Review Article

Effect of Variable Substances on Sexual Function: A Narrative Review

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Abstract

Background: Substance use disorders are among the most common psychiatric disorders worldwide, including Iran, and according to the latest studies, 2.8% of people have been affected in Iran. Sexual dysfunction is one of the most serious and most troublesome problems associated with substance use.

Methods: Research has been conducted on reliable and credible Persian and English databases regarding correlation between substance use and sexual dysfunction. By reviewing the Persian and English scientific bases, this article has been written.

Results: The effects of substance abuse on sexual function are different in terms of both the duration of use and the person's gender; for example, opiates such as opium, which are also found in narcotic pain medications, initially prolong the period of excitement and improve sexual activity in some individuals; however, for long term effects, they can reduce sexual desire and make erectile dysfunction. In addition, the use of stimulants and cannabinoids is mainly associated with the improvement and increased sexual desire. However, chronic and long-term use of these substances reduces desire and impairs the function. Similar cases about alcohol use are also evident.

Conclusion: Substance abuse positively correlates with sexual dysfunction with a variety of manifestations, and prevention or treatment of this commonly occurring disorder can lead to improved sexual health.

Keywords: Alcohol, Opiates, Sexual behavior, Sexual health, Substance-related disorders

Introduction

Substance-induced disorders based on the categorization of the Diagnostic Statistical Manual of Mental Disorder Fifth Edition (DSM-5) are divided into two main categories: substance use disorders and substance-induced disorders. Among substance-induced disorders, sexual dysfunction caused by the substance/medication (Substance/ Medication Induced Sexual dysfunction) can be mentioned (1). Although sexual dysfunction can be seen with all substances or drugs, but is clearly distinguishable for alcohol, amphetamines or related substances, cocaine, opioids, sedatives, hypnotics, or anxiolytics (2).

The incidence and prevalence of substance use varies across regions and countries and varies according to different cultures. According to the latest research conducted in Iran in 2011, during the one-year period, the prevalence of substance use disorder has been reported to be 2.8% (3). In a study carried out with a nationally representative sample of 7,841 individuals aged 15-64 years old in Iran, the prevalence of 12-month use disorders for any illicit drug according to DSM-5 criteria was 2.44% (95% CI=2.03-2.85%) and the most common use disorders were opioid use disorders, and opium in particular (4). Findings from national surveys in Australia, Europe, and the United States showed that cannabis is the most commonly used illicit drug, and that tobacco and alcohol are more extensively used than illicit drugs (5).

The statistics regarding sexual dysfunction due to substance have not been fully studied, but the most recent studies have shown that chronic consumption of substances is associated with more problems than their short-term use. The prevalence of sexual dysfunction has been reported in 60 to 70% of heroin users who are more than the consumers of stimulants. Chronic consumption of alcohol and nicotine has also been associated with high rates of erectile dysfunctions (1).

Considering the significant prevalence of substance use disorders in Iran and the importance of sexual health in the family, the current narrative review evaluates and discusses the role and impacts of substance use in sexual function of individuals.

Materials and Methods

The main method of collecting data and information was to refer to the main Persian and English psychiatric references and scientific databases in order to collect data and results regarding correlation between substance use and rates of sexual dysfunction. In the search for resources, the epidemiology of substance use was sought to be addressed in Iran.

Results

The DSM-5 classification of substance-related disorders encompassed 10 classes of drugs. These substance groups include alcohol, caffeine, cannabis, hallucinogens, phencyclidine, inhalants, sedative and hypnotics, opioids, stimulants, tobacco, and other substances. In the new publication of the DSM-5, pathologic gambling disorder has also been ranked for the first time in this category (1).

As mentioned above, sexual dysfunctions have been specifically addressed in relation to certain substances, such as alcohol, amphetamines or related substances, cocaine, opioids, sedatives, hypnotics, or anxiolytics (2). In this review, the role of these substances was evaluated on sexual function, and in addition to these substances, a short review of the sexual dysfunction caused by other substances is provided.

Alcohol

The extent of alcohol use is markedly higher than illicit drug use, although prevalence of dependence to it varies widely across countries, and precise statistics on the prevalence of it in Iran are not available (5). Alcohol is a Central Nervous System (CNS) depressant and acts by increasing the level of gamma amino butyric acid inhibitory neurotransmitter. Alcohol inhibits behavioral control and thus potentiates sexual desire (6).

Short-term use of alcohol can act as an anxiolytic and can play an important role in people whose anxiety leads to reduced sexual function. The study conducted by Eaton *et al* has estimated that 4.3 million Americans regularly use alcohol before engaging in sexual activity. In this study, regular pre-sex drinking's 12-month prevalence was 1.8% (2.6% of men, 1.0% of women) among the full sample of respondents (n=34 653) (7).

Although alcohol may begin to ease the activity by removing the inhibitors of sexual activity, chronic and prolonged alcohol consumption can be a contributing

factor to sexual dysfunction (5); chronic alcohol consumption has an effect on both women's and men's sexual function, which is attributed to its negative effects on cardiovascular and neurological systems. Alcohol also affects people's sexual function through hormonal effects. Alcohol use has been associated with reduction in testosterone levels in men, but increases testosterone levels in women (2,5). In addition, chronic alcohol consumption has negative effect on the structure of the liver and affects liver function and protein production. The reduction of body proteins decreases the sexual function of both sexes; it reduces the ability of the liver to metabolize estrogenic compounds, and especially in men, it can lead to loss of male characteristics and appearance of female characteristics (Testicular atrophy and enlargement of the breasts) (1,2,5).

In a study aimed at comparing sexual dysfunction between women with alcohol dependence syndrome and control group, it has been shown that all areas of sexual function have been affected by alcohol consumption, and factors such as the onset of consumption at lower ages, longer consumption and severe dependence were identified as the most important predictors of sexual dysfunction in users (8).

A cross sectional study conducted by Pendharkar *et al* showed that the most common alcohol-associated sexual dysfunction among alcohol-dependent men was erectile dysfunction, followed by problems in desire and premature ejaculation (9).

A meta-analysis of population-based studies showed that chronic alcohol consumption in men increases the likelihood of erectile dysfunction and high-dose consumption is more likely to be associated with this disorder (10).

Amphetamines and related substances

Amphetamines have been classified in the new DSM-5 classification in the stimulant group. Studies over the years have shown strong positive correlation between amphetamine use and increase in severe psychiatric symptoms such as psychosis. Unfortunately, amphetamine use has been rising in Iran over the past decade and currently, it is one of the serious concerns about mental health in the country as well as other countries in the Persian Gulf region (11).

Amphetamines can cause a variety of sexual function disorders that depend on factors such as the amount and method of consumption. Low level consumption increases enjoyment and delayed orgasms which may be useful to men with premature ejaculation, but a higher level consumption is associated with anorgasmia and reduced sexual desire. Long-term consumption of amphetamines has been accompanied by erectile dysfunction and delayed ejaculation in men and delayed orgasm in women (6).

Methamphetamine, which is a strong form of amphetamine, causes increasing social self-confidence, sexual disinhibition and the sense of increased physical energy. It is a sexual enhancer from the point of view of consumers, but there is no scientific evidence for its direct effect on receptors that can enhance sexuality. Amphetamines can induce a prolonged sexual desire in men with inadequate erections, known as "crystal dick" (6).

Although some users of these substances at first feel stronger and may be sexually active, ultimately prolonged use of these substances may then induce sexual dysfunction over time. Men usually have two stages of prolonged erection without an ejaculation, and then gradually loss of erectile ability (2).

Sometimes, in the treatment of major depression, psychostimulants such as amphetamines, methylphenidate and pemoline are used, which increase the plasma levels of norepinephrine and dopamine and therefore increase libido (2).

Cocaine

Diagnostic criteria for toxicity and dependence on cocaine based on DSM are similar to the amphetamines, and this is due to the similar performance of these two substances. The prevalence of this substance in Iran is unclear, but due to its high cost and lack of accessibility, it is lower in comparison with other psychotropic substances. One of the most common forms of cocaine in the world is Crack, but what is used in Iran as Crack contains no cocaine compound (12).

The effects of cocaine on sexual function are roughly similar to the effects of amphetamines and related substances (5). Initially, cocaine consumption increases sexual function in men, but long-term consumption can reduce desire and erectile ability and cause orgasm dysfunction (6).

Opiates

Opiates and, specifically opium are one of the

most common substances in Iran and are highly used particularly in psychiatric patients. In a study conducted by Habibisaravi *et al*, 67% of patients admitted to psychiatry ward were opium abusers and opium has been the most commonly abused substance (13). The study conducted in Fars province showed that 8.8% of the general population had a recent opium consumption and 17.9% of them have had opium use at least once in their lifetime (14).

The abuse of opiates and opioids nearly always depresses desire, although occasional users may experience sexual enhancement probably due to a change in consciousness (5). Opioids such as heroin cause sexual dysfunctions such as erectile dysfunction and decreased libido (5).

The effects of opioids abuse on sexual function have a dual model. At the onset of use, many patients experience improvement in the sexual function in the form of long ejaculation in men and the decrease of the symptoms of vaginismus in women, but with continued use in both sexes, there is a decrease in sexual desire and impaired ability to experience orgasm (6).

Chronic heroin abuse reduces the functioning of the testicles through the hypothalamus or higher centers and leads to a decrease in free testosterone level in plasma. These hormonal changes will become normal after discontinuation of heroin (6).

The prevalence of sexual dysfunction in methadone users has been reported more than buprenorphine, so sexual problems in patients on methadone maintenance treatment may decrease after changing their treatment to buprenorphine (15).

Ajo *et al* conducted a study on 750 patients with chronic non cancer pain attending an ambulatory pain clinic and receiving long-term oral and/or transdermal opioid treatment. This study showed that sexual dysfunction was common, although in addition to opioid use, there are multiple factors that might be associated with sexual dysfunction in these patients. Equivalent dose of morphine was higher in men than in women, and sexual dysfunction was reported more in men (33%) than women (25%); in this study, the morphine-equivalent dose was associated with severity of sexual dysfunction (16).

One of the most common sexual dysfunctions is premature ejaculation. The commonly prescribed pain medication, tramadol, which is a narcotic analgesic opiate, has been introduced as one of the effective treatments for premature ejaculation (17). However, there is insufficient evidence of the effect of tramadol on reducing sexual desire, erectile dysfunction, hypogonadism, anorgasmia, and high-risk sexual behaviors in patients with tramadol abuse (18).

The probability of being dependent on tramadol is different from the results of the various studies; a study has reported the likelihood of dependency low and another study has reported very high (17,19). Apart from the possibility of dependency on tramadol, its use can be problematic in several ways since there is a possibility of tonic-clonic seizure with tramadol alone, and especially in co-consumption with alcohol (20).

Anxiolytics

This family of drugs is one of the most commonly used substances in the community, especially younger people.

The major anxiolytic family is benzodiazepines (such as diazepam or valium) that have an effect on Gamma Aminobutyric Acid receptors (GABA) and are thought to interfere with memory, cognition, and motion control. Although benzodiazepines are one of the most medications all over the world, few studies (Mainly case reports and retrospective studies) have addressed the sexual side effects of benzodiazepines (21,22). Benzodiazepine drugs decrease the concentration of epinephrine in plasma and thus reduce anxiety. Therefore, these drugs may improve sexual function in people whose sexual activity has been hindered by severe anxiety (2,5). However, sexual dysfunctions including decreased sexual desire, erectile dysfunction, retarded ejaculation and anorgasmia, have been reported with different benzodiazepines (21-23). This finding has not been consistently replicated and in other studies, benzodiazepines haven't shown sexual side effects. For example, one study carried out in Argentina on 190 outpatients aimed to compare efficacy between sublingual and conventional tablets of alprazolam in the treatment of panic disorder; in this study, no statistically significant differences in Arizona Sexual Experiences Scale (ASEX) before and after treatment with alprazolam were found (24).

Buspirone is a serotonin partial agonist and a partial alpha-noradrenergic antagonist that is prescribed as an

anxiolytic. Buspirone may reverse sexual dysfunction caused by SSRIs (Selective Serotonin Reuptake Inhibitors) as an augmentation treatment (21,25).

A medication similar to barbiturates called methaqualone was known at one time as an enhancer of sexual desire, but later studies showed that this reputation is unfounded; as a result, that medication is not currently dispensed in the United States (2,5).

Other substances

Other substances can also have an effect on the sexual function, but this disorder is not coded according to DSM-5 (1). These include hallucinogens, cannabis, cigarettes and even tobacco.

In the case of hallucinogens, the occurrence of hallucination may interfere with the normal sexual function of a person and become problematic. Of course, other effects, such as but not limited to increased sexual function, anxiety, and delirium have also been reported (2).

In the case of cannabis, although its short-term use may increase sexual pleasure, it can interfere with sexual function in the long run (2). Some studies have shown that a low dose of cannabis has positive effects on women and men by prolonging the duration of intercourse, improving the quality of orgasm and increasing sexual satisfaction. The underlying mechanisms of these effects have been identified; for instance, disinhibited behavior, slowing of temporal perception, anti-anxiety effects, and expectancy effects are identified (26). Consumption of cannabis at high doses has been associated with erectile dysfunction, decreased levels of testosterone and sterility. In addition, consumption of cannabis has increased the risk of sexually transmitted diseases due to reduced use of condoms (26).

Nicotine is a potent vasoconstrictor that can reduce the genital blood flow of men and women during sexual activity. Nicotine reduces the vasoactive substances such as endothelium-derived relaxing factor, prostacycline, nitric oxide, and thromboxane in the endothelium of the genital vessels. In addition, nicotine has a negative effect on sex hormones such as testosterone and estrogen in men and women who smoke cigarettes. The negative impact of nicotine on the ability of a man to initiate or maintain an erection has been shown in some studies. The effects of cigarette smoking on erectile function are more visible in older men, but are also observed in men less than 45 years of age. Although the negative effects of smoking on sexual function are known, discontinuation of use even for a short period can improve the sexual function (6).

Herbal sexual enhancers

Herbal remedies and various dietary supplements have been introduced to strengthen sexual libido. Evidence also supports the stimulant activity of the extract of herbs used in traditional medicine (27).

Several natural products are known for the treatment of erectile dysfunction, one of which is Yohimbine, an extract from the bark of a tree in Africa. Yohimbine is known as a central amplifier of erection that may be useful in psychogenic erectile dysfunction (28). Yohimbine can dilate the penile artery (5). Some studies have shown that Yohimbine may be also effective for treatment of organic erectile dysfunction (28,29). However, further researches to reveal its molecular mechanisms of action and for validation of the medicinal benefits are needed.

Ginseng is a vital constituent of traditional Chinese medicine, and has been reputed as an aphrodisiac. Ginseng is used to treat sexual dysfunction as well as to enhance sexual performance and gonadal functions (30). In men with erectile dysfunction, the improvement in erectile performance and sexual satisfaction after taking Korean red ginseng had been reported (30). Ginseng has androgenic effects and its use in pregnant women can lead to androgenization of the neonate (5). Studies on the effect of ginseng on menopausal women have not always yielded the same results. A systematic review aimed to evaluate the evidence from placebo-controlled Randomized Clinical Trials (RCTs) of ginseng for menopausal symptoms provided positive evidence of ginseng's effect for sexual function (31). The study of Oh *et al* showed that oral administration of Korean red ginseng extracts improves sexual arousal in menopausal women (32). On the other hand, Chung *et al* found that Korean red ginseng significantly improves sexual desire, arousal, orgasm, and satisfaction domains in postmenopausal women; but, compared with placebo, there was no statistically significant difference (33). Further RCTs are needed to overcome the many limitations of the current researches.

Unfortunately, it has been proven that some of the herbal remedies and natural products have been made using synthetic drugs. Undeclared synthetic compounds and large numbers of adulterants were detected in dietary supplement and herbal remedies. The safety and toxicology profiles of these botanical products are often unknown; therefore, they can be dangerous even for public health (27).

Discussion

Substance use disorder is a significant problem in different societies and also in Iran. It can cause various problems that directly or indirectly affect community health. One of the problems associated with substance use is sexual dysfunctions which, in addition to the afflicted person, affect the performance and satisfaction of the partner.

In a study, the rate of sexual dysfunction has been reported to be 34.2% in women with substance dependence. Also, according to various studies, the risk of high-risk and sexually harmful behaviors is also high in substance abusers, and the possibility of transmission of sexually transmitted infections such as HIV is also higher in these individuals (34-36). In another study, the rate of any type of sexual dysfunction has been reported to be 14% in men and 33% in women, that among these disorders, painful sex and inhibited orgasm were reported more than other disorders (37).

According to conducted studies, the likelihood of a sexual dysfunction is different among consumers of different substances. Most studies have reported sexual dysfunction among opioid users, especially heroin, which has been more in comparison to stimulants users (38). Also, in a study, high risk sexual behaviors have been more observed in heroin users than the users of amphetamine-like substances (39).

So, with special attention to these problems, timely treatment and interventions by therapists especially psychiatrists are very effective. Reduction and, if possible, discontinuation of medication or substance abuse is the first action that in many cases causes recovery of the affected person. But if conditions are not provided for some reasons, including the lack of motivation for the person to discontinue the substance, suitable use of medications and non-medication interventions can be beneficial.

One of the medical treatments of sexual dysfunctions is the treatment of erectile dysfunction with 5-phosphodiesterase inhibitors (PDEI-5), such as sildenafil, commonly sold with trade name Viagra, and treatment of low sexual desire in women with bupropion or testosterone at specific conditions (40-42).

It should be noted that some people use substances such as opioids and tramadol to treat some sexual dysfunctions such as premature ejaculation. In these conditions, the treatments of the sexual dysfunction should be considered. For example, the behavioral techniques or medications such as SSRIs can be used for the treatment of premature ejaculation (43,44).

Conclusion

In general, it is advisable to pay special attention to sexual dysfunctions, especially in addiction treatment centers, by educating physicians about sexual problems. After recovering from substance dependency, patients may have difficulties in psychological readjustment to a nondependent state. Many of them have not experienced situations that are needed for learning social and sexual skills and have difficulty with intimate interactions (5). They may need psychotherapy to regain sexual function and psychiatrists can help them. Also, given the specific difficulties of treating sexual problems and the likelihood of potentially dangerous interactions, physicians are recommended to refer these patients to psychiatrists.

Conflict of Interest

The authors of this article have no conflict of interest.

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