Alcohol and Dementia

The number of older people is increasing in populations throughout the world. As we live longer, age-related maladies loom large unless we adjust our lifestyles and try to stay healthy but it is now emerging that alcoholic brain damage is catching up with Alzheimer's because oldies are drinking more and more (25). Alcohol use disorders in elderly people are a common but under-recognised problem associated with major physical and psychological health problems. Often described as a hidden problem, alcohol abuse may be due to a number of factors. (1)
Firstly, many elderly people do not disclose information about their drinking because they are ashamed. Many are isolated, with minimal social contact or networks, thereby making the problem more difficult to detect. It has also been suggested that older people may significantly underreport their drinking (2). Secondly, people in the helping professions seem reluctant to ask an older person about drinking, either because it makes them feel awkward or because of the stereotypical image of alcohol use disorders as a problem affecting mostly younger people (3). Thirdly, alcohol problems often present in a large number of non-specific ways such as accidents, depression, insomnia, confused states and self neglect, many of which are linked to the ageing process itself anyway.

Background

Alcohol use disorder may be described as being of early or late onset. Elderly people who fall into the early-onset category have had a lifelong pattern of problem drinking and have probably been alcoholics for most of their lives. American studies suggest that this category comprises two thirds of elderly alcoholics (4). Typically, there is a family history of alcoholism and these individuals had drinking problems in their early 20s or 30s. They are more likely to have psychiatric illness and brain syndromes. Alcohol adds to the risk of accidents and has been identified as one of the three main reasons for falls, which are a significant cause of mortality and ill health in older people (5). Alcohol abuse is clearly under-diagnosed. Signs and symptoms of alcohol abuse include cirrhosis of the liver, hypertension, cardiac disease, gastrointestinal disorders and certain types of cancers. Neurological signs include that of a peripheral neuropathy and wide-based gait, secondary to cerebella atrophy. Associated psychiatric disorders can include anxiety, depression and insomnia. Nutritional deficiencies secondary to dietary neglect can affect vitamin B12 and foliate levels. Recurrent falls during periods of intoxication are associated with trauma, including head injuries and fractures. Evidence demonstrates that individuals who experience problems with alcohol late in life (onset after the age of 45 years) differ from those with early-onset problems (prior to the age of 25 years). The late-onset alcoholics were better able to achieve abstinence, required fewer detoxifications, and had a lower alcohol consumption as well as lower psychiatric comorbiditiy compared to early-onset alcoholics. These differences contribute to a better treatment outcome. research indicates that treatment of elderly individuals with alcohol-use disorders can be beneficial. Given the comorbidity of other disorders, and that withdrawal tends to be more severe and protracted than in younger patients (8). Inpatient admission is generally preferred. Frequently of significance is that once an individual is able to achieve abstinence, cognitive impairment shows some degree of reversibility(6).

Relationship of Alcohol to Dementia

The relationship between alcohol use and dementia in the elderly is complex. Moderate alcohol use may have a protective effect against the development of dementia. There is some evidence to suggest that limited alcohol intake in earlier adult life may be protective against incident dementia later on. In older people, small to moderate amounts of alcohol consumption are associated with reduced incidence of dementia and Alzheimer's disease. The evidence is strongest for wine consumption but not conclusive.(7) However, excessive consumption has been associated with an

increased risk of dementia in the elderly. Given that anywhere between 2% and 10% of the elderly abuse alcohol or are alcohol dependent, the social impact of such behaviour is significant.(8)

Studies indicate that moderate alcohol consumption has a protective effect on the development of both Alzheimer's disease and vascular dementia. Heavy use increases the risk of developing vascular dementia and alcohol related dementia, but not Alzheimer's. Dementia may be either directly caused by alcohol use or secondary to alcohol use in the case of alcohol-related dementia. A definition has been proposed and is defined as "a significant deterioration of cognitive function sufficient to interfere in social or occupational functioning"(9).

Whether alcohol is beneficial or harmful depends upon the amount consumed. The elderly have a lower tolerance than younger individuals. Typically, blood alcohol concentration is higher in the elderly for a number of reasons, including decreased metabolism and blood flow, decreased lean body mass and decreased body water(10). Women have a lower tolerance than men due to significantly slower metabolism. Binge drinking is associated with increased overall risk of dementia.

Etiologies

In the view of current literature,(9), alcohol-related dementia encompasses a variety of etiologies, some of which will be described herein. Wernicke Korsakoff syndrome is the most common form of dementia related to alcohol use (11) and is associated with symptoms including a delirium and memory deficits, confusion and clinical signs such as opthalmoplegia and ataxia. However, it should be noted that the Wernicke Korsakoff syndrome often does not have a typical presentation. Pellagra is a rare condition associated with niacin deficiency and presents in the early stages with symptoms similar to physical disease or depression. More conclusive symptoms include confusion, hallucinations, paranoia, spastic weakness and a positive Babinski sign. Very rare and occurring primarily in men, Marchiafava-Bignami Disease is associated with the degeneration of the corpus callosum and a variable presentation. Diagnosis of this condition is very difficult and although CT scans and MRI assist in clarifying the presentation, diagnosis is typically made post-mortem. All of these conditions are largely related to nutrient deficiencies secondary to heavy alcohol use. Alcohol-related dementia also includes dementia directly caused by alcohol consumption, although controversy remains as to whether this phenomenon exists (11). This is because it has not been possible to clinically define this type of dementia as a separate entity from the Korsakoff symptom spectrum, and because there is no evidence for specific neuropathology.

The $ApoE_4$ Genotype

Genotyping research has been inconclusive. In some studies, individuals with an ApoE4 genotype who drank heavily were shown to be at greater risk of developing dementia than those who were negative for the genotype (12). To address the relationship of alcohol consumption and risk of dementia further a nested case-control study of alcohol consumption and risk of incident dementia in a cardiovascular health study, a prospective, population-based study of adults aged 65 years and older in the United States has been undertaken. Of the 664 participants who agreed to be tested, 171 tested positive for $ApoE_4$. Age-adjusted rates of incident dementia were 56 per 1000 among black participants and 36 per 1000 among white participants (14) In this case-control study, moderate alcohol consumption had an inverse relationship with the risk of dementia, even after multivariate adjustment and exclusion of former drinkers. Abstainers had odds of dementia that were about twice as high as the odds among consumers of between 1 and 6 drinks per week. Possible differences were found in the association of alcohol with dementia according to sex and $ApoE_4$ genotype. The inverse association of alcohol use with dementia was most pronounced among participants without an $ApoE_4$ allele, who are at lower risk of dementia. Among individuals with an $ApoE_4$ allele, alcohol use at or above 7 drinks per week appeared to be associated with a

substantially higher risk of dementia. These results parallel those of an epidemiology of vascular aging study, which found that alcohol intake was associated with a lower risk of cognitive deterioration among subjects without an $ApoE_4$ allele, but a higher risk in $ApoE_4$ carriers (13). Surprisingly, another study found that the lower risk of dementia associated with alcohol use was more consistent among individuals with an $ApoE_4$ allele (26).

Action of Alcohol on the Brain

Experimental studies have found that ethanol initially increases hippocampal acetylcholine release, which could conceivably improve memory performance (15). A review on the effect of alcohol on the frontal lobe noted that neuroradiological findings support the occurrence of morphological abnormalities in brains of chronic heavy drinkers, suggesting cerebral atrophy (27). Structural imaging using computed tomography scans of male alcoholics showed larger ventricles and wider cerebral sulci and fissures compared with controls (7). Functional imaging studies have reported decreased frontal lobe glucose utilisation and reduced cerebral blood flow. Various mechanisms have been attributed to the effects of alcohol on the brain including a direct neurotoxic effect of alcohol, oxidative stress, excitotoxicity, mitochondrial damage and apoptosis. Repeated withdrawal may be associated with greater cognitive impairment due to neuronal damage and may have a bearing on the dementing process. Those having two or more detoxifications showed a greater degree of cognitive impairment compared with those with one or none.

The protective effect of light-to-moderate alcohol consumption may be due to a number of direct and indirect mechanisms (16): increased serum concentration of high-density lipoprotein; lowering of cholesterol; beneficial effects on platelet function, clotting and fibrinolysis and improved insulin sensitivity. The non-alcoholic components may have antioxidant, anti-inflammatory and vaso-relaxant properties (17). It is still an open question whether different alcoholic beverages, such as beer, wine and spirits, have a similar effect. Some studies have shown a positive effect of wine only, which may be due either to the level of ethanol, the complex mixture that comprises wine or to the healthier life-style ascribed to wine drinkers. One study suggests (16) that light-to-moderate alcohol consumption is inversely related to incident dementia among individuals aged 75 years and older. There is no doubt that long-term alcohol abuse is detrimental to memory function and can cause neurodegenerative disease. Estimates from various studies have suggested the prevalence of alcohol-related dementia to be about 10% of all cases of dementia.

Given the neurotoxic effects of alcohol and the inexorable increase in per capita consumption, future generations may see a disproportionate increase in alcohol-related dementia. This could be compounded by the effects of increasing use of recreational drugs such as ecstasy, whose long-term effects on cognition are still uncertain.

A German Study (16)

The study was conducted in six centres (Bonn, Düsseldorf, Hamburg, Leipzig, Mannheim and Munich). A total of 3,327 patients were interviewed in their homes by trained investigators, 3,202 persons were without dementia. Information on current alcohol consumption was available for 3,180 subjects, 50.0% were abstinent, 24.8% consumed less than 1 drink per day with a small subgroup of 25 participants fulfilled the criteria of harmful drinking. One man and one woman reported an extremely high consumption of alcohol. Among the consumers of alcohol almost half (48.6%) drank wine only, 29.0% drank beer only and 22.4% drank mixed alcohol beverages (wine, beer or spirits). Alcohol consumption was significantly associated with male gender, younger age, higher level of education, not living alone and not being depressed. No association was found

between alcohol consumption and functional impairment, complex history of illness and multiple diseases , smoking, MCI or $ApoE_4$ status.
Although the consumption of alcohol generally decreases with increasing age, in Germany the current use of alcohol among the elderly is substantial (men: 73.5%; women: 37.6%). The study suggests that light-to-moderate alcohol consumption is inversely related, also among subjects aged 75 years and older, to both incident overall dementia and Alzheimer dementia. In dementia generally, it could be that participants who drank alcohol sensibly had a healthier lifestyle in terms of physical, dietary and mental perspectives. Key points from the study were:-
• Among a large sample of individuals (75 years of age and older) without dementia at the start, 50% consumed alcohol, in general less than 2 drinks per day.
• Persons who continue drinking alcohol throughout old age are the remainder population, exhibiting a survivor phenomenon.
• After controlling for a number of potential confounders current alcohol consumption was associated with a 29% decrease in overall dementia incidence.

The Finnish Study (18)

Results suggest that frequent alcohol drinking in middle age is associated with cognitive impairment in later life. For frequent drinking to be associated with increased risk of dementia, however, the presence of the $ApoE_4$ allele may be necessary. This observation that $ApoE_4$ may modify the effect of alcohol is in agreement with the concept that cognitive status is the consequence of both genetic and environmental factors. However, the mechanism by which moderate alcohol drinking could preserve cognitive function remains to be clarified. Is it alcohol as such or some other social and lifestyle factors that co-associate with certain drinking habits? Until all such factors and associations with cognitive functioning have been identified, care needs to be taken in how the results relating to alcohol consumption are interpreted. Current data indicates that frequent alcohol drinking has harmful effects on the brain, and this may be more pronounced if there is genetic susceptibility. One possible explanation could be that people with the $ApoE_4$ allele have less effective neural repair mechanisms (28) and thus they would be more susceptible to the deleterious effects of alcohol.

The London Study (19)

The study was undertaken in the London boroughs of Kensington and Chelsea, Westminster, and Hillingdon with a total population of 567 500 people. The aim of the study was to use a large, geographical catchment area and to use a combination of techniques to identify every known case of dementia starting **before the age of 65** years. Having identified cases, there was also interested in exploring the prevalence of the different causes of dementia, and using the results obtained to extrapolate estimates of the numbers of younger people with dementia in the UK. The cases identified included Alzheimer's disease (62 cases, 34%), vascular dementia (34 cases, 18%), frontotemporal dementia (23 cases, 12%), alcohol related dementia (19 cases, 10%), and dementia with Lewy bodies (12 cases, 7%). Other causes of dementia accounted for 35 cases (19%) Extrapolating the results of the survey to the UK as a whole, it was estimated that in 2001, there were 18,300 people under the age of 65 with dementia, 2255 between the ages of 30 and 64 years had alcohol related dementia and of those, 1910 were in the age bracket 45 to 64 years.

Summary

Alcohol consumption has escalated rapidly in many countries over the past decade. Evidence suggests a correlation between alcohol use and cognitive decline (20). The prolonged and excessive use of alcohol may lead to structural and functional brain damage, leading to alcohol related dementia. The cognitive deficits are most frequently observed in domains of visual perception of the spatial relationships of objects, memory and executive tasks, with a potential of partial recovery if

abstinence is maintained. However, there are doubts regarding the etiopathogenesis, nosological status, prevalence and diagnostic criteria for alcohol related dementia, due to difficulty in assessment and various confounding factors. With a growing cohort of young and middle-aged people, there is a probable risk of upsurge of alcohol related dementia. Presently, there are dilemmas over the diagnosis of independent alcohol related dementia hence there is a need to develop evidence-based guidelines for diagnosis and management of alcohol related dementia through further systematic studies.

Alcohol-related dementia has received little recognition as a distinctive clinical entity, predominantly due to doubts regarding the cause, profile and lack of a typical physiological processes profile. Recently, researchers have showed interest owing to its magnitude, ageing of population and focus of health bodies on alcohol-related issues across the world. There are doubts and debates concerning alcohol-related dementia whether the cognitive impairment or dementia is due to direct ethanol neurotoxicity, or representation of another underlying pathology (thiamine deficiency) or if it is multifactorial, neurotoxicity as well as multivitamin deficiency (21). Various confounding factors often complicate the assessment of alcohol related dementia. These may be the lifestyles of alcohol abusers, concomitant other substance abuse, associated complications like head injury, psychiatric issues, and a higher rate of vascular risk factors, which may independently predispose an individual for cognitive decline (17).

The correlation between the amount and duration of alcohol consumption and occurrence of alcohol related dementia is not well-established. This is due to different types and strengths of liquor available across the countries, varying definitions of leisure drinking and pathological drinking, different cultural beliefs, and different definitions of standard drink (22). Varying patterns of drinking (duration, quantity, binge, abstinent and withdrawal periods in between) along with difficulties in obtaining an accurate self-report of alcohol use (recall problems) may complicate attempts of correlating alcohol abuse to cognitive impairment.

The evidence from neuroimaging, neuropathological reports and autopsy evaluations suggest some degree of brain pathology in individuals diagnosed with an alcohol related disorder. Volume shrinkage, altered glucose metabolism and perfusion along with evidence of markedly decreased neuron density are commonly reported. Frontal lobe appears to be particularly affected (23). Computed tomography scans showed wider cerebral sulci and larger ventricles suggestive of atrophy. The evidence of neuro-circuit disturbances is seen in form of significant loss of white matter (most prominent in the prefrontal cortex, cerebellum and corpus callosum) on functional imaging. Neuronal loss is also noted in the superior frontal association cortex, cerebellum and hypothalamus (24).

Considering the growing proportion of ageing population and rise in per capita alcohol consumption, future generations are expected to see a disproportionate increase in alcohol-related dementia and neurocognitive impairment.

References

1. Dar K., Alcohol use Disorders in Elderly People., Adv. in Psychiatric Treatment., 12, 2006, 173
2. Naik P., Jones R G., Alcohol histories taken from Elderly People on admission., BMI., 308, 1994, 248
3. Deblinger l., Alcohol Problems in the Elderly., Patient Care., 34, 70, 2000
4. Atkinson et. al., Late versus early onset problem drinking in older Men., Clinical and Experimental Research., 14, 1990, 574
5. Wright et. al., Accident Prevention and Risk-taking in Elderly People., The need for Advice., Age Concern Inst. of Gerontology 1994

6. Carlen P L., et. al., Reversibility of alcohol-related Brain Damage. Clinical and Experimental Observations., Acta Med. Scand., 717, 18, 1987
7. Peters R., et. al., Alcohol, Dementia and Cognitive Decline in the elderly: a systematic Review., Age and Ageing., 37, 505, 2008
8. Farnik K., Persyko M., The Association between Alcohol use and Dementia in the Elderly., Can. Alzheimer Disease Review., 13, 2005
9. Oslin D W., Cary M S., Alcohol Related Dementia; validation of diagnostic Criteria., Am. J. Geriatric Psychiatry., 11, 4, 2003, 441.
10. Kalant H., Pharmacological interactions of Ageing and Alcohol., Research Monograph 33., US Dept. HJealth and Human Services., 99, 1998
11. Victor M., Alcoholic Dementia., Can. J. Neurol. Science., 21, 1994, 88
12. Mukamal K J., et. al., Prospective Study of Alcohol Consumption and risk of Dementia in older Adults. JAMA, 289, 11, 2003, 1405
13. Dufouil C., et. al., Influence of apolipoprotein E genotype on the risk of Cognitive Deterioration in moderate Drinkers and Smokers., Epidemiology, 11 2000, 280
14. Lopez O L., et. al., Evaluation of Dementia in the Cardiovascular Health Cognition Study, Neuroepidemiology, 22, 2003, 1
15. Fadda F., et. al., Chronic Ethanol consumption., Prog. Neurobiology, 56, 1998, 385
16. Weyerer S., et. al., Current Alcohol consumption and its relationship to incident Dementia: Resulta from a 3 Year follow-uo study among primary Care Attenders aged 75 years and older., Age and Ageing., 40, 2011, 456
17. Gupta s., Warner J., Alcohol Related Dementia; a 21st. centuary Silent Epidemic? Brit. J. Psychiatry, 193, 2008, 351
18. Anttila T., et. al., Alcohol drinking in middle age and subsequent risk of Cognitive Impairment in Old Age; a Prospective Population Study., BMJ., 10th.August 2004
19. Harvey R J., et. al., The Prevalence and Causes of Dementia in people under the age of 65., J.Neurol. Neurosurg. Psychiatry, 74, 2003, 1206
20. Sachdeva A., et. al., Alcohol Related Dementia and Neurocognitive Impairment; a Review Study., Int. J. High Risk Behav. Addict. 5, 3, 2016
21. Ridley N J., Alcohol Related Dementia: an update of the Evidence., Alzheimers Res. Ther. 5, 1, 2013, 3
22. Turner c., How much Alcohol is in a Standard Drink? An Analysis of 125 Studies., Br. J. Addict., 85, 9, 1990, 1171
23. Moselby H F., et. al., Frontal Lobe changes in Alcoholism; a Review of the Literature., Alcohol 36, 5, 2001, 357
24. Harper C et. al., Ethanol and Brain damage. Curr. Opin. Pharmacology., 5, 1, 2005, 73
25. Stoppard M., Boozy Pensioners risk 'Alcoholic Dementia' with the damage from Drink rivalling Alzheimer's., Daily Mirror 8th.Feb., 2016
26. Rutenberg a et.al., Alcohol Consumption and the risk of Dementia., Lancet, 281, 359, 2002
27. Gupta S., Alcohol related Dementia; a 21st Century Silent Epidemic?, British J. of Psychiatry., 193, 351, 2008.
28. Mahrw et.al., Apolipoprotein E: far more than a lipid transport Protein., Rev. Genomics Hum. Genet., 1, 507, 2000.