

Review Article

Interferences in Addictive Drugs and Ethanol Analysis

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Abstract

Addiction can be defined as an irresistible desire for an individual, an object, or a being, even though it harms the person psychologically or physically. In addiction, after starting to use the substance, negative effects such as the development of tolerance and withdrawal to the substance and changes in emotional states occur. Addiction is a chronic disorder evaluated from genetic, sociocultural, and neurodevelopmental perspectives. Medical laboratories are units where human biological samples or indirectly related samples are examined to evaluate health in humans, prevent, diagnose, monitor diseases, monitor treatment and predict prognosis, report and interpret the results, and provide services including recommendations for further examinations. Laboratory data plays a role in approximately 70% of disease diagnosis, patient treatment, hospitalization and similar decisions. Interference is defined as the effect of a substance present in the sample that alters the correct value of the result for the measured analyte and may lead to misdiagnosis of patients, incorrect treatment, failure to administer required treatments, and unnecessary or inaccurate test orders. This review provides information about the interferences encountered during laboratory analyses of opioids, ethanol, cannabis, cocaine, amphetamines and benzodiazepines.

Keywords: Addiction; Addictive drugs; Ethanol; Interference; Laboratory testing

Introduction

Addiction can be defined as an irresistible desire for an individual, an object, or a being, even though it harms the person psychologically or physically. In addiction, after starting to use the substance, negative effects such as the development of tolerance and withdrawal to the substance and changes in emotional states occur. Addiction is a chronic disorder evaluated from genetic, sociocultural, and

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neurodevelopmental perspectives [1]. The development of addiction is multifactorial. The individual's lack of education and love, anxiety about the future, and difficulty in expressing oneself are among the reasons that affect addiction [2]. While the substances that cause addiction vary, the symptoms that occur in addiction are similar. Withdrawal, development of tolerance to the substance, compulsive substance use, and a strong desire to consume substances are among the symptoms of addiction [3]. Addicted individuals feel an uncontrollable urge to repeat a certain obsessive state and continue this, despite the damage to their mental and physical health or social life [4]. Addiction in individuals can be physiological or psychological. In psychological addiction, the person feels a physical desire for the substance, whereas in physical addiction, substance use becomes a habit, and tolerance and withdrawal symptoms begin to be observed [1]. Substance addiction is a condition characterized by the inability to resist taking a substance even though it causes physical, mental, or social problems [3]. People first use addictive substances to relieve their anxiety, reduce stress, and feel happier, thus benefiting from the relaxing effects of addictive substances. The first use of the addictive substance coincides with periods when the person is tense and stressed. While the anxiety and stress decrease after the first use; the person feels stronger and better [1]. The first use of a substance does not immediately lead to addiction but continued and continuous use of the substance can cause addiction. The genetic characteristics of the person and the addictive potential of the substance lead to differences in the formation of addiction [5]. Addiction-causing substances can reshape neuronal circuits in the brain. The dopaminergic system and its receptors, the serotonergic system and its receptors, the GABAergic system and its receptors, and the glutamatergic system and its receptors play a role in the neurophysiology of addiction [1]. Opioids, alcohol, marijuana, cocaine, amphetamines, and benzodiazepines are among the addictive substances [6].

Medical laboratories are units where human biological samples or indirectly related samples are examined to evaluate health in humans, prevent, diagnose, monitor diseases, monitor treatment and predict prognosis, report and interpret the results, and provide services including recommendations for further examinations [7]. Laboratory data plays a role in approximately 70% of disease diagnosis, patient treatment, hospitalization, and similar decisions [8]. For this reason, the reliability of test results should be ensured in medical laboratories, and necessary precautions should be taken against problems that may be encountered in the pre-analytical, analytical and post-analytical phases [9]. Interference is defined as the effect of a substance present in the sample that alters the correct value of the result for the measured analyte [10]. Interference may threaten the security of the test results [9]. Interference may lead to misdiagnosis of patients, incorrect treatment, failure to administer required treatments, and unnecessary or inaccurate test orders [11]. This review aims to provide information about the interferences encountered during laboratory analyses of opioids, ethanol, cannabis, cocaine, amphetamines and benzodiazepines.

Opiate and Opioids

The term opiates refers to natural or semisynthetic alkaloids that occur naturally from *Papaver somniferum* and exhibit properties similar to the effects of morphine. Compounds such as morphine, codeine, thebaine, papaverine, and noscapine are natural alkaloids. Heroin, buprenorphine, hydrocodone, hydromorphone, oxycodone, and oxycodone compounds are semisynthetic alkaloids [12]. The term opioid refers to all compounds that have an affinity for opioid receptors and have similar pharmacological effects to morphine, although they have different chemical structures [13]. Opiates are among the drugs that have been used for a long time in history and are characterized by their pain-relieving properties. Opiates were synthesized legally and their addictive effects soon came to light. The risks involved in opioid use include misuse by patients, abuse, addiction, and death due to overdose. Genetic and personal characteristics and environmental and familial factors play a role in opioid use disorder [14]. Addiction to opioids can develop quickly. Opioid use can be prescription or non-prescription. Both situations may be considered as an increasing public health problem [15].

Opioids, which have pain-relieving properties, are widely used as analgesics for different types of pain. Short-term repeated use of opioids does not usually result in serious side effects. Opioids are substances with strong addictive potential. Non-medical and repetitive use occurs with addiction. High doses of opioid use can lead to sedation, inhibition of gastrointestinal activity, and respiratory depression, while an opioid overdose can lead to acute brain hypoxia, coma, and death. Heroin, morphine, oxycodone, and fentanyl are drugs in this group [16]. False positive results may occur due to poppy consumption. To prevent this situation; The Substance Abuse and Mental Health Services Administration guidelines recommend using 2000 ng/mL as the cut-off level for opioid immunoassay screening tests. The original cut-off for workplace urine opioid screening was 300 ng/mL, then in 1998, the cut-off was increased to 2000 ng/mL to eliminate false-positive opioid results after consuming products containing poppy seeds [4].

If the morphine concentration in urine exceeds 2000 ng/mL, 6-monoacetyl-morphine (cut-off 10 ng/mL) analysis is performed with immunoassay to distinguish whether the high morphine concentration is due to heroin use or hashish use [17]. The heroin metabolite, 6-mono acetyl-morphine, is an accepted biomarker for detecting heroin abuse [18]. 6-mono acetyl-morphine cannot be detected due to the consumption of food containing poppy seeds [19]. Generally, morphine concentrations are higher than codeine concentrations after consumption of food containing poppy seeds. Morphine-3-glucuronide is detected in urine after both heroin and poppy consumption [19]. Ofloxacin and Pentazocine may also cause false positive results [20].

Ethanol

Ethanol is the psychoactive substance most frequently identified in biological samples obtained [21]. The effects of ethanol vary depending on its concentration in the blood. It has the feature of depressing the central nervous system. Ethanol can cause coma and death depending on the dose [22]. Measurement of blood ethanol levels in toxicology laboratories is common all over the world [23]. Many laboratories use enzymatic methods to measure ethanol in plasma or serum. In enzymatic ethanol analysis, the alcohol dehydrogenase enzyme catalyzes ethanol to acetaldehyde. In this reaction, NAD is reduced to NADH and measured spectrophotometrically at 340 nm.

NADH formed in this reaction is directly proportional to the ethanol concentration in the sample. High lactate dehydrogenase levels may cause false positive results in studies [24]. Cleaning the skin with ethyl alcohol before taking blood from living people affects the analysis results. Ethyl alcohol contamination from gastric fluid may occur when a postmortem blood sample is taken for ethanol analysis [25].

Ethanol is a volatile substance that can be oxidized. The ability to reproduce analytical results by re-analyzing ethanol in biological fluids such as blood and urine after a certain period depends on the method and minimizing the loss of ethanol in the samples [26]. Therefore, after a certain storage period, the type and amount of anticoagulant substance does not matter if the analysis of plasma and whole blood samples is done within 4 hours after the sample is taken. It is sufficient that the anticoagulant substance does not interfere with the ethanol measurement and is in an amount that can prevent clotting. If ethanol analysis must be postponed, some precautions can be taken to prevent changes in the ethanol content of the blood. Sterile blood samples were preserved for 48 hours with a combination of potassium oxalate monohydrate (5 mg/mL blood; 2.7 Fmol/mL) and sodium fluoride (1.5 mg/mL blood; 3.6 Fmol/ml) to prevent changes in the ethanol content they contain and can be stored at up to 5°C [27]. Stability assessments are recommended to ensure that the storage conditions of the samples do not affect the analyte concentration [28].

Cannabis

Cannabis is generally smoked like a cigarette and has a rapid effect on the central nervous system, intense pleasure, and strong reinforcing properties [29]. Cannabis use causes physiological and behavioral changes. Euphoria, change in time perception, lack of concentration, paranoia, learning impairment, and behavioral changes may occur with marijuana use. In addition, dryness of the mouth and throat, vasodilation, decrease in respiratory rate, heart rate, diastolic blood pressure, changes in the endocrine and immune systems, and lung damage are among the other effects of cannabis use [30]. Cross-reactivity occurs between immune methods used in cannabis analysis and Efavirenz [31]. Analytical interference between cannabis and niflumic acid may occur [32]. Some Head-to-Toe Baby Wash products may cause false positive cannabis results [33].

Cocaine

Cocaine is an alkaloid produced biosynthetically by *Erythroxylum coca*. Cocaine grows in the Andes Mountains of South America and the northern regions of the Amazon. For many years, the natives of South America have consumed tea from this plant. By chewing the dried leaves of the plant with ash, they caused the release of cocaine in saliva. Natives used cocaine to alleviate hunger and thirst [34]. Cocaine is a naturally occurring alkaloid that has a local anesthetic effect. It is easily soluble in water and suitable for intravenous use [35]. Benzoylcegonine analysis is performed in immunoassay tests to determine whether there is cocaine in the urine. It is possible to detect this substance in urine within 48-72 hours [13]. False-negative results in cocaine analysis are important in immune methods. In cases of oral high-dose cocaine use, if sufficient time does not pass for benzoylcegonine to reach high doses in the urine, cocaine may not be detected by immunoassay even though it is in high doses, and the patient's test result may be negative even at the concentration where death occurred due to high-dose cocaine use [36]. It has been stated that the drug Levamisole has a disruptive effect on the integrity of the substance in cocaine analysis [37].

Amphetamine

Amphetamine has a stimulating effect on the central nervous system. Its use is legally restricted. It increases performance by increasing euphoria in the person. These properties have made it a frequently used doping substance. In medicine, it is used in the treatment of hyperactivity caused by narcolepsy, obesity, and attention deficit. Amphetamine has a high potential for abuse. Pseudoephedrine, found in cold medicines, may cause false positive results in immunoassays of amphetamine [38]. Additionally, medications containing chlorpromazine, labetalol, metformin, ofloxacin, and promethazine may also cause false positive results [20].

Benzodiazepines

Benzodiazepines potentiate GABA-mediated neural inhibition. They act on ionotropic GABA-A receptors in the central nervous system. Benzodiazepines require GABA but do not directly activate GABA-A receptors [39]. Consumption of efavirenz and sertraline may cause false positive results in benzodiazepine assays [20].

Conclusion

Laboratories are the units that play a role in diagnosing, treating and monitoring patients. The results obtained from the laboratory must be accurate and reliable. Reporting addiction-causing substance analyses as false negatives or false positives may result in inappropriate situations for the patient.

Conflict of Interest

None.

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