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Review Article

Overview of substance use disorders and available treatments

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Abstract

Substance use disorders are a major health problem worldwide. Substance use is a chronic disorder associated with significant mortality and morbidity. These diseases also cause significant healthcare utilization and medical costs. Substance use disorders occur when the use of alcohol, prescription drugs, or illegal drugs causes problems in his life and daily activities. Substance use disorders encompass a variety of behaviors, including but not limited to addiction, overuse, and behaviors caused by dangerous substances. Diagnosis is based on behavioral criteria, which include the inability to control substance use, dysfunction at school, home, or work, interpersonal problems caused or worsened by substance use, and risky or hazardous use of the substances. The first step in treating substance use disorders is to stop using the substance. In extreme cases of physical dependence, detoxification is necessary to help with withdrawal symptoms. Creating a supportive environment and eliminating triggers for substance abuse are essential to overcoming a substance abuse disorder. Treatment in management can be outpatient or inpatient, depending on the severity of the problem. Depending on the person's condition, a doctor may suggest individual counseling from a psychologist, psychiatrist, or addiction counselor. Family counseling is often important. A doctor may also recommend specific rehabilitation and/or treatment programs; Self-help groups for children and families with addiction problems are often very helpful. In this article, we would like to briefly review substance use disorders and treatment modalities that are available to treat them.

Keywords: *Substance use disorder, Alcohol, Cannabis*

Introduction

Substance use disorders are a major health problem worldwide. Substance use is a chronic disease associated with significant mortality and morbidity. These diseases also account for significant healthcare utilization and medical costs. Treatment for substance use disorder includes detoxification and relapse prevention. The main problem in treating patients with substance use disorders is relapse [1, 2]. Addiction is a chronic condition that requires long-term treatment. Anti craving agents play a key role in preventing relapse. These drugs generally reduce drug cravings and reduce the likelihood of relapse into compulsive drug use. Anti craving drugs are used along with other psychiatric drugs to treat substance use disorders. In India, drug abuse has infiltrated all sociocultural and economic strata, resulting in lost productivity. Substance abuse and mental illness are global public health crises that provide unique challenges to healthcare systems in both developed and developing countries. In poor nations, the treatment gap for mental health and substance use problems is over 90%, despite the prevalence of these conditions. [3, 4]. Mental problems and addiction are two of the most major noncommunicable diseases affecting developing nations. Most underdeveloped nations allocate a paltry percentage of their healthcare funds to mental health services (less than 2%). Drug addiction produces significant and lasting changes in brain chemistry and function. Effective medications are available to treat nicotine, alcohol, and opiate

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addiction, but not a stimulant or marijuana addiction. Adherence and relapse rates are similar for these disorders. Studies suggest that long-term treatment strategies of medication management and continuous monitoring bring lasting benefits to patients with substance use disorders. Substance abuse causes acute and chronic physical, psychological and social effects of varying degrees, as well as serious social problems in the form of crime, unemployment, family disorders and disproportionate use of medical care [5, 6].

Science has not fully explained the psychological processes leading to drug abuse. Substance abuse affects over 50 million people worldwide. The abuse of legally prescribed drugs is also increasing rapidly. In India, the abuse of alcohol, cannabis and raw opium is traditionally known. The abuse of synthetic narcotics and psychotropic substances is relatively new. Substance abuse has affected all sociocultural and economic classes, resulting in lost productivity. Family stress, lack of coping skills, peer pressure, personality disorders, psychiatric comorbidities, social stress and market forces act as risk factors. Surveys show that around 20-30% of adult males and 5% of adult females use alcohol, while 57% of male and 10.8% of female drug users use opiates in some form. A rapid substance abuse assessment survey shows that the most commonly abused drugs are heroin (36%), other opiates (29%) and cannabis (22%); 75% of addicts start using drugs before the age of 20; Heroin abuse is higher in urban areas, while cannabis abuse is higher in other locations [7-9].

Treatment of substance use disorders

Substance use disorder was conceived as a chronic relapsing disease with flares and remissions and a strong genetic component similar to type II diabetes and hypertension. The risk of recurrence is increased because the neurobiological changes in the brain pathways caused by long-term alcohol and/or drug use do not fully normalize after detoxification. The intensity and type of behavioral intervention can affect the treatment outcome of patients with SUD. The use of medication in the management of SUD may also play an important role in preventing relapse and facilitating prolonged periods of abstinence [10, 11]. Over the past 30 years, more and more effective drugs have been developed, meaning that pharmacotherapy has played an increasingly important role in treating addiction. Drugs are most commonly used as an adjunct to psychosocial treatments, and the role of pharmacotherapy in treatment depends on the specific type of SUD. Pharmacological agents have three main goals: treating acute withdrawal syndrome through detoxification, reducing cravings and cravings for illicit drugs (first recovery), and preventing relapse into compulsive drug use [12-14].

Treatment of nicotine dependence

Tobacco use is highly comorbid in patients with SUDs and is the leading cause of premature death and disability in patients recovering from other SUDs. Research suggests that smoking cessation may facilitate abstinence from alcohol and other drugs. Patients who use tobacco should be educated about these findings as a potential motivator for reducing tobacco use. Pharmacotherapy is considered the mainstay of smoking cessation treatment, and recommended therapies, including combinations of counseling and medication, result in abstinence rates of approximately 40% at one year [15]. First-line therapies (treatments recommended by the Food and Drug Administration [FDA] as having the most evidence of effectiveness) include nicotine replacement therapy (NRT), bupropion SR (Zyban), and varenicline (Chantix). NRTs replace the nicotine obtained from smoking to prevent withdrawal symptoms and improve smoking cessation outcomes. Substitute drugs are used because of the low success rate of total cold turkey from nicotine [16, 17]. Approved formulations include the nicotine transdermal patch, nicotine gum, nicotine lozenges, nicotine vapor inhaler and nicotine nasal spray. Behavioral therapies used in conjunction with NRT increase cessation rates [18, 19].

Treatment of alcohol dependence

Medications for detoxification and medical stabilization

Chronic alcohol dependence can lead to periods of severe withdrawal symptoms characterized by increased heart rate and blood pressure, anxiety and withdrawal attacks, and in severe cases, delirium tremens and even death. Medications for alcohol withdrawal syndrome include benzodiazepines, which act on gamma-aminobutyric acid (GABA) at the GABA receptors in the brain to stimulate the release of GABA. GABA is a neurotransmitter responsible for reducing activity throughout the nervous system, gradually detoxifying the patient from alcohol by reducing heart rate, blood pressure, sweating, and anxiety associated with alcohol withdrawal [20]. During detoxification, benzodiazepines are systematically reduced to meet the most important need, which is to prevent seizures and delirium from occurring. They should be avoided as a long-term strategy for controlling alcohol dependence because the physical tolerance of these drugs can set in quickly and lead to dangerous interactions if patients taking the drugs relapse into alcohol use. It is important to emphasize that the detoxification process is only a first step in medically stabilizing patients and supporting the transition from alcohol dependence to recovery. After detoxification, the patients must be actively treated with psychotherapy and behavioral therapy in order to remain abstinent from alcohol [21, 22].

Medications to Attenuate Substance Use and Reduce Relapse (Anti-craving agents)

Disulfiram (Antabuse) is the first FDA-approved drug for alcohol addiction and has been available for over 50 years. It inhibits aldehyde dehydrogenase, the enzyme that converts acetaldehyde to acetate when alcohol is broken down. As acetaldehyde builds up, the disulfiram ethanol reaction (DER) takes place. The DER includes uncomfortable and potentially dangerous symptoms such as sweating, nausea, vomiting, facial flushing, tachycardia, hyperventilation, shortness of breath, and hypotension. In severe reactions, cardiac arrhythmias and myocardial infarction, seizures, and death can occur. DER is an aversive state that aims to eliminate

an addictive behavior through negative reinforcement and behavior counterconditioning [23, 24].

Naltrexone (Revia) is a good example of an anti craving drug for the long-term treatment of alcohol addiction. Naltrexone is a competitive opioid antagonist thought to block the rewarding aspects of drinking by occupying opioid receptors. When naltrexone is present in the brain, alcohol cannot stimulate the release of dopamine, reducing the intoxicating effects of alcohol. Naltrexone has been shown to reduce the frequency and intensity of drinking, reduce the risk of relapsing into heavy drinking, and increase the percentage of abstinent days. The average dose is 50 mg daily. Naltrexone is usually well tolerated, and the most common side effects are mild nausea and headache. A depot injection formulation of naltrexone (Vivitrol) has been developed to be administered once a month with a slow release into the body. It has been shown to be effective in reducing the consequences of heavy drinking as it offers the benefit of increased medication adherence [25, 26].

Acamprosate (Campral) was approved by the FDA in 2004 as a drug to prevent alcohol addiction from returning. It affects various neurotransmitters and is structurally similar to GABA and glutamate. Glutamate is the primary neurotransmitter for increasing neurological activity. Acamprosate acts on gabaergic receptors, but primarily it modulates glutamate receptors. It can be considered either a glutamate modulator or a weakly potent and partial N-methyl-D-aspartate (NMDA) antagonist. This leads to its primary effect of reducing withdrawal. It is more effective when given in the initial phase after acute withdrawal has ended, possibly related to its action on NMDA receptors and its ability to reduce protracted hyper glutamatergic states that trigger relapse through negative reinforcement. In particular, acamprosate reduces alcohol cravings induced by the desire for relief from withdrawal symptoms [27-29].

Topiramate (Topamax) is a drug already approved to treat epilepsy. It has been studied for its ability to enhance GABA function and inhibit glutamatergic signaling pathways. These combined neurological activities can decrease dopaminergic activity and possibly alcohol reward. Therefore, patients taking topiramate will find it easier to reduce drinking or abstain. Topiramate is started with no initial abstinence. In two large controlled studies, topiramate was found to be more effective than placebo at reducing heavy drinking, drinks per day and increasing the percentage of days without abstinence. Topiramate is not FDA-approved (aka off-label) and prescribes it to treat alcohol addiction. More research is needed to determine which subpopulations of alcoholics would benefit most from topiramate. Topiramate has a range of side effects, including mild cognitive impairment, and requires low titration (the drug must be started at a low dose and increased gradually) over several weeks before reaching a fully effective dose [30-32].

Baclofen is a derivative of GABA and can activate the GABAB receptor with no known abuse potential. It has muscle relaxant and sedative properties and is primarily used to treat spasticity of neurological disorders, such as spinal cord injury, cerebral palsy and multiple sclerosis. Baclofen was first reported to be effective in inducing abstinence from alcohol and reducing alcohol cravings. Subsequently, it was reported that Baclofen was effective and well tolerated in alcohol-dependent patients with liver cirrhosis and that a higher dose (20 mg three times daily) had a greater effect than the common dose (10 mg three times daily) [33-35].

Research has been conducted using the newer antidepressants serotonin specific reuptake inhibitors (SSRI), for example, fluoxetine and citalopram, as adjuncts in the treatment of alcoholism. However, these medications have been found to be of limited utility. The findings suggest that SSRIs may be useful in reducing alcohol use in subpopulations such as those with depression and alcohol dependence [32, 36-39].

Treatment of opioid dependence

The most effective pharmacotherapies for opioid use disorders are agonist therapies. As mentioned above, by occupying the sites stimulated by opioids, agonist medications essentially ”turn on” the receptors. The therapeutic approach involves using medications that have similar actions to the abused drug but have different pharmacokinetic profiles. Medications like methadone are longer-acting, have fewer drug-like effects, and are, thereby, less reinforcing. In the case of opioids, methadone and buprenorphine are the most commonly used medications [40-43].

Once stabilized on methadone, individuals who are addicted to opiates and who use short-acting opioids such as heroin will no longer experience peaks of euphoria or the aversive effects of withdrawal, such as anxiety, agitation, diarrhea, and insomnia. As a result, the patient is no longer preoccupied with drug-seeking behaviors. When adequate doses are used, methadone maintenance also diminishes the intensity of shorter-acting opioids through cross-tolerance. This means that drug responses to a particular drug (e.g., methadone) transfer to other drugs from the same class (e.g., heroin) and reduce their reinforcing effects, which, in turn, decreases the intensity of cravings for the drug. The combination of control of aversive effects and prevention of reinforcement makes methadone maintenance an extremely effective treatment as objectively measured with opiate-free urine drug testing [44-46].

In accordance with the Drug Abuse Treatment Act of 2000, in Oct 2002, the FDA approved the use of buprenorphine (Subutex), an opioid partial agonist, as a Schedule II agent to treat opiate dependence in outpatient office-based practices. Buprenorphine is a long-acting (up to 48 hours) high-affinity partial μ opioid agonist, which causes it to act as a functional antagonist blocking the effects of pure μ agonists. Because it is a partial agonist, unlike methadone, a pure agonist, it is safer in overdose because it has a ceiling effect on respiratory depression. Buprenorphine is considered to cause a reduced euphoric effect compared to methadone and therefore is less likely to be diverted. To mitigate the potential for abuse of

the substance and diversion, buprenorphine has been developed in a sublingual (pills or film sheets that dissolve under the tongue) with naloxone (Suboxone). Suboxone has become the treatment of choice for detoxification from opioids. The typical maintenance dose of Suboxone is 12 mg-16 mg. Rarely doses higher than 16 mg might be useful but would necessitate a thorough reevaluation of the patient's treatment needs [47-49].

Naltrexone (Vivitrol) has been approved by the FDA for the treatment of opioid addiction in terms of adherence. Naltrexone's dopamine-blocking effects make it a potential alternative to opiate replacement treatment for opioid dependence. Patients addicted to opioids cannot get high from opioids while taking naltrexone, and it has been hypothesized that they do not want to use opioids, making them more likely to remain abstinent [46, 50, 51].

Conclusion

Substance use disorders are chronic, relapsing conditions that have adverse consequences for sufferers and society. Unfortunately, despite extensive research and an ever-evolving understanding of these conditions, current treatments are limited and ineffective. Therefore, investigating common mechanisms underlying addictive behavior is of paramount importance in the search for novel therapies. Without support and treatment options, substance use disorders are difficult to overcome. Substance use disorders can be a chronic struggle throughout a person's life, but treatment can restore emotional and physical well-being and help a person lead a substance-free life. Therefore, constant support from properly planned treatment therapy can help a person live a better life.

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