Pharmacotherapies of addiction

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ABSTRACT

Objective: Millions of drug addicts worldwide require proper treatment together with good quality care. This article aims to critically review the psychopharmacology of drug addictions.

Methods: MEDLINE was systematically searched for studies describing drug treatment of addictions. Numerous studies were obtained and grouped according to the drug used to treat addictions.

Results: Although there are many effective antiaddictive drugs in the therapeutic armamentarium of drug addictions, a great number of patients tend to develop poor drug compliance, multiple relapses, and continue to suffer from chronic addictions coupled with negative biopsychosocial consequences.

Conclusion: Aside from enhancing the public awareness of the devastating effects of drug addictions through regular and effective mass media campaigns, scientific efforts should be continued in order to develop new antiaddictive drugs with better clinical profiles for the treatment of patients with addictions.

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Drug addiction, a major public health problem, is conceptualized as a chronic, relapsing brain disorder that adversely affects both drug addicts and the society. In addiction to the development of tolerance, psychological and physical dependence and a specific withdrawal syndrome, drug addiction is also characterized by compulsive drug seeking and use despite an array of negative consequences. However, the significance of tolerance, psychological dependence, and physiological dependence is not at par with compulsive drug seeking and use. Notably, all addictive drugs similarly affect both the biological and the functional dynamics of the brain. Chronic consumption of addictive drugs results in an array of negative psychosocial and biological consequences such as violence and crimes, psychiatric conditions, cancers, liver and heart diseases, acquired immunodeficiency syndrome, and tuberculosis.[1,2] Drug addiction, a heterogeneous brain disease, is etiologically caused by biopsychosocial factors. Cultural factors also contribute considerably to the pathogenesis of drug dependence. Therefore, each individual with drug addiction requires comprehensive assessment, diagnostic evaluation and integrated treatment strategies, which are notably offered by mental health professionals including psychiatrists. However, the psychosocial mechanisms of drug addictions require that the psychiatrists should have additional training in drug addictions and, hence, competent skills[3] to deal with clients with drug problems. Reportedly, an addict goes through several stages that also necessitate different therapeutic approaches including motivation enhancing techniques and steps to maintain long-term improvement without relapses.[4-7] Over the past 2 decades, there have been pharmacological and psychotherapeutic revolutions in addictive therapies in the Western world.[1,5-7] Notably, the problems of drug abuse and addictions are ubiquitous. Nonetheless, there is no study that explored the true magnitude of addiction and its pharmacotherapies particularly in Arabian Gulf

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countries. Therefore, the main objective of this article is to review critically the psychopharmacology of addictions (**Table 1**). This paper will also bridge the information gap among physicians and mental health professionals on addictive drugs and its therapies. This article will also act as a stimulus to the local researchers for conducting studies in addictions in the Kingdom of Saudi Arabia (KSA).

Methods. In addition to manual exploration, the database MEDLINE was searched up to December 2001. First, the term "addiction" was used as a qualifier and combined with "antiaddictive drugs" and "pharmacotherapies". A 2nd search used the words "pharmacotherapies" and "addictions" as qualifiers and combined them with withdrawals, abstinence, relapse, animal models, vaccines, alcohol, opioids, cocaine, cannabis, nicotine, psychostimulants, hallucinogens, and volatile inhalant addictions. All published citations were also cross-referenced for other studies. The initial MEDLINE search yielded numerous peer-reviewed citations published over the past 2 decades. We looked for empirical studies and review articles that involved addicts who received some type of standardized assessment, antiaddictive treatment, and some measure of treatment outcome. Inclusion criteria were broad and allowed 1) a reasonable definition of addiction for the patient group, 2) a pretreatment systematic assessment of patients with addictions, 3) a standardized outcome measure, 4) a clear report on the treatment(s) received and whether treatment was controlled or uncontrolled. The studies were grouped according to the model used to assess addiction psychopathology and effects of pharmacotherapies. We restricted only to the qualitative review of these studies, as our objective was to highlight the new pharmacological developments in addiction generally, so we did not attempt a meta-analytical review. However, it is possible to present a meta-analysis type of review while considering a single addictive drug such as alcohol. In addition, all local addictive research, whether or not involving pharmacotherapies, was critically reviewed.

Table 1 - Medications for treatment of addictions.

Agonists*
methadone
L-α2-acetylmethadol [LAAM]
buprenorphine
nicotine preparations
Antagonists*
naltrexone
naloxone
cyclazocine
mecamylamine
Agonist-Antagonists*
nicotine plus mecamylamine
Anticraving drugs
bupropion
naltrexone
nalmefene
acamprosate
Medications that make intake aversive
disulfiram
silver acetate
Medications that mimic effects
clonidine
lofexidine
Vaccines
morphine antibodies
cocaine antibodies
nicotine antibodies
other stimulants antibodies
Other medications
anxiolytics
antidepressants
stimulants
anorectics
others including antipsychotics
* at specific opioid receptors, namely, mu, delta and kappa

Results. ***General principles.*** The somatic treatment of addictive disorders initially entails the proper management of acute withdrawal symptoms by detoxification. Further, medications are also needed for chronic protracted withdrawal and the maintenance phase of addiction.[8] Finally, addicts usually develop multiple relapses that are attributed to negative affective states, psychosocial cues, and an array of existential stresses. Hence, the prevention of relapses is an important aspect of addictive pharmacotherapies. Notably, there are several methods for detoxifying patients with addictions.[6] It is rather easy to achieve a drug free state in addicted persons, however, long-term maintenance is the most difficult task attributed to multiple relapses caused by aforesaid reasons. Other reasons are dysregulation in several homeostatic mechanisms that readapt when drug taking is discontinued by addicts.[9] Moreover, there are long-lasting biochemical changes in the brain of addicts which, if not reversed by pharmacotherapy, contribute to relapses.[10,11] Similar brain changes are reported in animal models of addiction.[10] Additionally, comorbid psychiatric disorders such as anxiety disorders, depression, personality disorders, and schizophrenia, further complicate the management, prognosis, and outcome of addictive disorders.[12] In this context, psychiatric disorders always require additional drug treatment. Addiction is a chronic brain disease. Therefore, the treatment approaches including drugs based on chronic disease model were also developed for addictive disorders. There is now a large body of research that substantiates the effectiveness of drugs in addictive disorders.[13] The treatment of addiction should address 1) reversing the pathological brain changes caused by prolonged exposure to addictive drugs, and 2) modifying etiological psychosocial factors by psychotherapies. Antiaddictive medications combined with one of the cognitive-behavioral therapies usually achieves better results and outcome in addicts.[14] Several specific drugs are recommended for patients addicted to nicotine, alcohol and opioids. These are used during phases of detoxification, abstinence and maintenance.[8,15] In contrast, no specific medications are available for

patients dependent on over-the-counter (OTC) medications, benzodiazepines and also psychostimulants such as amphetamines and its derivatives, cocaine, caffeine, hallucinogens, cannabis, and volatile solvents. Therefore, only psychosocial approaches are recommended for such addicts. Notably, the treatment of cocaine and amphetamine addiction is a challenging task worldwide.[15] Nonetheless, psychotropics are unspecifically used for aforesaid drug addictions coupled with comorbid psychiatric disorders.[1,8,11,15]

Treatment of specific drug withdrawals. Each addictive drug has its unique withdrawal symptoms and their immediate management is extremely crucial for overall outcome. Therefore, patients dependent on one of the addictive drugs initially need detoxification by suitable medications. Later, they certainly require proper drugs combined with one of the psychotherapies during the long-term maintenance phase in order to prevent future relapses.[16,17] The nonpharmacological modalities may be either cognitive-behavioral therapy or one of these types which include family therapy, group therapy, brief psychotherapy, counselling, and psychoeducation.

Treatment of nicotine withdrawal. The symptoms and signs of nicotine withdrawal are craving for nicotine, irritability, frustration, or anger, anxiety, low concentration, restlessness, bradycardia and increased appetite or weight gain and are coupled with mild to moderate discomfort, which may require low doses of nicotine given by multiple routes. Although most of the smokers develop previously mentioned withdrawal syndrome, many of them do not seek any drug therapy and hence tend to have relapses. However, only a minority of smokers succeed in giving up smoking without any treatment. Therefore, the majority of nicotine addicts require nicotine replacement therapy for months for blocking initial craving and preventing future relapses.[18-20] For more details, readers are referred to the American Psychiatric Association Practice Guideline for the treatment of patients with nicotine dependence.[18]

Treatment of alcohol withdrawal. Unlike nicotine withdrawal, alcohol withdrawal syndrome is potentially life threatening. An early detoxification of patients with uncomplicated alcohol withdrawal symptoms such as coarse tremors of hands, tongue, or eyelids; nausea and vomiting; malaise or weakness; autonomic hyperactivity; anxiety, depressed mood, or irritability; transient hallucinations or illusions, headache; and insomnia is reported to prevent its major complications in terms of trauma and accidents, hallucinosis, seizures, delirium tremens, metabolic derangements, dementia and amnestic syndrome, coma, and death. Reportedly, repeated alcohol withdrawals are accompanied by neuronal sensitization that is coupled with progressive severe withdrawal syndrome.[9,10] Hence, the early management of alcohol withdrawal would reverse sensitization state and lead to recovery from alcoholic addiction. Benzodiazepines are the most effective medications in suppressing alcohol withdrawals.[1] Additionally, the correction of electrolyte imbalance together with vitamin supplements would help in achieving a speedy abstinent state in preparation for a long-term psychosocial and rehabilitation programs.[7,14,21,22] Benzodiazepines are classified into 1) long-acting, and 2) short-acting. The long-acting benzodiazepines such as diazepam, chlordiazepoxide and chlorazepate are recommended in young adults with alcoholism. The short acting benzodiazepines such as oxazepam and lorazepam are preferred among elderly patients with alcoholism. Notably, chlormethiazole is used only in admitted patients with alcoholism,[6] as they develop respiratory depression and coma due to its interaction with alcohol. Further, alcoholics frequently report anxiety and depressive symptoms during the recovery phase and may benefit from anxiolytics and antidepressants. Nevertheless, anxiolytics should be used judiciously as these medications have a great potential for abuse by patients with alcoholism.[23] Notably, approximately 20-30% of alcoholic patients with comorbid mood and other psychiatric disorders get substantial benefits from the use of lithium, selective serotonin reuptake inhibitors (SSRIs), anticonvulsants, and atypical antipsychotics during the maintenance phase.[12,24,25] However, the results of controlled studies were not encouraging because of troublesome adverse effects associated with these medications.[23]

Treatment of opioid withdrawal. Opioid withdrawal is characterized by symptoms such as craving for an opioid; nausea or vomiting; muscle aches; lacrimation or rhinorrhea; pupillary dilation, piloerection, or sweating; diarrhea; yawning; fever; and insomnia. Methadone, a long-acting opioid, is used for detoxifying patients with opioid withdrawal syndrome. In case of legal restriction of methadone use, alternative drugs such as clonidine and lofexidine, which inhibit central adrenergic drive in the locus coeruleus (LC), are partially useful in ameliorating opioid withdrawals. The later medications are reported not to affect muscular pains and insomnia. Clonidine is an α_2-adrenergic agonist and binds to α_2-autoreceptors in the LC activated during opioid withdrawal. However, its use should be restricted to inpatients as clonidine is known to cause hypotension, rebound hypertension and sedation. Further, it should not be combined with antidepressants, which desensitize α_2-autoreceptors nullifying its therapeutic utility. However, a combination of naltrexone and clonidine achieve a rapid amelioration of opioid withdrawal.[23,26] Lofexidine hydrochloride, a clonidine structural analogue and centrally acting α_2-agonist, is also recommended for the management of opiate withdrawals. Lofexidine, available in sustained-release form, has a low incidence of adverse effects including hypotension as compared to clonidine.[15] Lofexidine could be used at home for detoxifying approximately 23% of individuals with stable use of opiates.[27] Buprenorphine is also reported to help better achieve complete detoxification from opiates.[28] Further, a combined use of trazodone-naltrexone versus clonidine-

naltrexone was studied in inpatients taking methadone with fairly good results.[29] Trazodone is a nontricyclic antidepressant, which acts antagonistically both at 5-hydroxytryptamine ($5HT_2$) receptors and alpha-1-adenoreceptors. In a study of detoxification of patients with heroin addiction, Yang and associates also reported good efficacy and safety of a regimen comprising of scopolamine, naltrexone and naloxone.[30] Notably, good results of detoxification of opioid withdrawal are not sustained in patients who opt for methadone or other opioid agonists during both the abstinence and maintenance phase. Conversely, patients who prefer drug free or opioid-antagonist drug regimens along with long-term rehabilitation tremendously benefit from detoxification and long-term improvement persists. As patients with opioid addiction frequently develop relapses requiring repeated detoxification, it is therefore wise to detoxify them in drug free community programs.

Treatment of psychostimulant withdrawals. The withdrawal symptoms of most of the aforementioned psychostimulants are dysphoric mood symptoms (depression, irritability, and anxiety), fatigue, insomnia, hypersomnia, psychomotor agitation, and lack of attention with poor concentration. These withdrawal manifestations often resolve within days without any specific drug treatment. Moreover, no specific drugs are available in the therapeutic armamentarium of most of the psychostimulant addictions. However, a variety of drugs including typical and atypical antipsychotics, SSRIs, and other antidepressants are used nonspecifically for the management of psychostimulants abuse and addiction.[1,6,23,31] Regarding long-term maintenance therapy in particular preventing future relapses, there should be continuing use of antiaddictive drugs coupled with psychosocial approaches.[14,17,32]

Medications used to treat drug dependencies. For the purpose of comprehension, we grouped antiaddictive medications into various categories (**Table 1**). In general, these drugs are used during different treatment phases of addiction. We now summarize briefly the clinical pharmacology of each drug used in the management of drug addictions.

Methadone. A slow-onset opioid agonist, acts on mu opiate receptors. It is long acting and usually given orally as liquid. Methadone prevents both heroin craving and euphoria if a maintained addict takes a dose of opiate. Reward is prevented through the mechanism of tolerance-insensitivity, namely, the tolerance acquired by the use of one drug in a category conveys tolerance to all drugs in that category.[1] The dose of methadone is adjusted to the purity of heroin abused by the individual. It is emphasized that if the dose of opioid is significantly higher than the maintenance dose of methadone, it will override the cross-tolerance effect. One of the advantages of adjusted doses of methadone is that the patients are maintained on methadone without relapses during the maintenance phase for many years. Methadone is coupled with intense withdrawal manifestations as compared to heroin.[33] The half-life of methadone is 24 hours and the usual oral dose is 20-30 mg/day. The dose of methadone should not be escalated more than 40 mg/day. Provided no craving, the patient could engage in productive activities with intact cognition and alertness. The adverse effects of methadone include nausea, vomiting, dizziness, mental clouding, pruritis and allergic urticarial reactions with injectable preparations.[34] Methadone nonspecifically induces release of histamine by degranulation of mast cells that is the probable cause of the urticarial reaction.[35]

L-α_2-acetylmethadol (LAAM). This new compound is used in patients with opiate addiction. Aside from other advantages, it is recommended both for opioid detoxification and maintenance purposes. It is a synthetic mu agonist and has long-acting active metabolites that block the development of withdrawal and craving for more than 72 hours. It is given 2-3 times per week. It is an alternative to the methadone maintenance therapy.[15,36]

Buprenorphine. Buprenorphine is a partial agonist at the mu receptor and an antagonist at the kappa receptor. It has 2 advantages: 1) overdose is rare as its partial agonist property makes it produce limited opiate effects, and 2) it effectively prevents the effects of other opiates such as heroin through its action on mu receptor. The disadvantage of methadone, LAAM and buprenorphine is that they themselves produce dependence. Notably, the withdrawal symptoms from buprenorphine are mild as compared to other agonists.[28] It is further reported that patients taking buprenorphine have less impaired driving skills compared to methadone.[13]

Dextromethorphan. This OTC compound is used for suppressing cough in the pediatric population. It is the D isomer of the codeine analog levorphanol with antitussive properties.[37] It elevates the threshold for coughing through its action on the brain. It has neither analgesic nor addictive effects. It loosely binds to the N-methyl-D-aspartate (NMDA) glutamate receptor and thus attenuates opioid addiction. However, it does not completely cripple the glutamate system, hence leaving the learning and memory processes more or less intact. Reportedly, it has no action on opioid receptors and also no adverse effects such as dysphoria and neurotoxicity.[38] Aside from reversal of morphine tolerance, this drug is found to block cocaine craving in rats.[39] Its mixture with ephedrine and diphenhydramine has a potential for abuse.

Naltrexone and naloxone. Naltrexone is a specific antagonist of mu receptors but has little effect on kappa and delta opiate receptors.[29,30] Unlike naloxone, naltrexone is a long-acting antagonist and has high affinity for opiate receptors. However, it has no effect on cellular events in the brain. Naltrexone, available in sustained-release form[15] and twice as potent as naloxone, is very effective in the treatment of opioid addiction. Naltrexone has also been used effectively in the treatment of alcoholism, especially in relapse

prevention.[40] It also blocks alcohol craving. Alcohol activates the endogenous opiate system in the brain, which is blocked by naltrexone. The adverse effects of naltrexone include elevation of liver enzymes and approximately 10% of patients have nausea and dysphoria. Therefore, laboratory monitoring of hepatic function is required.[40] It is administered orally but can be given parenterally in case of poor compliance. Naloxone is a specific antidote and diagnostic of opiate poisoning.

Cyclazocine and nalmefene. Cyclazocine is a narcotic antagonist. It is used in opioid detoxified patients. Its oral dose is 2 mg twice daily, which is titrated over a period of 2-6 weeks. Only highly motivated patients chose cyclazocine in preference to other available drugs. Nalmefene, a long-acting compound and an opiate receptor antagonist, is reported to reduce relapses in patients with alcoholism.[14] However, this drug is primarily used in opioid overdoses.

Bupropion and other antidepressants. Bupropion, an antidepressant, is often used in patients with depression. However, it has also been recommended for the treatment of nicotine dependence in patients with psychotic disorders such as schizophrenia. This drug, now available in sustained-release form, blocks craving for nicotine.[41] Although the exact mechanism is not known, nicotine and other receptors including dopamine in the brain may mediate this action. Moreover, clinical trials have revealed that bupropion decreases nicotine relapses, maintains abstinent state, and is useful in nicotine addicts who even have no depression.[42] Further, bupropion could be combined with a nicotine patch that is used for nicotine detoxification. This double-edge approach comprising of detoxification (nicotine patch) and anticraving effect (bupropion) at the same time is of special value during the maintenance phase. In light of bupropion efficacy both in nicotine addiction and cues-related craving without compulsive drug use, the researchers have criticized the concept of craving for addictive drugs.[41,42] Other antidepressants including nortriptyline, doxepin, tryptophan, imipramine, and fluoxetine are used successfully in nicotine addicts with depression, dysphoria, and post-cessation depression.[18] Likewise, patients with cocaine addiction show substantial improvement with SSRIs, but partial recovery with other antidepressants including desipramine, maprotiline, and trazadone.[43,44] Notably, fluoxetine is shown to have an anticraving effect both in animal experiments and humans abusing alcohol.[44] Cocaine addicts with manifest depression get greater benefit from antidepressant therapy. The assessment of depression in cocaine addicts is important because it complicates the treatment of cocaine addiction[45] and needs additional antidepressant therapy. Haloperidol, an antipsychotic and D_2 receptor antagonist, is reported to reduce cocaine craving induced by drug-cues,[46] but can not be used for long periods due to multiple reasons including development of troublesome tardive dyskinesia.[47]

Nicotine replacement therapies and other medications. Nicotine replacement therapies (NRT) such as nicotine patch, nicotine gum, nicotine nasal spray, nicotine inhalers, nicotine lozenges, and lobeline are used during nicotine withdrawal and maintenance phases. These nicotine preparations are effective in smoking cessation and attenuate nicotine withdrawal symptoms. The NRTs are associated with minor side-effects and have great potential for abuse.[42] However, lobeline, strictly not a replacement therapy, has no potential for abuse and addiction. It is not a nicotine drug but it shares cross-tolerance with nicotine. Other somatic therapies, used in nicotine addiction, are mecamylamine, naltrexone, clonidine, bupropion, silver acetate, benzodiazepines, and β-blockers including metoprolol, oxprenolol, and propranolol.[18,42] Nicotine-mecamylamine as agonist-antagonist combination has been found to be effective in stopping smoking. Anxiolytics associated with abuse potential and marked sedation are not recommended for the treatment of nicotine dependence. However, another anxiolytic, buspirone, an azaperone and partial serotonergic agonist of $5HT_{1a}$, lacks both sedation and potential for abuse and is a promising drug for nicotine addiction.[42] Although the results of several studies of buspirone versus placebo were inconsistent, smoking abstinence rate ranged from 36% to 89%.[48] Notably, smoking cessation has a tranquilizing effect,[49,50] which should be discussed with smokers who have strong wish to quit. Two psychostimulants, amphetamines and methylphenidate having potential for abuse, were used in the treatment of nicotine addiction. Only the later drug attenuated nicotine withdrawal. Two anorectics, phenylpropanolamine and fenfluramine, were used for combating post-cessation hunger and weight gain. But they decreased nicotine withdrawal symptoms and also increased abstinence period.[18,19] A variety of sensory therapies including black paper extract, capsaicin, denicotinized tobacco, flavorings, and denicotinized smoke decreased smoking craving as well as nicotine withdrawal.[18] Other medications including sodium bicarbonate, adrenocorticotrophic hormone (ACTH), anticholinergics, dextrose, and several homeopathic preparations have been used for the treatment of nicotine abuse but these drugs lack controlled trials.[18] For more detailed information on nicotine addiction and its therapies, the readers are referred to many comprehensive sources.[18,19,20,41,42]

Acamprosate. This compound, a structural analog of glutamate, deactivates NMDA receptor ion channels and decreases craving for alcohol.[40] Prolonged use of alcohol results in neuronal hyperexcitibility, which is attenuated by acamprosate.[51] This drug also acts by altering the excitatory amino acid (EAA) receptor gene expression. Acamprosate increases the abstinent period and decreases the duration of alcohol consumption if the patient 'slips' and drinks some amount of alcohol.

Although this drug was designed to treat idiopathic epilepsy, it was effective in alcohol-induced seizures. This medication also prevents relapses in alcohol addicts. This drug, if combined with naltrexone, will further prevent relapses as naltrexone is also known to prevent relapses in alcoholics. Unlike naltrexone, acamprosate has no effect on the endogenous brain opioid system. Further, acamprosate blocks the ability of glutamate to stimulate neuronal activity in rats.[1] Glutamate system, linked to long-term learning and memory, is implicated in alcoholic addiction. In a large-scale trial of acamprosate involving 4000 alcoholic subjects, 39% of patients were abstinent after one-year follow-up as compared to 17% of controls.[39] Acamprosate paradoxically activates the glutamate system in the hippocampus and nucleus accumbens. It is possible that neurons in these areas are abnormally quiet during alcohol withdrawal and this drug activates them to reduce withdrawal symptoms likely to trigger craving.[39]

Disulfiram. Disulfiram, a long-acting antidipsotropic, is used in the long-term management of alcohol dependence. It blocks the metabolism of alcohol by inhibiting hepatic aldehyde dehydrogenase. Thus, there is accumulation of acetaldehyde causing an aversive reaction that is characterized by nausea, vomiting, dizziness, and headache. This flushing reaction discourages patients to take alcohol. Its oral dose is 250 mg daily in the morning. The characteristics of patients who gain benefit from disulfiram therapy are, 1) old age, 2) social stability, 3) long history of heavy periodic drinking, 4) history of delirium tremens, 5) good motivation, and 6) no history of antidepressant treatment. Alcoholics without those features are unlikely to improve with disulfiram,[52] though it is debatable. One drawback of this therapy is patients' poor adherence, which could be circumvented by legal coercion and behavior therapies such as contracting.[1] Compliance can be checked by blood disulfiram analysis. Disulfiram is contraindicated in pregnant women[52] and in patients with cardiac and liver diseases.[40] Prolonged use of disulfiram may rarely lead to polyneuropathy.

Vaccines. Morphine and cocaine vaccines were developed in animals. Morphine-6-hemisuccinate-BSA (bovine serum albumin) produces antibodies against morphine. The morphine antibodies considerably reduced the desire of rats to self-administer heroin. However, these antibodies were not effective in cocaine abusers. Therefore, cocaine antibodies were developed in animals by administering a stable cocaine conjugate. The cocaine antibodies, effective in reducing the cocaine concentration in the brain, also decreased the rats' desire to self-administer cocaine. Further, cocaine antibodies suppressed the locomotor activity and stereotyped behavior induced by cocaine. However, amphetamine-induced locomotor activity and stereotypes were unaffected by cocaine antibodies. Cocaine antibodies, known to be peripheral blockers, block cocaine uptake into the brain of rodents. These antibodies are safe with immunogenicity.[11] The morphine and cocaine vaccines were not used in human trial, as naltrexone, an opioid receptor blocker, became available for clinical use both in opiate and alcohol abusers.[1,14,15,29] Recently, there is a renewal of interest in the production of morphine, cocaine, nicotine and other psychostimulants antibodies.[53-56]

Table 2 - Nonpharmacotherapies of addiction in general.

Behavior-cognitive therapies
Skills training and relapse prevention
Stimulus control
Aversive therapy
Social support
Contingency management
Cue exposure
Drug fading
Relaxation
Physiological feedback
Self-help material
Educational and supportive groups
Hypnosis
Exercise
Family counselling and family therapy
Motivation enhancing interview
Brief motivational interventions
Counselling
Biofeedback
Interpersonal therapy
Psychodynamic therapy
Others

Nonpsychopharmacological therapies of addictions. Although the primary goal of this article was to review pharmacotherapies of addiction, a brief summary of psychosocial therapies is also provided (**Table 2**). The psychotherapies are not the primary treatment of addictions, however, when combined with drug treatment, these therapies are reported to considerably reduce relapses, enhance the drug compliance, help in the rehabilitation programs, couple with good outcome, and finally better improve the overall quality of life of the addictive population.[1,5-7,14,16-18,21-23] The psychosocial therapies will be reviewed in the near future.

National scenario. There are no epidemiological surveys on drug addiction in KSA. However, the problems of drug addictions are impressively enormous. Therefore, the relevant authorities decided to provide comprehensive treatment services for patients with addictive disorders. As a corollary, 3 Al-Amal Hospitals, one each located in Jeddah, Riyadh and Dammam were established for this humane purpose. Soon after, Al-Qassim Psychiatric Rehabilitation Center was opened in Al-Qassim province. These special health facilities provide in and outpatient services for patients with drug addictions. The services include somatic treatments, psychosocial therapies, and rehabilitation programs. With special reference to medications, methadone and chlormethiazole are

commonly used for detoxification purpose. Nicotine replacement therapies, biofeedback therapy, and acupuncture are available at anti-smoking clinics established in various general hospitals. Although there are anecdotal researches on drug abuse and addiction,[57-71] there is an urgent need to accurately estimate the magnitude of drug addiction in KSA. The epidemiological data would help in planning adequate services for addicts. In brief, these anecdotal researches examined the pattern of drug abuse and psychiatric comorbidity (dual diagnosis) in psychiatric and nonpsychiatric population; explored the knowledge both of medical students and primary care physicians on drug abuse; highlighted the medical complications of drug addictions; described the positive effects of Islam on the prevention of alcoholic addiction; and reviewed the new concepts of drug dependence together with future challenges. Like other provinces, alcohol addiction is the most common form in Al-Qassim region. Unlike other regions, heroin addiction is very rare in this province. Furthermore, cigarette smoking was found to be largely very common among the psychiatric population and artane abusers.

Discussion. To our knowledge, this is the first review on pharmacotherapies of addiction that is mainly directed towards the medical community in Arabian Gulf countries. Drug addiction is a complex biopsychosociocultural problem and etiologically heterogenous brain disease. Hence, the management of drug dependence requires an integrated treatment approach, which also includes pharmacotherapies. Each drug dependency has a specific abstinence syndrome, which requires specific drugs for its management. Drugs are also needed for prophylaxis in order to prevent future relapses, which are frequently reported in the addicted population. To meet these demands, decades of research has developed several drugs and vaccines, for the effective management of drug addictions and prevention of impending relapses. Despite all this, a great majority of drug addicts continue to suffer from adverse consequences of drug addictions in addition to the unwanted effects of antiaddictive drugs. In contrast to huge western literature on pharmacotherapies of drug addiction, there is a dearth of relevant data in Arabian Gulf countries. As such, there are no epidemiological surveys on drug addiction in KSA. However, the problems of drug addictions are impressively enormous and hence comprehensive treatment services for patients with addictive disorders are offered through 4 major hospitals that provide in and outpatient services for patients with drug addictions in KSA. However in Arabian Gulf countries, there is a dearth of data on drug addiction and abuse, despite apparent epidemics of drug addiction problems. It is high time that the researchers explored different aspects of drug addictions that have potentially dangerous and devastating physical, psychological, sociopolitical, economic, and cultural consequences.

In summary, there are a variety of research and evidence-based psychopharmacological medications that could be used cost-effectively in the treatment of patients with addictive disorders. The effectiveness of pharmacotherapy is further improved when these drugs are supplemented with appropriate psychosocial therapies and rehabilitation measures. Further research is needed to develop drugs with better clinical profiles for the management of clients with drug addictions.

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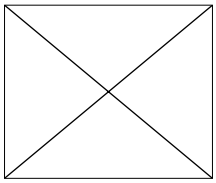

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Abstract

Objectives: To identify the characteristics, nutritional and health status of drug addicts hospitalized for detoxification in Jeddah Al-Amal Hospital. Also, to assess the detoxification therapy and its impact on the nutritional status. Methods: All patients admitted to Jeddah Al-Amal Hospital from January to June 1996 were examined and followed until the end of the detoxification therapy. Results: The majority of drug abusers were between 20 and 34 years and below university education. Unemployment was a common feature among 57.1% of them. Smoking, alcohol consumption and family history of drug and alcohol intake were important contributing factors. Most addicts (63.6%) used heroin intravenously. Depletion of body fat, muscle protein in addition to depleted visceral protein and depressed immune function were prevalent features. Liver damage was reflected by elevated mean aspartate transaminase. High prevalence of hepatitis C and B infections were detected. Human immunodeficiency virus infection, tuberculosis, and gastrointestinal disorders were also reported by some addicts. A significant gain in mean body weight was seen after detoxification therapy and 11.3% of patients experienced symptoms in the form of vomiting, nausea, constipation and loss of appetite. Failure of previous detoxification therapy was reported by 69.1% of patients. Conclusion: Drug addiction attacks the nutritional and health status of individuals who become more prone to various infectious diseases and less productive. Extensive health education programs, directed to all population categories, are crucial to prevent and control the spread of drug abuse. More research is recommended to identify the determinants of drug addiction and evaluate the detoxification therapy.