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# ALCOHOL USE DISORDERS IN THE ELDERLY: A BRIEF OVERVIEW FROM EPIDEMIOLOGY TO TREATMENT OPTIONS

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## Abstract

Alcohol-use-disorders (AUDs) afflict 1–3% of elderly subjects. The CAGE, SMAST-G, and AUDIT are the most common and validated questionnaires used to identify AUDs in the elderly, and some laboratory markers of alcohol abuse (AST, GGT, MCV, and CDT) may also be helpful. In particular, the sensitivity of MCV or GGT in detecting alcohol misuse is higher in older than in younger populations. The incidence of medical and neurological complications during alcohol withdrawal syndrome in elderly alcoholics is higher than in younger alcoholics. Chronic alcohol abuse is associated with tissue damage to several organs. Namely, an increased level of blood pressure is more frequent in the elderly than in younger adults, and a greater vulnerability to the onset of alcoholic liver disease, and an increasing risk of breast cancer in menopausal women have been described. In addition, the prevalence of dementia in elderly alcoholics is almost 5 times higher than in non-alcoholic elderly individuals, approximately 25% of elderly patients with dementia also present AUDs, and almost 20% of individuals aged 65 and over with a diagnosis of depression have a co-occurring AUD. Moreover, prevention of drinking relapse in older alcoholics is, in some cases, better than in younger patients; indeed, more than 20% of treated elderly alcohol-dependent patients remain abstinent after four years. Considering that the incidence of AUDs in the elderly is fairly high, and AUDs in the elderly are still underestimated, more studies in the fields of epidemiology, prevention and pharmacological and psychotherapeutic treatment of AUDs in the elderly are warranted.

### Keywords

alcohol use disorders; alcohol related diseases; elderly

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## 1. Epidemiology

Around 2 billion people worldwide consume alcoholic beverages. It has been shown that alcohol causes approximately 3.8% of all deaths world-wide (6.3% of men and 1.1% of women) and accounts for 4.6% of the global burden of disease (7.6% of men and 1.4% of women) (Rehm et al., 2009). In most European countries, alcohol consumption was responsible for 14.6% of all premature adult mortality (17.3% for men and 8.0% for women); moreover, in Eastern Europe, particularly in some industrialized cities of Russia, alcohol has been shown to be responsible for more than half of all deaths in younger men (15–54 years), and was a major cause of death in older men (55–74 years) and in women.

Over 76 million people have alcohol-use disorders (AUDs) consisting in alcohol dependence, alcohol abuse and dependence or harmful drinking. This latter definition consists of alcohol intake >14 drinks per week or >4 drinks per occasion for men and >7 drinks per week or >3 drinks per occasion for women, where a drink corresponds to 10–12 g of pure alcohol (Schuckit, 2009). AUDs are commonly found in all developed countries, and prevail in men; namely, AUDs were frequently found in Chinese, German, Thai, and US men, and in Brazilian and US women (Rehm et al., 2009). The lifetime risk of AUDs in men is more than 20%, with a risk of about 15% for alcohol abuse and 10% for alcohol dependence (Schuckit, 2009).

Almost 50% of the elderly (aged over 65) and almost 25% of subjects over 85 years old drink alcohol. AUDs afflict 1–3% of elderly subjects, and represent a cause of physical and psychiatric morbidity and social distress (Blazer and Wu, 2009). In addition, up to 30% of older patients hospitalized in divisions of general medicine, and up to 50% of those hospitalized in psychiatric divisions present AUDs.

The aim of the present review is to briefly analyze AUDs in the elderly population (>65 years old). A detailed discussion of prevention, epidemiology (that would imply the distinction between alcohol dependence, alcohol abuse and harmful drinking), pathogenesis, diagnosis and treatment, including psycho-pharmacological and social interventions, would go beyond the limits of this mini-review. Therefore, we mainly focused on alcohol-related disease that follow chronic misuse, even though other issues have been briefly dealt with.

## 2. Pathogenesis of alcohol related damage

After its ingestion, ethanol (almost 10%) is metabolized by the alcohol-dehydrogenase (ADH) in the gastric mucosa, undergoing the so called “first-pass metabolism”. The remaining amount leaves the stomach and is rapidly absorbed from by the upper small intestine. Then, via the portal vein, it reaches the liver, where it is largely metabolized to acetaldehyde by ADH in cytosol, and by cytochrome P-450-IIE1 in microsomes (Lieber, 2005). Acetaldehyde is quickly converted to carbon dioxide and water, primarily through the actions of aldehyde-dehydrogenase (ALDH) (Lieber, 2005). Excessive alcohol intake saturates this system, leading to the activation of the enzymatic microsomal ethanol oxidizing system (MEOS). In the elderly, a reduced activity of gastric and liver ADH leads to the elevation of blood alcohol level by 20–50%, and this, in turn, enhances the ethanol

effect on the central nervous system (Lieber, 2005). In addition, due to the frequent presence of co-morbidities, elderly subjects often have a high intake of medications. When the MEOS system is saturated by drugs, metabolism is hampered and medications accumulate in the blood (Moore et al., 2007) (table 1); on the other hand, when an excessive alcohol intake leads to enzymatic induction, the dosage of drugs metabolized by the MEOS system needs to be corrected due to their rapid elimination. Finally, alcohol metabolism is influenced by genetic polymorphism: gene variations of ADH can accelerate alcohol breakdown and lead to a greater acetaldehyde accumulation after drinking (inactive form of ALDH), as occurs in Asian populations (Schuckit, 2009).

Alcohol can induce mechanisms that promote cellular and tissue injury directly or via its metabolites (acetaldehyde and acetate). In particular, acetaldehyde forms neo-antigenic proteins that evoke an anti-body reaction which, as it occurs in the liver, may trigger tissue injuries (Lieber, 2005). In addition, acetaldehyde binding to proteins related with DNA repair and methylation forms DNA-adducts interfering with processes that control gene activity and the integrity of DNA itself. DNA adducts may subsequently lead to replication errors and point mutations. Indeed, there is convincing evidence that the carcinogenic effect of alcohol is due to the DNA mutagenic properties of acetaldehyde operating at multiple levels. Moreover, acetaldehyde is able to modify intracellular signaling pathways leading to the destabilization of the tight junction protein complex. This leads to the disruption of the barrier function provided by tight junctions, a process that becomes particularly relevant in gut epithelial cells as it increases permeability to the lipopolysaccharide (LPS) of the outer membrane of the Gram-negative bacteria. LPS absorbed in the gut and transported by the portal vein to the liver sensitizes the Kupffer cells to a molecular cascade of events with a final overstated transcription of pro-inflammatory cytokines (i.e. tumor necrosis factor alfa: TNF-α; interleukin-6: IL-6; transforming growth factor beta: TGF-β); while TNF-α and IL-6 are mainly involved in cholestasis and synthesis of acute-phase proteins, TGF-β is critically involved in fibrogenesis through the activation of hepatic stellate cells. The final scenario is the onset of necro-inflammation, apoptosis and fibrosis with a leading progression of ALD, finally culminating in cirrhosis (Gramenzi et al., 2006).

## 3. Diagnosis of AUDs

Several epidemiological studies have shown that the diagnosis of AUDs in the elderly is underestimated (Moore et al., 2002). This represents a worrying bias, as AUDs in the elderly have a greater probability to respond to treatment than those developed at an earlier age (6). There is a variety of conditions whose evaluation should include screening for a potential AUD such as: a) worsening of a chronic disease (hypertension, diabetes mellitus, osteoporosis, macrocytic anemia, hypercholesterolemia, gastritis, Parkinson’s disease, and gout); b) reduced or increased pharmacological effect of chronic therapies; c) onset of gastrointestinal disorders, urinary or fecal incontinence, accidental hypothermia, orthostatic hypotension, frequent falls, fainting, heart failure, aspiration pneumonia, dehydration and malnutrition; d) onset or deterioration of cognitive or psychiatric disorders (acute confusion, anxiety-depression syndrome, insomnia, Alzheimer’s disease, and Wernicke-Korsakoff syndrome) (Moore et al., 2002). The diagnosis of AUDs is based on a multidimensional assessment of the patient that involves physical and psycho-social examinations, with

interview of the patient and a family member. When alcohol misuse is suspected, alcohol consumption should be assessed by questionnaires. The four-item test with questions on Cutting down, Annoyance at criticism, Guilty feelings and use of Eye-openers (CAGE) (Culberson, 2006) (table 2), the short version of Michigan Alcoholism Screening Test-Geriatric Version (SMAST-G) (Johnson-Greene et al., 2009) (table 3), and the Alcohol Use Disorders Identification test (AUDIT) (Aalto et al., 2010) are the most common and validated questionnaires used to identify AUDs in the elderly. In particular, CAGE and MAST-G can be used together to improve their sensitivity, and the AUDIT, tailored at a cut-off of ≥ 5 points, is useful to identify HD (Aalto et al., 2010; Culberson, 2006; Johnson-Greene et al., 2009). The Diagnostic and Statistical Manual of Mental Disorders - 4$^{th}$ edition - Text Revision (DSM-IV-TR) criteria (American Psychiatric Association, 2000) can be used to make a diagnosis of alcohol abuse and dependence. Laboratory tests such as alanine aminotrasnferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transpeptidase (GGT), mean corpuscular volume (MCV), and carbohydrate deficient transferring (CDT) may be helpful (table 4). Some studies show that the sensitivity of MCV or GGT in detecting alcohol misuse is higher in older than in younger populations (Mundle et al., 1999).

## 4. Alcohol related diseases

The adverse effects of short-term (acute alcohol intoxication) and long-term (chronic alcohol abuse) excessive drinking outweigh its reputedly beneficial effects. Even an isolated episode of acute ethanol intoxication prior to another insult (i.e., traumatic injury resulting from driving under intoxication, burns) may exacerbate the suppression of the host defence and increase susceptibility to infections. Chronic alcohol abuse is associated with multiple diseases, involving liver, pancreas, gastrointestinal tract, respiratory tract, muscle, brain and the immune system. The individual propensity to develop alcohol-related disease is related to the pattern and duration of alcohol assumption, in association with other cofactors such as genetic predisposition, gender, dietary factors, and environment (Schuckit, 2009).

### 4.1 Alcohol and the cardiovascular system

Excessive alcohol intake increases cardiovascular risk (i.e. hemorrhagic stroke) (Mukamal et al., 2006). Indeed, alcohol misuse can negatively influence various determinants of cardiovascular risk such as glucose metabolism abnormalities, increase in waist circumference (Mukamal et al., 2006) and, in particular, increase in systolic pressure: in fact, there is evidence that alcohol intake more easily leads to hypertension in the elderly than in younger adults (Wakabayashi and Araki, 2010). In addition, individuals consuming more than 90 g of alcohol per day for more than 5 years can develop a non-ischemic dilated heart disease that can lead to ventricular dysfunction and heart failure (Piano, 2002).

Even though it is not appropriate to argue this topic here, it is worth noting that a cardiovascular protective effect of light to moderate alcohol consumption (1 drink/day for women or up to 2 drinks/day for men) has consistently been reported in adult and elderly populations (Mukamal et al., 2006; Costanzo et al., 2010). Indeed, the majority of studies dealing with alcohol intake have found J- or U-shaped risk curves with light to moderate

drinkers having a lower risk of atherosclerotic cardiovascular diseases than non-drinkers or heavy drinkers. In particular, a recent experience among 13,296 US Caucasian older adults showed that moderate alcohol consumption both in men and women was associated with a 15–30% decrease in cardiovascular risk (Paganini-Hill, 2011). A further interesting result drawn from a meta-analytic study showed a 30% reduced risk of type 2 diabetes in moderate alcohol consumers (Koppes et al., 2005).

### 4.2 Alcohol and the endocrine system

Chronic alcohol misuse may induce several alterations of the hypothalamo-pituitary glands axis. As an example, during a condition of chronic alcohol abuse and during an alcohol withdrawal syndrome, cortisol and adreno-corticotropic hormone (ACTH) levels may be found elevated with a return to normal levels within 2–6 weeks of continued abstention from alcohol. The increased cortisol levels may induce the so called *pseudo-cushing* state; however, due to many similarities in symptoms, this clinical condition remains difficult to discriminate from the primary form of Cushing Syndrome (Newell-Price et al., 2006).

### 4.3 Alcohol, liver, gut and pancreas

Elderly subjects with chronic alcohol abuse are more vulnerable to the onset of alcoholic liver disease (ALD). Symptoms and signs of ALD and its complications are similar to those seen in patients of all ages, and treatment is mainly focused on alcohol abstinence (Seitz and Stickel, 2007). Both acute and chronic alcohol consumption are responsible for other severe effects on the mucosa of the esophagus such as *Barrett's esophagus*. This clinical condition is characterized by metaplasia in the cells of the inferior portion of the esophagus with clinical symptoms of heartburn, dysphagia and hematemesis. The stomach may also be affected by acute and chronic ethanol ingestion; indeed, acute and chronic gastritis appear with an increasing risk of bleeding when ulcers develop. In addition, due to the chronic illness frequently found in older adults, the daily assumption of medications such as aspirin and proton-pump inhibitors in combination with alcoholic beverages leads to a reduction in the activity of gastric ADH with a consequent increase of blood ethanol levels and sedative effects. Moreover, acute and chronic alcohol ingestion may induce diarrhea which leads to malnutrition due to a reduction of micro-nutrient absorption. Furthermore, alcohol abuse is a common cause of pancreatitis, even though this appears to occur more in the young (30%) than in the elderly (5%) (Hall et al., 2005).

### 4.4 Alcohol and pulmonary disease

Besides the susceptibility of older age to pulmonary infections due to a physiological reduction of immune response, which is further worsened by excessive alcohol intake, alcohol abuse has been identified as an independent risk factor for the development of Adult Respiratory Distress Syndrome (ARDS), a severe form of lung injury mainly characterized by hypoxemia, increased permeability of the alveolar capillary membrane, and accumulation of interstitial protein and intra-alveolar edema. Indeed, among approximately 200,000 individuals who develop ARDS in the United States each year, nearly 50% have a history of alcohol abuse. Despite studies aimed at improving outcomes in patients with ARDS, mortality remains high (40%), and for those who abuse alcohol it is even higher (65%) (Boe, et al., 2009).

### 4.5 Alcohol and immune response

Alcohol intake definitely impairs innate immune responses. High doses of alcohol can directly suppress a wide range of immune responses by reducing both cell-mediated immunity and the humoral immune function, and it is associated with an increased incidence of a number of infectious diseases (Diaz et al., 2002). Indeed, T and B cell numbers are significantly decreased in patients with alcohol-induced disease. In addition, immunoglobulins produced by B cells against pathogens as the host defense response are usually increased in patients suffering from ALD. Finally, chronic alcoholism and ALD are accompanied by an increased cytokine production. In fact, cytokines (i.e. IL-6, IL-10, IL-12) are elevated in alcoholics with respect to control subjects (Dıaz et al., 2002;, Szabo and Mandrekar, 2009).

### 4.6 Alcohol and bone-joint fractures

Alcohol misuse is an important risk factor for falls and the development of spontaneous bone fractures since it can cause: a) acute confusion, and orthostatic hypotension; b) distal sensory-motor neuropathy and myopathy; c) reduced ability of spatial assessment and ataxia; d) reduced bone mineral density, particularly if associated with smoking (Johnston and McGovern, 2004). It should be remembered that elderly subjects with reduced autonomy and high fragility should be advised to avoid alcohol consumption.

### 4.7 Alcohol and tumors

The consumption of more than 40 g of alcohol per day represents a risk factor for the onset of tumors in many organs, including: oropharynx, larynx, esophagus, liver, colon-rectum and breast (Bagnardi et al., 2001). Notably, the relationship between alcohol consumption and onset of tumors is dose-dependent. In particular, in menopausal women, an increased risk of breast cancer has been described, an effect likely attributable to the alcohol-induced increase in estrogen blood levels. Recently, even a moderate intake of alcohol (from 3 to 6 glasses per week) has been found to be an independent risk factor for the onset of breast cancer in older women (Chen et al., 2011). The presence of gastrointestinal symptoms such as constipation, loss of weight, diarrhea, dysphagia and abdominal pain, in elderly subjects with a positive anamnesis for heavy drinking must arouse the suspicion of alcohol-related cancers that must be investigated. Finally, it is worth noting that in Japan, cancer was the most important alcohol-attributable burden of disease category for both sexes (Rehm et al., 2009).

### 4.8 Alcohol and the brain

Alcohol acts on the central nervous system via both direct and indirect effects. The former results from changes in cell membrane fluidity, impaired cell functioning, increased inhibitory activity of gamma amino-butyric receptor receptors, and inhibition of the excitatory activity of N-methyl-D-aspartate receptors. Indirect effects are mainly mediated by malnutrition, which causes deficiencies in thiamine, nicotinic acids, B vitamins and folate. Thiamine deficiency facilitates excessive glutamate release leading to neuronal damage (Wernicke-Korsafoff syndrome and Marchiafava Bignami disease). By contrast, alcohol dementia, in its degenerative and vascular forms, generally occurs in the absence of nutritional deficit; in this case, a direct neurotoxic effect of alcohol is presumably

implicated. In the elderly, the prevalence of dementia is almost 5 times higher in alcoholics than in non-alcoholic individuals, and approximately 25% of elderly patients with dementia also present AUDs (Moriyama et al., 2006). From a clinical standpoint, it is important to differentiate alcohol-related from other types of dementia. In this respect, alcohol-related persisting dementia is a specific diagnosis included in the DSM-IV-TR (American Psychiatric Association, 2000).

Even though a protective effect of moderate alcohol intake in slowing cognitive decline and the progression to Alzheimer's Dementia remain controversial (Lobo et al., 2010), it has been shown that abstainers have poorer cognitive function than light drinkers (Rodgers et al., 2005); in addition, a recent study has demonstrated that greater adherence to a Mediterranean-type diet, characterized also by a moderate intake of wine, could be associated with a slower cognitive decline, a reduced risk of Alzheimer's disease and a decreased all-cause mortality in patients with Alzheimer's Dementia (Solfrizzi et al., 2011).

### 4.9 Alcohol and psychiatric disorders

Almost 20% of individuals aged 65 and older with a diagnosis of depression have a co-occurring AUD (Gunn and Cheavens, 2008). Conversely, more than 90% of older subjects with AUDs have a history of depression. The relationship between AUDs and late life depression is complex and it is important to understand whether depression is the result of the AUD or vice versa. Moreover, when associated with AUDs, depression and anxiety disorders are responsible for more than 70% of suicides, and are an important cause of domestic violence, separation/divorce, and social and economic decline. Depressed patients who discontinue the use of alcohol progressively improve their psychiatric condition compared with those who continue drinking. Nevertheless, the management of anxiety and depression symptoms remains a crucial point during the treatment of AUDs. Despite the lack of scientific evidence indicating a specific strategy for treating elderly patients with both depression and AUDs, the importance of treating both problems is recommended.

## 5. Treatment of alcohol use disorders

### 5.1 Detoxification

The incidence of medical (myocardial ischemia, aspiration pneumonia, arrhythmias, orthostatic hypotension) and neurological complications (hallucinations, delirium tremens, dizziness, convulsions) during alcohol withdrawal syndrome (AWS) in elderly alcoholics is higher than in their younger counterpart (Letizia and Reinbolz, 2005). Controlled clinical studies evaluating the efficacy of medications for the treatment of AWS in elderly patients are not available. However, in order to avoid any risks of sedation, short-acting benzodiazepines (BDZs) (i.e. lorazepam, 30–60 mg orally every 4 h or oxazepam 1–2 mg orally or i.m. or i.v. every 4 h for the first day and then tapering the dose by 50% on days 2 and 3) are recommended. Elderly patients are particularly susceptible to the onset of some complications of AWS, such as Wernicke-Korsakoff syndrome characterized by peripheral neuropathy, ataxia, ocular paralysis, confusion and confabulation, and amnesia due to reduced serum levels of magnesium. Thus, in addition to BDZs, the treatment of AWS

should include the administration of magnesium and of intramuscular or intravenous thiamine for three to five days.

In cases of severe agitation associated with severe sleep or behavioral disorders, when BDZs alone are unable to control the symptoms of AWS, haloperidol may be cautiously associated. Beta-blockers (i.e. atenolol) have proven to be effective in controlling tachycardia or hypertension, but should be used with caution due to the elevated risk of hypotension in the elderly population. In cases of delirium tremens, the administration of 30–60 mg/day of diazepam i.v., magnesium, thiamine 100–250 mg/day i.v., and electrolytes (if necessary) is warranted (Letizia and Reinbolz, 2005).

### 5.2 Rehabilitation

The goals of rehabilitation for AUDs are the same as for any chronic relapsing disorder: to help keep motivation high, to change attitudes toward recovery, and to reduce the risk of relapse. The prevention of drinking relapse in older alcoholics is crucially important, as the outcomes are comparable and, in some cases, better than in younger patients. More than 20% of treated elderly alcohol-dependent patients remain abstinent after four years (Satre et al., 2004). Moreover, women seem to maintain abstinence, both in the short- and long-term, better than men (Satre et al., 2004; 2007).

Among the medications approved for alcohol dependence, disulfiram is not generally recommended due to the increased risk of serious adverse effects (Oslin et al., 1997; Satre et al., 2004; 2007). In addition, naltrexone (μ-opioid antagonist) given at 50–100 mg per day (or 150 mg three times a week) might help alcohol-dependent patients by reducing craving and feelings of reward or pleasure when drinking and most studies have reported a longer time before relapse or lower alcohol intake on drinking days with an improved outcome of a modest 20% (Schuckit, 2009). Thanks to its safety profile, naltrexone (50 mg daily) is suggested as a pharmacological agent for relapse prevention in older alcoholics (Oslin et al., 1997). Moreover, due to the elderly's predisposition to forgetfulness, some hypotheses have been raised regarding the possible usefulness of the injectable extended-release formulation of naltrexone (380 mg/month for 4 months) after a period of abstinence of 3–5 days (Johnson, 2010). Furthermore, even though specific studies in older populations have not been performed yet, acamprosate (N-methyl-D-aspartic acid-glutamate receptor inhibitor) has been shown to be able to increase the time to relapse, to decrease the number of drinks per drinking day, and to help in maintaining abstinence with a rate of improved outcome similar to naltrexone. Combined naltrexone and acamprosate might be slightly better than either drug alone, although not all studies agree (Schuckit, 2009). Finally, GABA-ergic drugs such as sodium oxybate (approved in some European Countries for the treatment of alcohol dependence), baclofen and topiramate have been shown to be efficient and promising drugs in maintaining alcohol abstinence and in reducing the number of episodes of heavy drinking (Addolorato et al., 2011; Caputo et al., 2010; Johnson, 2010).

Cognitive-behavioral therapy and attendance at self-help groups, such as Alcoholics Anonymous, have proved beneficial if associated with a pharmacological approach (Oslin et al., 1997; Satre et al., 2004; 2007). On the other hand, depression, interpersonal conflicts, solitude and major life stressor events are important risk factors for relapse in the elderly

population. Thus, a multidimensional approach, including pharmacological, psychological and socio-behavioral treatment, is crucial in maintaining abstinence in alcohol-dependent elderly patients.

## 6. Conclusions

The incidence of AUDs in the elderly is fairly high; however, AUDs in the elderly are underestimated, and data collection of alcohol-related harm in older adults by the European Union and also by the World Health Organization are incomplete and sparse (Lee et al., 2008). Filling this scientific gap may identify cost-effectiveness intervention for AUDs in older adults, improving the sustainability of public finances and reducing health inequalities (Scafato, 2010); additional research is needed to identify the best implementation strategies.

Thus, the diagnosis and treatment of AUDs in elderly subjects should always be pursued, since it is just as effective as in younger patients; more attention should be paid to the fragility of older patients during AWS and to the need for a multi-dimensional approach in the prevention of relapse. More studies on the pharmacological and psychotherapeutic treatment of AUDs in the elderly are warranted.

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**Table 1**

Interactions of alcohol with some medication (Moore et al., 2007).

| MEDICATION | EFFECTS |
|---|---|
| Opioids | ↑ sedative effect hypotension |
| Anxiolytics<br>Antihistamines<br>Cimetidine | ↑ sedative effect |
| Aspirin<br>PPIs | ↓ gastric ADH activity (*first pass metabolism*) |
| Antidepressants<br>Antipsychotics | ↑ sedative effect hypertension |
| Phenytoin | ↑ toxicity (acute alcohol intoxication)<br>↓ efficacy (chronic alcohol abuse) |
| Carbamazepine | ↑ sedative effect |
| Beta-blockers<br>Calcium-channel blockers<br>Nitrates | hypotension (acute alcohol intoxication)<br>hypertension (chronic alcohol abuse) |
| Digoxin | ↓ digitalis effect |
| Oral hypoglycemia-regulating drugs | hypoglycemia (chronic alcohol abuse)<br>↑ risk of lactic acidosis (metformin) |
| Heparin<br>Warfarin<br>Aspirin and NSAIDs | ↑ risk of bleeding (i.e.gastro-intestinal tract) |
| Statins<br>Paracetamol<br>Isoniazid<br>Lithium<br>Methotrexate | ↑ hepatic toxicity (acute hepatitis) |
| Cephalosporins<br>Chloramphenicol<br>Ketoconazole<br>Metronidrazole | ↑ acetaldehyde blood levels (during disulfiram administration) |

ADH: alcohol-dehydrogenase; NSAIDs: non-steroidal anti-inflammatory drugs; PPIs: proton-pump inhibitors.

**Table 2**

The **CAGE** test: two or more positive answers suggest the presence of an alcohol-related problem (Culberson, 2006).

| |
|---|
| **C (cut-off):** have you ever felt that you should cut down on your drinking?<br>**A (annoyed):** have people annoyed you by criticizing your drinking?<br>**G (guilty):** have you ever had guilty feelings about drinking?<br>**E (eye opener):** have you ever had a drink first thing in the morning to steady your nerves or get rid of a hangover? |

**Table 3**

Short Michigan Alcoholism Screening Test - Geriatric Version (**SMAST-G**): two or more positive answers suggest the presence of an alcohol-related problem in the past 12 months (Johnson-Greene et al., 2009).

| | |
|---|---|
| **1** | When talking with others, do you ever underestimate how much you actually drink? |
| **2** | After a few drinks, have you sometimes not eaten or been able to skip a meal because you didn't feel hungry? |
| **3** | Does having a few drinks help decrease your shakiness or tremors? |
| **4** | Does alcohol sometimes make it hard for you to remember parts of the day or night? |
| **5** | Do you usually take a drink to relax or calm your nerves? |
| **6** | Do you drink to take your mind off your problems? |
| **7** | Have you ever increased your drinking after experiencing a loss in your life? |
| **8** | Has a doctor or nurse ever said they were worried or concerned about your drinking? |
| **9** | Have you ever made rules to manage your drinking? |
| **10** | When you feel lonely, does having a drink help? |

## Table 4

Prevalence of the alterations of laboratory markers of chronic alcohol abuse in elderly patients compared to young subjects (Mundle et al., 1999).

| Serum parameter | alterations (%)(patients aged ≥ 65 yr) | alterations (%)(patients aged ≤ 65 yr) |
|---|---|---|
| ↑ AST | 56 | 42 |
| ↑ GGT | 55 | 48 |
| ↑ MCV | 44 | 17 |
| ↑ Glucose | 32 | 36 |
| ↑ Uric acid | 21 | <1 |
| ↓ Albumin | 17 | 3 |
| ↑ Alkaline phosphatases | 11 | 15 |
| ↑ Triglycerides | 16 | 15 |

AST: aspartate aminotransferase; GGT: gamma-glutamyl transpeptidase; MCV: mean corpuscular volume.