Holiday Heart Syndrome Revisited after 34 Years

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Abstract

The cardiovascular effects of alcohol are well known. However, most research has focused on the beneficial effects (the "French paradox") of moderate consumption or the harmful consequences, such as dilated cardiomyopathy, associated with heavy consumption over an extended period. An association between the ingestion of acute alcohol and onset of cardiac arrhythmias was first reported in the early 70's. In 1978, Philip Ettinger described "Holiday heart syndrome" (HHS) for the first time, as the occurrence, in healthy people without heart disease known to cause arrhythmia, of an acute cardiac rhythm disturbance, most frequently atrial fibrillation, after binge drinking. The name is derived from the fact that episodes were initially observed more frequently after weekends or public holidays. Since the original description of HHS, 34 years have passed and new research in this field has increased the volume of knowledge related to this syndrome. Throughout this paper the authors will comprehensively review most of the available data concerning HHS and highlight the questions that remain unresolved.

Introduction

Alcohol is one of the oldest known drugs and is the most used recreational drug in the United States of America[1] and probably the rest of the world as well. Alcohol can have health benefits when consumed moderately because it appears to offer some degree of cardiovascular protection due to various mechanisms including activation of the fibrinolytic system, lower platelet aggregation, antioxidant effects, lipid profile improvement, and improved endothelial function. These cardioprotective effects are known as the "French paradox"[2]. However, alcohol abuse can lead to several diseases in humans, such as alcohol addiction, alcoholic liver disease, dilated alcoholic cardiomyopathy, and even cancers of the oral cavity and esophagus[3].

Keywords

Alcoholism / complications; Arrhythmias, Cardiac / etiology; Holidays; Atrial Fibrillation; Review.

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Among the cardiovascular effects, regular alcohol abuse appears to increase blood pressure, leading to arterial hypertension, which by itself is a risk factor for other cardiovascular diseases[4] and for sudden death[5]. It is also associated with procoagulant changes after acute ingestion, hypocoagulation with chronic abuse, and thrombocytosis after withdrawal. In addition, it can also reduce regional cerebral blood flow by affecting cerebral metabolism due to chronic abuse or lead to vasoconstriction of cerebral arteries with acute intake. All these aforementioned effects can lead to stroke, and regular abuse is also associated with intracranial hemorrhage, which can be fatal[6].

There is also a higher risk of sudden cardiac death with alcohol abuse, which increases with the amount ingested, regardless of the presence of previous heart events like ischemic heart disease or myocardial infarction[5].

Chronic consumption of large amounts of alcohol is associated with alcoholic cardiomyopathy, a subtype of secondary dilated cardiomyopathy, known to be associated with not only cardiac failure but also with atrial fibrillation (AF) and other cardiac arrhythmias[7-9].

Alcohol appears to be able to cause cardiac arrhythmias in healthy people either following acute excessive alcohol ingestion, commonly known as "binge drinking," or chronic ingestion. Arrhythmias due to binge drinking have been described as "Holiday heart syndrome" (HHS) and will be further discussed in this article. Arrhythmia due to chronic drinking appears to be significantly associated with consumption of >36 g alcohol/day, but this correlation is less clear with light and moderate drinking[10,11].

As alcohol consumption and binge drinking are common, it is important to illuminate the medical community and general population to the perils of HHS because the condition can be diagnosed more easily and preventive measures can be taken. In addition, because it has been 34 years since the original description of HHS by Ettinger et al and questions surrounding this condition remain unanswered, we propose it is time to organize ideas and put things into perspective.

Methods

An electronic search in PubMed was performed using the following string: "alcohol intake AND (AF OR arrhythmias OR atrial fibrillation OR atrial flutter) OR holiday heart" from January 1960 to September 2012. We obtained 436 articles from this main search. After analyzing each abstract, we identified 10 relevant papers concerning HHS and potential alcohol mechanisms behind its arrhythmogenicity.

Papers focusing only on chronic alcohol intake and its effects on cardiac function were not included. We also manually examined the reference lists from these identified articles for more relevant articles, repeating the process again, which resulted in four additional articles being added to our list. Six other articles were added from manual searches on specific subjects related to HHS and/or alcohol mechanisms behind its arrhythmogenic properties (Figure 1).

HHS: History and definition

HHS was first recognized in the early 70's when Philip Ettinger noticed an association between acutely intoxicated patients and cardiac arrhythmias[12,13], even though at that time most textbooks did not suggest that alcohol could cause cardiac arrhythmias in apparently healthy non-alcoholic individuals[7].

The term was officially introduced in 1978 by Ettinger et al for describing the occurrence of an acute cardiac rhythm disturbance in apparently healthy people after an episode of heavy drinking, i.e., "binge drinking." This disturbance disappeared with subsequent abstinence, leaving no residual heart disease. These occurrences had the particularity of being more frequent after weekends or holidays like Christmas or New Year's Eve, which are known to be associated with increased alcohol ingestion, hence the name[14]. However, in a later study, Koskinen et al showed that this association between arrhythmias caused by recent alcohol intake and weekends or holidays was not always present[15].

HHS is mainly associated with supra ventricular arrhythmias, with AF being the most common cardiac arrhythmia in this syndrome. However, other less frequent types of arrhythmias can also occur, such as atrial flutter, paroxysmal atrial tachycardia, and isolated ventricular premature beats[14].

HHS can occur in regular and non-regular drinkers. However because all the patients in Ettinger's study consumed alcoholic beverages heavily and on a regular basis, initially HHS was considered to be linked more to people with a background of chronic alcohol consumption than those without the background[14]. Nevertheless Ettinger et al[14] also describe the case of a healthy non-regular drinker who presented with AF after alcohol consumption, hinting that HHS could also occur in this group of subjects. This was later confirmed by other studies showing similar cases of sudden onset of cardiac arrhythmias after heavy drinking in non-alcoholic healthy people[7,16].

It is important to note that patients with HHS are apparently healthy, with no personal or family history of palpitations or other suggestive symptoms of structural cardiac anomalies or any clinical evidence of heart disease such as cardiomyopathy, cardiac valvular disease, coronary heart disease, or other conditions that could lead to cardiac arrhythmias, such as abnormal electrolyte levels or elevated thyroid hormone levels. Laboratory and other tests are usually normal and after returning to normal sinus rhythm, the electrocardiograms are also mostly normal[7,13-15].

Another particular characteristic of HHS is the lack of new episodes with alcohol abstinence and the recurrence of symptoms with continued alcohol abuse. This observation further strengthens the role of alcohol in the development of these arrhythmias and also the importance of avoiding alcohol binging or consumption to prevent the occurrence of new events[7,12,13,17].

The most frequent symptom reported by patients with HHS is palpitations. Other symptoms commonly reported are precordial pressure or pain, syncope[14], and dyspnea[7]. However, it is important to note that cardiac arrhythmias, such as AF, can also occur without any clinical symptoms,

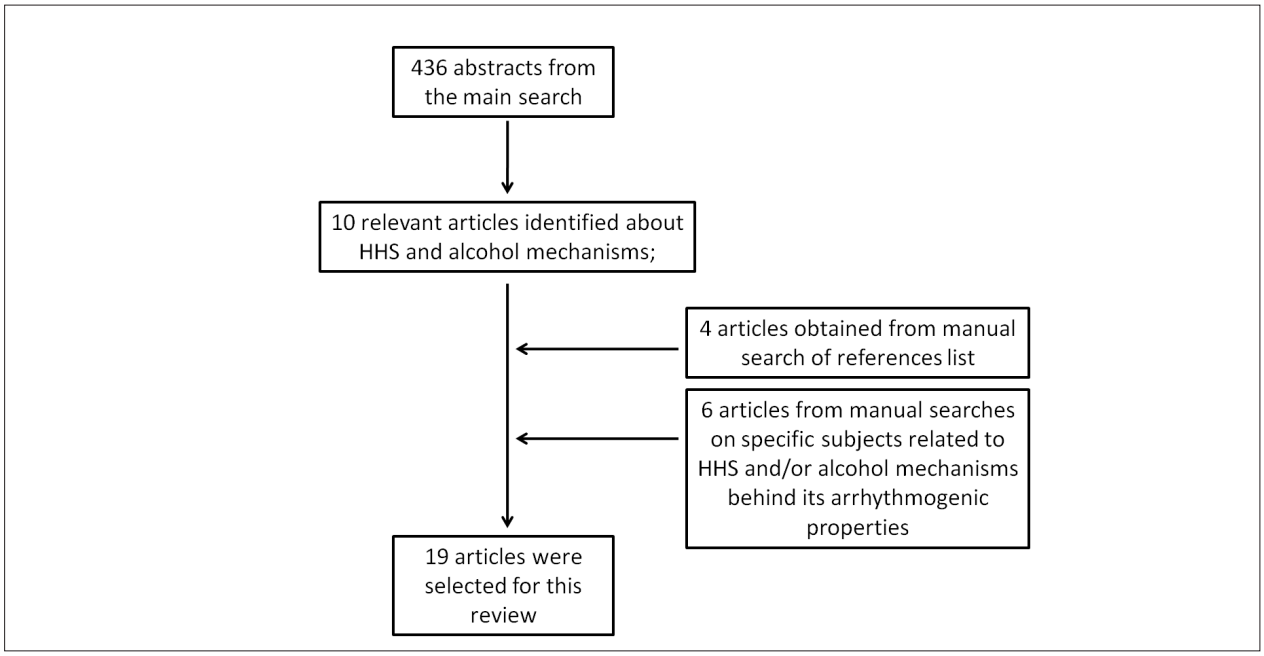

Figure 1 - *Article selection process.*

making some episodes of HHS harder to diagnose, which can lead to an underestimation of its incidence[18].

AF, the most frequent cardiac arrhythmia in HHS, has been shown to be a major risk factor for stroke[19] and increased mortality[20], indirectly suggesting an association between HHS and stroke or death. Nevertheless, there is no clinical data assessing these outcomes specifically in association with HHS. Moreover, arrhythmia associated with HHS after binge drinking can lead to sudden death, which may explain some of the sudden death cases commonly reported in alcoholics[5,14].

Pathophysiology

The mechanisms behind the association of alcohol and cardiac arrhythmias remain unresolved. These may be direct (alcohol myotoxicity) or indirect (by alcohol derived metabolites or effects on other organs such as adrenal glands). However, there are some facts about alcohol arrhythmogenic properties that have been accepted among the scientific community (Figure 2).

Cardiac conduction interference: It is believed that acute alcohol ingestion interferes with the cardiac conduction system through slowing of conduction, which is important because it facilitates re-entry, which is one of main mechanisms underlying the development of cardiac arrhythmias, namely AF.

In an experimental study with dogs, Ettinger et al[21] did not observe prolongation of the HV interval or QRS widening after acute alcohol infusion. However, these parameters were only measured in two dogs. A bigger sample, namely one composed of humans, may be necessary to confirm this theory. In fact, later in the original HHS study, prolongation of PRc, QRS, and QTc intervals[14], which are known to be associated with AF, was observed[22]. Cardy et al[23] have also shown prolongation of P and QRS waves in 13 humans after acute ingestion of alcohol, suggesting atrial and ventricular slowing of conduction due to alcohol. Although controls also showed prolongation of these waves, changes in the alcohol group were significantly more pronounced.

A recent study, using the patch clamp technique, has shown that ≥ 2 g/L alcohol has an inhibitory effect on cardiac sodium channels, providing a possible mechanism for the cardiac conduction interference caused by acute alcohol ingestion. This may happen directly or even indirectly since the inhibition of sodium channels can increase sodium-calcium-exchanger activity, prolonging the action potential and repolarization, with subsequent prolongation of intervals, such as the QT interval, thereby facilitating the onset of cardiac arrhythmias. For concentrations <2 g/L, inhibition was not significant, indicating that this mechanism is more likely to occur with acute heavy ingestion, i.e., binge drinking[24].

Refractory period shortening: Alcohol can shorten the atrial refractory period, which can lead to cardiac arrhythmias in rat atrial tissue[25]. However, in a study of 11 alcohol abusers, Engel *et al*. did not find significant alterations in the atrial refractory period after whiskey consumption. Therefore, there can be additional and significant focal conduction changes that can facilitate re-entry and lead to the cardiac arrhythmias observed in this study[16].

Increased sympathetic activity: Alcohol can increase the release of catecholamines, secreted by the adrenal gland medulla or locally by the myocardium itself[7,16]. This increase of systemic and intramyocardial catecholamines can lead to the prolongation of P-waves, which is known to be associated with atrial arrhythmias[8,9].

However, Maki et al[26] did not find a significant increase of catecholamine levels after alcohol consumption in individuals with or without a personal history of AF episodes caused by binge drinking. Yet, catecholamine levels in the AF group displayed a trend toward being higher, which can synergistically work with the other arrhythmogenic mechanisms of alcohol, increasing the likelihood of cardiac arrhythmias. The same

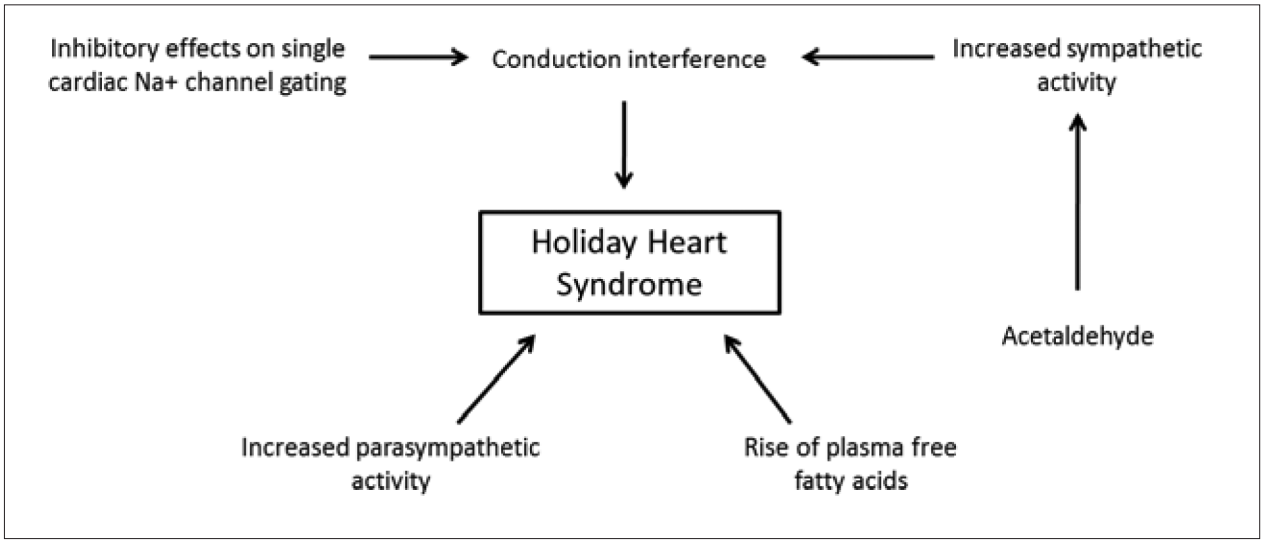

Figure 2 - *Potential mechanisms involved in the onset of cardiac arrhythmias after acute alcohol ingestion (binge drinking).*

authors observed an increase of beta-adrenergic receptors along with a predominance of cardiac sympathetic activity in patients with a previous drinking-related AF history[26].

Rise in plasma free fatty acids: With alcohol intake there is a rise in plasma free fatty acids, which are believed to be arrhythmogenic in nature[7,9]. Although the mechanisms are still not completely understood, a significant association between elevated free fatty acids and AF was observed in elderly people in a recent analysis of the Cardiovascular Health Study, strengthening this theory[27].

Acetaldehyde arrhythmogenic effects: The primary metabolite of alcohol also appears to exhibit arrhythmogenic properties, possibly by increasing systemic and intramyocardial catecholamines[23,26]. An experimental study by Gallardo-Carpentier et al[28], using dog Purkinje fibers, has shown that acetaldehyde has an arrythmogenic effect, which appears to be caused by an increase in adrenergic activity. Hence, acetaldehyde could cause the onset of arrhythmias some time after alcohol ingestion. Conversely, arrhythmia has been observed shortly after whisky intake even before significant amounts of acetaldehyde could be produced[16].

Increased parasympathetic activity: Despite the aforementioned data supporting increased sympathetic activity after alcohol intake as a cause for cardiac arrhythmias[26], a recent study by Mandyam et al[29] identified a connection between vagal activation and paroxysmal atrial fibrillation (PAF). It also suggested that alcohol could trigger AF by vagal activation because patients reporting alcohol as a trigger were more likely to report vagal activation as a trigger[29].

Clinical evidence

In addition to Ettinger's original description, the link between binge drinking and the onset of cardiac arrhythmias has been consistently observed (Table 1).

Engel et al[16] tested the vulnerability to AF and flutter after whiskey consumption. In their study, two of three non-alcoholic patients with sinus bradycardia, but without heart failure, developed AF or flutter after consuming whisky.

A case series by Thornton[7] showed four cases of cardiac arrhythmia after alcohol intake in persons who did not consume alcohol regularly.

Koskinen et al[15], in a case-control study with 100 patients, including 35 with no evidence of cardiac disease, also verified a link between recent alcohol intake (previous two days) and AF. However, unlike the original HHS study, most cases did not occur during weekends or after holidays, but rather on Wednesday, Thursday, and Friday. The authors justify this distribution by citing the increased mental and physical stress during work days, which can increase sympathetic tonus, further enhancing the arrhythmogenic effect of alcohol. This study estimated that approximately 15%–30% of idiopathic AF cases are related to alcohol abuse.

Although only indirectly related to HHS, Wannamethee and Shaper[5], in their prospective study about alcohol and sudden death, noticed that patients between 40 and 49 years of age without ischemic heart disease and with occasional drinking habits had an incidence of sudden death similar to that of heavy drinkers, suggesting that some of these occasional drinkers may have partaken in binge drinking, which is associated with HHS, leading to cardiac arrhythmias that could result in sudden death.

Another retrospective study of young adults by Krishnamoorthy et al[17], focusing not only on alcohol but also on illicit drug use, confirmed alcohol as a major trigger for AF. Of 88 patients admitted with AF, 20 had consumed alcohol before the onset of symptoms and one was admitted for cocaine abuse. The same study followed-up some of the patients, verifying relapses in all those who continued alcohol abuse, which strengthens the motivation to suggest abstinence as a prophylactic measure.

Mandyam et al[29] also observed an association between alcohol and PAF. Their study had the particularity of comparing PAF patients against patients with supraventricular tachycardia (SVT) to assess whether alcohol intake precipitates PAF more frequently than that probably expected. Alcohol consumption is common and PAF is also quite frequent; therefore, alcohol would appear to trigger PAF in the absence of a true causal association. Patients with PAF had 4.42 higher odds of reporting alcohol ingestion before a PAF episode compared with the SVT group[29].

In a recent study, Liang et al[30] analyzed the role of both regular alcohol intake and binge drinking in AF risk using participants from the Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial and Telmisartan Randomized Assessment Study in ACE Intolerant Subjects with Cardiovascular Disease trials. Within the moderate alcohol intake group, binge drinkers (defined as alcohol intake of >5 drinks/day) were associated with an increased risk of AF compared with non-binge drinkers, reaching a similar risk of AF as heavy drinkers (>3 drinks/day for men and >2 drinks/day for women).

Unsolved questions

Although there have been considerable developments related to HHS, there are still some important questions requiring further research.

Long-term vs non-drinkers: do chronic drinkers have an increased risk of HHS? Although there is a link between chronic alcohol abuse and alcoholic cardiomyopathy, which is known to lead to cardiac arrhythmias[8], there has been considerable research, including several epidemiological studies showing an association between chronic alcohol consumption and an increased risk of AF in apparently healthy individuals without evident heart disease, namely alcoholic cardiomyopathy. This link appears to be stronger with heavy abuse, but it is less clear in cases of moderate and light alcohol ingestion.

Djoussé et al[4], using data from the Framingham study, found a significant increase in the risk of AF (1.36, $p = 0.006$) for chronic alcohol intake of >36 g/day (approximately 3 drinks / day); however, the increased risk was non-significant for amounts below that level. In a review paper about dietary factors including alcohol by Gronroos et al[10], a similar

Table 1 - Characteristics of the reference studies

Authors	Year of Publication	Design	Study sample	n	Key findings
Ettinger et al[14]	1978	Observational	Patients aged 25 to 62 years of both genders, admitted at Martland Hospital and Englewood Hospital between January 1972 and January 1976	32	Original description of HHS. Association between binge drinking and cardiac arrhythmias.
Engel et al[16]	1983	Prospective observational	Men aged 43 to 75 years	14	Increased vulnerability to AF and atrial flutter after whisky ingestion.
Thornton [7]	1984	Case series	Hospital-based, both genders, aged 34 to 47 years	4	AF induced by binge drinking in non-alcoholic people.
Koskinen et al[15]	1987	Case-control	Consecutive patients aged 21 to 64 years , of both genders, admitted at Helsinki University Central Hospital between 1 January and 20 September 1985	100	A link between recent alcohol intake (previous 2 days) and AF was described. Weekend and Holidays prevalence of AF onset weren't observed.
Wannamethee and Shaper[5]	1992	Cohort Prospective	Men aged 40 to 59 years selected at random from one general practice in each of 24 towns in England, Wales and Scotland	7 735	Similar incidence of sudden death between occasional drinkers and heavy drinkers. Possible association between occasional binge drinking and sudden death.
Krishnamoorthy et al[17]	2009	Case series	Patients aged ≤ 45 of both sexes, admitted at City Hospital, Birmingham between June 2000 and June 2006	88	20 patients reported alcohol consumption before onset of symptoms. Recurrences were observed in all patients who continued with alcohol abuse.
Mandyam et al[29]	2012	Case-control	Consecutive patients of both sexes presenting at electrophysiology laboratory at the University of California, San Francisco, Between September 2004 and March 2011	223	Patients with PAF had 4.42 bigger odds of reporting alcohol consumption before the PAF episode when compared to SVT group.
Liang et al[30]	2012	Cohort prospective	Patients aged ≥ 55 years, with personal history of cardiovascular disease or diabetes with end-organ damage, followed for 56 months	30 433	Binge drinking, in patients with moderate alcohol intake, was associated with increased AF risk when compared to non-binge drinkers

HHS: Holiday heart syndrome; AF: Atrial fibrillation; PAF: Paroxysmal atrial fibrillation; SVT: Supraventricular tachycardia.

conclusion was drawn, with a consistently significant increase in the risk of AF observed for heavy drinkers, but no increase associated with moderate alcohol consumption. An analysis of Prospective Study of Pravastatin in the Elderly at Risk in a study by Macfarlane et al[22], despite the sample being based on elder people, also demonstrated that alcohol intake was significantly higher in patients with AF than in patients without AF.

In a recent meta-analysis, Samokhvalov et al[11], verified a dose–response relationship between the daily amount of alcohol consumed and risk of AF, with a relative risk of 1.08/drink. However, the risk of AF was only significant for intake of >3 drinks/day (36 g/day) for men and >2 drinks/day (24 g/day) for women, implying a possible threshold above which there is a significantly increased risk of AF. Ingestion below these levels had the same risk as non-drinkers[11].

One theory that can explain the lack of association of AF with moderate alcohol ingestion is that this type of consumption may be protective against AF due to its anti-ischemic effects, providing protection from possible cardiac events that can result in structural damage and lead to AF. However, in another recent meta-analysis, by Kodama et al[18], apart from observing a dose–response relationship similar to the previously cited meta-analysis, their data also suggested that moderate intake could produce a higher risk of AF compared with not drinking at all. More studies with bigger samples and follow-up are needed to clarify this matter.

Contrary to previous studies, a recent analysis from the Framingham study performed by Shen et al[31] did not observe a link between long-term alcohol consumption and AF. There was an increased risk for alcohol consumption above 35 g / day and 25 g/day for men and women, respectively, but this did not reach statistical significance. However, heavy drinkers were under-represented, which may have rendered this study underpowered for that purpose. A bigger sample and longer follow-up may be needed prior to drawing further conclusions[31].

Overall, the risk appears to be consistently increased with heavy chronic drinking; therefore, the risk of HHS may further increase by superimposing binge drinking episodes on this already risky chronic background.

Moreover, experimental studies with dogs have shown long-term alcohol abuse can lead to microscopic structural changes and cardiac conduction interference before any clinical evidence of macroscopic structural heart changes are evident[21,32]. These micro-structural and cardiac conduction changes may facilitate the occurrence of HHS after a binge drinking episode.

Another point to consider is that chronic drinkers may be more prone to binge drinking during holidays, weekends, or other special occasions.

Does the presence of cardiac comorbidities increase HHS risk?

Previous studies suggest that in patients with cardiac disease that increases the chance of cardiac arrhythmias, namely AF, alcohol can be a trigger for arrhythmia episodes[15,17,30]. However further studies are needed to quantify this risk.

Other questions:

-Is the incidence of HHS underestimated? HHS is most probably under-diagnosed because some of the cardiac arrhythmias, namely AF, can occur without symptoms.

- Is there a genetic background associated with a higher susceptibility to alcohol arrhythmogenic effects? For example, Ettinger and colleagues related a case where the patient had only taken one drink before the onset of symptoms[14]. These reports are also common in our daily practice.

- Does the type of drink affect the risk? There are many types of beverages: beer, wine, and distilled drinks such as vodka and whisky. Therefore, it is important to be aware if some of these types of drink confer an increased risk of HHS. For example, beer was more frequently associated with PAF than wine or spirit drinks in the study by Mandayam et al[29]

- Is there a threshold for acute alcohol intake above which the risk of HHS increases significantly?

- Do patients with HHS have a higher risk of thromboembolic events compared with those with PAF independent of alcohol ingestion?

- Is the risk of HHS higher than the benefits of moderate intake?

- Does the speed of intake affect the risk of HHS? Does faster intake increase the risk?

- Is the risk different if the binge drinking takes place during fasting or after a meal?

Conclusion

Alcohol has a definite role in cardiac arrhythmia, either by chronic abuse or by binge drinking. It is important for physicians to recognize HHS and be aware of the role of alcohol in its genesis, sparing patients from complex investigations when there is no clinical evidence of cardiac pathologies.

During admission of a patient with palpitations or other symptoms associated with cardiac arrhythmias, a high suspicion of HHS should occur if the patient exhibits signs of alcoholic intoxication or had a recent episode of binge drinking. After confirming the cardiac arrhythmia and excluding evident heart diseases, the physician should explain the syndrome to the patient and recommend alcohol abstinence in an effort to prevent new episodes of HHS.

Author contributions

Conception and design of the research, Writing of the manuscript and Critical revision of the manuscript for intellectual content: Tonelo D, Providência R, Gonçalves L; Acquisition of data and Analysis and interpretation of the data: Tonelo D.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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