

Mini Review

## Caffeine, Energy Drinks and Atrial Fibrillation: A Mini-Review

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### Abstract

The present mini-review analyzes the relationship between caffeine and atrial fibrillation (AF) and specifically referred to the association between energy drinks (EDs) and occurrence of AF. The topic is very actual whereas data in literature are controversial. The quantity of caffeine in EDs is really high and is often underestimated by users. Several case-reports suggested a risk of AF in subjects assuming high quantity of EDs and it is becoming a social problem due to the wide use of mix drinks (EDs and alcohol) among youth.

**Key Words:** Energy Drinks; Caffeine; Atrial Fibrillation; Younger

The present mini review analyzed the relationship between caffeine intake and arrhythmias specifically, atrial fibrillation (AF). The topic has been evaluated by several studies exploring the association between AF and coffee and/or caffeine intake. Recently the wide diffusion of EDs, beverages that contain high dose of caffeine reveal new data supporting the hypothesis that caffeine could act as trigger for arrhythmias. The wide use of EDs among young people lead to a social problem especially when EDs were taken mixed with alcohol and drugs. This mini-review intends to analyze recent data on this phenomenon.

### Effect of Caffeine on Atrial Fibrillation

Caffeine is one of neuroactive substances most prevalent in Western countries. Its cardiovascular effects are well known, as well as the different cardiovascular responses observed in individuals who usually take caffeine from beverages and foods regularly than those who take it occasionally [1,2].

Caffeine is an alkaloid that exerts many effects on the autonomic nervous system. Caffeine is a non-selective competitive antagonist of adenosine receptors, both A1 and A2A subtypes. All tissues with adenosine receptors may be influenced by caffeine assumption. The plasmatic concentration reaches its peak after coffee consumption. Antagonize adenosine receptors, whether other caffeine effects, such as inhibition of phosphodiesterase or calcium release from intracellular stores, occur at higher concentrations [1,2]. Acting as a psycho stimulant substance, caffeine increases mental alertness, wakefulness, and restlessness.

In addition caffeine exerts a stimulating action on the heart, which increases contractility and stroke causing at the same time a coronary vasodilation. While coronary vessels dilate brain vessels constrict and blood flow to the brain decreases. This effect is useful in some cases of headache or migraine, but could be dangerous if

added to cerebral effect of alcohol [1,2].

Among its pro-arrhythmic effects palpitations, ventricular tachycardia (VT) and atrial fibrillation (AF) has been reported [3,4,5,6]. However, there are still many discrepancies on the effects of caffeine and despite the theoretical relationship between caffeine and arrhythmias, there is no evidence, in humans, that caffeine at doses with which is commonly consumed, can directly cause abnormal heart rhythms. However EDs contained very high dose of caffeine, much higher than the dose commonly assumed by drinking coffee.

Moreover there are some differences between caffeine intake and coffee intake. Coffee is the main source of caffeine in industrial Countries but other different sources have been reported: i.e. tea, chocolate, soda and recently energy drinks (EDs). Caffeine, in fact, is present in various foods. Not only it is contained in the range of 40-180 mg in coffee, but it is also contained in the range of 24-50 mg in tea, 15-29 mg in Coca Cola, 1-36 mg in chocolate per serving [2,3].

Food Standards Authority of Australia and New Zealand defined caffeine intake levels as low, moderate and high: 80-250 mg/day "low intake" (1.1-1.3 mg/kg in a 70kg weight adult), 300-400 mg day "moderate intake" (4-6 mg/kg in a 70kg weight adult), > 500 mg/day "high intake" (7 mg / kg in a 70kg weight adult).

The half-life of caffeine in a healthy adult ranges from 2.5 to 10 hours. The long-term consumption of caffeine and the assumption of large amounts may prolong the half-life. The maximal plasma level is reached only after 2 hours, although plasmatic levels increase after 30 minutes [2,3]. Plasmatic levels are influenced by the contemporary assumption of food. [7,8].

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## Clinical Studies on Caffeine and AF

Several studies investigate the relationship between caffeine (or coffee) and atrial fibrillation.

In the Multifactor Primary Prevention Study, consumption of 1-4 cups of coffee/day was associated with an increase risk of atrial fibrillation, on contrary drinking more than 4 cups a day was not associated with a risk of atrial fibrillation [9].

The Danish Diet, Cancer and Health study did not find any risk of atrial fibrillation or flutter associated with caffeine consumption [10]. The strength of the Danish Diet study is the large number of patients with atrial fibrillation and the incidence rate for atrial fibrillation was the same reported from the Framingham study and the Manitoba Follow-up Study [11,12].

In a case-control study it was found that increasing level of coffee consumption was associated with a significantly greater risk of acute atrial fibrillation [13]. High espresso coffee consumption (>3 cups a day) was associated with an increase risk of atrial fibrillation and the risk is more marked in non-habitual coffee drinkers. This effect could be the consequence of the more marked sympathetic activation induces by caffeine in nonhabitual coffee drinkers.

Some studies suggested a protective effect of high coffee consumption on cardiovascular risk factors mainly due to its antioxidant properties, which appear to reduce the risk of cardiovascular disease [14]. In this study the intake of antioxidants by coffee was quite high. However the selection of a population that had a strong adherence to Mediterranean diet could have influenced the results.

The hypothesis that coffee consumption would lower the risk of cardiovascular disease is also supported by a recent study, which showed that women who regularly consumed coffee had a lower risk of stroke than women who did not consumed. This association was only partially mediated by bioactive substances contained in coffee [15].

The topic is controversial and the effects of coffee consumptions seem to be mediated by several other factors, mainly the Diet, the modality of preparation of coffee (filtered or not) and the interference of food and drugs on its bioavailability.

A recent case report underlines the correlation between the appearance of arrhythmia in an adult following the consumption of chocolate and taking salbutamol. The salbutamol is a short-acting selective  $\beta_2$  adrenergic receptors agonist. The combined effects of methylxanthines contained in the coffee/tea and chocolate and salbutamol would increase the probability of triggering of arrhythmia [16].

Another study reported a clinical improvement in a patient, 58 years old, with AF, dilated cardiomyopathy immediately after stopping excessive consumption of coffee/caffeine [17].

We also observed an association between the consumption of drinks with high caffeine content and the development of AF in

youth [1,18].

## Energy Drinks and Atrial Fibrillation

In recent years consumption of “Energy Drinks” (EDs) beverages that contain a high amount of caffeine has become very popular among young people.

The amount of caffeine varies widely in EDs and it is estimated between 80 to 114 mg/can. These drinks are very popular within young people because they increase supervision during the evening hours. Moreover, they are sold in cans, are unrestricted and marketing campaign identify it as safe products able to improve the physical and mental performance.

Currently, there is not a basic formula or ingredient necessary to define the energy drinks. However, there are a number of substances, i.e. methylxanthines, often present in high quantities that give the beverage certain characteristics (psychostimulants). The EDs contain substances such as caffeine, B vitamins, taurine, maltodextrin, inositol, carnitine, creatine and glucuronolactone; there are also plants and herbs such as guarana (containing caffeine), ginseng and ginkgo biloba [19].

The caffeine content is very variable: generally a quantity slightly higher or slightly equivalent to 80-85 mg of a cup of coffee and superior to 23 mg of a classical Soda Cola. On the basis of discrepancies regarding the effects of the consumption of coffee/caffeine, the FDA (Food and Drug administration) recognized as “safe” intake of some popular beverages containing a concentration of 0.02% of caffeine [20,21].

Comparing the different energy drinks in the market, a can of a popular ED of 8.2 grams contains about 80 mg of caffeine (0.03%), while a can of another popular ED contains about 141 mg of caffeine [22,23].

In addition these EDs contain several other source of caffeine, i.e. guarana. The guarana plant and berry has one of the highest naturally occurring levels of caffeine at around 7–8%, and there are also traces of theophylline and theobromine. Instead of referring to caffeine, many companies and websites market their products using the term ‘guaranine’. Other companies clearly label their products with the caffeine content, but the impression may be given to consumers that there is something additionally special about guarana [24].

The presence of herbs in the EDs could also induce some side effects. It is well known that herbs interact strongly with medications and could have direct effects on cardiovascular and hemostatic system [25]. One of the effects is the QT interval prolongation leading to a pro-arrhythmic status. Although herbal remedies are perceived as being natural and therefore safe, many have adverse effects that can sometimes produce life-threatening consequences [25].

Furthermore, these beverages are very often taken in combination with alcoholic drinks, triggering arrhythmias. Nowadays an online drinking game called “Nek Nomination” is really popular among

young people who are required to film themselves while drinking as much as possible of an alcoholic beverage and share their performance on the Internet challenging other friends to do the same within 24 hours.

The EDs have now a prevalent role in the enjoyment of alcohol. Among young people, the intake of EDs based cocktails is now a common habit [26,27].

We also reported a case of a boy that had consumed a popular ED mixed with an alcoholic drink in order to increase his alertness and eventually developed AF [18]. Several similar cases in the literature are reported, among which the case of two teenagers who showed evidence of changes in heart rate due to consumption of alcohol together with ED [28,29].

A paper described the cases of two boys (14 and 16 years old) without previous cardiac event that developed AF after consuming EDs [20]. The first one developed palpitations and chest pain after taking an energy drink containing high dose of caffeine. The same symptoms had been warned five days before having consumed another popular ED. Physical examination also showed irregular heart rhythm (130 b/m approximately), while the ECG, showed tachycardia with intermittent FA. The second boy experienced vomiting, attention problems, hyperactivity, asthma and chest pain after taking a mix of ED, spirits, vodka, together with amphetamines and a number of medications. Physical examination showed an irregular heart rhythm (160 b/m approximately), while the ECG showed atrial tachycardia and AF with a rapid ventricular response. In this patient the level of ethanol in the blood was 155 mg/dl [20].

Unfortunately, data on the side effects of these drinks are still partially unknown. The damages that the regular consumer of EDs and alcohol are facing arrhythmias and renal impairment. The intake of high amounts of caffeine, about 1gram per day, and the combination alcohol-EDs can alter both the central and peripheral nervous system. The increase of heart rate can cause major side effects such as anxiety, mood changes, insomnia, hypertension, and cardiac arrhythmias. EDs associated with alcohol have been associated with renal impairment that seem to be related to the effects of taurine on the excretory system. The hypothesis that kidney damage is induced by taurine in EDs is supported by a recent study reporting renal failure developed after a high consumption of EDs. The first case was a 17-year-old boy who had taken about 3liters of EDs and 1liter of vodka, and in another case, an athlete who had taken a large quantity of EDs, both developed renal failure [30].

In addition, the mix generates a potential risk of dehydration because both alcohol and EDs have diuretic properties. The risk of dehydration is due to both an increase in diuresis and an increase in sweating. Cases of deaths from dehydration and alteration of the electrolytes during intense physical activity associated with high consumption of EDs have been reported [31]. Moreover the

indiscriminate use of EDs and alcohol can lead to alcohol addiction and alcoholism in youth.

## Conclusion

Despite the enormous popularity worldwide in some European and non-European countries, it has not been granted the marketing authorization of EDs.

In France, the Ministry of Health ruled that EDs may have undesirable effects on the metabolism and on blood pressure and classified them as medicinal, effectively preventing the distribution. Similarly other European Countries are evaluating restriction to ED market. Even Denmark and Norway have not authorized the sale in younger. In Britain, however, trade in such drinks is allowed freely, but is not recommended for pregnant women, younger and persons with cardiovascular risk.

At EU level, specific provisions are foreseen for the labeling of energy drinks in the EU Labelling Directive 2000/13/EC and in the recently implemented Food Information to Consumers Regulation (EU) No 1169/2011. According to the latter regulation, labeling of energy drinks includes the indication "High caffeine content. Not recommended for children or pregnant or breast-feeding women" followed by the indication of the amount of caffeine per 100ml in brackets. This legislation constitutes harmonized European law and is directly applicable in all EU member states.

What we hope for the future is that at least in adolescents the purchase and consumption of these drinks will be limited because, as psychostimulants and containing various substances, can cause different negative effects on the organism. Moreover, frequent consumption can have a debilitating effect on a body that is still growing.

Not much information is available on direct effects of EDs and caffeine on heart. Existing data suggested that the effects are strongly influenced by interaction with food and alcohol, which impact bioavailability of caffeine in blood.

More information is needed on this topic and also medical practitioner needs to be informed on these potential detrimental effects.

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