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Drug alcohol interactions – a review

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Abstract

Chronic Alcoholics can induce interactions with various drugs. Mainly the pharmacokinetic and pharmacodynamics interactions between drugs and alcohol play an important role. Alcohol can cause potentially harmful effects. When people are unaware of known drug interactions, knowingly combine due to negligence, as a tool to facilitate a crime. Most of the drugs involved are benzodiazepines, cocaine, NSAIDs, metronidazole. Caution, awareness, and education about the consequences should be enhanced within the alcoholic abusers who are in medication which can cause potential interactions and secondary effects. The elderly and chronic drug abusers are at risk mostly.

Key Words: Drug-Alcohol, Interactions, Pharmacokinetics, Pharmacodynamics.

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Introduction

Alcohol and drugs can affect each other's absorption, distribution, metabolism, and excretion, drug absorption, gastrointestinal blood flow and drug availability can be altered. Mainly two types of alcohol-medication interactions exist: (1) pharmacokinetic interactions, in which alcohol interferes with the metabolism of the medication, and [2] pharmacodynamic interactions, in which alcohol enhances the effects of the medication, particularly in the central nervous system (e.g., sedation). At the pharmacodynamic level, alcohol can increase the effects of sedatives, certain anxiolytics, sedative antidepressants and antipsychotics, and anticholinergic agents, on performance. Mechanisms of lethal interactions between moderate overdoses of ethanol and anxiolytics / opiates / sedatives are poorly understood. On the other hand, certain peptides, 'nonspecific' stimulants, dopaminergic agents and opiate antagonists can antagonise alcohol-induced inebriation to a significant degree [3]. Alcohol metabolism occurs

mainly in the liver, where in abstainers the alcohol dehydrogenase (ADH) pathway plays the major role. After chronic alcohol consumption, the microsomal ethanol-oxidizing system (MEOS), involving the ethanol-inducible cytochrome P450 2E1, increases in importance with a four- to ten-fold increase in the contribution to alcohol metabolism. Because of the fact that this enzyme system catalyses not only the metabolism of ethanol but also activates a great number of drugs, it is a very common site of alcohol-drug interactions. Only a small amount of alcohol is metabolized outside the liver, mainly in the stomach by gastric ADH, which leads to first-pass metabolism of ethanol. Its significance in alcohol metabolism is reviewed. The only way to prevent severe alcohol-drug interactions is to make medical doctors as well as their patients more aware of these possible secondary effects [6].

Mechanisms of drug interactions with alcohol

Pharmacokinetic and pharmacodynamic factors play vital roles in alcohol-drug interactions. The combination of acute administration of alcohol and many other drugs may result in potentially harmful interactions especially when central nervous system depressants are involved. Often the mechanisms responsible for an adverse

alcohol-drug interaction include inhibition of biotransformation and enhancement of the central depressant effects. Long-term ingestion of alcohol can lead to hepatic enzyme induction and in many instances to enhanced biotransformation of numerous substances, usually resulting in reduced therapeutic effectiveness. Alcohol-drug interactions do not generally result in death, however, there is evidence for a contributory role of alcohol in many drug-related fatalities. The elderly and chronic drug users and abusers are especially at risk.

The groups of drugs significantly interacting with ethanol include

1. The central nervous system depressants (hypnotics, opioids, psychotropic drugs, sedative H₁-antihistamines, anticonvulsants), the combined effects being mostly additive and without any important pharmacokinetic component;
2. Agents provoking antabuse reaction (disulfiram, carbimide etc.);
3. Vasodilating agents, which may lead to unexpected collapse;
4. Antidiabetic drugs (poor control of diabetes; antabuse reaction);
5. Coumarin anticoagulants (unstable kinetics during drinking spells);
6. Non-steroidal anti-inflammatory drugs (gastrointestinal toxicity, central interactions possible);

Few effects of Drugs-Alcohol interactions

Aspirin – aspirin increases gastric emptying, leading to faster alcohol absorption in the small intestine;

Acetaminophen – alcohol enhances drug metabolism into a toxic product – liver damage.

Phenytoin – chronic alcohol consumption induces phenytoin breakdown.

Diphenhydramine – induces drowsiness, sedation.

Hydroxyzine – seen more in elderly patients.

Warfarin – increases warfarin metabolism.

Glipizide – hypoglycaemia

Metformin – increase levels of lactic acid in the blood.

Phenobarbital – increases barbiturate metabolism by cytochrome p450.

Ranitidine – increases gastric emptying over time.

Benzodiazepines – alcohol increases the effects of these agents on the CNS, giving rise to sedation.

NSAIDs- alcohol consumption increases the risk of gastrointestinal bleeding.

Opioids- alcohol induces drowsiness, and sedation.

Tricyclic antidepressants- orthostatic hypotension.

Immune modulators- liver damage

Potential harm can occur in three ways

- 1) When people are unaware of known drug interactions
- 2) Knowingly combine due to negligence
- 3) As a tool to facilitate a crime [4].

Alcohol with neurotransmitters

Evidence suggests alcohol affects multiple neurotransmitter systems in the brain. Brain functions balance between excitatory and inhibitory neurotransmission. An important finding is the demonstration that alcohol can affect the function of specific neurotransmitters [5].

Metronidazole and alcoholic

This well-known disulfiram or Antabuse-like reaction stems from the ability of metronidazole, like disulfiram, to inhibit the enzyme acetaldehyde dehydrogenase in the ethanol degradation pathway, resulting in an accumulation of acetaldehyde in the bloodstream. While not life-threatening, the drug interaction can produce flushing, headache, nausea, and cardiac palpitations and because of this there were once thoughts of employing chronic metronidazole therapy in the treatment of alcoholics. The interaction is supported by numerous anecdotal reports and several studies with varying rates of occurrence. Alcohol consumption should be avoided during metronidazole therapy, and for at least 3 days afterwards [7].

Non-steroidal anti-inflammatory drugs and ethanol-

The combined use of alcohol and non-steroidal anti-inflammatory drugs significantly increases the risk of fecal blood loss associated with gastrointestinal erosions and ulcers. Not only are both alcohol and non-steroidal anti-inflammatory drugs (especially non-selective cyclooxygenase-inhibiting nonsteroidal anti-inflammatory drugs) capable of damaging the gastrointestinal mucosa, but alcohol may also stimulate gastric acid secretion, aggravating the gastrointestinal toxicity of non-steroidal anti-inflammatory drugs. It has been recommended that aspirin and alcohol consumption be separated by at least 12 hours. Probably the short course of analgesic therapy after routine dental procedures limits the severity of this interaction in dental outpatients. However, warnings appear on the labels of all non-steroidal anti-inflammatory drugs containing products of enhanced gastrointestinal toxicity in combination with alcohol if three or more drinks per day are consumed [8].

Alcohol Interactions with Benzodiazepines and Cocaine

A rational management of alcoholic patients requires an understanding of alcohol interactions with other drugs. The effect of alcohol may be indirect by producing liver disease and secondary impairment of drug metabolism, or direct following acute or chronic alcohol administration. The acute administration of alcohol suppresses the oxidative metabolism of chlordiazepoxide and diazepam and their metabolites. This finding may account partly for the enhanced psychomotor impairment following combined benzodiazepine-alcohol ingestion. The conjugation of lorazepam is also decreased, oxazepam remains normal. Data are insufficient to establish the effect of chronic alcohol administration on benzodiazepine disposition, especially in man. On the other hand, with respect to cocaine, chronic alcohol exposure causes induction of hepatic microsomal enzyme activity and enhances the production of metabolites that prove injuries to the liver, thereby causing the hepatotoxic effect of alcohol.

Conclusion

Caution should be taken while using drugs with alcohol. Major and minor drug interactions with alcohol may lead to unwanted and undesired effects of the drug.

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