Atrial Fibrillation & Alcohol

A Review of the Pathophysiology

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Background

Excess alcohol consumption is ever present in Western societies. 53% of Americans consume alcohol on a regular basis, whilst 44% have consumed ≥ 5 standard drinks, on a single occasion, in the last month (1). Although modest amounts of alcohol are believed to have an overall cardio-protective effect, its effects on the development of atrial fibrillation (AF) are less well understood. The aim of this editorial is to explore the possible mechanisms involved in alcohol associated AF.

Introduction

The association between excessive acute alcohol intake and cardiac rhythm disorders was first described in 1978 (2) due to an increased frequency of atrial arrhythmia related hospitalisations occurring between Sunday and Tuesday, and following public holidays. Over the next 4 decades the association between habitual alcohol consumption and the risk of AF development has been studied in detail (3) with some studies suggesting a possible dose response association (4). It has been estimated that 35% to 62% of AF cases presenting to the Accident and Emergency department are precipitated by alcohol, the so called ‘holiday heart syndrome’. The mechanisms underpinning this relationship remain unclear (5, 6).

AF represents an increasingly significant burden to modern healthcare systems and represents an emerging epidemic within cardiovascular medicine. AF is associated with both morbidity and mortality (7) and is increasingly prevalent in an ageing population with worsening lifestyle factors. Rates of alcohol consumption and acute alcohol intoxication also remain significant in the United Kingdom.

Pathophysiology

Electrophysiological effects at a cellular level

Cardiac conduction velocity

The electrophysiological effects of alcohol on excitable cardiac tissue have been studied in both animal and human subjects. Klein et al (8) have demonstrated that ≥ 2g/L of alcohol can lead to inhibition of Na^+ channels and an increase in Na^+ / Ca^{+2} exchanger activity, leading to prolongation of the action potential and repolarisation periods. Rabbit atria tissue infused with alcohol over a 5-day period, has been shown to experience a significantly reduced L-type Ca^{+2} and Na^+ current density (9). Cardy et al (10) have also demonstrated prolonged P and QRS wave duration in 13 human subjects following acute ingestion of alcohol. This suggests that both atrial and ventricular conduction velocities are reduced by alcohol. The slowing of cardiac tissue conduction, facilitates the formation of re-entry circuits, which is believed to be one of the principal mechanisms responsible for the development of a suitable substrate for cardiac arrhythmias, such as AF (11).

Refractory period shortening

Alcohol has been demonstrated to shorten the atrial refractory period and possibly result in arrhythmias in rat atrial tissue (12). In a study involving 48 AF patients (13) atrial effective refractory periods were significantly shorter in drinkers compared to controls. Although similar observations have not been replicated in alcohol abusers (14).

Hypokalaemia

Hypokalaemia has been implicated as a possible contributing factor in the development of AF in both acute alcohol ingestion and chronic alcohol use. In the acute setting, hypokalaemia is aggravated by emesis, whereas in chronic drinkers hypokalaemia is primarily mediated by inappropriate kaliuresis. This is the result of coexistent hypomagnesaemia which is present in approximately 30% of heavy drinkers (15). Voskoboinik et al (16) argued that a hypokalaemic state can lead to hyperpolarization of the cellular membrane, which in turn can increase recruitment of Na^+ channels, leading to a faster upstroke. Thus an increase in tissue excitability could predispose individuals to AF. The diuretic effect that alcohol induces may also contribute to further electrolyte imbalances which could contribute to a pro-arrhythmic state.

Autonomic nervous system-mediated effects

Increased sympathetic activity

Exposure to alcohol can potentiate the release of catecholamines, both systemically, via the adrenal medulla, and locally, by the myocardium itself (14, 17). The elevated levels of systemic and intra-myocardial catecholamines can result in prolongation of P waves, which has previously been associated with increased risk of atrial arrhythmias (18). Maki et al (19) demonstrated increased sympathetic activity across a wide spectrum of alcohol concentrations in patients with previous binge drinking induced AF. However, although the catecholamine levels in the AF patient group trended towards higher values, the study failed to demonstrate a statistically significant increase of catecholamine levels in those individuals.

Increased parasympathetic activity

A recent study by Mandyam el al (20) has explored the role of vagal activation as a potential trigger for episodes of paroxysmal AF. In this study, individuals reporting vagal triggers for episodes of AF were also likely to report alcohol as a trigger, giving rise to the hypothesis that alcohol may stimulate a vagal response. This seems to contradict the aforementioned data regarding increased sympathetic activity, suggesting that a more complex interaction between the different components of the autonomic nervous system, which might be responsible for the link between alcohol exposure and risk of AF.

Elevated plasma free fatty acids

Free fatty acids are known to become significantly elevated following alcohol intake (17). Although the exact mechanisms mediating this effect are not fully appreciated, a significant link between increased levels of free fatty acids and AF has been observed by Khawaja et al (21). Further research in this area is needed to fully elucidate the underlying mechanisms of this interaction.

Raised acetaldehyde

Gallardo-Carpentier et al (22) have demonstrated the arrhythmiogenic effect of acetaldehyde in an experimental study using canine Purkinje fibres. The observed effect is at least partially mediated by the increase in systemic and intramyocardial catecholamine concentration. Since acetaldehyde is alcohol's primary metabolite (17), this notion is at least partially supported by the fact that although a significant number of individuals develop AF during their intoxicated state, others present 12 to 36 hours after binge drinking (23).

Structural effects of alcohol to atrial tissue

Atrial remodelling

Daily alcohol consumption has been shown to be an independent multivariate predictor of discrete atrial fibrosis, in a patient population undergoing pulmonary vein isolation (PVI) for paroxysmal AF (24). In addition, a study performed by Ettinger et al (25), showed that animals exposed to alcohol for >1 year exhibited structural changes at a cellular level, including localised dilatation and cystic changes in intercalated disks responsible for cell-to-cell impulse propagation.

Atrial tissue inflammation and oedema

Alcohol and its primary metabolite, acetaldehyde are known to have direct cardiotoxic effects (16). They have been implicated in the inhibition of Ca^{+2} release by the sarcoplasmic reticulum, lipid peroxidation and direct protein damage, leading to cardiac contractile dysfunction (26). Supporting this notion, is the observation that otherwise healthy binge drinkers have been shown to have T2 signal intensity suggestive of ventricular myocardial oedema and hyperaemia on cardiac magnetic resonance imaging (CMR). These changes on CMR were associated with elevated troponin concentrations suggesting an acute cardiac tissue inflammatory state following binge drinking, which could be extended to the atrial myocardial tissue.

Other contributing factors

Alcohol is responsible for 16% of hypertensive disease (16, 27) and hypertension affects up to two-thirds of AF patients (28). Since AF is often preceded by LVH and atrial hypertrophy it is possible that some of its effects are mediated through hypertension. In addition, obesity is a known determinant of left atrial size and a recognised risk factor for the development of AF (1:54). Traversy et al (29), amongst others, have shown that excessive alcohol consumption (>21 drinks per week) can lead to increased body mass index (BMI). Finally, sleep-disordered breathing, including obstructive sleep apnoea (OSA) could be a possible mediator for the effect of alcohol on the development of AF. Sympathetic hyperactivity, acute hypertension and left atrium stretching secondary to large negative intra-thoracic pressure swings could occur with higher frequency during apnoeic episodes (30-32).

Conclusion

Moderate and chronic exposure to alcohol has significant impact on the development of AF. This effect is likely mediated by a combination of physiological mechanisms, including but not limited to; direct alteration of the electrophysiological properties of the atrial myocardial cells, autonomic nervous system mediated mechanisms and altering of the structure of the myocardial tissue, especially in the setting of chronic alcohol intake.

More research is however required to further characterise the contribution these individual pathways have in the development of AF, to elucidate their association with different patterns of drinkin and to better understand their interplay in the development of AF.

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