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Moderate alcohol use and health: An update a Consensus Document

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Abstract. Excessive alcohol consumption is associated with increased incidence of several degenerative diseases and ill health. However, in 2013, Poli et al. published a Consensus document in which they thoroughly and critically reviewed all available evidence in support (or against) the moderate and alimentary use of alcohol. We added further evidence to the aforementioned by searching and selecting according to relevance and novelty the recent literature on alcohol and health, published since the appearance of that paper and conclude that it appears convenient to educate consumers and health professionals on the appropriate use of alcoholic beverages, within the framework of a healthy lifestyle.

1. Introduction

Excessive alcohol consumption is associated with increased incidence of several degenerative diseases and ill health. However, moderate use is being constantly associated with reduced cardiovascular risk and all-cause death. International regulatory bodies such as the WHO seldom acknowledge this notion, mostly because they fear misinterpretation of alcohol-related health messages.

In 2013, Poli et al. [1] published a Consensus document in which they thoroughly and critically reviewed all available evidence in support (or against) the moderate and alimentary use of alcohol. The Consensus was signed by representatives of about 20 Italian Scientific Societies. The evidence-based conclusions were that cumulated evidence clearly shows a statistically significant association between moderate alcohol consumption, i.e. not more than two or three drinks/d or 24–36 g of ethanol/d for men and one-two drinks/d or 12–24 g of ethanol/d for women and risk reduction of specific clinical events. Also, the well-known "J"-shaped curve graphically describes the association between ethanol intake and all-cause mortality. Therefore, even though no abstainer should be advised to drink for health reasons and some patients and population groups should use alcohol (if any) with extreme caution, consumption of alcoholic beverages within 30 g ethanol/d, i.e. ~two drinks/d for men and 15 g/d, i.e. ~one drink/d for women in adults at low risk of dependence should not be discouraged. The Consensus document conclusions are summarized in Box 1.

We added further evidence to the aforementioned by searching and selecting according to relevance and novelty the recent literature on alcohol and health, published since the appearance of that paper [1].

Box 1

1) In adults and in the elderly (regardless of sex), spontaneous consumption of alcoholic beverages within 30 g ethanol/d, that is two drinks/d, for men and 15 g/d, that is one drink/d, for women are to be considered acceptable and do not deserve intervention by the primary care physician or the health professional in charge. In fact, there is no evidence to suggest complete abstention from alcohol drinking by moderate users.
2) Patients with increased risk for specific diseases, for example women with familiar history of breast cancer, or subjects with familiar history of early CVD or cardiovascular patients should discuss their drinking habits with their physician.
3) No abstainer should be advised to drink for health reasons.
4) Alcohol use must be discouraged in specific physiological or personal situations or in selected age classes (children and adolescents, pregnant and lactating women and recovering alcoholics). Moreover, the possible interactions between alcohol and acute or chronic drug use must be discussed with the primary care physician.

2. Moderate alcohol and health: Mechanisms of action

In terms of mechanisms of action (which are always sought after, specifically to verify if the observed correlation between moderate alcohol consumption and health is causal) most of the cardioprotective effects of ethanol might be due to its HDL-raising properties. However, as reviewed elsewhere [1], the actions of alcohol on human health are manifold and not fully elucidated. To address this issue, Mathews et al. [2] constructed an integrated interaction system that produced a "connection graph", linking the various measurable serological biomarkers (from more than 1 million subjects) with health outcomes. The conclusions restate that moderate alcohol consumption is associated with a lower risk of CHD, independent of the type of beverage consumed. This effect can

be largely explained by increases in HDL-c and adiponectin concentrations and insulin sensitivity, together with decreased inflammation.

2.1. Cardiovascular disease

The J-shaped curve correlation between alcohol and health (mostly consequent to the cardioprotective effects of moderate alcohol use) has been confirmed by a recently-created lifestyle-based prediction model [3] (called the Healthy Heart Score, computing data from 61 025 women in the Nurses' Health Study and 34 478 men in the Health Professionals Follow-up Study), which can be usefully employed as a tool for the long-term prevention of cardiovascular disease and in a study on the risk of total mortality in 449 US male physicians with prevalent heart failure (HF) [4]. In addition to showing a J-shaped association between alcohol intake and mortality in patients with HF, the latter reported no relation between beverage preference (beer, wine, or liquor) and mortality [4].

In terms of cardiovascular heath, an interesting paper has been published by Bonaccio et al. [5], who tried to disentangle the various contributions to the lower mortality they observed in diabetic subjects who followed the Mediterranean diet. This study is part of the large Moli-sani investigation, and the authors concluded that major contributions were offered by moderate alcohol consumption (14.7% of the observed effect), high intake of cereals (12.2%), vegetables (5.8%) and reduced consumption of dairy and meat products (13.4% and 3.4% respectively) [5].

Part of the vascular effects of alcohol appears to be mediated by lower inflammatory status, at least according to van Bussel et al. [6], who reported that consumption of more fresh fruit, wine, and poultry, and fewer high-fat dairy products, was associated with less low-grade inflammation using longitudinal data from 557 participants at increased CVD risk from the CODAM (Cohort on Diabetes and Atherosclerosis Maastricht).

A controversial Mendelian randomization meta-analysis of 56 epidemiological studies [7] reported that individuals with a genetic variant associated with non-drinking and lower alcohol consumption had a more favorable cardiovascular profile and a reduced risk of coronary heart disease than those without the genetic variant. However, this study has been criticized due to patent methodological issues. As an example, no statistically significant effects were observed in the groups of "light drinkers", "moderate drinkers", and "heavy drinkers" when these clusters were analyzed separately; additionally, carriers of the mutation not only drink less alcohol, but also have lower blood pressure, smaller BMI, and less inflammation (expressed as log of IL-6 plasma concentrations) even if they belong to the abstainers group. This clearly shows that the mutation is in itself protective (and not necessarily through the reduction of alcohol intake), therefore violating one of the basic principle of the Mendelian randomization approach. Of note, people with a genetically less active form of another alcohol dehydrogenase, ADH1C (a.k.a. ADH3), had a lower risk of CHD than those with the gene for the more active form [8]. This difference suggests that longer exposure to alcohol – due to its slower metabolism associated with the variant ADH1c – exerts a protective effect on CHD risk [8].

Finally, lifestyle associated with alcohol use appears to be of utmost importance because a meta-analysis of genome-wide association studies of plasma fibrinogen concentrations, computing 80,607 subjects of European ancestry, found no strong evidence of interaction between genetic variants and smoking status, alcohol consumption or BMI on fibrinogen concentrations [9].

2.2. Alcohol and cancer

As extensively reviewed by Poli et al. [1], the relation between alcohol use and cancer incidence is rather multifaceted.

In a very large (572 studies, including 486 538 cancer cases) dose-response meta-analysis Bagnardi et al. [10] investigated the effect of alcohol on 23 cancer types. The results of this analysis confirms that excessive alcohol use increases risk of cancer of oral cavity and pharynx, oesophagus, colorectum, liver, larynx and female breast. One prominent example is of oral and pharyngeal cancer, for which relative risks (RRs) for heavy drinkers compared with nondrinkers and occasional drinkers were 5.13, with a clear dose–risk relationship.

La Vecchia et al. [11] correlated the documented decrease in alcohol consumption in Southern Europe with the observed decrease in upper digestive tract neoplasms. Of note, the decrease in tobacco consumption can only partially account for these data.

As far as general alcohol toxicity is concerned, a systematic review and meta-analysis indicated positive independent associations of baseline levels of GGT and ALP (liver enzymes markers of liver function and dysfunction) with all-cause mortality, consistent with linear dose–response relationships [12]. Indeed, a linear relationship with increasing alcohol intake in drinkers appears to exist, with estimated excess risk of 46% for 50 g of ethanol per day and 66% for 100 g per day. A systematic review by Turati et al. [13] suggests a moderate detrimental role of consumption of 3 or more alcoholic drinks per day on liver cancer, and a lack of association with moderate drinking. In this respect, the precise mechanisms of alcohol hepatotoxicity remain to be elucidated [1,13]; yet, it appears advisable to closely monitor such enzymes in subjects for which excessive alcohol consumption is suspected.

2.3. All cause mortality

A recent meta-analysis has evaluated, in British cohorts, the association between alcohol intake and overall mortality [14]. The authors conclude that protective effects of alcohol intake on all-cause death are observed among men 50–64 years of age and women >65 years of age. These data fully agree with previous meta-analyses [15] suggesting a 20–25% reduction of all-cause death risk associated with moderate alcohol intake. Some methodological flaws of the Knott et al. paper have also been pointed to (see, as an example, http://www.bmj.com/content/350/bmj.h384/rr) and can explain the limited magnitude of the positive effects observed.

2.4. Excessive alcohol use

Any "alcohol and health" investigator cannot disregard the major health issues brought about by excessive ethanol use and by insalubrious patterns of consumption, e.g. binge drinking. This approach to alcohol ingestion has been repeatedly associated with unfavorable health outcomes; for example, Larsson et al. [16] published a meta-analysis on high alcohol consumption and risk of atrial fibrillation (AF). Although this association is not new, the dose-response data reviewed by the current meta-analysis reaffirms the potential causality of the link between alcohol intake and AF [17].

In this regard, several public health initiatives are being taken worldwide, especially in Northern European countries and in the USA. The foremost preventive policy is implemented by raising alcohol-related taxes and, therefore, the price of alcoholic beverages. An interesting systematic review by Nelson [18] shows that these strategies have no discernible effect of binge drinking. In particular, young adults are reluctant to alter their higher-than-recommended levels of alcohol consumption and try to compensate with other healthy behaviors such as increased physical activity, at least in a UK cohort [19].

In terms of overall, i.e. regardless of consumption patterns, alcohol intake O'Keefe et al. [20] underscore that: Heavy alcohol use is one of the most common causes of reversible hypertension, accounts for about one-third of all cases of nonischemic dilated cardiomyopathy, is a frequent cause of atrial fibrillation, and markedly increases risks of stroke-both ischemic and hemorrhagic. In keeping with Poli et al. [1], the authors recognize that people who abstain from alcohol should not be advised to begin, even though moderate ethanol intake is associated with decreased risks for total mortality, coronary artery disease, diabetes mellitus, congestive heart failure, and stroke.

3. Conclusion

Although randomized clinical trials are impracticable in alcohol research – as they entail important ethical issues – strong evidence is steadily being built that allows us draw firm conclusions.

The first one is the existence of a J-shaped curve describing the association between alcohol use and all-cause mortality. In practical terms, this translates into the concept that consumption up to one (for women) or up to two (for men) drinks per day is safe and might even be advantageous to most people. The main contributor to this J-shape is the effect of ethanol use on cardiovascular health, which can be – at least partly – explained with its positive actions on several risk factors and surrogate markers. Indeed, accrued evidence points to the ethanol-induced HLD-raising activity as the main responsible for the cardioprotective effects of moderate alcohol consumption; however, anti-inflammatory and hormonal effects, e.g. on adiponectin do play important roles.

Inordinate alcohol use is harmful and should be actively discouraged. Of note, raising taxes on alcoholic beverages does not appear to be an effective solution. Unhealthy patterns of consumption, e.g. binge drinking should also be tackled from a public health viewpoint.

In summary, it appears convenient to educate consumers and health professionals on the appropriate use of alcoholic beverages, within the framework of a healthy lifestyle.

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