ISSN 1669-9106

SUPPLEMENT

MEDICINA (Buenos Aires) 2023; Vol. 83 (Suppl. I): 23-26

ALCOHOL AND CARDIOVASCULAR DISEASE

PASCUAL VALDEZ, SILVIA CORTESE, MARINA RISSO, HOMERO PUELLO, EMILIO CASARIEGO, LORENZO DÍAZ SALAZAR, ROSALÍA GARCÍA PEÑA, AGUSTINA MARCONI

Current state of knowledge

Alcohol is a toxic and mind-altering substance that leads to dependence. The term "social use" often downplays the health and social harm it causes or contributes to. "It plays a crucial role in more than 200 diseases and disorders[1].

In 2016, 32.5% of people worldwide were current drinkers (defined as individuals aged 15 or older who reported consuming alcohol in the last 12 months), with 25% being women and 39% men. On a global scale, the average daily alcohol consumption was 0.73 standard drinks for women and 1.7 for men. It's important to note that various types of beer, wine, and spirits have different alcohol content levels. An average of 10 grams of pure ethanol per serving is considered a 'standard drink,' which is roughly equivalent to 200 ml of beer, 100 ml of wine, or 30 ml of spirits.

Alcohol consumption contributes to 3 million deaths each year worldwide (5.3% of all deaths), causing disabilities and health problems (mental disorders, noncommunicable diseases such as cirrhosis, neoplasms, and heart disease) for millions of people. It is responsible for 5.1% of the global burden of disease (7.1% in men and 2.2% in women), calculated in terms of disability-adjusted life years (DALYs)[1].

The percentage of deaths attributable to alcohol consumption among men is 7.7% of all deaths, while it is 2.6% in women[1].

In a comprehensive analysis of 694 sources of alcohol consumption data, along with 592 prospective and retrospective studies[2], it was found that alcohol consumption ranked as the seventh risk factor for both mortality and years lived with disability. It accounted for 2.2% of female deaths and 6.8% of male deaths. Among the population aged 15-49 years, alcohol consumption emerged as the primary risk factor, contributing to 3.8% of female deaths and a significant 12.2% of male deaths. A significant proportion of the disease burden attributable to alcohol consumption consists of intentional or unintentional injuries (traffic incidents, violence, and suicide), generally in relatively younger age groups[1].

Alcohol is the leading risk factor for premature mortality and disability among people aged 15 to 49 years (10% of all deaths in this age group). Among people aged 20 to 39, 13.5% of total deaths are attributable to alcohol[1]. During pregnancy, it can cause fetal alcohol syndrome and prenatal complications[1].

Alcohol consumption results in significant social and economic losses for both individuals and society as a whole[1].

Besides chronic consumption, there is a phenomenon known as excessive episodic alcohol consumption (EEAC), which is defined as the consumption of five or more standard drinks for men or four or more for women in a span of two hours or less, within the last 30 days. This pattern of consumption heightens the risk of enduring structural and functional brain damage, as well as an increased likelihood of traffic accidents, public violence, and engaging in unprotected sexual activity. Young individuals engaging in this type of consumption are four times more likely to develop dependence compared to those who commence drinking in adulthood[3].

Risks

In several studies, the J curve determines cardio protection at low consumption levels compared to nonconsumers, and when consumption is high, there is a clear association with elevated risk. However, there is some controversy about the initial assertion.

In a study from Lancet[2], the amount of alcohol intake that reduced harm to health outcomes was ZERO standard drinks per week. This contradicts guidelines advocating for cardiovascular health benefits linked to consuming up to two standard drinks per day. However, these results imply that alcohol control policies should be reconsidered globally, emphasizing efforts to decrease/eliminate overall consumption in the population, echoing other studies[4,5]. The study[2] findings indicate that alcohol consumption (irrespective of quantity) results in health decline across all populations. Although some protective effects were found for ischemic heart disease and diabetes among women,

these effects were diluted compared to general health risks due to the strong association between alcohol consumption and the risk of cancer, injuries, and transmissible diseases. These findings emphasize the importance of evaluating how alcohol consumption affects the health of the population throughout life and leaving aside the classic concept of risky or harmful consumption (more than two average standard drinks per day in men and more of one in women.).

From a cardiovascular point of view, consumption is associated with atrial fibrillation[6] and to a lesser extent, with sinus tachycardia, and a reduction in physiological respiratory arrhythmia (due to autonomic imbalance). It is also linked to sudden cardiovascular death (ventricular arrhythmia due to ischemia or alcoholic cardiomyopathy).

A comprehensive review of 44 observational studies[7], encompassing almost a million patients and nearly 40,000 coronary events, compared moderate consumers (those consuming less than two standard drinks daily) with non-consumers, was unable to conclude a beneficial effect for all consumers.

A meta-analysis[8], encompassing 45 studies and involving 3 million patients with 65,000 deaths, revealed an overall lower risk among moderate consumers compared to non-consumers. However, this pattern has not been consistently demonstrated in studies of higher methodological quality or those evaluating global cardiovascular health.

Two European studies[4,9], involving a total of 315,000 cases, failed to establish a causal link between alcohol consumption and cardiovascular protection.

13% of asymptomatic alcoholic patients have subclinical cardiomyopathy[10].

The clinical manifestations of alcoholic cardiomyopathy are typically observed in alcoholic patients over 35 years of age with a daily alcohol intake between 112 and 380 grams (mean 185 ± 52) over a period ranging from 10 to 40 years (mean 23 ± 7)[11].

Alcoholic cardiomyopathy accounts for 21-32% of dilated cardiomyopathies, although this figure could be higher in countries with a higher rate of alcoholism[12].

Recommendations

There are population-level and individual level interventions.

From the population-level, reducing the burden of harmful alcohol consumption, public health measures are proposed that are beyond the scope of this document[3].

From an individual level, different clinical situations that all involve problematic alcohol consumption must be considered[1,2,13,14]:

• Dependence or alcoholism or alcohol addiction (main reason for addiction consultations).

• Regular or chronic risky consumption without dependency.

• Consumption in vulnerable populations such as adolescents or pregnant women.

• Episodic excessive alcohol consumption (EEAC).

What tools should doctors apply in the consultation to reduce alcohol consumption?[3]. Firstly, terminology must be handled carefully. It would be more prudent to speak about problematic consumption to acknowledge that this issue is difficult to define, and represents a social problem with multiple dimensions, that require a multidisciplinary approach. The significance of alcohol as a psychoactive drug, akin to marijuana and cocaine, should not be overlooked due to its pervasive presence in people's lives. It is crucial for internists and other healthcare professionals to be cognizant of the detrimental effects associated with problematic alcohol consumption. This awareness enables them to seamlessly integrate discussions on alcohol-related issues into their routines and provide appropriate guidance to their patients.

The patient can consult for:

• Addictive behavior.

• Problems directly related to alcohol.

• Problems where alcohol arises from the interview and physical examination (tremors, tachycardia, hypertension, rhinophyma, parotid hypertrophy, telangiectasias, hepatomegaly, splenomegaly, polyneuritis) or other findings from complementary methods (macrocytosis -with or without anemia-, increased transaminases, increased gamma glutamyl transpeptidase, ultrasound with fatty liver)[15].

Alcohol problematic consumption can occur even if the preceding situations are not present, raising the question of how to identify an alcoholic patient. Tools to identify it are CAGE and AUDIT questionnaires, both validated in primary care. Health professionals must ask about the presence and type of consumption. It should be suspected in patients with mood changes, weight loss or other symptoms without adequate explanation[15].

Once chronic consumption has been identified, the presence of physical and psychological dependence and target organ damage must be evaluated.

Consider that those with a family history of alcoholism, tobacco use, trauma, traffic incidents, or those taking medications that interact with alcohol (paracetamol, NSAIDs, anti H2, isoniazid, phenytoin, warfarin, sulfonylureas, benzodiazepines, methotrexate, opioids, tricyclic antidepressants, metronidazole) may have an increased risk either of developing alcoholism or experiencing interactions with alcohol[15,16].

Questionnaires such as CAGE (detects issues related to abuse and dependence)[17], and AUDIT (identifies disorders related to alcohol intake)[18] should be used. There are other less commonly used methods (Trauma test, T-ACE, TWEAK, RAPS4). These questionnaires, especially AUDIT, are useful for detecting low-risk consumption,

excessive or risky consumption, and dependence or alcoholism[18,19].

Simple advice and brief interventions prove to be effective measures in reducing alcohol consumption and mitigating associated risks. For individuals with low-risk alcohol consumption, it is crucial to consistently counsel them on the perils of alcohol intake while operating machinery or vehicles, in conjunction with specific medications, during pregnancy, and in adolescence. In cases of risky consumption, brief interventions are recommended. These are concise (lasting 3 to 5 minutes) and low-intensity actions that involve providing feedback, along with simple advice, to enhance motivation for reducing or ceasing alcohol consumption. Patients may not always comprehend the potential harm of alcohol consumption, making the intervention by healthcare professionals particularly effective. For individuals with alcohol dependency, a more intensive treatment approach is necessary. This could involve outpatient treatment or, in severe cases, may require hospitalization depending on the specific circumstances. Physical withdrawal (tremor, anxiety, seizures, delirium, autonomic hyperactivity) may or may not be present in a patient with alcohol dependence, and if present, requires immediate pharmacological intervention. Consider hospitalization in cases of severe depression, particularly when suicidal ideation is present, severe co-existing psychiatric disorders, insufficient family support, or if outpatient management proves ineffective[15,20,21].

Available drugs can be fundamentally grouped into those used for the treatment of alcohol withdrawal and dependence, and those used for the prevention of complications related to nutritional deficiencies associated with chronic alcohol consumption[15, 20, 22,27].

Administration of thiamine with or without magnesium replacement is recommended for the prevention or treatment of neuropathies and Wernicke's encephalopathy.

The objective of treating alcohol withdrawal is to prevent the occurrence of seizures, delirium tremens, and alleviate withdrawal symptoms. Benzodiazepines are the primary medications used in the first line, with antipsychotics employed as adjuvant drugs (especially in cases of delirium, always in conjunction with benzodiazepines to mitigate the risk of seizures by lowering the seizure threshold). Beta-blockers may be used in instances of autonomic hyperactivity, while carbamazepine or valproic acid may be considered for cases with mild or moderate symptoms.

For individuals with alcohol dependence, there are anticraving medications designed to reduce the urge to drink. Naltrexone is the preferred choice, with acamprosate being an alternative in the absence of naltrexone or if there is some degree of liver damage. In certain cases, aversive drugs like disulfiram can be employed, particularly for highly motivated patients aiming to maintain abstinence.

There are other drugs under study (topiramate, nalmefene, serotonin reuptake inhibitors, ondansetron).

References

1. WHO. Alcohol. At: https://www.who.int/es/news-room/fact-sheets/detail/alcohol; consulted July 2022.
2. GBD 2016 Alcohol Collaborators. Alcohol use and burden for 195 countries and territories, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet* 2018; 392:1015-35.
3. Cortese S, Sánchez Cabezas A, Pavlovsky F, Valdez P. Latin American champions in alcohol consumption: a reason for analysis. *Rev Arg of Medicine* 2018; 6: 129-34.
4. Holmes MV, Dale CE, Zuccolo L, et al. Association betweenalcohol and cardiovascular disease: Mendelian randomization analysis based on individual participant data. *BMJ* 2014; 349: g4164.
5. Chikritzhs T, Stockwell T, Naimi T, Andreasson S, DangardtF, Liang W. Has the leaning tower of presumed health benefits from 'moderate' alcohol use finally collapsed? *Addiction* 2015; 110: 726-27.
6. Reyes Caorsi W. Alcohol, arrhythmias and coronary heart disease. *Rev Urug Cardiol* 2020; 35:12-20.
7. Roerecke M, Rehm J. The cardioprotective association of average alcohol consumption and ischemic heart disease: a systematic review and meta-analysis. *Addiction* 2012; 107:1246-60.
8. Zhao J, Stockwell T, Roemer A, Naimi T, Chikritzhs T. Alcohol consumption and mortality from coronary heart disease: an updated meta-analysis of cohort studies. *J Stud Alcohol Drugs* 2017; 78:375-86.
9. Lawlor DA, Nordestgaard BG, Benn M, Zuccolo L, Tybjaerg-Hansen A, Davey Smith G. Exploring causal associations between alcohol and coronary heart disease risk factors: findings from a Mendelian randomization study in the Copenhagen General Population Study. *Eur Heart J* 2013; 34:2519-28.
10. Urbano-Marquez A, Estruch R, Navarro-Lopez F, Grau JM, Mont L, Rubin E. The effects of alcoholism on skeletal and cardiac muscle. *N Engl J Med* 1989; 320:409-15.
11. Estruch R, Sacanella E. Alcohol: cardiovascular tonic or toxic? *Clin Invest Arterioscl* 2005; 17:183-95.
12. Vázquez-Ramírez EM, Mata-Vicente JF. Cardiomyopathy secondary to alcohol consumption. *Med Int Méx* 2016; 32:93-102.
13. OPS. Development of the action plan (2022-2030) for the effective implementation of the Global Strategy to reduce the harmful use of alcohol. Regional technical consultation on the working document. Pan American Health Organization, 2021. In:https://www.paho.org/es/documentos/elaboration-action-plan-2022-2030-for-effective-implementation-global-strategy-to-reduce; consulted October 2022.
14. Babor TF, Caetano R, Casswell S, et al. Alcohol: a product of non-ordinary consumption. OPS 2010. ISBN 978-92-75-33144-6. At: https://iris.paho.org/handle/10665.2/2836; consulted October 2022.
15. Pendino JC. Alcoholism. In Greca A, Gallo R, Parodi R,

Carlson D. Ambulatory Medicine. Rosario: Corpus, 2016, p 191-200.
16. González-González JS, Zúñiga-Lemus O. Interactions between drugs and alcohol. *Health and Administration* 2015; 2:61-4.
17. Ewing JA. Detecting alcoholism. The cage questionnaire. *JAMA*1984; 252: 1905-07.
18. Babor TF, Higgins-Biddle JC, Saunders JB, Monteiro MG. AUDIT. WHO 2001. In: https://apps.who.int/iris/bitstream/handle/10665/331321/WHO-MSD-MSB-01.6a-spa.pdf;consulted October 2022.
19. Córdoba García R, Camarelles Guillem F. Cribado e intervención breve en consumo de alcohol. Aten Primaria 2022; 54:102349.
20. Monte-Secades R., Rabuñal Rey R. Clinical practice guide: Treatment of alcohol withdrawal syndrome, 2toedition. *Galicia Clin* 2011; 72: 51-64.
21. Monte R, Rabuñal R, Casariego E, Bal M, Pértega S. Risk factors for delirium tremens in patients with alcohol withdrawal syndrome in a hospital setting. *Eur J Intern Med* 2009; 20:690-4.
22. Gupta PK. Neurotoxic agents. In: Gupta PK. Fundamentals of Toxicology. *BSP* 2016, p 221-44.
23. Burnette EM, Nieto SJ, Grodin EN, et al. Novel agents for the pharmacological treatment of alcohol use disorder. *Drugs* 2022; 82: 251-74.
24. Swift RM, Aston ER. Pharmacotherapy for alcohol use disorder: current and emerging therapies. *Harv Rev Psychiatry* 2015; 23: 122-33.
25. Poncea G. Jiménez-Arrieroa MA, Rubio G. Pharmacological treatment of alcohol dependence. *Addictive Disorders* 2003; 5:27-32.
26. Maisel NC, Blodgett JC, Wilbourne PL, Humphreys K, Finney JW. Meta-analysis of naltrexone and acamprosate for treating alcohol use disorders: when are these medications most helpful? *Addiction* 2013; 108: 275-93.
27. Novo-Veleiro I, Herrera-Flores J, Rosón-Hernández B, et al. SEMI Group, Alcohol and Alcoholism Group, Spanish Society of Internal Medicine (SEMI). Alcoholic liver disease among patients with Wernicke encephalopathy: a multicenter observational study. *Drug Alcohol Depend* 2022; 230:109186.