Alcohol-medication interactions: A review

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Abstract

Some medications when taken with alcohol cause accumulation of acetaldehyde by inhibiting aldehyde dehydrogenase (ALDH) enzyme. Acetaldehyde causes toxic effects in the body which are characterized by nausea, vomiting, facial flushing, hypotension and tachycardia, symptoms known as disulfiram-like reactions/antabuse effects or acetaldehyde syndrome. Alcohol interacts with many medications, thereby altering the metabolism of medications and/or alcohol. Alcohol dependence is an increasing and pervasive issue in today's world. Withdrawal symptoms of alcohol are because of dependence syndrome and are seen mostly in hospitals. The signs and symptoms of alcohol withdrawal syndrome can be mild to severe. The severe and complicated alcohol withdrawal may manifest as seizures, hallucinations and delirium tremens. This article aims to review various alcohol-medication interactions.

Keywords

Alcohol medications interaction, alcohol withdrawal syndrome, antabuse, disulfiram reaction, fetal alcohol syndrome

Introduction

A minor portion of alcohol gets metabolized immediately in the stomach, and the major portion of alcohol is absorbed into the blood vessels mainly from intestine and stomach. After absorption of alcohol, through portal vein, it is transported to the liver. A portion of the alcohol during its initial passage via liver is metabolized and the remaining portion of alcohol enters in the systemic circulation after leaving from the liver, this metabolism initially during the passage via liver is called as first pass metabolism.

Alcohol is primarily metabolized in the liver. Alcohol is transported to the liver from systemic circulation, where it gets broken down by many enzymes; most important among them are alcohol dehydrogenase (ADH) and cytochrome (CYP) P450. Alcohol is converted into acetaldehyde (toxic substance) with the help of enzyme ADH and acetaldehyde is responsible for various adverse effects. This adverse reaction is the basis of aversion therapy from alcohol, which is used in the treatment of chronic alcoholism, as the aversive drugs inhibit the ADH enzyme and promote the accumulation of acetaldehyde which is manifested by toxic effects such as facial flushing, nausea, vomiting, facial flushing, hypotension, and tachycardia. Alcohol is further metabolized by an enzyme aldehyde dehydrogenase (ALDH) to acetate [Figure 1].

Apart from ADH, the alcohol metabolizing enzyme CYPP450 (also called microsomal ethanol oxidizing system, i.e.) plays an important role in alcohol-medication interactions.

In addition to alcohol, numerous other chemical compounds and drugs such as acetaldehyde, acetaminophen, antibiotics, and barbiturates can also be metabolized by CYP2E1. Thereby, in many interactions between alcohol and medication, an important role has been played by CYPE1. Alcohol-medication interaction that can occur in the liver and involve CYPP450 enzymes are as follows:

1) DRUG $\xrightarrow{\text{CYP}}$ DRUG METABOLITE $\xrightarrow{\text{EXCRETION}}$

CYP activity is relatively low in the absence of alcohol. The medication is metabolized with the help of CYP, and the metabolites are excreted.

2) DRUG $\xrightarrow{\text{CYP}}$ DRUG METABOLITE $\xrightarrow{\text{EXCRETION}}$

After consuming moderate amount of alcohol, alcohol and medication is metabolized by CYP. Alcohol and the medication compete for CYP and results in reduction of medication's metabolism. Thereby, the production and excretion is reduced, which results in higher levels of medication in the body.
In sober chronic heavy drinkers, the activity of CYP is increased, which will result in increase in metabolism of medication through CYP and the level of drug metabolites along with their excretion is increased, thereby results in insufficient medication levels in the body. Furthermore, toxic metabolites of medications can accumulate.

In intoxicated chronic heavy drinkers, the activity of CYP is enhanced, but mostly alcohol makes use of this enzyme for its metabolism, resulting in the reduced metabolism of other drugs which are metabolized by CYP, and hence their metabolite levels and excretion decreases.

**Disulfiram Reaction**

Disulfiram (also known as antabuse) is a drug which is used for aversion therapy from alcohol. This drug acts by inhibiting ALDH enzyme, therefore, promoting the acetaldehyde accumulation which manifests toxic effects, such as facial flushing, nausea, vomiting, hypotension, and tachycardia. These manifestations are called as antabuse effect. This mechanism causes intolerance to alcohol and encourages withdrawal from alcohol.

**Disulfiram-like Reactions**

Some medications, when combined with alcohol, can also inhibit ALDH enzyme and can induce disulfiram-like effects. Certain anti-infectives, as nitroimidazoles, cephalosporins, furazolidone, nilutamide, and chlorpropamide, as well as dermatological preparations such as tacrolimus and pimecrolimus, can produce disulfiram-like reactions.

**Anti-infective drugs**

Disulfiram-like reactions can be caused by cephalosporin, which can be manifested as bronchospasm, tachycardia, vomiting, flushing, and sweating. A group named methylthiotetrazole which is present in cephalosporin resembles the disulfiram structurally, therefore, resulting in accumulation of acetaldehyde due to inhibition of enzyme ALDH.

**Dermatological preparations**

Erythematous flushing can occur after consumption of even a small amount of beer or wine with tacrolimus or pimecrolimus, cream and ointment, respectively.

Disulfiram-like reactions can occur when topical sulfiram is coadministered with alcohol. Although sulfiram is a weak inhibitor of enzyme ALDH in vitro, but it is photo converted to disulfiram, which explains the reason why after the sulfiram topical therapy, there is an adverse reaction to ethanol.

**Others**

Chlorpropamide and Abacavir with concomitant use of alcohol decreases the activity of ALDH.

Nilutamide, an antiandrogen also shows disulfiram-like reactions, manifested as skin rash and hot flashes.

**Management of disulfiram and disulfiram-like reactions**

Adrenaline and noradrenaline (pressor agents) can be given for severe hypotension that will result from a disulfiram-alcohol reaction. In this condition, adrenaline or noradrenaline is used as drugs of choice together with the other treatments which will stabilize hemodynamics and reverse the neurological symptoms. Fomepizole is safe as well as effective treatment for a severe form of disulfiram-alcohol reaction. 1 dose of fomepizole is advised and can be given for severe disulfiram-alcohol reaction with angioedema unresponsive to antihistamines or for hypotension which is unresponsive to the fluid resuscitation.

**Other Alcohol-medications Interactions**

There are two general categories for alcohol-medication interactions: Pharmacokinetic and pharmacodynamic. In pharmacokinetic interactions, the normal metabolism of the medication can be altered directly by the presence of alcohol. This interaction can be of two forms:

- The medication competes with the alcohol for the metabolism by CYPP450 and thereby excretion of the affected medications is delayed.
• The activity of medication-metabolizing CYPs is increased by alcohol; therefore, there is increase in metabolism of the affected medications. The CYPs’ activity is increased because alcohol is not there to compete with CYP, which will increase the rate of elimination of medications that are metabolized by these enzymes.

Most commonly the pharmacodynamic interactions of alcohol and medication take place in the central nervous system (CNS) where the effects of the medication have been altered by alcohol without changing the concentration of medication in the blood. These interactions can be synergistic.

Some Specific Alcohol-medication Interactions

Medications are mostly metabolized by various CYPP450 enzymes; thereby many potential pharmacokinetic interactions with alcohol are observed. Some such interactions are as follows:

Antibiotics

Alcohol absorption in the intestine is increased by the antibiotic erythromycin which accelerates gastric emptying, thereby increasing the blood alcohol levels.

Isoniazid should not be taken with alcohol, as isoniazid causes liver damage, which can be increased by daily intake of alcohol.

Antidepressants

Alcohol increases the sedative effect of antidepressant medications, including selective serotonin reuptake inhibitors, tricyclic antidepressants, atypical antidepressants, and monoamine oxidase inhibitors, through pharmacodynamic interactions.

Barbiturates, benzodiazepines, and antihistamines

Concomitant consumption of alcohol while taking these agents enhances the sedative side effects of these medications synergistically through pharmacodynamic interaction. It is observed that both benzodiazepines and barbiturates along with alcohol can impair the memory.

Histamine H₂ receptor antagonists (H₂RAs)

According to Caballera et al. (1991), ADH activity in the stomach mucosa is reduced by these drugs.

Muscle relaxants

Narcotic-like reactions such as dizziness, agitation, confusion, euphoria, and extreme weakness are seen when muscle relaxant such as carisoprodol, cyclobenzaprine, and baclofen is taken with alcohol.

Anti-inflammatory medications, non-narcotic pain agents and opioids

The risk of toxic effect related to acetaminophen on the liver increases when it interacts with alcohol.

The risk of bleeding from gastric mucosa increases because the alcohol enhances the damaging ability of NSAIDs.

Alcohol exacerbates the sedating effect of opioids. Overdoses of opioids and alcohol can be lethal.

Warfarin

Even small amounts of alcohol can acutely alter the anticoagulant effect.

Alcohol Withdrawal Syndrome

When an individual ceases suddenly or decreases the alcohol intake after chronic consumption, he or she can suffer from alcohol withdrawal syndrome which is a group of signs and symptoms.

Excessive liquor usage and its continuation can cause physical dependency and tolerance. In the absence of alcohol, there is hyperexcitable reaction of the CNS which is the main cause of withdrawal syndrome.

The manifestations of alcohol withdrawal can differ from minor symptoms such as sleep instabilities and nervousness to severe and life-threatening indications such as hallucinations, autonomic unpredictability, and delirium.

Fetal Alcohol Syndrome (FAS)

A distinct dysmorphology is seen in the children who are born to mothers who consume alcohol during pregnancy, this dysmorphology is called as FAS (Lemoine et al., 1968, Jones and Smith, 1973).

A triad of abnormalities is seen in the newborn, which is typical for FAS, includes:

1. CNS dysfunction
2. Cluster of craniofacial abnormalities
3. Pre- and/or post-natal growth stunting.

References
