodiazepines were linked to sexual dysfunction (Hosseinzadeh Zoroufchi et al., 2021). Clonazepam has the maximum propensity to cause sexual dysfunction compared to alprazolam, diazepam, and lorazepam in male veterans with post-traumatic stress disorder (PTSD). The prevalence of sexual dysfunction, primarily ED, has shown to have a prevalence as high as 42.9% with clonazepam (Fossey and Hamner, 1994). The alprazolam was also found to have dose-dependent sexual problems, i.e., decreased libido, erectile dysfunction (Kaufman et al., 2018; Lydiard RB et al., 1987). There are anecdotal reports of sexual disinhibition and increased promiscuous behavior with clonazepam and diazepam withdrawal (Fava and Borofsky, 1991; Nutt et al., 1986).

Cocaine use and sexual function

Cocaine, a psychostimulantand a potent dopamine agonist, can be used as snort, smoke, or injection (Nestler, 2005). The global prevalence of cocaine dependence is estimated to be around 52.5 per 100 000 (Peacock et al., 2018). In India, a small proportion of the population (male-0.18%, female-0.01%) currently use cocaine (Ambekar A et al., 2019).

The short-term use of cocaine can enhance sexual function, but chronic cocaine use may result in sexual dysfunction, including decreased sexual desire and erectile dysfunction (Warner, 1993; Weatherby et al.,

1992). The prevalence of ED was found as high as 66% in regular cocaine users for 1 year or longer (Cocores et al., 1988). Moreover, increased sex trading and drug paddling are fairly associated with crack use (Weatherby et al., 1992). The intracavernosal injection of cocaine is known to cause priapism (Jansen and Theron, 2006).

The effect of cocaine on FSD is far less explored; contrary to the widespread assumption that cocaine acts as an aphrodisiac, cocaine use was found to reduced sexual desire and increasedsexual dysfunction (Henderson et al., 1995).

Use of amphetamine-type stimulant (ATS), 'designer drugs' and sexual function

Right after discovering amphetamine in 1920, a series of amphetamine-based stimulants was synthesized, and soon their abuse potential was recognized. These amphetamine-based stimulants later popularised as amphetamine-type stimulants (ATS) (Rasmussen, 2015). The use of ATS is perhaps highlighted due to its association with risky sexual behavior and sexually transmitted diseases (STDs) (Jia et al., 2013). In India, a modest proportion of 0.18% (i.e., about 19.4 lakh individuals) is estimated to use ATS in harmful or dependent patterns (Ambekar A et al., 2019). Range of sexual problems such as decreased sexual desire, increase latency, and ED found associated with amphetamine use (Bang-Ping, 2009; Chou et al., 2015). Amphetamines most likely interfere with the central nervous system and act as neurotoxins, probably impair penile smooth muscle and endothelial function (Chou et al., 2015).

Another ATS, 3,4-Methylene dioxymetha mphetamine (MDMA or Ecstasy), has hallucinogenic property. One-year prevalence of hallucinogen use in India is about 0.12% of the population, i.e., approximately 12.6 lakh individuals (Ambekar et al., 2019). MDMA is associated with high-risk sexual behavior due to sexual dis inhibition and enhanced sexual experience (Bang-Ping, 2009). In one of the studies, the use of MDMA associated with increases sexual desire delayed but an intense orgasm and 40% of ED among male subjects (Zemishlany et al., 2001). Amphetamines, due to their sympathomimetic property, result in vasoconstriction, therefore, causes vascular erectile dysfunction (Abekawa et al., 2001).

Methamphetamine, one of the amphetamine derivatives, popularly known as 'crystal meth', 'ice', 'crank', and 'speed'. Like other designer amphetamines, this drug also produces feelings of energy, euphoria, and a 'high' (Comer et al., 2001). However, it induced central dopamine depletion and cause neurotoxicity (Abekawa et al., 2001).

Methamphetamine, gamma-hydroxybutyrate (GHB), MDMA, ketamine ('Special K'), lysergic acid diethylamide (LSD) and Rohypnol (flunitrazepam) collective popularised as 'club drug' or 'party drug' (NIDA, 2004). Use of these drugs popular among youth in special circuit parties with loud techno-rock music, laser light, and 'night clubs' termed as 'rave party' (Rome, 2001). The growing popularity of rave culture or 'rave party' in India also a matter of concern (Chakraborty et al., 2011). These drugs can decrease sexual inhibition and intern enhances vulnerability for risky sexual practices. A strong link has been found between the sexual choices of bisexual men and gay with the use of club drugs at circuit parties (Colfax et al., 2001).

The 'club drug' especially important due to its connexion with 'chem sex' representing sexual practice where 'club drug' usedduring sex to enhance the sexual experience; it

mainly popular among communities of men who have sex with men (MSM) (Bourne A et al.,2014). The use of 'club drug' prevalent among gay and bisexual men (Isaiah Green and Halkitis, 2006).

Gamma-hydroxybutyrate (GHB) impart increase feelings of relaxation, euphoria, and sexual dis inhibition (Miotto, Jack Darakjian, Janice Basc, 2001). Although, it is known as a 'date rape' drug as it can be mixed with alcohol in liquid form without altering its taste, the increased sexual feeling and amnesia under its intoxication incapacitate the victim of sexual abuse of a perpetrator (Schwartz et al., 2000).

Ketamine, the anaesthetic agent, was abused owing to cause technicolor, vivid visual and auditory hallucinations (Wong and Jenkins, 1974). Chronic use of ketamine is most likely associated with ED (Shang et al., 2017).

It can be concluded that SUD is entwined with several bio psycho social and cultural factors and poses serious implications to sexual functions manifested as a range of sexual dysfunctions. Many of these substances are perceived to have sexual enhancing properties, but most research supports their deleterious impact on sexual function on long-term use.

Summary box: impact of SUD on sexual function

1. Cannabis
- Most widely cultivated and consumed substance worldwide
- A strong image of an aphrodisiac and wider entheogenic acceptability
- Chronic use associated with orgasmic dysfunction in men, ED and poor semen quality.

2. Tobacco
- Smoking; an independent factor for ED
- Smoking; an independent risk factor for FSD

3. BZDs
- Range of sexual problems like ED and decreased libido associated with chronic use of clonazepam and alprazolam.
- Scattered reports of sexual disinhibition and increase libido also present.

4. Cocaine
- Chronic use of cocaine causes sexual dysfunction, including decreased sexual desire and erectile dysfunction.

5. ATS
- The use of ATS is associated with risk-taking sexual behavior and sexually transmitted diseases (STDs).
- MDMA causes delayed orgasm and ED.

6. GHB
- Has a reputation of 'Date rape' drug.

7. Ketamine
- Long-term use of ketamine found to cause ED.

Acknowledgements: None

Declaration of interests: None

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