



# Substance Use, Pharmacotherapy and Impact of Pharmacotherapy for Renal System: A Review

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## Abstract

Increase of the substance abuse, especially narcotic drugs and psychotropic substances, is a major challenge faced by entire region of the world. The use of narcotic drugs and psychotropic substances without medical supervision is associated with significant health risks to the individual who depend on drugs. Therefore, providing of proper treatment services and interventions is important and it must be based on scientific evidence, and match the specific needs of individual patients at a particular phase or severity of their disorder. As a part of that medications can be very helpful in managing and/or treating a variety of drug use disorders and health conditions due to drug use, such as acute intoxication and overdose, withdrawal syndromes, as well as a variety of comorbid disorders. Pharmacological interventions should be administered, when appropriate, alongside psychosocial interventions. Majority of these abusive drugs, medications or their metabolites are excreted through the kidneys. Therefore renal complications including wide range of glomerular, interstitial and vascular diseases leading to acute or chronic renal failure of these drugs are very common. The present review discusses the possible renal complications associated with pharmacotherapy.

**Keywords:** Renal; Pharmacotherapy; Substance

## Introduction

### Global Overview of Drug Abuse

According to the World Drug Report 2022, an estimated 284 million people worldwide aged between 15 -64, had used drug within the year of 2020. It corresponds to approximately 1 in every 18 people in that age group (5.6%) and further it represents a 26% increase on 2010. Further, according to the world drug report 2022, observation made on overall increase in the use of cannabis and in use of methamphetamine in 2020 and use of opioids remain stable in most countries. Stimulant drug can refer to cocaine and

ATS, as well as 'ecstasy' type stimulants, cathinones and some other NPS due to their stimulant effects on the central nervous system. There are some National differences to which stimulant drug is most used. The reason for this differences lie in a complex interplay of drug markets dynamic and other factors [1]. Now a day poly drug use is common phenomenon and it includes a wide spectrum of substance combinations used either concurrently or sequentially. People who use multiple drugs do so for variety of reasons, such as to achieve a cumulative or synergistic effect which increases the overall psychoactive experience, lack of availability or decreases in purity or increases in price of their preferred drugs [2].

## Substances Used to Abuse

Traditionally, most psychoactive drugs were mainly plant based substances, such as cocaine, heroin and cannabis. But due to the increased global trade and travel, the market for plant-based substances that were previously largely confined to specific regions. In recent decades, new psychoactive substances synthesized in illicit laboratories have become more widely available and are consumed in every region [3].

## Opioids

Opioids includes compounds that are extracted from the poppy plant (*Papaver somniferum* L.) as well as semisynthetic compounds such as heroin and synthetic compounds such as fentanyl, and pain relievers available legally by prescription, such as oxycodone, hydrocodone, codeine, morphine sulphate, tramadol and many others with similar properties that can interact with opioid receptors in the brain. Fentanyl is a potent synthetic opioid that is used as a pain reliever and as an anesthetic drug. It is approximately 50-100 times more potent than morphine. Fentanyl in various formulations is on the WHO Model List of Essential Medicines [4].

Opioids have analgesic and sedative effects and commonly used as a pain medication. According to the pharmacological effects, it can cause difficulties with breathing, and overdose which leads to death. Their regular non-medical use, prolonged use, misuse and use without medical supervision can lead to opioid dependence and other health problems. Use of opioid can lead to death due to the effects caused by the opioids on the part of the brain which regulates breathing. Mostly fentanyl and its chemically similar analogues including carfentanil, acetylfentanyl, butyrfentanyl, and furanyl fentanyl strongly associated in deaths from opioid overdose [4].

## Treatment Methods of Drug Use Disorder

The use of narcotic drugs and psychotropic substances without medical supervision is associated with significant health risks to the individual who depend on drugs. Disorders due to drug use comprise a broader category of health conditions that include drug intoxication, withdrawal syndrome and a range of drug-induced mental disorders. In addition to drug use disorders, some individuals who use drugs develop other health conditions that are associated with drug-related health risks and behaviors. People who inject drugs are at high risk of exposure to blood-borne infections such as HIV, as well as to tuberculosis (TB) infection. There is an increased risk of fatal overdose, road traffic and other injuries, cardiovascular and liver problems, violence and suicides. Further, Drug use disorders often take the course of a chronic and relapsing disorder [4]. Various

psychosocial factors may lead the risk of both the initiation to drug use and development of drug use disorders. Family-related factors such as early childhood neglect, child abuse and parental modelling of substance use may contribute towards harmful patterns of drug use and drug dependence. As a societal or community level factors such as extreme poverty, displacement, favorable inputs given by the media towards drug use have been shown to increase the vulnerability to drug use disorders.

Drug use disorders can effectively treated by using a range of Biophysical interventions (pharmacological) and psychosocial interventions. For the management of drug use disorders, aim of the treatment method should apply to improve the health and quality of the life of people with drug use disorders, and ultimate objective should address to help individuals achieve recovery to the extent possible. Specifically, treatment goals should address to improve health, well-being and social functioning of the affected individual by preventing future harms by decreasing the risk of complications and relapse [4]. Treatment services and interventions must be based on scientific evidence, and match the specific needs of individual patients at a particular phase or severity of their disorder. The services include community-based outreach, inpatient and outpatient treatment, medical and psychosocial treatment, long-term residential or community-based treatment or rehabilitation and recovery-support services [4]. Pharmacological interventions can be helpful in managing or treating a variety of drug use disorders and health conditions arise due to drug use, such as withdrawal syndromes, acute intoxication, overdose, and variety of comorbid disorders. Pharmacological interventions should be administered, when appropriate, alongside psychosocial interventions [4].

## Pharmacological Treatment for Opioid

Opioid medicines such as methadone and buprenorphine are used for maintenance treatment of opioid dependence [3]. As a pharmacological treatment for opioid withdrawal, mainly involves in short-term drug treatment with methadone, buprenorphine, or alpha-2 adrenergic agonists such as clonidine or lofexidine. If these medications are not available, another option is to use of decreasing doses of weak opioids, as well as medications to treat the specific symptoms that appear. However, people with opioid dependence generally respond better to long-term opioid agonist treatment because, on its own, detoxification leaves them at greater risk of overdose. Main goal of withdrawal treatment is to stabilize a patient's physical and psychological health condition while managing the symptoms of cessation or reduction of drug use [4]. Therefore, it is necessary to manage withdrawal before starting successive treatment with opioid antagonists. The reason is that recent periods of

abstinence are major risk factors for fatal opioid overdose due to reduced tolerance and the great danger of miscalculating opioid dosage. According to the availability, it is safe and effective to treat opioid detoxification using supervised doses of methadone and buprenorphine over a period of one–two weeks according to the overview of physicians. Low doses of clonidine or lofexidine or gradually reduced weaker opioid medications can use along with the specific medications, to treat the symptoms of opioid withdrawal. If available, naloxone given to people with opioid dependence and their families to take home in case of an opioid overdose. (UNODC-WHO International Standards Treatment Drug Use Disorders)

## Method

This review include the articles published between 2000 and 2023 and search was done on the terms substance use, opioids, pharmacotherapy, methadone, naltrexone, toxicity, poisoning, kidney, renal, and nephrotoxicity through PubMed, Google Scholar.

## Nephrotoxicity of Pharmacological Treatment for Opioid

Methadone is a synthetic mu-opioid receptor agonist widely used to treat opioid dependence and it has pharmacokinetic and pharmacodynamic properties that make it attractive for treating patients with opioid dependence. As other opioid medications, methadone has a possible potential for abuse. Opioids influence renal functions, through various mechanisms may leads or exacerbate a wide range of kidney diseases. Chemical structure of methadone is differing from typical structure of opioids and it administered via oral, intravenous, rectal, subcutaneous, sublingual and intrathecal routs. It has an oral bioavailability of 70 to 90% and reaches peak plasma concentrations within 2–4 hr after ingested. Its analgesic effect appears almost 15 min after a subcutaneous injection and it has a long but variable plasma half-life of 15–55 hr with a mean of approximately 24 hr. Mostly up to 40% of a dose of methadone is eliminated through kidney and it depends on the pH of urine. As a direct or indirect result of exposure to illicit drugs nephrotoxicity can occur and sometimes it cause acute kidney injuries. Acute kidney injuries induced by methadone consumption usually results from rhabdomyolysis. Rhabdomyolysis due to methadone is by means of an increase in the muscular demand for oxygen that augments muscle ischemia. Further, opioids

decrease the renal function by reducing glomerular filtration and methadone can cause pulmonary edema. Methadone intake and narcotic or intravenous (IV) drug abuse have been associated with this renal pathology and methadone substitution have renal lipidosis associated with a positive history of narcotic abuse [5].

The main indication of buprenorphine is the long-term treatment of opioid use disorder [6]. Mainly, buprenorphine use as a medical treatment for medically supervised opioid withdrawal. Evidence from numerous studies has shown buprenorphine to be effective for the treatment of opioid use disorder [6]. According to the Zuin, et al. Was suggested that therapeutic doses of Buprenorphinr can induce life-threatening acute hepatitis and renal failure [7].

## Limitations and Future Works

Most of the studies indicated that pharmacotherapy induced renal failure but it is very important to carry out more intervention and group studies to understand the mechanism, causal factors and consequence of renal toxicity induced by pharmacotherapy for opioid use.

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