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Risks of Combined Alcohol-Medication Use in Older Adults

Alison A. Moore, MD, MPH¹, Elizabeth J. Whiteman, MD¹, and Katherine T. Ward, MD¹

¹David Geffen School of Medicine at UCLA, Department of Medicine, Division of Geriatrics

Abstract

Background—Many older adults drink alcohol and use medications that may be harmful when consumed together.

Objective—This article reviews the literature on alcohol and medication interactions with a focus on older adults.

Methods—Relevant articles were identified through a search of MEDLINE (1966-August 2006) for articles on alcohol medication interactions, diseases worsened by alcohol use, alcohol metabolism, absorption and distribution. Additional articles were identified by a manual search of the reference lists of the identified articles and review articles.

Results—Many older adults drink alcohol and take medications that may interact negatively with alcohol. Some of these interactions are due to age-related changes in the absorption, distribution and metabolism of alcohol and medications. Others are due to disulfiram-like reactions observed with some medications, exacerbation of therapeutic effects and adverse effects of medications when combined with alcohol, and alcohol's interference with the effectiveness of some medications.

Conclusions—Older adults who drink alcohol and who take medications are at risk for a variety of harms depending on the amount of alcohol and the type of medications consumed. It is important for clinicians to know how much alcohol their older patients are drinking to be able to effectively assess their risks and to counsel them about safe use of alcohol and medications. Similarly, it is important for older adults to understand the potential risks of their combined alcohol and medication use to avoid the myriad of harms possible with unsafe use of these substances.

Keywords

alcohol; medications; alcohol medication interactions; aged

INTRODUCTION

While national estimates of the combined prevalence of alcohol and medication use among adults aged 65 years and older in the United States are unknown, approximately 40–50% of older adults drink alcohol ¹ and more than 90% of older adults take medications.² Older

adults are susceptible to adverse effects from the combined effects of alcohol and medications, in part, because of changes in the body with increasing age that affect the distribution and metabolism of these substances and increase the brain's sensitivity to their effects.^{3, 4} In addition to these physiological changes that increase their susceptibility to alcohol-medication related adverse reactions, older adults have reduced homeostatic capacity, often take multiple medications with potential to interact with alcohol, and have chronic conditions that may be worsened by concomitant alcohol use.⁵⁻⁷

Alcohol has the potential to adversely interact with many, many prescription and non-prescription medications through a variety of mechanisms including raising blood alcohol levels, altering the metabolism of many drugs, interfering with the effectiveness of medications and exacerbating their side effects.^{8, 9} Although some of the interactions between alcohol and medications occur primarily among those who drink heavily (e.g., 3 or more drinks per occasion), many of these interactions may occur with lower amounts of alcohol use, that is light to moderate drinking (e.g., 1-2 drinks per occasion).

In the following sections we will review what is known about the prevalence of alcohol-medication interactions in older adults, the absorption, distribution and metabolism of alcohol and how that is affected by alcohol and aging, and the types of risks that may occur with alcohol and medications. This paper builds on the information provided in two prior reviews of alcohol and medication interactions by Adams¹⁰ and Weathermon and Crabb.¹¹

Prevalence of alcohol-medication interactions in older adults

Others have investigated the prevalence of alcohol-medication interactions in older adults. Using data from the Pennsylvania PACE program, a state-funded program providing prescription benefits to older persons with low to moderate incomes, the researchers found that 19% of those consuming alcohol took medications that could have negative interactions with alcohol.¹² In another study among drinkers in three retirement communities, 38% used drugs that could have negative interactions with alcohol.⁵ A third study among a sample of older adults living in New York State estimated that 25% of them drank alcohol and took medication that could negatively interact with alcohol.¹³ A fourth study, using data from the Italian Group of Pharmacoepidemiology in the Elderly (GIFA) study found the prevalence of adverse drug reactions among hospitalized persons aged 65 and older was 3.7% among abstainers and 4.1% among those who drank less than 40g of alcohol per day (approximately 3 drinks. After adjusting for potential confounders, moderate drinkers were 24% more likely to experience an adverse drug reaction compared to abstainers.¹⁴ A fifth study among older adults considered at-risk drinkers found that more than 70% of them were considered at-risk because of the amount of alcohol they drank combined with the medications they took.¹⁵ These data provide evidence for the considerable potential for alcohol-medication-interactions among older adults.

Alcohol and Medication Absorption, Distribution and Metabolism in Aging Persons

In this section we will review the absorption, distribution, and metabolism of alcohol and how aging affects these processes. We will also provide examples of combinations of alcohol and medications that may influence their absorption, distribution and/or metabolism.

Gastrointestinal Absorption and Metabolism—When alcohol is consumed, a small amount is metabolized in the stomach by the enzyme alcohol dehydrogenase (ADH).¹⁶ Women have lower levels of ADH as compared to men^{17, 18} and older adults have lower levels of this enzyme as compared to younger persons.¹⁹ Most of the remaining alcohol is subsequently absorbed into the systemic circulation from the gastrointestinal tract, predominantly from the stomach and the upper small intestine. This absorption happens slowly from the stomach but rapidly from the upper small intestine. Aging prolongs gastric emptying²⁰ but this does not appear to affect the absorption of most drugs.²¹ After the alcohol is absorbed, it is transported to the liver through the portal vein and part of the alcohol is metabolized during this initial passage through the liver. The rest of the alcohol leaves the liver, enters the systemic circulation and is distributed throughout the body. Eventually the alcohol is transported back to the liver and metabolized there. The metabolism of alcohol or any other substance that takes place in the gastrointestinal tract and during the initial passage through the liver is called “first-pass metabolism”.

First-pass metabolism is likely responsible for, at most, metabolism of 10% of consumed alcohol.¹¹ Some medications may either inhibit ADH activity such as aspirin and H₂ receptor antagonists (e.g., ranitidine, cimetidine)²² or may accelerate gastric emptying (e.g., metoclopramide) and thereby increase blood alcohol levels (BALs).

Distribution—The alcohol remaining after first-pass metabolism enters the bloodstream and is distributed throughout the body water. Aging has clinically important effects for the distribution of alcohol and medications as the proportion of body water and fat differs both between men and women and younger and older persons. Women and older adults have higher amounts of body fat and less body water than do men and younger adults.³ These differences affect the blood alcohol levels (BALs) reached with a given alcohol dose so that women and older adults, whose lower body water creates a smaller fluid volume in which alcohol is distributed, tend to have higher BALs than do men and younger adults after consuming the same amount of alcohol. Fat soluble medications, such as many of the benzodiazepines, will have a larger volume in which the medication is distributed and may consequently have longer half-lives and remain in the body for a longer period of time.^{23, 24} The combined effects of alcohol and benzodiazepine use in an older adult may result in prolonged and excessive sedation and/or problems with coordination given the changes in distribution of these substances with aging.

Hepatic Metabolism—Alcohol is metabolized primarily in the liver. Alcohol is transported in the bloodstream to the liver where it is metabolized by several enzymes, the most important of which are ADH and cytochrome P450 enzymes. Part of the cytochrome P450 enzyme system having an important role in alcohol metabolism is the microsomal ethanol oxidizing system (MEOS).²⁵ ADH converts alcohol into acetaldehyde, which is a toxic substance to the liver. Acetaldehyde is metabolized further by aldehyde dehydrogenase (ALDH).

Of note, many persons of Asian descent experience facial flushing, nausea and vomiting when they ingest alcohol as they have an inborn variation in the enzymes used to break down acetaldehyde. The medication disulfiram (Antabuse) uses this mechanism (inhibition

of ALDH) to cause those who drink alcohol to experience the flushing reaction. Other medications can induce a disulfiram-like reaction including several antibiotics, nitrates and some of the sulfonylureas.

Although there are age-related decreases in hepatic blood flow and liver mass, these changes do not appear to have clinical importance.²⁶ There also do not appear to be any age-related changes in the functioning of the cytochrome P450 enzyme system.³ The cytochrome P450 system metabolizes only a small fraction of alcohol among those drinking only occasionally, but the activity of the P450 system can increase 10-fold among those who drink alcohol chronically and heavily.²⁷ The increased enzyme activity causes more rapid breakdown of many medications with resulting lower blood levels of these medications and reduced effectiveness. Some of the more important drugs affected by induction of the P450 system are warfarin, phenytoin, diazepam and other benzodiazepines,²⁸ propranolol and isoniazid, and some highly active anti-retroviral therapy (HAART) drugs.²⁹ Among those who engage in episodic heavy drinking (that is drinking much more on an occasion than is usual for that individual), these medications compete with alcohol for metabolism by the P450 system resulting in higher blood levels of these medications and potential drug overdose.³⁰ Wide variation exists in the activity of the P450 system and metabolic rates for medications broken down by this enzyme system (e.g., acetaminophen). Some of this variation may be genetically determined but the specific underlying mechanism is unknown.^{31, 32} An individual's P450 enzyme activity could influence his or her susceptibility to alcohol-medications interactions involving this enzyme.

Risks of Alcohol-Medication Combinations

Negative interactions between alcohol and a variety of medications in older adults can occur in a variety of situations that differ based on age-related changes in the body and brain, the amount of alcohol consumed, the types and amounts of medications used, the timing of alcohol and medication ingestion, the types and number of chronic conditions, and functional status. In this section we will review the types of adverse effects possible with alcohol and medications and we will describe which of these may worsened by concomitant age-associated changes (see Table 1).

Increased blood alcohol levels—Particular H2 blockers, including ranitidine and cimetidine, when combined with alcohol in even small amounts, raise blood alcohol levels to an extent that interferes with cognitive and fine motor functions.^{33–35} Use of these drugs with alcohol is even more risky in older adults because, even in the absence of these drugs, older adults develop higher blood alcohol levels and have increased brain sensitivity for a given dose of alcohol as compared to younger persons.^{3, 4}

Increased drug metabolism—Persons who are long-term heavy alcohol users induce the cytochrome P450 system to increase the rate of metabolism of alcohol and many drugs including benzodiazepines, warfarin, phenytoin, propranolol, tolbutamide and isoniazid, and highly active anti-retroviral therapy (HAART) drugs.³⁶ This increased metabolism serves to lower the blood levels of these drugs and higher doses of the drug are needed to achieve a therapeutic effect. This increased metabolism may persist for weeks after alcohol use is

reduced. Therapeutic failure is the major risk of this type of interaction such as inadequate anticoagulation among those using warfarin, and increased risk for seizures among those using phenytoin.

Another result of enzyme induction by chronic heavy drinkers is the increased production of toxic metabolites to the liver during the metabolism of drugs like isoniazid, phenylbutazone and acetaminophen. As many older adults take medications other than these that may have hepatotoxic effects (e.g., statins), those who drink 3 or more drinks per day may have increased risk for liver toxicity.

Decreased drug metabolism—Short-term heavy alcohol consumption can have the opposite effect on the cytochrome P450 system, that is, inhibition of hepatic drug metabolism. Because alcohol competes with drugs such as benzodiazepines, narcotics, and warfarin, such medications will be metabolized more slowly and result in increased concentrations of these medications in the blood so that lower doses of the drug are needed to achieve a therapeutic effect and the risk of overdose of these medications is increased. Older adults are particularly at-risk for sedation and psychomotor effects of benzodiazepines and narcotics and this effect may be intensified among those who drink heavy amounts episodically. Depending on the usual drinking habits of the individual, the amount of alcohol placing an individual at risk could be as low as 2 or 3 drinks on an occasion.

Disulfiram-like reactions—Several medications can induce a disulfiram-like reaction when alcohol is consumed. These medications include certain beta-lactam antibiotics such as cefmandole, cefoperazone and moxalactam,^{37, 38} nitrates,³⁹ and longer acting sulfonyleureas such as chlorpropamide and tolbutamide.^{40, 41}

Exacerbation of therapeutic effects and adverse effects of medications when combined with alcohol

Gastrointestinal bleeding: Nonsteroidal anti-inflammatory drugs (NSAIDs) and aspirin when combined with alcohol can increase risks for gastrointestinal bleeding by injuring the gastric mucosa and increasing bleeding time.^{42, 43} Since arthritis and other musculoskeletal problems causing pain are among the most common problems older adults have, this risk is important to consider among those who consume alcohol and use these medications. The negative gastrointestinal effects of NSAIDs are higher in older adults,^{44, 45} so the combined risks of gastrointestinal toxicity from use of alcohol and NSAIDs are potentially large.

Sedation, Impaired Psychomotor Function: Older adults are more susceptible to the sedating effects of alcohol and, when used with drugs that can cause sedation, the effect may be severe. Drugs in this category are benzodiazepines, tricyclic antidepressants, muscle relaxants, narcotics, sedating antihistamines, some of the drugs used to treat seizures or neuropathic pain (e.g., phenobarbital, gabapentin), and barbiturates. The combination of alcohol and these types of medications may result in additional sedation and impairment with motor skills and judgment.^{4, 46} Kava (*Piper methysticum*) is an herbal supplement used for anxiety. There is some data suggesting that when this herb is used with alcohol, the combination causes motor and cognitive impairment.^{47, 48}

Hypotension: Alcohol potentiates orthostatic hypotension by impairing vasoconstriction.⁴⁹ The combination of alcohol and drugs that may cause orthostatic hypotension such as vasodilating drugs, tricyclic and monoamine oxidase inhibitor antidepressants, drugs used for Parkinson's disease, and barbiturates may cause a severe drop in blood pressure³⁶ and cause dizziness and fall-related injuries.

Hypertensive crisis: Foods and beverages containing tyramine, including red wine and beer can increase risk for a hypertensive crisis when consumed with non-selective monoamine oxidase inhibitors used for depression (e.g., tranylcypromine, phenelzine).⁵⁰

Interference with the effectiveness of medications—Another common type of interaction between alcohol and medications occurs when alcohol adversely affects the illness for which the medication was prescribed. Many of the illnesses common in older adults can be worsened by particular amounts of alcohol. Such conditions include hypertension, diabetes, upper gastrointestinal conditions, gout, insomnia, depression, and cognitive impairment. Other conditions, not necessarily more prevalent in older adults, may also be worsened by concomitant alcohol use such as liver disease, breast cancer, and seizures. In this section, when possible, we provide data on the amounts of alcohol that have been associated with causing or worsening each of the conditions. Many of these data were obtained from a comprehensive review of amount of alcohol consumption to burden of disease by Jurgen Rehm et al.⁵¹

Hypertension: Alcohol is known to double the risk for hypertension among women consuming 2 or more drinks daily and for men consuming 4 or more drinks per day.^{51–53} Consuming this amount of alcohol can make it more difficult to treat hypertension.

Diabetes: Light to moderate alcohol use in diabetics has been associated with reduced risk for coronary heart disease (CHD) and CHD-related deaths.^{54, 55} But known risks of heavier alcohol use among diabetics include exacerbation of diabetic neuropathy,⁵⁶ and retinopathy.⁵⁷ Also even among those diabetics who drink moderately, those who drink alcohol without eating risk hypoglycemia as alcohol suppresses hepatic gluconeogenesis.^{58, 59} Further, alcohol may worsen diabetic control among those who drink sweet alcoholic beverages and has been associated with worsening adherence to diabetes care and hypoglycemia unawareness among both heavy and moderate drinkers.⁶⁰ Both the American and British Diabetes Association guidelines recommend limits of no more than 1 drink per sitting.^{61, 62}

Upper gastrointestinal conditions: Alcohol can cause gastric irritation. Risks of upper gastrointestinal bleeding are increased approximately 40% among those consuming 7–27 drinks per week and almost 300% among those consuming 28 or more drinks per week as compared to abstainers.⁶³ Persons who are being treated for ulcer disease should not drink alcohol.

Alcohol may also be associated with gastroesophageal reflux disease (GERD), though data on this is mixed. Most studies find no association between alcohol use and the prevalence of GERD^{64, 65} but lifestyle modifications, including avoidance of alcohol is still recommended

by the American College of Gastroenterology⁶⁶ and some studies find an association between consumption of alcohol and GERD.^{67, 68} Given that age is also a risk factor for GERD,⁶⁹ older adults with GERD and who drink up to 1–2 drinks daily should be advised to observe whether this amount of alcohol use worsens their symptoms and avoid alcohol if symptoms do worsen.

Gout: Consuming any amount of beer or spirits has been associated with an increased risk of gout.⁷⁰ As compared to no alcohol use, drinking 1 beer a day increased the risk of gout by 50%, while drinking one shot of spirits per day was associated with an increase in the risk of gout by 15%.⁷⁰ Given these data, older adults with gout should be cautioned against daily consumption of even light to moderate amounts of beer or spirits to avoid gouty attacks.

Insomnia: Among heavy drinkers, alcohol interferes with falling asleep and staying asleep and older alcoholics are also more likely to have sleep-disordered breathing as compared to younger alcoholics.^{71, 72} Among lighter drinkers, alcohol initially helps one to fall asleep but tolerance rapidly develops for this effect.⁷³ Alcohol is, therefore, not an effective sleep aid, and may disrupt sleep among those who drink heavily.

Depression: Several studies examining changes in depressive symptoms when heavy or dependent drinkers abstain from alcohol provide evidence that depressive symptoms dramatically improve within days to weeks of abstinence.^{74–77} It is recommended then, that those with depression avoid alcohol when starting therapy and limit alcohol intake to 1–2 drinks per day.

Cognitive impairment/Dementia: While mounting evidence suggests that light to moderate drinking can prevent cognitive impairment,^{78–81} there is insufficient data on the effects of alcohol use among those with pre-existing cognitive impairment.⁸² However, given that alcohol has sedative effects and neurotoxic effects on the brain, it is not recommended that those with cognitive impairment drink alcohol.^{83, 84}

Liver disease: Drinking 2 or more drinks daily among women and drinking 4 or more drinks per day among men increases risk for cirrhosis 9 times that as compared to those who do not drink alcohol.^{51, 53, 85–88} Other liver conditions such as chronic or acute hepatitis, particularly hepatitis C infection, can be worsened by smaller amounts of alcohol given its toxicity to the liver.⁸⁹ Alcohol also reduces the responsiveness to interferon, accelerates disease progression, and increases the risk for hepatocellular cancer.^{90, 91}

Seizures: Drinking 2 or more drinks daily among women and drinking 4 or more drinks per day among men increases risks for a seizure disorder more than 7 times as compared to non-drinkers.^{51, 53, 85–88, 92} While alcohol may not directly cause seizures except for those experiencing withdrawal, it is likely a risk factor for those with pre-existing brain injury or disease. It is recommended that those whose medications are controlled with seizure medications be cautious about drinking alcohol and those whose seizures are not controlled well with medications, abstain from drinking alcohol.⁹³

Breast Cancer: The risk of breast cancer increases 7% with every drink consumed per day as compared to those women who do not consume alcohol.^{94, 95} Although there is no data on risks of breast cancer recurrence with varying amounts of alcohol use, given that alcohol is associated with breast cancer development, breast cancer survivors should be cautioned about alcohol use.

CONCLUSIONS

Older adults who drink alcohol and who take medications are at risk for a variety of harms depending on the amount of alcohol and the type of medications consumed. Types of risks include increased blood alcohol levels, increased and/or decreased drug metabolism, disulfiram-like reactions, exacerbation of therapeutic effects and adverse effects of medications, and interference with the effectiveness of medications. These risks may cause harms such as liver and gastrointestinal disease, sedation, dizziness, problems with coordination leading to falls and motor vehicle accidents, gouty flares, therapeutic failure or overdose, hypotension, hypertension, insomnia, breast cancer, worsening of depression and poor control of seizure disorders and diabetes. It is important for clinicians to know how much alcohol their older patients are drinking to be able to effectively assess their risks and to counsel them about safe use of alcohol and medications. Similarly, it is important for older adults to understand the potential risks of their combined alcohol and medication use to avoid the myriad of harms possible with unsafe use of these substances.

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