

Special Article

A Literature Review of the Prevalence of Dementia and Cognitive Impairment Associated with Alcohol Use in the Elderly

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Abstract

Purpose: The purpose of this paper is to describe the effects of alcohol abuse, mainly at cognitive functioning among the elderly population.

Material and Method: Thirty-four articles of the last decade, studies, and researches related to the subject were examined.

Results: Alcohol-related dementia (ARD) is a form of dementia caused by excessive and prolonged use of alcohol. It is related to brain damage as a direct effect of alcohol's neurotoxicity. The direct effects of alcohol abuse result in a continuous cognitive dysfunction and behavioral change. It is known that excessive alcohol consumption can cause serious and sometimes permanent cognitive impairment, including alcohol-abuse dementia, withdrawal syndrome, frontal lobe syndrome, Wernicke-Korsakoff encephalopathy as well as amnesia syndrome via thiamine. Mechanisms of alcoholic effects in cognition are complex. In addition to direct and indirect effects, genetic predisposition and environmental factors can modify the clinical manifestations accordingly. Since dementia, stroke and cardiovascular disease are the main causes of mortality in the elderly in developed countries, the better knowledge of mechanisms that stimulate the effects of alcohol intake may be useful in both medical management and policy-making for the social health. Finally, in the elderly alcohol-drug interactions and age-related physiological changes must be taken into account.

Conclusions: Alcohol increases the risk of exposure to potentially harmful causes such as head trauma, hepatic encephalopathy, greater susceptibility to infections and simultaneous abuse of other neuroactive substances. In elderly patients should be taken into account the alcohol-drug interactions and the age-related physiological changes.

Keywords: alcohol, alcohol use, cognitive disorders, dementia, elderly

Introduction

Alcohol acts on the central nervous system and modifies the fluidity of cell membranes by interacting with calcium and chlorine channels, resulting in the impairment of cell function. Ethanol does not act on a particular receptor, but

on several nerve networks that are served by different neurotransmitters. The results appear to be dose-related since at low doses alcohol affects the monoaminergic transmission and causes inhibition and euphoria, while at high doses it causes anxiolytic and sedative effects, increasing

Gamma-Aminobutyric Acid (GABA) activity and inhibiting the excitatory amino acids (Littleton et al, 2001).

The main neurotoxic effect of ethanol appears to be caused by glutamic acid, as alcohol blocks N-methyl-aspartate (NMDA) receptors, which chronic inhibition causes increased release of glutamic acid with excitotoxic effects (Brust 2010; Harper 2007). Direct effects are mainly caused by malnutrition, which is common in alcoholics and lead to deficiencies in thiamine, nicotinic acid, vitamin B complex and folic acid (Roberto et al. 2004). Probably through regulation of glutamate receptors and down regulation of the GABA receptor, the abrupt abstinence after prolonged drinking may lead to tremor, hallucinations (visual, auditory, or tactile), seizures or delirium, hyperactivity, internal agitation and gait instability (Martin et al, 2003; Harper 2007).

Effects of alcohol on cognition

The effects of chronic alcohol abuse on cognitive function are known. In the elderly, also it should be taken account the complexity of neurobiology of alcohol, in particular the interaction of alcohol effects with genetic predisposition and environmental factors, as well as age-related changes that emerge with age. The neurological complications of alcohol abuse include different clinical manifestations of cognitive disorders (Geibprasert et al, 2010).

Wernicke-Korsakoff syndrome and Marchiafava-Bignami disease are both associated with nutritional deficiency, in particular with thiamine. Whereas, «alcoholic dementia» or «alcohol-related dementia» occurs generally in the absence of nutritional deficits or other forms of brain damage that are caused, for example, by brain trauma and hepatic insufficiency. In these cases, it is likely that an immediate neurotoxic effect of alcohol is involved. This view has not been substantiated yet (Sullivan and Pfefferbaum 2009). The degree of neuropsychological deficiencies is related to gender, overall duration of abuse and the amount of alcohol intake. Women are possibly more vulnerable to the effects of alcohol, displaying earlier changes as well as faster recovery on abstinence (Gupta and Warner 2008).

An important factor is also the age of onset of abuse for the development of a future cognitive impairment. Alcoholism causes changes in brain morphology such as enlargement of the abdominal system, especially the third ventricle, and cerebellar atrophy while in later stages shrinking of the frontal and pre-frontal areas associated with neuropsychological deficits that have been reported. Cognitive disorders as well as brain abnormalities in alcoholics may partially recover by abstinence (Geibprasert et al, 2010; Savage 2015). Although more recent data suggest that repeated withdrawal episodes may be associated with decreased plasticity of the brain, as evidenced by the delayed recovery from carelessness and disturbed executive functions in contrast to those having one or none detoxifications (Davies et al, 2005).

Alcohol and dementia

The direct effects of alcohol abuse are depicted on neuroimaging and neuropathology. The key feature of alcohol-induced brain injury is the reduction in «white matter» in the frontal cortex which is responsible for Fronto- cerebellar. The neuropsychological profile of alcohol-related dementia has not been adequately studied, but there are indications that the linguistic malfunction is unlikely in comparison with Alzheimer's disease. It seems to be better performance in semantic tasks and in speech memory recognition, whereas worse in audiovisual tasks. However, many patients who have Wernicke-Korsakoff syndrome features often referred to precursor amnesia, have reduced recall of past events and executive function (Letenneur 2004; Luchsinger et al. 2004).

It remains a need for further investigation whether the degree of alcohol abuse can aggravate the primary degenerative and vascular dementia as well as if traumatic brain injury and alcohol related brain damage caused by substance abuse and other bodily disorders can affect the cerebral function (Peters et al, 2008).

There are 3 different diagnostic criteria of ARD(**table 1**). The first is based in the DMS system, the second to the provisional criteria proposed by Oslin and the last one, on the International statistical classification of disease system (Oslin and Carry,2003). In clinical practice ARD is mostly under diagnosed because the diagnosis is largely dependent on primary

care doctors individually and their ability to take a full medical history and to identify alcohol abuse in the elderly. The clinical manifestations of ARD are similar to other types of dementia and as a result there is difficulty in the diagnosis (Cheng et al, 2017; Chari et al. 2015). In particular, the presence of prolonged and abnormal alcohol intake and the persistence of symptoms for more than three weeks after withdrawal from alcohol are required for diagnosis. Patients that develop progressive multi-sectoral cognitive disorder, and rarely dementia are usually because of Wernicke-Korsakoff syndrome. However, the morphological substrates are different, since in alcoholic dementia the neuroimaging exhibits diffuse atrophy while in the Wernicke-Korsakoff

syndrome a selective involvement of the frontal cortex and the thalamus during the acute phase has been reported (Panza et al, 2009; Lobo et al, 2010).

Also, a cognitive dysfunction, mainly related to memory and executive functions, can be detected in chronic "inadequate" alcoholics (Mechtcheriakov et al, 2007). Early-onset dementia (EOD), onset of dementia before the age of 65 years, is mainly attributed to Fronto-temporal dementia (FTD), Alcohol-related dementia (ARD), traumatic brain injury and Huntington’s disease. As a consequence, there is always a possibility of hidden alcohol consumption in EOD and it should always be taken into account.

Table 1. Assessment of Alcohol- Related Dementia

Index	Description
High Index of Suspicion	In confused patients with alcohol use/disorders and/or dietary deficiency/malnutrition and comorbid medical illness.
Thorough history taking	Specially noting the quantity, frequency, pattern, duration of alcohol use, and time of last use; attempts at abstinence, number of detoxification attempts and severity of withdrawal symptoms. Detailed history of amnesia, apraxia, visuo-spatial deficits, aphasia and difficulty in daily functioning, and its temporal relationship with alcohol use.
Detailed clinical examination	Eliciting dietary deficiency/malnutrition; Oculomotor abnormalities-nystagmus, ophthalmoplegia, diplopia, miosis, anisocoria, papilloedema and retinal hemorrhages; Cerebellar dysfunction (ataxia, nystagmus); Mild memory impairment or delirium; Autonomic disturbances like tachycardia, hypotension, hypo or hyperthermia. Other features like seizures, hearing loss, spastic paraparesis or acute psychosis
Investigations	Complete blood counts; electrolytes; liver function tests; renal function tests; thyroid function tests; blood sugar level; coagulation profile; serum levels of folate, B12, magnesium, calcium and phosphate. Raised gamma glutamyl transferase and macrocytosis are useful biological markers of alcohol consumption. Magnetic resonance imaging of brain may support Wernicke encephalopathy’s diagnosis. Treatment with thiamine should be started immediately without waiting for the results. Thiamine pyrophosphate levels and erythrocyte transketolase activity may be helpful

Neuropsychological testing	<p>Determines the degree of cognitive impairment. Folstein Mini-Mental Status Examination (MMSE) is the minimum screen for dementia.</p> <p>The Montreal Cognitive Assessment (MoCA) Test appears to be the most appropriate screening test for detection of cognitive impairments in these patients, as it is more sensitive than MMSE for mild-to-moderate cognitive impairments.</p> <p>Detailed assessment of cognitive impairments may be performed by a clinical neuropsychologist.</p> <p>A number of test batteries may be used for different domains such as memory (e.g., California Verbal Learning test), working memory (Digit Span and Letter-Number Sequencing test) executive functions (e.g., Trail Making Test part B and Wisconsin Card Sorting Test, the Stroop Color Word test, and the Letter Fluency Test) and processing speed (Digit Symbol-Coding)</p>
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Source: (Sachdeva et al, 2016 ; Mehlig et al, 2008 ; Paul et al, 2008)

Table 2.Data based on the global report on the state of the Alcohol and Health in 2014

Worldwide, 3.3 million deaths each year result from the harmful use of alcohol.
Harmful use of alcohol is a causal factor in more than 200 disease and injury conditions.
A total of 5.1% of the world's burden of illness and injuries is due to alcohol as measured in the DALYs (Disability – Adjusted Life Years).
Drinking alcohol causes death and disability relatively early in life. In the 20-39 age groups about 25% of all deaths attributed to alcohol.
There is a causal relation between harmful alcohol use and a series of mental and behavioral disorders and injuries.
The latest causal relations have arisen between harmful alcohol consumption and the incidence of infectious diseases such as tuberculosis as well as the course of HIV / AIDS.
Apart from the health consequences, harmful alcohol use brings considerable social and economic losses for individuals and society in general.

Source: (WHO 2014; Ilomaki et al, 2015)

Alcohol as a protective factor for health

Dementia and cognitive decline are associated with diseases of the cardiovascular system. Whereas alcohol in large quantities seems to have negative effects on the cardiovascular system, in smaller controlled amounts it acts beneficially. The effect of alcohol intake may be

more important in the elderly as it affects their cognitive function (Peters et al, 2008).

Despite the fact that chronic alcohol abuse causes progressive neurodegenerative disease, several studies have shown that alcohol intake within limits and consumption of certain types of alcoholic beverages mainly wine, are both associated with a reduced risk of developing

dementia or cognitive dysfunction. According to the bibliography, there are several mechanisms that are associated with the protective effect of light-to-moderate alcohol consumption (Paul et al, 2008). For example, the antioxidant properties of flavonoids in wine can help to prevention of the oxidative damage that is involved in dementia. Alcohol also increases the levels of HDL cholesterol and fibrinolytic factors leading to lower aggregation of platelets and possibly lower risk of stroke, ischemic episode. Alcohol consumption has been associated with decreased cardiovascular risk and possible enhancement of insulin sensitivity or decreased of inflammatory response. A study from even in the context of the economic crisis from health professionals did not suggest high levels either in the frequency or quantity of alcohol consumption, nor was consumption considered by participants to be a management tool to deal with stressful situations experienced in their working life (Saridi et al., 2016)..

Given that the relationship between vascular dementia, vascular function and the increasing number of elements suggesting that Alzheimer's disease can be affected by vascular factors, it can be concluded that this cardiovascular protection reduces the casual dementia and cognitive impairment (Sabia et al. 2014). In France, the PAQUID study reported that even three to four glasses of wine a day can reduce the risk of dementia (Nourhashémi et al, 2003).

Since dementia, stroke and cardiovascular disease are the main causes of mortality in the elderly in developed countries, the better knowledge of mechanisms that stimulate the effects of alcohol intake may be useful in both medical management and policy-making for the social health (Sinforiani et al, 2011; Sabia et al, 2014).

Discussion

According to World Health Organization (WHO,2012), 5.9% of all global deaths were attributable to alcohol, although there is wide geographical variation in alcohol-related deaths. In 2013 alcohol became the sixth leading cause of morbidity and there are 60 different types of diseases that alcohol plays a major causal role (WHO, 2014). The total number of dementia patients worldwide in 2015 is estimated at 47 million and is expected to rise to 82 million by

2030 and to triple by 2050. Deaths due to Alzheimer's disease and other dementias was the 5th leading cause of mortality worldwide in 2016, whereas in high-income countries was the third (WHO, 2012). As far as public health is concerned there are mixed reports on the role of alcohol consumption and the development of dementia (**table 2**).

In a United Kingdom clinical study in people aged 56 years, it was found that alcohol consumption more than 32 units per week caused impairment in cognition, memory and executive functioning after a decade (O'Dowd 2008). These cognitive impairments exceed the neuropsychological profile of amnesia syndrome. There is evidence of minor improvement after abstinence in people with alcohol-related dementia (Savage 2015).

In a study conducted in 2011 in New South Wales Hospital, Alcohol-related cognitive dysfunction was studied, in approximately 450 hospital patients, alcohol users, with an average age of 50 years. The results showed that excessive alcohol consumption can cause severe cognitive impairment whereas in some cases the damage is permanent and irreversible. Significant clinical and neuropathological overlap between disorders such as deprivation syndrome, frontal lobe syndrome and Wernicke-Korsakoff encephalopathy has been reported. Alcohol-related cognitive disorders often become apparent in hospital patients during the early days of hospitalization due to alcohol abstinence. They usually have a major withdrawal syndrome (Draper et al, 2011; McQueen et al, 2009; Rao and Draper, 2008).

In a similar study, conducted in 2006-2007, in an Australian hospital, HDS, in the dementia program, people with an average age of 50 years were studied, as there are relatively few cases of dementia under this age. The results were that 8.2% had been diagnosed with dementia (Wobrock et al, 2009). More specifically, 3.2% had diagnosis of dementia due to alcohol abuse, 1.8% had a mixed dementia diagnosis, 1% represented patients diagnosed with another type of dementia, and the other 2% were patients with other mental behavioral disorders are due to the use of alcohol based on the classification scale F10, ICD-10-AM, and subcategories, acute poisoning, addiction syndrome, delirium

withdrawal status, amnesic syndrome, mental and behavioral disorders, psychotic disorder (APA 1994; Draper et al, 2011; Roberto et al, 2004).

In 2011, a 3-year follow up German study among primary care at tenders aged 75 years and older investigated the relationship between alcohol intake and incident dementia. It was found that light-to-moderate alcohol consumption was in general associated with good mental and overall health. But according to the researchers that could be due to other factors such as healthier lifestyle choices in terms of diet, exercise and mental well-being (Weyerer et al, 2011 ; Draper et al,2011).

Finally, in a clinical study in Sweden, which studied people with an average age of 43 years-old, based on the quantity, frequency and type of alcohol they consumed with a follow-up period of over 20 years, the results were that average alcohol consumption of over 12 grams, there is a risk of increased dementia. The type of alcohol beverage seems to play key role in developing dementia (Sachdeva et al, 2016). Nurk et al (2008), also, conducted a population-based study and examined the relationship of cognitive test performance and regular intake of flavonoid-rich food such as chocolate, wine and tea and found that there is dose dependent association between flavonoids and cognitive function. Light-to-moderate wine consumption in particular seems to have the strongest beneficial effect on cognition (Nurk et al, 2009; Lee et al, 2010).

With the number of cases of dementia at steady rise due to aging of the population, the researchers have focused on modifiable prevention factors for future appearance of dementia. The development of dementia can be an interrelation of genetic and environmental factors, which can be aggravated by poor individual lifestyle choices of a person's lifestyle such as lack of physical activity, malnutrition and smoking (Harwood et al, 2010).

Conclusions

From the thirty-four articles studied, there were fifteen studies with a follow-up duration of over ten years and up to 25 years. Twelve were population studies and three clinical studies. The majority of studies originated in Europe, mainly in northern Europe. Three studies looked into

only at AD dementia, eleven studies focused on cognitive decline, and the rest assessed the alcohol abuse and the incidence of dementia.

The results from all studies reported that there was a significant correlation between alcohol intake and dementia, as well as significant cognitive decline. Given that the samples of the studies were quite heterogeneous, we should be very careful in interpreting the results of the investigations. The differences in study design, inclusion criteria, beverages, alcohol, alcohol intake duration, and follow-up periods are sources of variability in the results. Moreover, there is a lack of statistical data in ARD, probably because in clinical practice ARD is usual underdiagnosed. But if there is an early diagnosis the negative effects may be reversed or by abstinence. Moreover, the potential environmental and genetic factors may cause further confusion in the results. Mechanisms of alcoholic effects in cognition are complex. In addition to direct and indirect effects, the genetic predisposition and environmental factors can modify differently the clinical manifestations.

Also, alcohol increases the risk of exposure to potentially harmful causes such as head trauma, hepatic encephalopathy, greater susceptibility to infections and simultaneous abuse of other neuroactive substances. In elderly patients should be taken into account the alcohol-drug interactions and the age-related physiological changes. The role of alcohol in cardioprotection and neuroprotection should be further clarified, as dementia, stroke and cardiovascular diseases are the main causes of mortality in older people in developed countries.

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