REVIEW ARTICLE

Current addictive drugs: A review

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Abstract

Introduction: Addictive drugs and its abuse are a major health as well as social concern all over the world. Around 40 million people are regularly abusing drugs throughout the world. The problem is matter of concern for India as well. Most importantly substance abuse is widely getting popular among young generations including medical students. This article is an endeavor to address current status of addictive drugs. **Methods:** Scientific literature regarding addiction were collected from various data bases from Google Scholar, PubMed, Embase, Indexed Research Journals, and Textbooks using the keywords Addiction, Substance abuse, Addictive, Drug dependency. The collected data were critically reviewed and results were drawn. **Results:** The critical review of the data revealed that, nearly ten different types of addictive drugs are used currently. The majority of users are from adolescent age or students. Even though both sexes are involved prevalence rate is more in males. Among all the additives alcohol and tobacco are the most common. The common health issues include tolerance, physical dependence, sensitization, craving, relapse, depression, intense anxiety, hopelessness, helplessness, and irritability. The statutory control over narcotic drugs was exercised in India through a number of Central and State enactments like the opium Act, 1857, the Opium Act, 1878 and the Dangerous Drugs Act, 1930. But in spite of all these efforts the drug dependence is a major concern for globe. **Conclusion:** Drug abuse and addiction are affecting the quality of life of people around the world and hence awareness about the health hazards and availability of de-addiction measures for all strata of population is recommended.

Key words: Drug abuse, Addictive drugs, Drug dependence, Substance abuse

INTRODUCTION

Addictive drugs and its abuse are a major health as well as social concern all over the world.[1] Addiction can also be defined as a chronic disorder which is characterized by compulsive use of drugs resulting in physical, psychological, and social harm and continued use in spite of evidence of that harm.[2] Instead of using the former term, "drug addiction," the World Health Organization (WHO), and the American Psychiatric Association currently use the term "substance dependence."[3]

According to Ministry of Health and Family Welfare (MOH and FW), at least 40 million people throughout the world regularly abuse drugs. The problem is increasing in India also and it is estimated that 3 million people are abused to alcohol and other drug of which 5–6 lakhs are dependent, requiring medical treatment and rehabilitation.[1]

Considering the impact of addictive drugs in society on the level of physical-mental-social and economic health, it is necessary to address this global problem. This article is an endeavor to review the current status of addictive drugs in regards of types, prevalence in accordance of addictive drug, associated health disorders, and the preventive measures for de-addiction.

METHODS

Scientific literature regarding addiction were collected from various data bases from Google Scholar, PubMed, Embase, Indexed Research Journals, and Textbooks using the keywords Addiction, Substance abuse, Addictive, and Drug dependency. The collected data were critically reviewed and results were drawn.

RESULTS

The results drawn from the collected data have been categorized under the headings Prevalence, Types of addictive

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drugs, pathophysiology of development of addiction, health impact due to addictive drugs, legal provisions to encounter drug abuse in India.

Prevalence

An estimate done by the WHO, (2014) shows there are around 2 billion alcohol users, 185 million drug users and 1.3 billion smokers all over the world.[4] In a study conducted worldwide, it was estimated that a prevalence rate of substance abuse is to be around 20–40% among students from various streams including the medical field. It was reported that more than 75% of the users' used substances for "feel good factor" and were using despite knowing their harmful effects. The common reasons being psychological stress and occasion celebration followed by to reduce tiredness, peer pressure, easy availability, experimental use, and community acceptance. From a study conducted in India, it was noted that nearly 50% of the undergraduate medical students were reported experiencing stress of variable severity, predisposing to substance abuse. It was also noted that a higher proportion of children were found to be using any of the substances when one or both of their parents were doctors or para-medical professionals.[5]

Among various additives tobacco and alcohol are the most common. The National Household Survey of Drug on documenting the nationwide prevalence of drug use reports - alcohol (21.4%) was the primary substance used (apart from tobacco), followed by cannabis (3.0%) and opioids (0.7%). While The Drug Abuse Monitoring System, which evaluated the primary substance of abuse in inpatient treatment centers, noted that the major substances were alcohol (43.9%), opioids (26%), and cannabis (11.6%) and The World Drug Report of 81,802 treatment seekers in India (2004–2005), 61.3% reported use of opioids as 15.5% cannabis, 4.1% sedatives, 1.5% cocaine, 0.2% amphetamines, and 0.9% solvents. Considering Punjab, "drug abuse" is observed as a raging epidemic, especially among the youngsters. According to a survey, 66% of the school going students in the state are consuming "gutka" or tobacco and every third male and every tenth female student are into some form of drugs and seven out of ten college-going students are into drug abuse.[6]

In a study conducted among randomly selected population in a community in a city in Gujarat, it was found that overall prevalence of substance abuse was 18.86%. The most common substance to be abused was tobacco (38%) which is followed by alcohol (34%). This may be due to alcohol ban in the Gujarat state. The survey also reported that the mean age of onset for drug use was inferred as 26.9 years. It was noted that the proportion of substance abuse found to be greater among males (79.84%), those who were from Class IV (68.37%), those who belongs to joint families (61.67%), and who were literate (55.73%), whereas females shown high prevalence for chhikni or bajjar (80.39%).[7]

The diagnostic criteria for drug dependency include following symptoms as per diagnostic and statistical manual of mental disorders (DSM-VTR) of American Psychiatric Association[3]

- Tolerance means every time larger amount of drug is required to achieve desired effect of pleasure which eventually increases the amount of consumption
- Withdrawal is the physical and mental symptoms that occur after stopping or reducing intake of a drug
- Unsuccessful attempts or desire to control use - drug addiction or substance abuse, affects the brain, making it difficult to stop taking the drugs, even if the person want to
- Considerable time spent obtaining the substance - the substances are often taken in larger amounts or over a longer period than intended and a great deal of time is needed in activities necessary to obtain the substance, use the substance, or recover from its effects
- Reduction of social and occupational activities due to abuse - drug abuse results in lost productivity (The National Drug Intelligence Centre) leading to reduced labor participation, incarceration, premature mortality, hospitalization, and participation in treatment programs away from work along with arguments with spouse about consequences of intoxication, physical fights.

Continued use of a substance despite physical or psychological problems, etc. Neurochemical actions of the drug are responsible for the repeated drug use which produces positive reinforcing effects leading to neurobiological changes in the brain reward circuits and behaviors.

Types of Addictive Drugs

The various categories of addictive drugs consumed are as follows:[5]

1. Alcohol
2. Tobacco
3. Opioids (morphine, heroin, oxycontin, etc.)
4. Cannabis (Marijuana)
5. Cocaine
6. Amphetamines and others
7. Hallucinogens (Lysergic Acid Diethylamide [LSD], phencyclidine)
8. Sedatives, tranquillizers, and hypnotics (Barbiturates, Benzodiazepines [BDZs], etc.)
9. Inhalants (Solvents, Ether, etc.)
10. Miscellaneous-Datura, Caffeine, Analgesics, etc.

Alcohol

Alcohol is the most commonly abused drug in the world.[2] They are hydroxyderivatives of aliphatic hydrocarbons and are produced by fermentation of sugar by yeast.[5] It is estimated that 60% of males and 40% of females are engaged in chronic alcohol consumption.[2] Alcohol addiction is a leading risk factor for death (2.2% of female deaths and 6.8% of male deaths) and disability (2.3% in female and 8.9% in male) as per a data in 2016.[8]

Alcohol is absorbed rapidly from stomach (20%) and small intestine (80%). Strong alcoholic beverages are distilled after fermentation which increases the alcohol concentration and hence absorbed slowly as higher concentration of alcohol inhibits gastric peristalsis thus delaying gastric emptying.[5]

The action of ethyl alcohol or alcoholic intoxication is mainly due it its depressing action on CNS by dissolving in the cell's lipid membrane causing disorganization of lipid matrix. Alcohol also acts as a diaphoretic, appetizer, and hypnotic agent. Alcohol initially has a stimulant action due to the depression of higher inhibitory centers which normally controls human behavioral attitudes, followed by depression of vital centers of medulla thus causing cardiorespiratory failure and alcoholic coma leading to death.[9] Most of the individuals start use of alcohol for euphoric feelings or recreational effect, later tolerance develops due to the desensitization of gamma aminobutyric acid (GABA) receptors, and/or liver enzyme activation finally leading to an uncontrolled intake.[9]

Chronic administration of ethanol, which is sufficient to produce dependence, and increased ethanol intake may result in GABA release in the amygdala leading to increased sensitivity to GABA agonists. It is also noted that GABAergic interactions with the brain stress neurotransmitter corticotropin-releasing factor, in specific elements of the extended amygdala may be an important factor responsible for the motivation for excessive drinking associated with the transition from social drinking to addiction.[10]

GABA is the major inhibitory neurotransmitter of the central nervous system. Ethanol, BDZs as well as some anticonvulsant drugs have direct impact on GABA receptors producing similar anxiolytic, sedative, hypnotic, and anticonvulsant effects. Due to the proven efficacy of BDZs in enhancing symptoms and in decreasing the risk of seizures and delirium tremens, they are the drug of choice for the management of alcohol withdrawal syndrome. However, while considering its addictive potential and lack of safety when combined with alcohol, BDZs are generally not recommended for the treatment of alcohol abstinence.[11]

Alcoholism is characterized by salience of drink-seeking behavior, loss of control over consumption, awareness of a compulsion to drink excessively and development of tolerance and dependence and also impaired social and occupational functioning. Like most of the addictive disorders, alcoholism is also characterized by chronic vulnerability to relapse after cessation of drinking.[12] Alcoholic individuals are at high risk of anxiety, depression, impaired cognition performance, and illicit drug use. They are also comorbid with liver diseases such as liver cirrhosis and alcoholic hepatitis, which is a major cause of personal death and disability worldwide.[9]

Withdrawal symptoms of alcohol include anxiety, shakiness, sweating, vomiting, tachycardia, and mild fever and severe symptoms such as seizures, visual and auditory hallucinations, and delirium tremens can be seen.[9]

Nicotine

It is the second most common and abused drug in the world after alcohol.[1] According to WHO tobacco kills more than 8 million people each year.[13] In India, tobacco use is characterized by a high prevalence of smoking and smokeless tobacco use. Among the estimated 28.6% of total tobacco users in India, only 10.7% consumes in the form of cigarettes and bidis whereas 21.4% uses smokeless tobacco in the form of pan, pan masala, and gutka and mishri (GATS 2017).[14]

Nicotine is the major addictive component in tobacco products and is a stimulant of central nervous system which acts on nicotine receptors present in central nervous system, spinal cord, neuromuscular junction, adrenal medulla etc.[5] Nicotine also stimulates the reticular activating system with favorable effects on memory, attention and anxiety, when taken at moderate doses and on high dose it leads to convulsion and tremors.[15] By the hemodynamic consequences of sympathetic neural stimulation and systemic catecholamine release, nicotine may contribute to cardiovascular diseases. Cigarette smoking accelerates atherosclerosis, producing premature atherosclerosis at epicardial coronary arteries, the aorta, the carotid and cerebral arteries and large arteries in the peripheral circulation and is also associated with an increased risk of acute cardiovascular events, including acute myocardial infarction, sudden death and stroke.[16]

Nicotine binds to nicotinic acetylcholine receptors which are allosterically regulated ligand-gated ion channels widely distributed throughout the central nervous system and are normally activated by the endogenous neurotransmitter acetylcholine leading to activation of reward centers in the CNS ultimately leading to addiction.[17]

While smoking a cigarette, smoke particles carry the nicotine into the lungs, where it is rapidly absorbed into the pulmonary venous circulation. It is then entered into the arterial circulation and from there nicotine moves quickly from the lungs to the brain, where it binds to nicotinic cholinergic receptors (ligand-gated ion channels that normally bind acetylcholine). This binding of nicotine at the interface between two subunits of the receptor opens the channel, thereby allowing the entry of sodium or calcium will further activates voltage-dependent calcium channels, allowing more calcium to enter. The stimulation of nicotinic cholinergic receptors releases a variety of neurotransmitters in the brain [Figure 1] like, dopamine which provides pleasurable experience and is critical for the reinforcing effects (effects that promote self-administration) of nicotine.[19]

It has been recently advocated that calcium channel blockers have potential for alleviating nicotine addiction by selectively

decreasing the incentive motivational properties of drug and may be beneficial as smoking cessation.[19]

Caffeine

Caffeine is one of the world's most popular psychoactive substances which acts as central nervous system stimulant and produces dose-dependent symptoms and intoxication with overconsumption. Caffeine is also known for its addictive properties and discontinuation may results in withdrawal syndrome.[20] It is materialized in numerous prescriptions and over-the-counter medications, coffee, tea, chocolates, colas, and other carbonated and non-carbonated beverages.[21]

Caffeine use raises multiple concerns especially among the youth population such as (1) regular use can result in "dependence"; and daily users (as young as 13) may experience withdrawal symptoms. (2) Children who consume moderate amounts of caffeine can experience anxiety/nervousness, hyperactive behavior and disrupted sleep, which may lead to adverse impact on learning and developmental processes. (3) Small to moderate amounts of caffeine have positive and immediate effects on mood, mental alertness, and motor performance but chronic use have more potent impact and have delayed consequences such as development of addictive behavior. (4) The effects of caffeine may act synergistically with other substances, reinforcing the development of unhealthy behaviors. Ex. caffeine in sugary drinks can substantiate poor dietary habits and contribute to obesity.[22]

Caffeine can cause caffeine-intoxication, caffeine-induced anxiety disorder, caffeine induced sleep disorder, and caffeine-related disorders not otherwise specified. Consumption of three or more cups of caffeinated coffee a day can results in delayed conception and spontaneous abortion and daily consumption of 400 mg of caffeine during pregnancy may increase the risk for sudden infant death syndrome. Symptoms such as headache, lethargy, irritability, and mental fuzzy-headedness are seen in caffeine withdrawal.[23]

Cannabis

Cannabis is the world's most commonly used illicit drug which occupies fourth place among most popular psychoactive drugs.[24] "Cannabis' is the botanical name of a genus within the Cannabaceae family that includes three species- C. sativa, C. ruderalis, and C. indica and hops also comes under this family. All Cannabis plants contain secondary compounds called "Cannabinoids".[25]

The most common way to use cannabis is smoking herbal cannabis (i.e., *marijuana, pot,* or *weed*). Intoxication by this route occurs as soon as 2 min after the first inhalation and peak drug effect occurs about 30 min after use. Hashish is a crude product of cannabis consisting of the compacted sticky resin glands of the plant with tetrahydrocannabinol

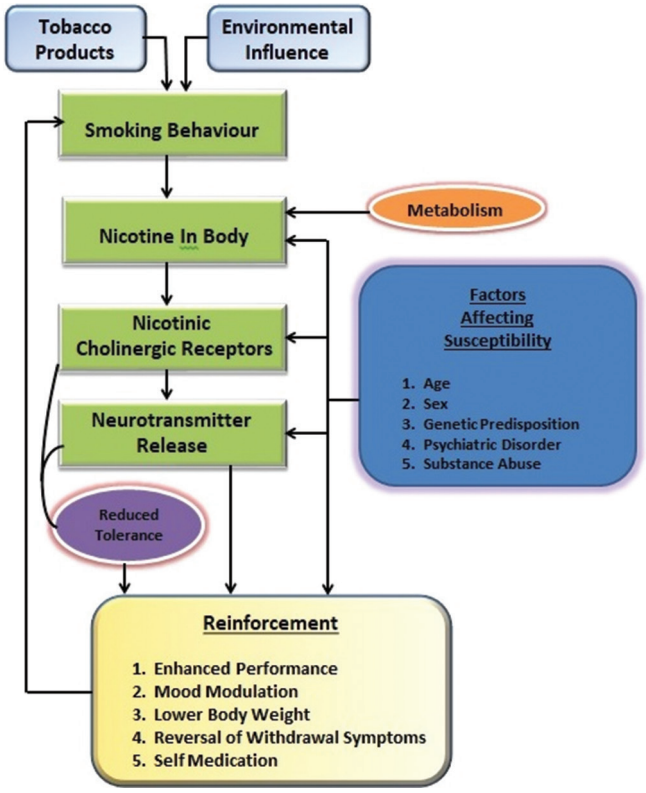

Figure 1: Mode of action of Tobacco[18]

(THC) ranging from 15% to 30% by weight.[26] Cannabis are delivered in various modes such as smoked or vaporized dried herb, cannabis mixed or rolled with tobacco, vaporized liquid form, hashish, hash oil, concentrates, edibles, liquids, tinctures, topical ointments, and fresh flower/leaf.[27]

Cannabis is not as highly addictive as other substances such as heroin and cocaine but cannabis-dependent individuals still greatly surpass those reporting dependence on other illicit drugs and the number of people seeking treatment for cannabis dependence are increasing every year (SAMHSA, 2011).[25] The most commonly abused form is Marijuana especially among adolescence, which is eaten alone or drunk in beverage or smoked. Other forms include Hashish (charas), Ganja, Majun, and Bhang.[28]

Tobacco and cannabis (marijuana) are often used in combination and cannabis is the most frequently used drug among tobacco users.[29] Among the active principles, 9-THC is responsible for most of its psychoactive effects. It acts on specific receptor regions of brain concerned with pain perception, memory, reward, and motor coordination.[29]

Cannabis contains various cannabinoids such as cannabidiol and delta-9-THC, which induce clinical effects through their influence on the endogenous endocannabinoid system. The psychoactive component of cannabis involves effects produced primarily by THC's partial agonistic effects on cannabinoid-1 receptors thus generating the feeling of "high" in users.[30] Basal ganglia and cerebellum show highest

density of receptors producing dose-related impairment in cognitive and behavioral functions. Cortex, hippocampus, and dentate gyrus show moderate level of binding resulting in effects on cognition and short-term memory. Brain stem regions showing low receptor density is responsible for "lack of lethality" of cannabinoids.[29]

Withdrawal symptom of cannabis includes irritability, anger or aggression, nervousness or anxiety, sleep difficulty, decreased appetite or weight loss, restlessness, depressed mood, chronic irritability, malaise, and dysphoria and physical symptoms causing significant discomfort such as shakiness or tremors, sweating, fever, chills, and headaches during acute and protracted abstinence from a drug of abuse. Apart from these sleep disturbances characterized by trouble falling asleep, decrease in total sleep time, and the presence of nightmares and strange dreams are also seen.[31]

The consumption of cannabis resin (charas) was prohibited in India in 1930 s during British rule and ever since its cultivation and production is diminished. Under the Narcotic Drugs and Psychotropic Substances Act (NDPS Act) in India, it is illegal to produce, manufacture, possess, sell, purchase, transport, use, consume, import, export any narcotic drug, or psychotropic substance except for medical or scientific purposes. Violation of this may be punishable with maximum penalty for repeat offence can be as high as a death penalty.[32] In 11 US states (Alaska, California, Colorado, Illinois, Maine, Massachusetts, Michigan, Nevada, Oregon, Vermont and Washington, and the District of Columbia), recreational or 'non-medical cannabis has been legalized and was legalized federally in Canada on 17 October 2018.[33]

Opioids

Opioid use disorder and opioid dependence are a problem of global concern.[34]

Opioid addiction is a chronic and complex mental illness that causes the addicted individuals to experience many relapse and remission. When compared to smoking and alcohol, opioid addiction is less common but has imposed a heavy burden on both healthcare systems and the criminal justice system.[35] In recent years opioid-related overdose deaths, rates of abuse and dependence of prescription opioids have risen dramatically.[29]

All opioids including morphine, heroin, and prescription analgesics (Vicodin and OxyContin) have extremely high abuse potential and dependence on these drugs is associated with a multitude of health and social problems, such as increased risk for human immunodeficiency virus, mortality, crime, unemployment, legal issues, and interpersonal breakdowns. Morphine is a drug derived from the natural juice of opium poppy and is considered to be the most potent analgesic painkiller available and the drug is known to induce relaxation and euphoria.[36]

Generally individual start use of opioids for euphoric feelings or pain relief and later on tolerance develops due to the desensitization of opioid receptors, leading to an uncontrolled intake. On withdrawal, symptoms such as severe muscle ache, bone pain, tearing, runny nose, yawning, diarrhea, abdominal cramps, agitation, anxiety, and sweating will appear and individuals use opioids again to alleviate these intolerable feelings.[35]

Opioid receptors are G protein-coupled receptors distributed across the brain, spinal cord, skin, and gastrointestinal tract. The mu-opioid receptor (MOR) was the first discovered opioid receptor and can trigger euphoria, thus essential for brain reward circuits which are highly dynamic and also plays an important role in goal-directed behavior such as drug-seeking behavior for pleasure.[35] Opioids induce dopamine release directly by interacting with opioid receptors (MOR) and indirectly by decreasing GABA-inhibition via l-opioid receptors in the ventral tegmental area. Repeated opioid administration leads to the activation of cAMP pathway resulting in phosphorylation of the transcription factor CREB (cAMP response-element binding protein), in turn inducing transcription of many genes. Another theory states that the reward mechanisms become dysregulated by continued drug use, diminishing the pleasurable effects of the drug ("liking"), while increasing the incentive effects ("wanting" or "craving"), leading to compulsive drug-seeking.[37]

Cocaine

Cocaine is an alkaloid which is found in significant quantities in leaves of two species of coca shrub-*Erythroxylum coca* and *Erythroxylum novogranatense*.[38] It is one of the most addictive drugs due of its immediate and powerful rewarding effects. Cocaine dependence is a chronic, complicated and destructive illness with somatic, psychological, socio-economic, and legal complications that is often difficult to treat.[39,40] The highest rates of cocaine use are young males aged between 15 and 24 years.[41]

Most of the psychoactive drugs that cause addiction in humans activate the meso-cortico-limbic system by increasing dopamine release within the nucleus accumbens. In case of cocaine, it directly increases synaptic dopamine levels in this meso-cortico-limbic system by blocking the transporter that pumps dopamine out of the synapse into the presynaptic nerve terminal which significantly contributes to the reinforcing effects of cocaine. Cocaine also blocks the serotonin and norepinephrine presynaptic transporters and also influences other neurotransmitter systems including glutamate, GABA, endocannabinoid, and corticotrophin-releasing hormone. These neurotransmitter systems modulate and interact with the reward, motivation, and memory systems in the brain.[41]

During the 1st year of use 5% of cocaine users will develop substance-dependence and 20% of these will become long-term cocaine-dependent patients.[41] Cocaine addiction does not cause any gross physiological gross syndrome.

Cocaine initially induces profound subjective wellbeing with alertness, increase in self-confidence and self-perception of mastery and so anxiety is decreased initially. Social inhibition is reduced, facilitating interpersonal communication.[42]

Cocaine dependent individuals often experience cognitive impairments, strong use-related social and environmental issues, and high levels of life stress from repeated cocaine use. It also affects areas of the brain related to motor function, inhibition, memory, concentration, problem-solving, learning, planning, attention, and discrimination. Apart from the high risk for abuse and dependency, cocaine use implies health risks including respiratory failure, cardiovascular complications, gastrointestinal problems, and mental disturbances such as paranoia and other serious consequences that can further lead to death.[40]

Antidepressants

Antidepressants are one of the most widely used drug classes which are prescribed for a wide range of indications[43] (75% of all prescriptions) including neurological and rheumatoid diseases rather than depressive and anxiety disorders. Antidepressant drugs are associated with many adverse effects resulting in withdrawal symptoms when used for a long time.[44]

Most commonly used antidepressants include[45]

a. Selective serotonin reuptake inhibitors - citalopram, escitalopram, fluvoxamine, etc.
b. Serotonin-noradrenaline reuptake inhibitors-duloxetine, milnacipran, venlafaxine
c. Noradrenaline and specific serotonergic antidepressants - mirtazapine
d. Serotonin antagonists and reuptake inhibitors-nefazodone, trazodone
e. Tricyclic antidepressants (TCAs) - imipramine, amitriptyline, clomipramine, desipramine, etc.
f. Monoamine oxidase inhibitors (MAOIs)
    - Irreversible and non-selective classical MAOIs - isocarboxazid, phenelzine, tranylcypromine
    - Reversible inhibitor of MAOIs: Moclobemide
g. Norepinephrine and dopamine reuptake inhibitors - bupropion
h. Norepinephrine reuptake inhibitor: Reboxetine

Antidepressant discontinuation reactions usually appear within a few days of stopping an antidepressant or less commonly reducing the dose. Such reactions are more common with higher doses and longer courses of treatment and are rare unless treatment has continued for more than 5 weeks. Most antidepressant discontinuation reactions are short-lived but occasionally symptoms can last several weeks or even months too.[46]

The TCAs have complex actions resulting in diversity of features on over dosage. They block the reuptake of noradrenaline into peripheral and intracerebral neurons which results in increased concentration of monoamines in these areas.[37]

Barbiturates

Barbiturates are basically derived from barbituric acid and are used as sleeping tablets, anesthetics and anti-epileptic drugs. The drug is highly abused widely because of the seductiveness'. In combination with alcohol, it is more dangerous as alcohol is CNS depressant and its effects get multiplied when used in conjunction. Overdose death is hence frequent when alcohol and barbiturates are mixed either accidentally or deliberately. These acts as a CNS depressant and also have cumulative effects and hence its metabolism and excretion are very slow. It binds to specific sites on GABA sensitive ion channels which inhibits neurotransmitters in CNS.[10]

All barbiturates are physiologically addicting with a potential to produce a life-threatening abstinence syndrome.[47] In smaller doses they are used as daytime sedatives and in larger doses as hypnotics.

Barbiturates can be classified according to the duration of their action. The ultrashort-acting ones (only intravenous use) are used exclusively as agents producing quick, superficial general anesthesia for short surgical procedures or induction of general anesthesia and play no part in drug abuse. The most frequently abused is the short-and intermediate acting barbiturates which is widely prescribed as sleeping pills and sedatives and is effective for 2–6 h. Long-acting barbiturates being generally used as sedatives or hypnotics (effective for >6 h) are often employed as anticonvulsants and are less often abused.[2,48]

The pattern of barbiturate abuse is very similar to alcohol abuse - a one-night affair, a binge of a few days' or a few weeks' duration, or continuous use. When they are used continuously the development of tolerance and on abrupt discontinuation of the drug, withdrawal symptoms may appear such as motor incoordination, impaired thinking, and lack of emotional control, aggressive behavior, and staggering.[49]

Hallucinogens

Hallucinogens have been broadly defined as agents that alter thought, perception, and mood without producing memory impairment, delirium, or addiction.[49] Hallucinogens refer to certain group of drugs which produce visual illusions, sensory perceptual distortions, depersonalization, and de-realization. It is more appropriately labeled as psychedelics. The classic hallucinogens are LSD, Dimethyl tryptamine, morning glory seeds, the psychotomimetic amphetamine, psilocybin, etc. All these hallucinogens are potentially psychologically hazardous to humans and results in symptoms such as anxiety, panic attack, depression, paranoid reaction, mood swings, confusion, and inability to distinguish reality and fantasy.[10]

LSD is a semisynthetic product of lysergic acid which is a natural substance found in the parasitic rye fungus called

Claviceps purpurea. Its clinical dose is 100 µg and after administration, psychomotor functions (coordination and reaction time) are frequently impaired.[50] It also has potent psychotropic effects (inducing "mystical experiences"), alterations of the state of consciousness, euphoria, enhanced capacity for introspection, altered psychological functioning, a sense of unity, transcendence of time and space, positive mood, feelings of joy, feeling of blessed and peace, a sense of sacredness and a positive attitude toward others, and the self.[51]

LSD stimulates the sympathetic system, causing hyperthermia, sweating, palpitation, the elevation of blood pressure, convulsions, an increase in muscle tension, tremors, and muscular incoordination and at a medium dose of 100–200 µg *per os*, it induce psychotic-like state. In vulnerable subjects, LSD may induce a real psychosis which includes panic, paranoia and distrust, suspicious feelings or delusions of grandeur, confusion, impairment of reasoning, regret, depression, loneliness and/or somatic discomfort, all of which can be of monumental proportions. And at high doses they activate the dopaminergic system, producing psychosis and similar effects.[52]

Amphetamines

Amphetamines are man-made chemicals which resemble many naturally occurring substances and had great impact on 20th century and still are in therapeutic use. It acts as appetite suppressants to counteract obesity and in the treatment of children suffering from ADHD.[52] Amphetamine is now a days enjoying a resurgence of popularity around the world as a recreational drug which account for the widespread domestic synthesis of the drug. In many domains, amphetamine has surpassed cocaine as the stimulant drug of choice among users.[53] These drugs were earlier prescribed for abolition of fatigue and to suppress appetite. But due to its abuse potential, it's therapeutically use is highly restricted these days.[37]

It has stimulant action to CNS by increasing the dopamine concentrations in the synaptic cleft. When compared to cocaine, which stimulates CNS by blocking the reuptake of dopamine into the presynaptic neuron, the amphetamines stimulate presynaptic production and release of dopamine into the cleft.[45]

High doses of amphetamine can cause temporary psychosis which resembles schizophrenia. This drug induced and schizophrenic psychosis is caused due to the excessive release of the chemical messenger dopamine in the brain.[54]

Pathophysiology of Development of Addiction

The pathophysiology of addictives are as shown in Figure 3. Addiction may be regarded as the disease of the brain reward system which is closely related to the system of emotional arousal located in limbic structures of brain. The prime neurotransmitter involved in the reward is dopamine, but other monoamines and acetylcholine may also take part.[55]

Drug's neurochemical actions arising due to repeated drug use produce positive reinforcing effects, progressively leading to neurobiological changes in the brain reward circuits and behaviors characteristic of addiction such as tolerance, sensitization, dependence, withdrawal, and craving.[3]

Mechanism of Addictive Drugs[5]

As shown in Figure 2, the addictive drugs may mimic, block or increase the natural transmitters leading to drug dependency.

a. Mimicking or substituting the natural transmitters as
   - Alcohol-GABA-A/endorphin
   - Opioids-endorphin/encephalin
   - Cannabis-anandamide
   - LSD-5-HT
   - BDZs-GABA-A

b. Blocking the natural transmitters as
   - Alcohol and barbiturates-glutamate

c. Increasing endogenous transmitter release as
   - Cocaine-dopamine
   - Amphetamine-dopamine

Method to Diagnose Addiction

Following examination helps diagnosis of drug abuse.[6]

- Record blood pressure
- Pulse rate
- Temperature
- Pupil size
- Pupillary reaction towards light
- Glasgow coma scale
- Romberg's test
- Orientation of time/person/place
- Coordination
- Gait
- Tremors at rest
- Speech
- Auscultation of chest
- Rhinorrhea
- Gooseflesh etc.

Complications of Drug Abuse[5]

1. Medical complications: Malnutrition, pulmonary embolism, dental decay, self-neglect, thrombophlebitis, septicemia/cellulitis, psychiatric complications, and even death
2. Social complications: Social isolation or aloofness, antisocial behavior, violence, crime or theft.

Legal Provisions to Encounter Drug Abuse in India

India has exercised various statutory control over narcotic drugs through a number of Central and State enactments and its approach towards Narcotic Drugs and Psychotropic

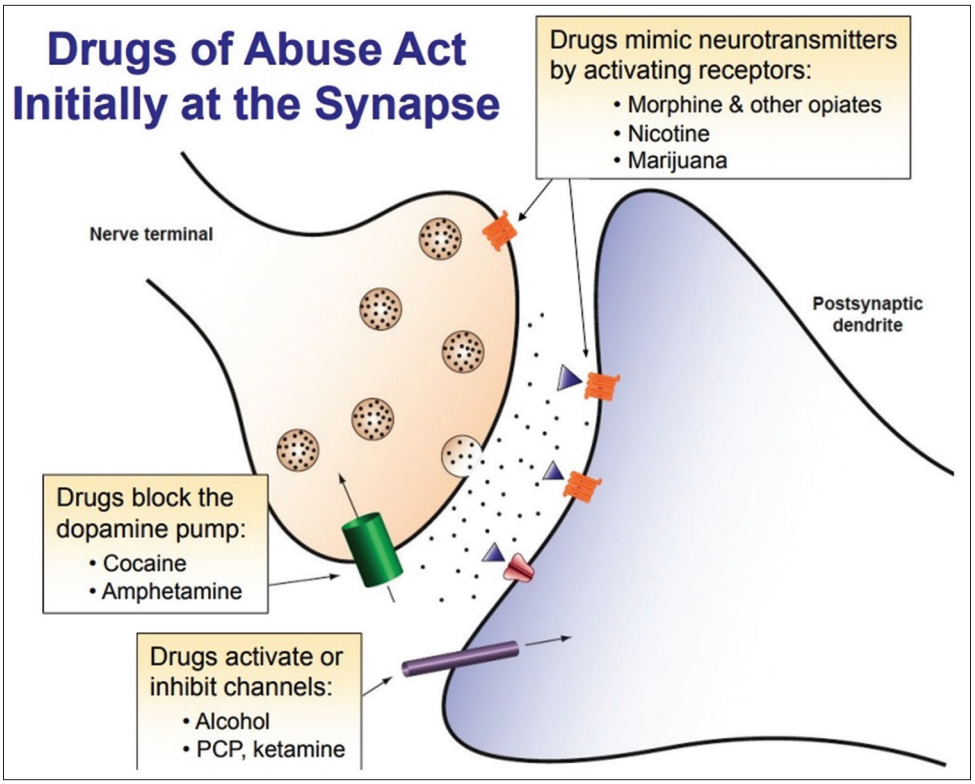

Figure 2: Pathophysiology of various addictive drugs[56]

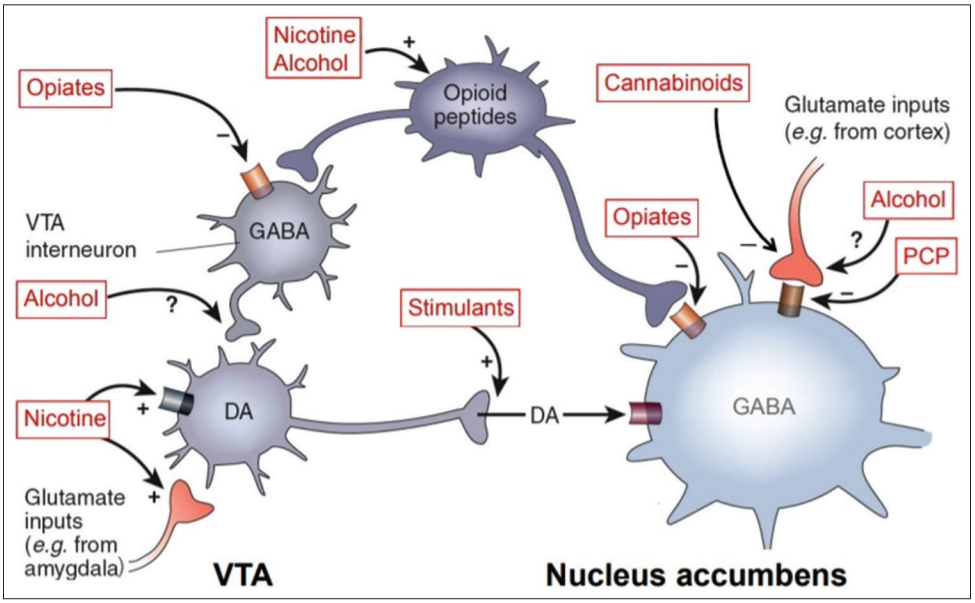

Figure 3: Mode of action of addictive[57]

Substances is enshrined in Article 47 of the Constitution of India which instructs that the "State shall endeavor to bring about prohibition of the consumption except for medicinal purposes of intoxicating drinks and of drugs which are injurious to health."[1]

Services offered for De-addiction in India is through the government, private, voluntary and the non-governmental organization (NGO) sectors. The components of the services to the substance using population involving the pharmacotherapy, psychotherapy and rehabilitation services, and service provision models through inpatient, outpatient and community settings.[57]

The statutory control over narcotic drugs was exercised in India through a number of Central and State enactments such as the opium Act, 1857, the Opium Act, 1878 and the Dangerous Drugs Act, 1930.[1]

NDPS Act came into existence on 14 November 1985 by Parliament of India is made with the purpose to control cultivation, manufacture, transport, distribution, export, import and use of Narcotic Drugs, and Psychotropic Substances.[58] This act bans around 200 psychotropic substances and hence not available over the counter for any walk-in individual. Violation of this law may result in punishment including rigorous imprisonment or fine or both depending on the harshness of the case.[59]

As per this act penalty is categorized into 2:

- Rigorous imprisonment up to 1 year or fine up to Rs. 20,000 or both in case of consumption of cocaine, Morphine and Heroin
- Imprisonment up to 6 months or fine up to Rs. 10,000 or both in case of other drugs.[58]

MSJE (Ministry of Social Justice and Empowerment) works for prevention of alcoholism and substance abuse since 1985–86 by creating awareness and educate people about the ill-effects of alcoholism and substance abuse. The main objectives of MSJE are identification, motivation, counseling, de-addiction, rehabilitation of drug dependent persons, training, and capacity building of the service providers.[58]

The narcotics control bureau was set up by the Central Government in 1986 with the broad remit to coordinate drug law enforcement nationally.[1]

DISCUSSION

Around 40 million people are regularly abusing drugs throughout the world. The prevalence rate of substance abuse is to be around 20–40% among students from various streams including the medical field. Among all the additives alcohol and tobacco are the most common. In India around 5–6 lakhs people are dependent.[1]

The critical review of the available data revealed that, nearly 10 different types of addictive drugs are used currently. Alcohol and tobacco are the most common additives followed by caffeine, cannabis, opioids, cocaine, antidepressants, barbiturates, and amphetamines.[2,28] The availability of alcohol and tobacco is free and no major legal restrictions are involved in consumption of alcohol and tobacco may be the reason for its more use. The majority of users are from adolescent age or students. This may be due to the, influence of social media, inquisitiveness about the addictive, peer pressure, false beliefs to relive the stress, and fantasy feeling about the drug. Even though both sexes are involved prevalence rate in India is more in males may be due to social acceptance and trend is favorable for male in India.

Addiction may be regarded as the disease of the brain reward system which is closely related to the system of emotional arousal located in limbic structures of brain. Drug's neurochemical actions arising due to repeated drug use produce positive reinforcing effects, progressively leading to neurobiological changes in the brain reward circuits and behaviors characteristic of addiction such as tolerance, sensitization, dependence, withdrawal and craving, unsuccessful attempts or desire to control use, considerable time spent obtaining the substance, reduction of social and occupational activities due to abuse, continued use of a substance despite physical or psychological problems.[1] Development of withdrawal symptoms in the form of anxiety, termers, etc., and craving for the substance abuse is the cardinal and essential symptoms of addiction diagnosis.

The common health issues include tolerance, physical dependence, sensitization, craving, relapse, depression, intense anxiety, hopelessness, helplessness, and irritability. Chronic toxicity due to the substance is another matter of concern.[2,9]

The statutory control over narcotic drugs was exercised in India through a number of Central and State enactments such as the opium Act, 1857, the Opium Act, 1878, and the Dangerous Drugs Act, 1930. But in spite of all these efforts the drug dependence is a major concern for globe.[1]

CONCLUSION

Drug abuse and addiction are affecting the quality of life of people around the world and hence awareness about the health hazards is recommended.

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