Alcohol binge drinking: getting to the heart of it

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CHRONIC ALCOHOLISM IN CONJUNCTION with its acute and chronic deleterious consequences ranks among the top five risk factors for disease and death (7). While clinical evidence suggests that low to moderate daily consumption of alcoholic beverages (particularly red wine) is associated with favorable consequences on cardiovascular mortality (1, 6), chronic and heavy drinking promotes cardiac dysfunction or subsequent cardiomyopathy/heart failure and increases the risk of sudden cardiac death (9, 12).

Increasing is the number of people who binge drink, which is the most common form of alcohol abuse in young adults (10, 13). According to a national survey, close to 60% of college students ages 18-22 drank alcohol in the past month, and over 60% of them engaged in binge drinking during that same time frame (10). Binge drinking is associated with adverse cardiovascular effects, such as macro- and microvascular dysfunction in young adults (5), and enhanced myocardial injury (14).

Although animal studies have investigated the cardiovascular effects of either acute or long-term ethanol (EtOH) consumption, there are no good mouse models that mimic human drinking patterns and lead to alcoholic cardiomyopathy (3). In this issue of the American Journal of Physiology-Heart and Circulatory Physiology, Matyas et al. (8) describe new mouse models of alcoholic cardiomyopathies [National Institute on Alcohol Abuse and Alcoholism (NIAAA) models] induced by feeding mice with a liquid Lieber-DeCarli diet containing 5% ethanol for 10, 20, and 40 days combined with single or multiple EtOH-binges (5 g/kg body wt) (8). They characterize detailed hemodynamic alterations by using both echocardiography and invasive pressure-volume (P-V) conductance approaches. While chronic alcohol feeding for 10 and 20 days induced no significant changes in load-independent indexes of myocardial contractility (measured by the P-V approach) compared with isocaloric pair-fed control animals, the more prolonged alcohol feeding for 40 days was associated with declined left ventricular function (8). However, when the alcohol feeding was combined with single or multiple binges (10 days + 1 binge, 20 days + 2 binges, and 40 days + 4 binges), it resulted in dramatic reduction of left ventricular systolic and diastolic function compared with controls or animals fed with EtOH diet for the same duration without binges.

The chronic plus binge drinking was also associated with marked impairment of vascular function, including decreased arterial elastance and total peripheral resistance, as measured by P-V conductance system, leading to hypotension and impaired ventriculo-arterial coupling. Remarkably, even the shortest period of alcohol feeding (10 days) combined with a single binge was sufficient to induce marked cardiac and vascular dysfunction. Importantly, to avoid the acute effects of alcohol binge on cardiac performance, the authors evaluated hemodynamics 9 h following the administration of the binge when the blood alcohol levels were returning to baseline in mice.

Interestingly, the conventional load- and heart rate–dependent markers of cardiac function measured by echocardiography, such as ejection fraction and fractional shortening, were not different among groups. In a way, this is not entirely surprising based on the marked effects of the chronic plus binge drinking on total peripheral resistance and heart rate. This finding emphasizes the limitation of small animal echocardiography measurements in cardiovascular pathologies when the loading conditions are altered and the importance of using the P-V conductance system for evaluating the hemodynamic effects of alcohol in vivo (11).

To explore the mechanism of the observed cardiac dysfunction, the authors evaluated markers of oxidative/nitrative stress, metabolism, mitochondrial function, and biogenesis. They found mitochondrial dysfunction in their alcoholic cardiomyopathy models (complex I activity was decreased in the 10 days + 1 binge model, whereas complexes II and IV activities were attenuated by increasing the number of binges and the duration of EtOH feeding), increased oxidative and nitrative stress, and decreased mitochondrial biogenesis.

The impaired renin-angiotensin system plays a critical role in alcohol-induced cardiomyopathy both in humans and rodents (2, 4). Consistently with these observations, an increase of angiotensin-II type-1 receptor expression was found in hearts of animals on alcohol diets (8). Alcohol consumption in mice was also associated with mild cardiomyocyte hypertrophy without significant fibrosis (8).

Different cardiovascular diseases have been associated with an excessive amount of steatosis in the myocardium (15). One of the most interesting aspects of the study by Matyas et al. (8) is the demonstration of cardiomyocyte lipid accumulation after as early as 10 days of EtOH consumption, which was markedly enhanced by EtOH binge and paralleled with upregulation of myocardial acetyl-CoA carboxylases (ACC 1 and 2), suggesting upregulation of the triglyceride synthesis pathways (8).

Collectively, the new mouse models of cardiomyopathy and vascular dysfunction induced by chronic plus single or multiple EtOH binges (i.e., NIAAA models) mimic many features of alcohol-induced cardiovascular pathology in humans (5, 14). This study also suggests that binge drinking may significantly enhance the deleterious cardiovascular effects of excessive EtOH consumption (8). This binge-induced injury may contribute to the 1,825 EtOH-related deaths of college students between the ages of 18 and 24 annually (10) and warrants further investigation.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).
AUTHOR CONTRIBUTIONS

J.D.G. drafted, edited, revised manuscript, and approved final version of manuscript.

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2. Cheng CP, Cheng HJ, Cunningham C, Shihabi ZK, Sane DC, Wan-Bryson CL, Mukamal KJ, Mittleman MA, Fried LP, Hirsch CH, J.D.G. drafted, edited, revised manuscript, and approved final version of manuscript.


