

Opiate Addiction

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Article is published in FIMA Year Book 2014- Addiction Medical, Psychosocial and Islamic

Abstract

Drug addiction is rapidly increasing in most parts of the world resulting in escalating healthcare cost, fatalities and serious negative familial and social consequences. The opiate addiction is the most serious form of drug addiction and it is extremely difficult to treat and keep the patient sober.

The article covers the historical perspective, genetic and environmental factors contributing to the addiction behavior and the brain mechanisms for addiction. It will discuss the diagnostic criteria and the current methods of treatment available including use of opiate agonists, opiate partial agonists, opiate antagonists and psycho social treatments.

The article also includes a brief discussion about the current situation related to drug use in the Muslim World and proposes some guidelines for treatment and control of the spread of drug use in the Muslim World.

Keywords: Drug addiction, Opiate use disorders, neurologic mechanisms, causes of addiction, treatment of addiction, history, Islamic perspective.

Introduction

The death of Philip Seymour Hoffman, the brilliant Oscar winning actor, created headline news about mortality due to overdosing on opiates. One of the statements he made created this

renewed interest in this subject when he stated, “if one of us dies of an overdose probably 10 people who were about to won’t.”¹

Opiate dependence is a significant worldwide public health issue. Globally, between 24 and 35 million adults between the ages 15 and 64 years used an illicit opiate in 2010.² Alcohol and illicit drugs are harming millions of people in many countries around the world. Alcohol and drug use account for 5.4% of the world’s annual disease burden. In some Eastern European countries, 16% of the population suffers from “Alcohol use disorder”.³ Some of the most common drugs of abuse are opiates and opioids. Opiates are derived from the poppy seeds and is known as heroin. Opioids are semi synthetic products such as Morphine, Oxycodone, Percocet, Tylox, Oxycontin, Hydrocodone, Vicodin, Tramadol, Ultram, Pentazocine, Talwin and Fentanyl. The heroin is used intravenously, as a smoke or as an inhalant and all opioids are used orally.

According to the USA Centers for Disease Control and Prevention (CDC), 12 million Americans used opiates in 2010 and that every day 100 people die from drug overdoses, 75% of which are caused by prescription opiates. The rate has tripled in the last two decades. There have been more than 17 deaths linked to the possible use of Fentanyl-contaminated heroin in Pittsburgh, Pennsylvania alone from January 24, till March 23, 2014. In the first two weeks of January, there were 22 such deaths reported in the state of Rhode Island due to heroin overdose. Heroin is always an extremely intoxicating drug of abuse with a wide array of risks including overdose and increased exposure to Hepatitis C and HIV/AIDS and other infectious diseases. It often contains other ingredients which render it potentially more harmful or in some cases deadly.⁴ Opiates become more dangerous when mixed with benzodiazepines and can be fatal.

In 2009, slightly over 120 million visits were made to the emergency departments in general hospitals in the United States and at least 4.5 million of these visits were drug related. Drug-related emergency department visits have increased by over 80 percent since 2004. This increase primarily reflects greater numbers of medical emergencies associated with adverse reactions, accidental drug ingestions, and misuse or abuse of prescription drugs and over-the-counter medications.⁵

Countries around the world spend billions of dollars fighting drugs and treating and rehabilitating those addicted. In addition to personal and social problems, alcohol, drug use and

other addictions lead to criminal behavior. Hundreds of thousands of individuals are arrested for possession and /or sales of drugs, or for committing crime to obtain them. Drug intoxication results in traffic accidents which may cause fatalities. One-third of AIDS cases occur in IV drug users and children are born with AIDS to the female drug users.

What is Addiction?

Addiction is an obsessive and compulsive behavior which includes taking drugs (alcohol, opiates and other drugs), engaging in gambling, computers and being pre-occupied with persistent sexual thoughts and pornography in spite of negative consequences, which influence health, relationships and work. In other words, addiction has many forms; some of them are related to substances while the others are related to psychological dependence on behaviors. The addiction alters the brain's function and structures affecting mood, perception and consciousness leading to physical, psychological and psycho-social problems.

Addiction is a primary, chronic disease of brain's reward, motivation, memory and related circuitry. Addiction affects neurotransmission and interactions within reward structures of the brain, including the nucleus accumbens, anterior cingulate cortex, basal forebrain and amygdala, such that motivational hierarchies are altered and addictive behaviors, which may or may not include alcohol and other drug use, supplant healthy, self-care related behaviors. Addiction also affects neurotransmission and interactions between cortical and hippocampal circuits and brain reward structures, such that the memory of previous exposures to rewards (such as food, sex, alcohol and other drugs) leads to biological and behavioral responses to external cues, in turn triggering craving and/or engagement in addictive behaviors.⁶

Historical Perspective

Contrary to common belief, the contemporary drug problems are not new. In fact, the use of psychotropic substances seems to be an almost universal phenomenon which has long been a great social concern. Today, there are only a few isolated societies in which psychoactive substances are not used. It is stated that the very desire to alter consciousness, whether by drugs or some other means "is an innate, normal drive analogous to hunger or the sexual drive." Blum identified only four out of 247 cultures where people do not use any substance which alters the

mind. The only people without a traditional intoxicant are the Eskimos, “who had the misfortune to be unable to grow anything and had to wait for white men to bring them alcohol.”⁷⁻⁹

Human beings have always had a desire to consume substances that make them feel relaxed, stimulated, or euphoric. People started chewing leaves, herbs and other natural products, and they cultivated plants which they used for food, for alleviating pain or recreational purposes. Some of these preparations produced euphoria, and many of these were used in religious rites. The later discovery of fermentation of fruits or juices was closely followed by the production of alcohol. One of the oldest drinks was a juice extracted from Palm trees(Palm toddy) (an incision is made on top of the stem of the tree during the night and the juice is collected early morning)²²; after being left in the sunshine for a few hours, it becomes fermented and gives the same effect as alcohol. It is still commonly used in South Asia. Initially, these drugs were used as natural products and were less harmful. As their potency is increased by distillation and other mechanisms, they become more intoxicating and harmful.

In the recorded history from ancient times, alcohol was the only drug mentioned causing problems in the Greek and Roman periods. I am sure there were other drugs used which alter mental conditions causing stimulation, relaxation and euphoria but alcohol was mentioned as causing significant social problems. The earliest recorded example of concern related to alcohol use is the prohibition of its use in the 7th century under the Islamic law based on the commandment of God recorded in the Glorious Qur’an. Muslims are strictly forbidden from using alcohol and other intoxicants which alter consciousness and from an addictive behavior that is gambling.⁶⁴

In the 11th century, the technique of distillation became known in Europe, making it possible to produce more potent alcoholic beverages. In the 16th century, drunkenness was mentioned in England for the first time as a crime, and laws were passed against its use. In European colonies, drunkenness was prominent, but it was not considered a major problem or stigmatized behavior. In England, the consumption of beers and wines, particularly home-brews, was integrated into every aspect of family life.⁷

In the 12th century, the chewing of coca leaves was common in the Inca Empire (South America), mostly in religious and special social functions. The coca plant was also viewed as a divine gift of the Sun God giving energy and euphoria.

In the 14th century, coffee was initially used in Ethiopia for medicinal purposes. The technique of roasting made coffee cheaper and more pleasant to consume. Cultivation and use of coffee expanded into Arabia. In the 15th century, Arabs spread the use of coffee to the Muslim countries. Use of coffee became predominant because wine is prohibited according to Islamic law. Initially coffee was prohibited in Turkey (Middle East) and the coffee houses were closed but the ban was lifted some time later when it was realized that people did not stop drinking coffee. Coffee became a popular drink throughout the Middle East. When coffee was introduced in Europe from Muslim Turkey, it was banned on religious grounds as it was regarded as “infidel’s drink.” Later during the 16th century, its use was sanctioned.

Tobacco chewing and smoking were first observed by Europeans when they landed in America. Later, they cultivated and transported tobacco to Europe due to great financial rewards. Tobacco seeds were transported from Brazil to France and England for cultivation. Within a century, tobacco use became widespread in most European countries.⁷

In 7th century, the opium poppy was introduced in India and China by Arabs, and its use was limited to medicinal purposes. However, its use increased significantly especially in China. Later, British opium traders from India established depots at Canton and Macao and its trade became very profitable. As opium smoking spread and the number of Chinese addicts significantly increased compromising their productivity, the emperor of China prohibited its sale. The effort was initially successful with the destruction of all British opium stock in 1839. However, to protect this trade, Britain declared war on China. The first opium war was from 1839 to 1842 and the second opium war was from 1856 to 1860. China was defeated and the war ended with the Treaty of Nanking, which protected foreign opium traders from Chinese law. It is ironic to see how far the imperialist governments will go to destroy humanity for financial gains. The Maoist revolution ended drug addiction quickly. By 1952, there were no more addicts, no more pushers, and no more drugs smuggled. In only three short years, China went from 70 million drug addicts to none.¹⁰

Cocaine and opiate addiction in the United States became increasingly identified with the underworld and organized crime. In 1914, Congress passed the Harrison Act which regulated and taxed the production, importation and distribution of opiates and coca products. It required all persons authorized to handle or manufacture narcotic drugs to register, pay a fee, and keep a record of the drugs in their possession. The act did not prohibit the supply of opiates to users by registered physicians.

Temperance movements for alcohol use have been active since 1840s by religious organizations and finally the 18th amendment to the USA constitution was passed as “the national prohibition act of 1919” which required licensures for businesses that brew, distill and wholesale alcoholic beverages. The prohibition act and the religious movement of temperance were hoped to curtail the sale and use of alcohol. Unfortunately, underground breweries and distilleries became very popular throughout the country to supply the demand for alcohol. The sale of alcohol in the black market and importation of alcohol from other countries by illegal means became widespread. This resulted in forcing Congress to repeal the 18th amendment by 21st amendment (the 18th amendment is the only constitutional amendment that was repealed by another amendment – the 21st amendment).⁷

Cannabis, opium, coca, tea, coffee, tobacco, and alcohol became the most commonly used substances in the world. Tobacco, alcohol, and caffeine became the major three drugs of addiction in Europe and America. There was an initial opposition for their use but due to their widespread use, these substances were not regarded as drugs of addiction. The use of alcohol in Western countries is well accepted, and no criminal sanctions are imposed on alcohol use. In Muslim countries alcohol is prohibited, however its use along with other drugs has increased considerably during the last decade. Alcohol and tobacco are now recognized as highly addictive drugs causing severe detrimental effects on health.

What Causes Addiction?

Most addictions with drugs such as alcohol and opiates or pleasurable behaviors such as gambling and pornography start as pleasurable or recreational activities, but continued use or engagement in such behavior results in dire consequences. Many addicts do not recognize this at

the early stages. Only when the behavior becomes out of control and causes problems to themselves and others that it is recognized.

There are some controversies about which of the behavioral addictions are validated as true addictions. There has been no agreement among professionals on this controversial issue and more research is needed to have a clear definition and to establish the criteria for diagnosis. The gambling disorder is included in the DSM-V, and requires five criteria to diagnose patients with clinically significant gambling related disorders.¹¹

Most people exhibiting addictive behaviors are emotionally stressed and or unstable and thus psychologically vulnerable to develop dependence on drugs. Research also showed that there are some genetic predispositions for drug dependence. Recent studies of twin families with history of drug abuse indicate that drug abuse is substantially heritable.^{12, 13}

Genes of the dopamine system are likely candidates to harbor risk variants, as dopamine neurotransmission is involved in mediating the rewarding effects of drugs of abuse. These data demonstrate the importance of dopamine gene variants in the risk for opioid dependence and highlight a functional polymorphism that warrants further study.¹⁴

While genetics plays a role in drug addiction, it is important to recognize that environmental factors also play a significant role in the transmission of this disease. Recent research confirms the role of environmental factors such as the influence of parents and siblings on adolescent drug use. When one member of the family household is using a drug, it places the other members of the family at risk. Socio-economic conditions of the family, neighborhood level of social deprivation also affects the risk for drug abuse, beyond family socio-economic status.^{15, 16}

How drugs influence brain and behavior

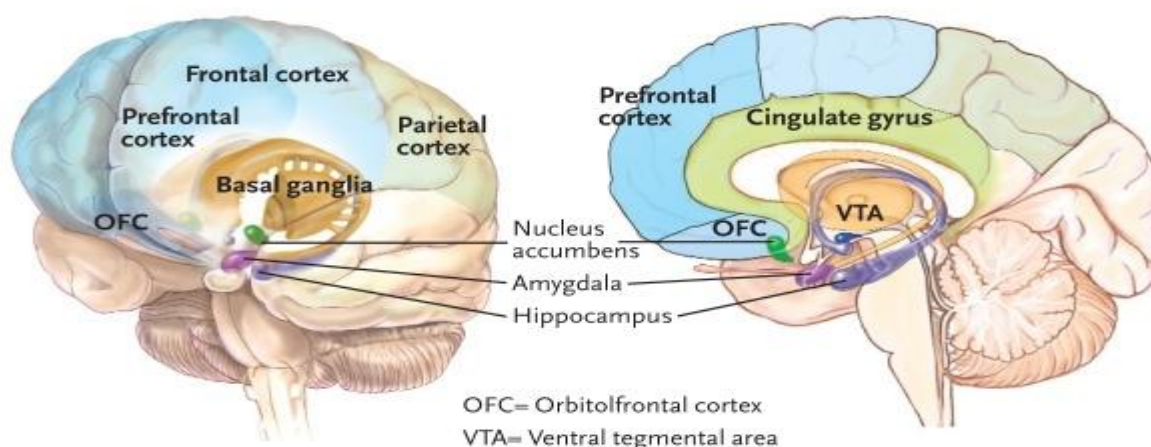
Most drugs of abuse directly or indirectly affect the brain's reward system through the neurotransmitter dopamine. The limbic system contains the brain's reward circuit and through the complex neuronal system links with cerebral cortex and mid brain structures including the hypothalamus, amygdale and other areas which process information resulting in perception of anger, fear, happiness and other emotions. The limbic system is activated by drugs, which results

in mood-altering behavior. These parts of the brain are also responsible for executive functions and decision making. Thus, excessive drug use influences decision making behavior.

Amphetamine and cocaine stimulate the neurons to release large quantities of the neurotransmitter dopamine, resulting in excessive stimulation leading to excitement, pleasurable feelings and euphoria. This pleasurable experience is remembered which results in continuous use of drugs and dependence on drugs.

Brain imaging studies have provided information on the drugs' neurobiological effects, explained the causes and mechanisms of vulnerability to drug abuse, and yielded important insights into abusers' subjective experiences and behaviors, including their struggles in recovery. Recent neuroimaging studies suggest that people living with a drug addiction have considerable decrease in dopamine D2 receptors and in dopamine release, which may contribute to both the rewarding properties of substances and difficulties in abstaining despite adverse consequences. Brain areas such as the prefrontal cortex have been identified as being directly involved in assessing the reward potential of decision-making and vulnerability for relapse. Abnormal hippocampus and anterior cingulate functioning are associated with challenges in the ability to cope with stress, in addition to problems in cognition.¹⁷

Structural MRI provides information on the location, shapes, and sizes of the brain's various regions such as prefrontal cortex, cingulate gyrus and basal ganglia



Sagittal sections of human brain showing Orbitofrontal cortex (OFC) and Ventral tegmental area (VTA)

A structural MRI study found that individuals with a history of abusing drugs have smaller prefrontal lobes. It also showed that chronic substance abusers' frontal lobe tissues contained a lower proportion of white matter than those of matched controls.¹⁸

Researchers have used functional MRI to obtain detailed information about the roles of different brain areas in producing cocaine-induced euphoria and subsequent craving. An influx of cocaine described as a drug rush occurs during a brief period when a set of areas, including the caudate (an area of the basal ganglia), cingulate, and most of the lateral prefrontal cortex showed higher levels of activity. The participants' reports of craving commenced when the euphoria subsided and persisted as long as a different set of brain areas—including the nucleus accumbens (NAc)—remained activated. Positron Emission Tomography (PET) and single-photon emission computerized tomography (Spect) have also shown the presence and actions of drugs of abuse in the brain's reward system with their euphoric properties and their ability to preoccupy addicted individuals. Dopamine flow in these areas is a main determinant of how much pleasure is derived. A PET study also revealed that while methamphetamine temporarily hyper-activates the dopamine system, chronic exposure to the drug reduces the availability of dopamine transporters, which may indicate a loss of dopamine cells.¹⁹

Opiate Dependence

Opiate dependence is a major public health problem, and the illicit use of opiates contributes to the global burden of disease and can result in premature disability and death. Incidence and prevalence of blood borne viruses (e.g., HIV, hepatitis B, and hepatitis C) are higher in injection drug users.²⁰

The United States has seen a significant increase in the illicit use of prescription opiates. Prescriptions for opioid analgesics increased from about 75.5 million to 209.5 million in 10 years. Admissions for opiate drug dependence have increased from approximately 280,000 to 421,000 during a 10 year period (1999-2009).²¹ In a study of Jordanian opiate dependent patients, the major cause of premature death was accidental overdose, along with infectious disease. Moreover, a high prevalence of criminal activity and psychosocial difficulties are also found among Jordanian heroin users.²³

Addiction to opiates can be caused either by the recreational use of opiate based drugs, or it may be caused by prescribed use of the drugs. Opiates create a feeling of euphoria. The initial feeling of euphoria wears off in a short period and a user starts feeling withdrawal symptoms. They then use larger doses to reduce withdrawal symptoms and experience pleasure.

Often times, opiates such as Oxycontin, Oxycodone or morphine are prescribed for the treatment of chronic pain associated with degeneration of bones, arthritis, post surgical pain, cancer and other diseases. Unfortunately, many people who are prescribed opiate painkillers do not realize the risk of opiate addiction and believe that they are under no danger if they take the medication as prescribed by their doctor. Seventy five per cent of high school seniors perceive using heroin once or twice as dangerous, but only 40% perceive similar use of prescription opiates as dangerous²⁴. Unfortunately, indiscriminate use of prescription opiates creates a major problem in the USA. Physicians are prescribing narcotic analgesics without proper justification. Patients are becoming addicted and in some cases they sell the drugs on the streets. While pain management clinics help patients with chronic pain, they are also the major contributors in creating prescription drug dependence. Iatrogenic drug addiction has become a major problem. No strict guidelines have been developed for the use of these highly addictive drugs. Many physicians do not have a protocol about stopping drug use until it is too late. The new regulations and law enforcement efforts have curtailed the supply of prescription drugs and the cost of these drugs in the open market has increased considerably. This has resulted in many users switching to a cheaper drug – heroin.

Environmental factors such as availability of opiates, psychosocial stresses and lack of coping strategies also influence the risk of developing opiate addiction. Traumatic lifetime experiences such as post-traumatic stress disorder may increase the risk for opiate addiction. Weak parental bonds also increase the risk for illicit drug use during adulthood.²⁵

The risk for developing opiate addiction is a complex interaction between genetics, environmental factors, and the pharmacological effects of opiates. Genetic loci associated with opiate self-administration have been identified; and selective disruption of the gene encoding the mu opioid receptor, the principal target of opiates, can eliminate opiate self-administration and conditioned place preference.²⁶ Prolonged opiate use leads to changes in neuronal connections

that result in an inability of the body to cope with or stop pain. Once in the brain, the primary target for abused opiates is the mu opioid receptor. Located throughout the brain, the highest density of this receptor occurs in areas modulating pain and reward (e.g., thalamus, amygdala, anterior cingulate cortex, and striatum). Activation of mu opioid receptors inhibits GABA-mediated dopaminergic neurons in the ventral tegmental area²⁷. Human imaging studies have identified ongoing reductions in dopamine D2 receptor binding potential in opiate addicts and that this reduction correlates with the duration of opiate use.²⁸ The details of how the interaction between genes, environment, and drugs contributes to the development, persistence, and relapse to addiction have yet to be elucidated. This interaction forms the hypothesized foundation for the persistence of addiction vulnerability even in those who have discontinued drug use and indicates that long term relapse prevention strategies need to include both environmental and pharmacological interventions beyond the immediate period of withdrawal.

Diagnostic Criteria for Opioid Dependence

DSM-5 Opioid Use Disorder - Diagnostic Criteria, American Psychiatric Association

In the **DSM-5**, Substance Use Disorder is the singular diagnosis which combines substance abuse and substance dependence. It is defined as such:

A problematic pattern of opioid use leading to clinically significant impairment or distress, as manifested by at least *two* of the following, occurring within a *12-month* period:

- 1) Opioids are often taken in larger amounts or over a longer period than was intended.
- 2) There is a persistent desire or unsuccessful efforts to cut down or control opioid use.
- 3) A great deal of time is spent in activities necessary to obtain the opioid, use the opioid, or recover from its effects.
- 4) Craving, or a strong desire or urge to use opioids.

- 5) Recurrent opioid use resulting in a failure to fulfill major role obligations at work, school, or home.
 - 6) Continued opioid use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids.
 - 7) Important social, occupational, or recreational activities are given up or reduced because of opioid use.
 - 8) Recurrent opioid use in situations in which it is physically hazardous.
 - 9) Opioid use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance.
 - 10) Tolerance, as defined by either of the following:
 - (a) A need for markedly increased amounts of opioids to achieve intoxication or desired effect.
 - (b) A markedly diminished effect with the continued use of the same amount of an opioid.
 - 11) Withdrawal, as manifested by either of the following:
 - (a) The characteristic opioid withdrawal syndrome
 - (b) Presence of either of the following:
 - Cessation of (or reduction in) opioid use that has been heavy and prolonged (i.e., several weeks or longer).
 - Administration of an opioid antagonist after a period of opioid use.
- Three (or more) of the following developing within a minute to several days after the cessation of (or reduction in) opioid use*

Dysphoric mood, nausea or vomiting, muscle aches, lacrimation or rhinorrhea, pupillary dilation, piloerection, sweating, diarrhea, yawning, fever, and insomnia.³⁰

Side Effects of Opiates

Opiate side effects include sedation, dizziness, nausea or vomiting, constipation, and respiratory depression which may lead to death in cases of overdose. People receiving prescriptions from several different providers, and take high daily doses of opiates are more prone to have an overdose.

Treating Opiate Intoxication

Mild to moderate opiate intoxication does not require treatment. Overdose of opioids results in respiratory depression. It requires treatment in an emergency department. Naloxone is usually used to reverse the respiratory depression.

Initial signs of dependence: Dependence is indicated by extreme fatigue, sleeping more than usual, or episodes of “nodding off” during normal activities. Pinpoint and fixed pupils that are unresponsive to changes of light as well as changes in appetite and weight (both will often decrease drastically), loss of interest in usual activities, and constipation .

Common features of opiate addiction: lack of control over drug consumption, exhausting all financial resources, spending more and more time using drugs, denial or thinking that there is no problem and lying or hiding the drug use, using drugs despite known negative consequences such as financial breakdown, effects on physical health, family problems, occupational and legal problems, inability to maintain social relationships, and multiple failed attempts to quit.

Withdrawal symptoms: The main features of opioid withdrawal are nausea, vomiting, diaphoresis, yawning, fatigue, aches and pain, muscle cramps, diarrhea, mydriasis, and piloerection. Other symptoms include chills, irregular heartbeat, itching, restless leg syndrome, flu-like symptoms, diarrhea and weakness. As tolerance goes up, susceptibility to withdrawal

becomes marked. Withdrawal symptoms can be excruciating and include muscle aches, anxiety, sweating and insomnia. Subjective symptoms are much greater than objective signs. Cravings begin 4 to 6 hours after the last dose of short-acting opioids, leading to active drug-seeking behavior. This is followed by anxiety, diaphoresis, and agitation after 8 to 12 hours. Peak withdrawal discomfort is usually experienced after 36 to 72 hours and decreases thereafter.²⁹

Treatment of Opiate Use Disorder

The main objective of treatment is to reduce dependence and issues associated with use. It is important to realize that treatment for opiate addiction requires long-term management. Discontinuing opiates without medical supervision is not only difficult but it is also dangerous. Opiates cause physical changes within the body and the brain that can make quitting cold turkey almost impossible except in prisons or in hospitals under medical supervision. Generally, it is not advisable to quit opiates without at least tapering the drugs off or being under the direct care of a healthcare professional because there is a risk of opiate withdrawal symptoms leading to deadly consequences.

Behavioral interventions alone have extremely poor outcomes, with more than 80% of patients returning to drug use. Most often, a combination of medical intervention and psychological counseling is needed in order to effectively help an individual overcome opiate addiction. Because this addiction is medically recognized as a central nervous system disorder, much attention has been placed on medical intervention and treatment of opiate addiction through medication replacement therapies.

The cravings and withdrawal symptoms associated with quitting opiate use are very strong and difficult to overcome. It is for this reason that medication-assisted treatments are often recommended. These therapies address the changes that drugs have caused in a user's brain. The pharmacotherapy with methadone, buprenorphine and naltrexone combined with psychosocial services are effective in reducing opiate use, dangerous behavior, and criminal activity, while improving the mental health of patients.³¹ Medication-assisted therapies are safe in that they are administered by trained physicians in measured daily doses. They are not taken intravenously

and thus eliminate the risk of HIV and other IV-related diseases; when taken correctly they eliminate the risk of overdose.

Pharmacological Treatments for Opiate Disorder

The three medications approved by the USA Federal drug Administration (FDA) for long-term treatment of opiate dependence are: the opioid agonist methadone, the opioid partial agonist buprenorphine, and the opioid antagonist naltrexone. Oral naltrexone is effective in treating opiate addiction but recent studies using extended release naltrexone injections have shown good results in patients who lack strong motivation.

For many years, methadone, an opioid agonist, was the main pharmacologic treatment option for opioid dependence, but its availability in the United States was limited to licensed programs. The introduction of another opioid agonist in the form of sublingual buprenorphine, which can be prescribed in office-based practices, has greatly expanded access to treatment for individuals with opioid dependence. The opioid antagonist naltrexone has been available as a treatment for opioid dependence for many years, but its use has been limited, particularly in countries where agonist treatment is available.

Sometimes, opiate addiction treatment takes place in hospitals or residential treatment centers. Because of the severity of withdrawal symptoms that are associated with opiate dependence and addiction, opiate addiction requires a longer stay in a residential treatment setting before safely integrating into an outpatient treatment setting.

Methadone and methadone maintenance clinics: Methadone is the oldest of these kinds of treatments and has been used since the 1960s. It must be taken in certified, specialized methadone clinics. Methadone is given each day in sufficient quantity to counteract the withdrawal symptoms. Methadone is a synthetic mu opioid receptor agonist, administered orally in liquid or tablet form. Following oral administration, peak plasma levels are reached within 2–4 hours and the elimination half-life at the steady state is approximately 28 hours, allowing for once daily dosing. Methadone safety is well established. Like other opiate agonists, methadone has the potential to induce respiratory suppression. Recent increases in methadone associated

deaths are primarily related to its minimally regulated use in the treatment of pain and not due to its use in the treatment of opiate dependence.^{32, 33}

Methadone response appears to be dose related with most patients stabilizing at doses between 60 and 120 mg daily. Response is most frequently measured in terms of retention in treatment and discontinuation of opiates, other drugs and improvement of psycho-social functioning. At our clinic, all patients with opiate dependence are initially evaluated by the physician and have a physical examination and laboratory work. Once the diagnosis is established, they receive an initial oral dose of methadone 20-30 mg daily in either tablet or liquid form. The dose is increased between 5 -10 mg daily until it reaches 50 mg. During the initial evaluation, patients are instructed to stop use of opiates, benzodiazepines, and other drugs due to serious side effects. Patients who are using benzodiazepines are required to discontinue the benzodiazepines after consulting with the prescribing physician or gradually discontinuing them in 4 to 6 weeks. All patients are required to consult with a physician to increase the dose of methadone. All patients are seen weekly by a trained counselor who assesses psycho-social functioning and develops a treatment plan to help the patient as needed. The treatment approach is problem-oriented and focuses on achieving well-defined goals. Providing intensive psychosocial services and counseling may improve treatment outcomes.

Methadone maintenance for patients with opiate disorders is effective in decreasing opiate use, psychological and medical morbidity associated with opiates, improving social functioning, reducing the spread of HIV infection and decreasing criminal activity. The most common side effects of methadone are constipation, increased sweating and sexual difficulties.^{34, 35} Retention in methadone treatment clinics and adherence to the treatment regimen are similar to or exceed results for other medically managed diseases such as hypertension, dyslipidemia, and diabetes mellitus.³⁶

When the patient is well stabilized on a specific dose and does not experience any side effects and shows improvement in psychosocial functioning, gradual detoxification can be started. Detoxification period varies from patient to patient depending on the patient's self-confidence, social circumstances, marital stability, occupational stability and coping capabilities. Methadone is an effective means for an addict to discontinue opiates and move forward with a

more productive life. It is much safer and cleaner than opiates and allows people to successfully hold a job and manage other aspects of their lives. A small percentage of patients will continue to use opiates.

Buprenorphine

Buprenorphine is a semi-synthetic mu opioid with weak partial agonist effects. It has less abuse potential than other opioids because the intensity of the rewarding effect is milder and plateaus at higher doses.³⁷ It produces a normalizing effect in individuals with opioid addiction already in withdrawal. Sublingual buprenorphine has a long half-life (24 to 60 hours, mean 37 hours). Suboxone contains 2 active ingredients; buprenorphine and naloxone at the ratio of 4:1. Naloxone is intended to deter individuals from abusing the medication. Naloxone blocks the effect of opiates. While a patient is on Buprenorphine (which contains Naloxone) takes opiates he will not feel any euphoric effect of opiates and therefore it acts as a deterrent for relapse. The intravenous use of opiate gives a surge to the individual and he will not experience this when taking. Therefore, Suboxone must be given after the total discontinuation of the opiate, and the patient is already in withdrawal.

The literature on safety evaluation of buprenorphine maintenance is less developed than that of methadone, but is considered to be quite safe. During maintenance treatment, patients have reduced illicit opiate use but following buprenorphine taper, some patients return to illicit opiate use. In one study comparing heroin addicts to prescription opiate addicts, the heroin addicted patients had more severe addiction and did not do as well with buprenorphine treatment as the less ill prescription opiate dependents. Buprenorphine is a safe treatment with expected side effects of sedation, constipation, headache, nausea or vomiting, and dizziness, and it carries a lower risk of respiratory depression than full opioid agonists. There are rare reports of hepatotoxicity, in addition to a few reports of death when combined with benzodiazepines.^{38, 39}

Buprenorphine, was approved by the FDA in 2002 and can be prescribed by physicians and can be taken in physicians' offices rather than solely in specialized clinics like methadone. It is taken as a tablet or sublingually once a day. For the induction phase, patients can be started on buprenorphine (maximum 8 mg on day 1, as per the drug monograph, in single or divided doses)

12 to 24 hours after the last opioid dose. Dosage can then be adjusted based on clinical symptoms. Patients should be observed medically for at least two hours after the initial dose.⁴⁰ It is well established that moderate to high doses (8 to 16 mg) have significantly higher efficacy. Although the maximum dose recommended by the manufacturer is 24 mg, doses of up to 32 mg have been used in some trials. Buprenorphine's long half-life and slow dissociation from opioid receptors allows for the possibility of less-than-daily dosing.⁴¹

Buprenorphine is an effective detoxification agent for opioid dependence. Although methadone remains a slightly superior substitution treatment, buprenorphine's lower abuse potential and good safety profile make it particularly appealing for family physicians. Those patients that fail to respond are then referred for methadone maintenance. Moderate to high doses (8 to 24 mg) of buprenorphine are usually required. Use of buprenorphine-naloxone in primary care settings is efficacious, safe, and feasible within reasonable time constraints.⁴²

Naltrexone: Naltrexone is an opioid receptor antagonist used in treatment of opioid dependence. It helps patients overcome opioid addiction by blocking the drug's euphoric effects. Naltrexone should not be confused with Naloxone (which is used in emergency cases of opioid overdose) as it can cause acute opioid withdrawal symptoms. Return to opiate use following detoxification is caused by negative reinforcement of environmental stimuli (e.g., cues and social stressors) and if an antagonist prevented the addict from relieving this negative state through opiate use, then the behavior of turning to opiates in these situations would eventually cease. Naltrexone can block the effect of opiates for approximately 24–48 hours after oral dosing. Naltrexone is a useful non-addictive pharmacotherapy for opioid addiction. Naltrexone is non narcotic and non addictive drug. Therefore there is no chance of a patient becoming addicted to Naltrexone whereas Methadone and Suboxone contain opiates which are narcotics and has potential for abuse. In Russia and some Muslim countries (like Jordan) opiate agonists such as Methadone or Suboxone are not approved to be used for treatment of opiate addiction.

While some patients do well with oral Naltrexone, it must be taken daily and a patient whose cravings become overwhelming can take opioids simply by skipping the dose before taking the opioids. A monthly injection of long acting depot naltrexone can be used for patients to motivate themselves to stick to a treatment regime which is very useful. The plasma levels

sufficient to block 25 mg of heroin are approximately 1–2 ng/ml, a level maintained for 21–28 days following 380 mg of the intramuscular extended release formulation.⁴³ In 2010, the FDA approved extended-release injectable naltrexone for the treatment of opioid dependence. This approval was partly based on the results of a trial conducted at 13 addiction treatment centers in Russia where opioid agonist treatment is prohibited. Extended release naltrexone may improve treatment outcomes because non-adherence to daily oral regimens is reduced by delivery of a once monthly injection. Currently, there is limited data regarding the extended release intramuscular injection. A larger trial in Russia retained 53% of patients at 6 months compared to 38% for placebo. Patients receiving extended release naltrexone also had significantly fewer days of illicit opiate use.⁴⁴ Naltrexone should be given after a week of abstinence from opioids due to risk of acute withdrawal. Common side effects are diarrhea and abdominal cramps. High doses may cause liver damage.

Research studies recently showed that a higher retention rate can be achieved with Naltrexone implants. The implants are not currently approved and are not available in USA.⁴⁵

Tramadol versus methadone for treatment of opiate withdrawal

Tramadol may be as effective as methadone in the control of withdrawal and could be considered as a potential substitute for methadone to manage opioid withdrawal. Seventy patients randomly assigned to two groups received either prescribed methadone (60 mg/day) or tramadol (600 mg/day). The withdrawal symptoms of patients were evaluated before and after rapid opiate detoxification. No significant differences existed between the two groups. Dropout rates were similar in both groups. Side effects in the tramadol group were as or less common than in the methadone group except for increased perspiration with Tramadol.⁴⁶

Treatment of opiate dependence in pregnant patients

Opioid use may result in poor nourishment, general medical complications, miscarriage and preterm birth. Fifty percent of the infants born to women with opiate dependence are physiologically dependent on opioids and may experience withdrawal symptoms. The placenta is metabolically active and can increase clearance of both methadone and buprenorphine. Methadone is the standard of care for pregnant women and has been shown to reduce illicit

opioid use, enhance compliance with obstetric care, and improve neonatal outcomes. Since methadone does not have active metabolites, patients may experience early withdrawal and may require increases in or splitting of methadone dose during the second and third trimesters. It is recommended that neither naloxone nor naltrexone be administered during pregnancy thus buprenorphine should be administered as the mono product and naltrexone should be avoided. In a small Cochrane meta-analysis of maintenance treatment in pregnancy, there were no differences in maternal or fetal outcomes between groups taking buprenorphine or methadone. Recent trials have suggested buprenorphine to be superior in terms of fetal outcomes, with less severe neonatal abstinence syndrome.⁴⁷⁻⁴⁹

Psychosocial Treatment of Opiate Use Disorder

Individuals with substance use disorder are often ambivalent about giving up their habit. They deny and minimize the negative consequences of their behavior. They struggle with the emergence of cravings and thoughts about using the drugs. Other stresses such as influence of friends and family members who are using drugs, unemployment, hopelessness, despair and persistent pain make the individual more vulnerable to relapse. They need supportive therapy and guidance to strengthen their coping mechanism. Psychosocial treatment for opiate use disorder helps in bringing about better patients' behavior, thought process and social functioning. The primary goal of this treatment is enhancing motivation to stop drugs, teaching coping with stress, changing reinforcement contingencies, fostering management of pain effects and enhancing social support and inter-personal functioning. Sustaining motivation is required to forgo the rewards of substance use, to tolerate the discomfort of withdrawal symptoms and to cope with the cravings. Coping skills are required to manage and avoid situations that place the individual at risk of relapse. It is reported that successful improvement occurred in patients receiving both opiate agonists (methadone or suboxone) treatments as well as psychosocial treatment services.³⁴

Drug Rehabilitation

Some people do not want to go with medication-assisted therapy and therefore, do not wish to take part in a methadone maintenance program. For those who decide not to quit cold

turkey but also not to take part in a medication replacement program, drug rehab is an option. Drug rehab involves a combination of medical intervention, monitoring, peer support and counseling to effectively help patients overcome opiate addiction. Many drug rehabilitation programs do utilize methadone maintenance or Suboxone for a short period but most provide alternatives that are also effective at helping patients get past the strongholds of opiate addiction and move on with their lives.

There are several different kinds of drug rehabilitation facilities, and the one that works for a certain individual may not work for another. The main difference in programs is that in some facilities housing is provided. These facilities are called residential centers, and they provide around the clock care, daily counseling in either one-on-one, group settings or both. They are usually more costly than the alternative outpatient programs and usually require people to leave their job, family, and other parts of their lives for the duration of treatment.

Is Addiction Primarily a Brain Disease??

There is no single theory or approach that can offer a complete explanation for the existence of any social problem. The view of addiction as primarily a brain disease disregards the extensive body of research that suggests neurogenetic explanations of mental illness contribute to negative perceptions towards people with mental illness, and substance use problems. The brain disease model implies that addicted individuals are unable to exercise any degree of control over their substance use. This focus on a biological model may bring about unintentional consequences on a person's sense of identity, responsibility, notions of autonomy, illness, and treatment preference.

Addiction consists of interacting biological and psychosocial mechanisms because the mechanism (e.g., the behavior) contributing to addiction involves action within a social system. Every learned action, whether pro-social or anti-social, may be prompted by social conditions such as a lack of resources, conflicts, social norms, peer pressure, an underlying drive (cravings similar to hunger and sex drive) or a combination of these factors. Factors such as drug availability within the environment can increase craving and consequently, the vulnerability for relapse.

It is believed that laws and policies that are lenient to substance use are linked with greater prevalence of use and criminal activity. However, research findings have not confirmed this claim. In one study comparing cannabis use in San Francisco (where cannabis is criminalized) and Amsterdam (de-facto decriminalization), there was no evidence to support claims that criminalization laws reduce use or that decriminalization increases use. In fact, San Francisco reported a higher cannabis use rate than Amsterdam.⁵⁰ Similarly tobacco Smoking has become less acceptable as a normative method of social interaction due to the medical interventions for smoking cessation as well as social and public health efforts to curtail smoking behavior. It shows that social and public health efforts in curtailing the smoking behavior are more effective than laws prohibiting the smoking.

Drug use is a pleasure-oriented desire and continued medicalization of addiction will obviate all responsibility for behaviors associated with drug use. The opinion that people with addictions lack decision-making capacity is supported by research in both addiction neuroscience and the neuroscience of decision-making. Substance use influences voluntary brain mechanisms and renders individuals incapable of making rational decisions. The brain responds to particular social cues that may provide instant pleasure. Brain systems that moderate feeling, memory, cognition, and engage the individual with the world influence the decision to consume or not consume a drug, or participate in a specific behavior or series of actions. The degrees in which self-control is exerted, free choice is realized and desired outcomes achieved are dependent on these complex interacting bio-psycho-social systems. The complex combination of biological, psycho-social and systemic factors may explain why it is so difficult for some individuals to refuse or stop consuming illicit drugs in the face of increasingly negative consequences⁵¹ There is no question that the addictive behavior is genetically determined and mediated by neurotransmitters which promotes “reward behavior”. However in my opinion the humans are capable of resisting genetic predispositions which may lead to negative consequences. Our experience with treatment of alcohol addiction shows that psychosocial interventions including spirituality play a significant role in overcoming this problem.

The current situation of drug use in Muslim world

Alcohol is forbidden in the Muslim world, but the alcohol consumption has nearly doubled across the Islamic world in the last decade. The French newspaper *Le Monde* reported that between 2005 and 2010, the average consumption of alcohol by the French dropped from 104.2 liters of alcohol per year to 96.7, while in the same period in the Middle East and Africa it increased by 25%. In countries like Iran, Saudi Arabia, Libya and Pakistan where alcohol is legally banned, drinking is still commonplace.^{52,53}

Contrary to the Islamic teaching, unfortunately Muslims are heavily involved in planting, harvesting, refinement, smuggling and distributing heroin and cannabis to the Western countries. Morocco is the largest cannabis exporter to the Europe through Spain. Afghanistan, Pakistan and Iran are the major producers and exporters of heroin. In 2007, Afghanistan produced an extraordinary 8,200 tons of opium (34% more than in 2006), becoming practically the exclusive supplier of the world's deadliest drug (93% of the global opiates' market).⁵⁴ Taliban initially opposed the production of heroin, but they realized that these narcotics provided an invaluable source of income, and they supported its production. They argued that it is permissible because it is consumed by non-believers in the West. Islam does not permit the production and sale of narcotics for Muslims or non-Muslims.

According to *United Nations Office on Drugs and Crime* (UNODC) in 2009, Afghanistan has around one million heroin and opium addicts aged between 15 and 64 years out of a population of 30 million, making it the world's top user per capita. Sixty thousand women in Afghanistan regularly take illegal drugs. HIV epidemic among injection drug users increased from 3% (2005), to 7% average in three main cities (2009). Iran has 1.2 million "drug users," and 2.26 percent of the population aged between 15 and 64 are addicted to opiate. In 1979, Pakistan has no heroin addicts but 20 years later, there were 5 million addicts. In 2011, nearly six percent - or 6.4 million adults used drugs. Most of the heroin in Europe is transported via Turkey. British Muslims are also heavily involved in drug use and the sale of the drugs. These young men were seldom educated in understanding and respecting the Islamic values or the dangers of drug use. In United Arab Emirates, alcohol and prescription-drug use has been on the rise for the past 10 years and Tramadol, a painkiller similar to opiates such as morphine, has been a commonly prescribed drug of addiction. Community surveys conducted in Dubai and al-Ain, United Arab Emirates have further confirmed a high prevalence of drug disorders.⁵⁵⁻⁵⁸

In Saudi Arabia, amphetamine abuse is most prevalent. Saudi authorities confiscated 12 metric tons of amphetamine (the world drug report in 2010 UNODC. Professor Jallal Toufiq, founder of the Middle East and North Africa “Harm Reduction Association,” told the USA Cable News Network (CNN): There is a worsening of the drug situation in the whole region. However, there is a void in terms of data and information. In many Muslim countries, there is a lack of political willingness to accept that a drug problem exists. People just do not want to deal with this problem. Peer pressure is a significant factor influencing the young people to use the drugs. Saudi Arabia has strict laws for drug importation and sale (death penalty). However, so far, not enough attention is given to education or treatment.⁵⁹

The incidence of alcohol and drug use among Muslims is gradually increasing in USA, but it has not reached the same level as among non-Muslims. Strict religious prohibition against the drugs plays a major role in curtailing the drug seeking and using behavior. The exact data about the Muslim minorities' drug use is not available as data is not collected based on religious preferences. The actual incidence may be much higher than observed as there is denial by addicts and their family members. They tend to minimize the issue until it is too late. Even if the family members are aware of the problem they do not talk about it. They do not seek help due to shame and guilt, and the fear that the problem will become known in the community. Alcohol use is relatively more common than the use of other drugs.

Islamic Perspective

Shari`ah (Islamic Law) established in the 7th century based on Qur’anic commandment. The warning against using intoxicants was revealed by Allah (ﷻ) and was gradually introduced to the people until the total prohibition was declared. Allah (ﷻ) says,

*“They ask you (O’ Muhammad) about khamr (alcohol) and gambling. Say: ‘In them there is great sin, and some profit, for men, but sin is greater than the profit’”*⁶²

The prophet Muhammad ﷺ said there is a prohibition of Khamr, which may be made from the juice of grapes, dried dates, unripe dates, raisins and other things that intoxicate.⁶³

Islam stops the wrong behavior before its inception so that it will not become a major problem. By declaring that *Khamr* is prohibited, taking intoxicants became a major sin and for a strong believer, this commandment serves as a preventive measure.

People who are addicted to alcohol, opioid and other substances must seek medical and psychological treatment, but they can also get the benefit from spiritual guidance. It is a responsibility of the Muslim community to support and help persons who need treatment for addiction rather than stigmatizing or out casting them. These patients also require guidance in improving their social relationships, getting employment and gaining respect in the community.

As discussed earlier, there are multiple factors, which may cause addictive behavior. Current research points out that there is a genetic predisposition for addiction. However, an individual has a capacity to control these tendencies. Sexual desire is genetically determined and controlled by neuronal and hormonal discharges. In spite of this, an individual should have full control on the expression and fulfillment of the sexual desires. Similarly, an individual can control the desire to take drugs, although there may be genetic predisposition.

According to Islamic beliefs, the human soul is composed of three elements:

- 1) *Al-Nafs al-Ammarah* (soul commanding of evil or evil-inciting soul)
- 2) *Al-Nafs al-Lawwamah* (self-reproaching soul)
- 3) *Al-Nafs al-Mutma' innah* (tranquil, peaceful soul)

The goal of every Muslim is to be aware of the stage of the development of his or her own soul and discipline himself in obedience of God. He / She must strive to control *al-Nafs al-Ammarah* and achieve *al-Nafs al-Mutma' innah*.⁶⁰

Freud described human's basic instinctual drives (id), human's perceptual, intellectual-cognitive, and executive functions (ego) and human's capability of controlling self desires, reflecting social standards learned from parents, culture and religion (super ego) as parts of the personality structure. 'id' is primarily an instinctual desire, and the 'ego' represents the self, and it mediates between the demands of primitive instinctual drives (id) and internalized parental and social prohibitions (super ego). Super ego is associated with ethics, values and self-critical assessment.

It is influenced by parents, teachers and the religious beliefs. This is the part of conscience development. The hunger, sexual derives, etc. are genetically determined and influenced by id. However, the super ego controls or directs its appropriate expression.

There is no question that the desire to use a drug is genetically determined and mediated through the brain's neuronal system. However, humans have the capacity to control and restrain its use. This capacity of restraining is influenced by parenting and religious guidance. The Glorious Qur'an has described these psychological interactions in 6th century in terms of *al-Nafs al-Ammarah*, *al-Nafs al-Lawwamah*, and *al-Nafs al-Mutma'innah*.

Allah (ﷻ) says in the Qur'an:

"O you who believe, intoxicants, gambling, the altars of idols and game of chance are admonitions of the devil; you shall avoid, that you may succeed." ⁶⁴

In overcoming addiction, one needs to feel guilty for allowing one self to be controlled by the lower desires and seek help from Allah (ﷻ) to give him strength to overcome the habit. Allah

(ﷻ) says:

"And be you not like those who forgot Allah. He made them forget their own souls. Such are the rebellious transgressors." ⁶⁵

The solution to the drug problem is not simple. It must be recognized that environment plays a significant role in causing drug addiction. Affluence, easy access to the drugs, permissive environment, and peer pressure are major contributing factors. The Muslim community must be educated about the importance of early upbringing, parental guidance and developing strong religious beliefs, which will help in building a super ego or consciousness (*al-Nafs al-Lawwamah*, the self-reproaching soul). This is necessary to develop a strong ego which will resist temptation (*al-Nafs al-Ammarah*) for drug use and to achieve *al-Nafs al-Mutma'innah*. A strong belief in Allah ﷻ and the respect for *Shari`ah* law as well as use of consciousness in decision making is necessary. A Muslim addict must be encouraged to adopt the Islamic way of life. Educational programs must be developed for middle and high school children informing them about negative consequences of drug use, resisting peer pressure and adopting Islamic way

of life. The most effective strategy is prevention but unfortunately in most countries of the world this strategy is not implemented. Islam provides clear direction for every aspect of life. The Qur'anic legislation concerning the prohibition of using intoxicants gives Islam a distinct place in comparison to other religions.

The treatment of drug addiction must be regarded as a medical treatment and all addicts must be encouraged to seek medical and psychosocial treatment. Islam does not "shame" its believers when they seek treatment, and Allah forgives the shortcomings. The community has the responsibility to support and assist in recovery whenever possible.

The prescription and the dispensing of the narcotics must be reviewed, as the prescription opioid abuse became the most serious problem in the world today. Many young men do not realize that prescription opiates are potentially dangerous drugs.

Abstinence-oriented treatment programs are preferable in Muslim majority countries. The recently introduced anti-opioid medication naltrexone (by injection and possibly as an implant) is effective in blocking the euphoric effects of opioid. The effects of long acting naltrexone last 3-4 weeks and this will be a useful deterrent for opioid use. This medication along with psychosocial support system, guidance to improve the family life and occupation may be the best options of treatment in Muslim majority countries. There is no risk of abuse, dependence and diversion of this drug. The opioid agonists such as methadone and buprenorphine have a risk of abuse, dependence and diversion. Many Muslim governments do consider the use of opioid agonists as *haram* (forbidden) and this must be respected. However, the use of methadone and buprenorphine for opioid drug addiction must be acceptable in Muslim countries where their dispensing is permissible.

For Muslim patients psychotherapy and counseling should focus on spirituality, strong belief in God, asking for forgiveness and mercy. These will increase the hope and give strength to the coping mechanisms. The positive affective status of spiritual experience may affect the brain reward system, and the patient may recognize the new cues for pleasure, redirecting the pleasure reward system to the new religious experiences.⁶¹ Religious guidance can also direct the patient to adopt a healthy lifestyle.

Various Islamic countries have instituted support groups of Alcoholic Anonymous (AA) and Narcotic Anonymous (NA) for patients with addiction. They have modified the ‘twelve steps’ and replaced the word ‘higher power’ with Allah ﷻ. These support groups are also helpful in the recovery of the Muslim patients when presented with Islamic spiritual beliefs. Prayers and *Dhikr* (remembrance of Allah ﷻ) should be incorporated in the treatment regime.

Strict control of drug trafficking, and manufacturing of narcotics and pharmaceutical products containing opioid are absolutely necessary. Close monitoring of prescriptions can avoid iatrogenic dependence. Stigma should be removed, and addicts should be treated as victims and patients rather than criminals. Legal statute should be applied equally to affluent and non-affluent residents of the country.

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