Mini Review

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Journal of Clinical Nutrition & Dietetics
ISSN 2472-1921

2016
Vol. 2 No. 1:3

http://dx.doi.org/10.4172/2472-1921.100010

Coffee Consumption and Coronary Heart Diseases: A Mini-Review

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Citation: Shateri Z, Djafarian K. Coffee Consumption and Coronary Heart Diseases: A Mini-Review. J Clin Nutr Diet. 2016, 2:1.

Abstract

Background: Coffee contains thousands of chemical compounds such as chlorogenic acid, caffeine, potassium, niacin, magnesium and tocopherols. Only caffeine in coffee shows pharmacological effects. Based on relevant studies, caffeine in coffee has many side effects such as increasing blood pressure, homocysteine, plasma renin; catecholamine and arrhythmia, which are considered as risk factors for coronary heart diseases (CHD). Several epidemiological studies have investigated this association which conflict each other.

Materials and method: The current research was conducted based on articles published in medical journals from 2000 to 2014 applying the PubMed database from which 56 articles were selected.

Results: According to the research, coffee can affect the risk of myocardial infraction. Furthermore, coffee's effect on blood pressure depends on the duration of coffee consumption. Coffee can increase homocysteine concentration which is one of the risk factors for coronary heart diseases.

Conclusion: It seems that coffee can affect coronary heart diseases, but these effects depend on many factors too, consisting genetic polymorphism.

Keywords: Coffee; Caffeine; Coronary disease

Received: November 18, 2015; **Accepted:** January 18, 2016; **Published:** January 25, 2016

Introduction

One of the most popular drinks worldwide is coffee that contains dietary antioxidants, and its name is derived from the name of province Keffa which is located in Ethiopia. Coffee has been discovered by shepherds from Ethiopia in the sixth century. This beverage wasn't popular until was used in Islamic population in thirteen century. 200 years later, it was sold in Europeans so this new drink was introduced in western culture [1]. Coffee has thousands of chemical compounds which can name chlorogenic acid, caffeine, potassium, niacin, magnesium and tocopherols [2] Coffee has two diterpenoids named Cafestol and Kahweol which involve in increasing cholesterol [3], but only caffeine in coffee has pharmacological effects [4]. The amount of cafestol and kahweol in coffee depends on the method of brewing [5]. The most of amount this two materials release when was contacted boiled water [3]. Soluble dietary fiber contents of brewed coffee are significant (0.47-0.75 g/100 mL of coffee). Principle non-digestible polysaccharides in coffee are cellulose, arabinogalactan type II (AGII) and galactomannan (GM) [6]. According to studies, caffeine in coffee has roles such as increasing blood pressure, homocysteine, plasma renin; catecholamine and arrhythmia, which all of them are risk factors for coronary heart diseases [5]. It has been shown unfiltered and boiled coffee increases the serum cholesterol, particularly the level of low-density lipoprotein cholesterol [7]. Several epidemiological studies have investigated this association which conflict each other. The purpose of this article was to review the literature to give a comprehensive outline about the association between coffee consumption and coronary heart diseases.

Compounds in coffee

Caffeine

An alkaloid that is in coffee beans is caffeine (1, 3,7 thrimethylxanthin) [5]. Additional coffee, caffeine is in tea, soft drinks, energetic drinks and chocolate, but coffee is the most major source of it in adults [4]. Caffeine is readily absorbed from the gastrointestinal tract [8]. Caffeine has different acute

effects on the heart and vessels such as effect on blood pressure, circulating catecholamine, arterial stiffness and endothelial dependent vasodilation [4]. Caffeine is A1 and A2 receptor antagonism [9]. Caffeine is a methylxanthine that important biological effect is competitive antagonism of adenosine receptor [10, 11]. Adenosine receptors are affected by caffeine and its abstinence cause muscle fatigue in those addicted to coffee [12]. The caffeine content is 83 mg/cup in instant coffee, cola sodas 42 mg, regular tea 36 mg and chocolate snakes 6 mg [13]. Caffeine content depends upon the brew time [14].

Chlorogenic acid

Chlorogenic acid (CGA) is the ester from caffeic acid and quinic acid, which is a main phenolic acid composition of coffee [15, 16]. Chlorogenic acid has antioxidant properties in vitro. It is shown that chlorogenic acid might have an antagonistic impress on glucose transmission [17]. Coffee drinkers consume approximately 1 g chlorogenic/quinic acid in daily intake [18]. A main source of chlorogenic acid is coffee in human diet [19] **(Figure 1)**.

Apples, pears, berries, almond, artichoke and aubergines are the other sources of chlorogenic acid [20].

Cafestol and kahweol

Diterpenes of Cafestol and Kahweol are part of boiling coffee, which is responsible for increasing blood cholesterol [21]. Their amount in a coffee beverage is affected by the brewing manner [22]. Coffee is contributing significantly to the increase in LDL-C, TC and TG especially unfiltered coffee, and the changes were associated with the level of intake [23]. Surveys have shown dose-dependent effect of Cafestol and Kahweol on elevating serum cholesterol levels [24]. Boiled coffee contains the highest concentrations such as Scandinavian-style and Turkish-style while, trace amounts see in instant, drip-filtered and percolated coffees [22]. Each 2 mg of consumed Cafestol increase serum cholesterol by 1 mg/dL [25]. Cafestol down-regulated and up-regulated LDL receptor and acyl-CoA: cholesterol ester transferase (ACAT) in HepG2 cells and HSF, respectively. In addition to, in transgenic mice fed Cafestol suppress the HMGCoA reductase activity and bile acid synthesis [3].

Cafestol down regulated CYP450s of the CYP7 and CYP27 family accordingly, suppressed bile acid synthesis in rat hepatocytes, a mechanism that may be involved in hypercholesterolemia [26]. Cafestol increases plasma triacylglycerol by elevating the generation rate of VLDL [1] apo B, via increased aggregation of $VLDL_1$ in the liver [27, 28].

Materials and Method

A search was conducted on articles published in medical journals from 2000 to 2014 using the PubMed database. The relevant studies were identified through search engine using a combined text word and MeSH (Medical Subject Headings) search strategy. Articles with case-control, cohort, interventional (clinical trials), review, meta-analysis and systematic review design published between 2000 and 2014 were evaluated through PubMed using keywords such as “coffee”, “caffeine”, “ingredient” and “coronary disease”. We searched the bibliographies of target studies for additional references. The inclusion criteria were animal, intervention and observational studies and appropriate comparison group. The exclusion criteria were poorly defined comparison group and inaccessibility to the full-text. A total of 56 articles were selected **(Figure 2)**.

Results

The results of the current review article are listed below on the basis of conducted epidemiological research.

Risk of myocardial infarction

In a case-crossover study on 503 incident cases of nonfatal myocardial infarction have been shown in the hour after coffee intake relative risk (RR) of myocardial infarction was 1.49 and in occasional coffee consumers (1 cup/day, n=103) was a RR of

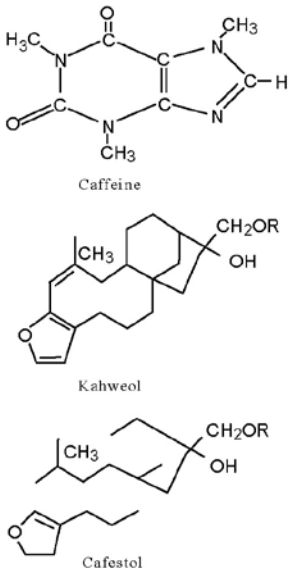

Figure 1 Structure of Caffeine, Kahweol and Cafestol.

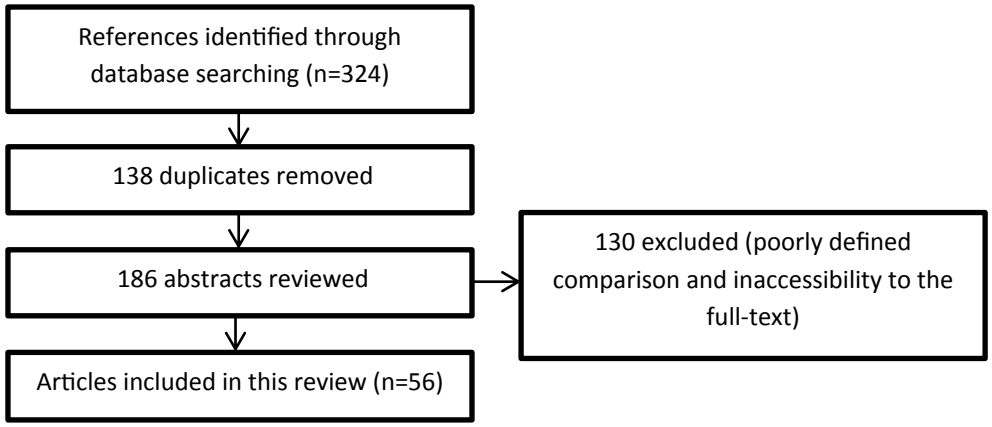

Figure 2 Flow diagram for literature search and study selection.

myocardial infarction of 4.14 (2.03– 8.42) and in moderate coffee consumers (2–3 cups/day, n=280) was a RR of 1.60 (1.16–2.21), and in heavy coffee consumers (4 cups/d, n=120) had a RR of 1.06 (0.69–1.63; P 0.006, test of homogeneity). This study indicated that coffee intake may trigger myocardial infarction (28). Coffee is the main source of caffeine that is metabolized by polymorphogenic cytochrome P4501A2 [5]. In the research of coffee, CYP1A2 genotype and risk of myocardial infarction done by Cornelis. et al showed that intake of coffee was related to an elevated risk of nonfatal MI only among persons with slow caffeine metabolism, representing that caffeine take part in this relationship [29]. Rosner et al showed coffee drinking of ≥ 5 cups/week was non-significantly reversely related to myocardial infarction risk among older Swedish women [30]. A research represented that drinking of filtered coffee was positively related to the risk of a first myocardial infarction in men [31]. In total, coffee could affect risk of myocardial infraction **(Table 1)**.

Effect on blood pressure

One of the strong independent risk factors for heart attack and coronary heart diseases is hypertension. Coffee consumption has been associated with acute increases in blood pressure (BP) in caffeine-naive people, but exerts negligible effects on the long-term levels of BP in habitual coffee drinkers [32]. The probable mechanisms of the cardiovascular effects of caffeine contain blocking the adenosine receptors present in the vascular tissue to produce vasoconstriction [33]. A study was concluded in which caffeine increases blood pressure in short-term studies [34]. However, the above effects of caffeine could be transient, because partial tolerance might develop after several days of use [35].

Coffee administration has shown that increase significantly blood pressure in men, but not in women [36]. In a systematic review and meta-analysis, it was concluded that caffeine intake produces an acute increase in blood pressure for 3 hours in hypertensive individuals. Their results do not support a relationship between long-term coffee consumption and elevation in blood pressure [37]. One study showed that coffee and caffeine caused a significant blood pressure in non-habitual coffee drinkers while habitual coffee drinkers showed no elevation in blood pressure [38]. Another study showed that regular caffeine intake increased blood pressure [39]. It was found that chlorogenic acid from green coffee bean extract was impressive in decreasing blood pressure and safe for patients with mild hypertension [40]. However, more research shows that regular intake of caffeinated coffee does not increase the risk of hypertension [41]. Winkelmayer et al found no linear relationship was between caffeine and hypertension [42] **(Table 2)**.

Effect on homocysteine

In nondiabetic individuals, a moderate increase in plasma homocysteine concentrations is related to an increased risk for cardiovascular events independent of common risk factors [43]. A significant influence of coffee beverage on plasma levels of homocysteine have been reported in some studies during recent years [36]. They recognized that coffee drinking was as main lifestyle determinant of plasma homocysteine distribution in the population [44]. In an intervention study, it seemed that avoiding the consumption of coffee for 6 weeks really reduced the total plasma homocysteine concentration about 1.5 µmol/l in participants who were utilized to drinking ≥ 4 cups per day, showing a causal association [4]. Consumption of both filtered and unfiltered coffee for 2 weeks significantly increased plasma homocysteine levels [4]. Olthof et al showed with chlorogenic acid that is one of the other components of coffee, a 7 day treatment elevated plasma homocysteine concentrations [45]. Grubben et al showed that unfiltered coffee could elevate plasma homocysteine concentrations in volunteers with normal initial concentrations [46]. Concentrations of tHcy have been positively associated with coffee drinking in a dose-dependent manner in several cross-sectional studies in Europe, Scandinavia and the US [5]. Supplementation of healthy men and women in a randomized, placebo-controlled crossover trial with folic acid (200 mcg/d) prevented increasing in plasma tHcy due to the drinking of 600 ml/d of filtered coffee for 4 weeks [47] **(Table 3)**.

Discussion

Coffee consumption is related to increasing in several cardiovascular disease risk factors, such as plasma homocysteine [48]. “The homocysteine-increasing effect of coffee is partly due

Table 1 The effect of coffee drinking on myocardial infarction.

Researchers	Type of research	Results
Baylin A et al (2006)	A case-crossover	Coffee intake may trigger myocardial infarction.
Cornelis M et al (2006)	A case-control	Coffee intake is related to an elevated risk of nonfatal MI that is depended on caffeine metabolism.
Rosner S et al (2007)	Prospective study	Coffee drinking of ≥ 5 cups/week has not reverse association with myocardial infarction risk
Nilsson L et al (2010)	A case-control study	Drinking of filtered coffee relate to the risk of a first myocardial infarction in men.

Table 2 The effect of coffee drinking on blood pressure.

Study	Type of research	Results
Okeefe J et al (2013)	Review	Coffee intake exerts negligible effects on the long-term levels of BP in habitual coffee drinkers.
Hartley T et al (2004)	Clinical trial	Caffeine increases blood pressure in short-term.
Lopez-Garcia E et al (2006)	Cohort study	Partial tolerance might develop after several days of caffeine intake.
Sofi F et al (2007)	Meta-analysis	Coffee administration increase blood pressure in men, but not in women.
Mesas A et a l (2011)	Systematic review and meta-analysis	Long-term coffee consumption isn't related to elevation in blood pressure.
Corti M et al (2002)	Clinical trial	Drinking of coffee in habitual coffee drinkers show no elevation in blood pressure.
Noordzij M et al (2005)	Mata-analysis	Regular caffeine intake increases blood pressure.
Geleijnse J (2008)	Perspective study	Regular intake of caffeinated coffee does not increase the risk of hypertension.
Winkelmayer et al (2005)	Cohort study	No linear relationship is observed between caffeine and hypertension.

Table 3 The effect of coffee drinking on homocysteine.

Study	Type of research	Results
Nurk E et al (2004)	Perspective study	Coffee intake induces elevation of plasma homocysteine.
Riksen N et al (2009)	Review	Avoiding the consumption of coffee reduces the total plasma homocysteine concentration.
Olthof et al (2001)	Crossover	Chlorogenic acid elevates plasma homocysteine.
Grubben et al (2000)	Clinical trial	Unfiltered coffee can elevate plasma homocysteine concentrations.
Higdon J et al (2006)	Review	Concentrations of tHcy are associated positively with coffee drinking.
Strandhagen E et al (2003)	Crossover trial	Supplementation with folic acid (200 mcg/d) prevents increasing in plasma tHcy due to the drinking of filtered coffee.

to caffeine. Also, chlorogenic acid can increase homocysteine. It seems that reactions of o-methylation that happen during the metabolism of chlorogenic acid cause increasing homocystein" [49].

A study has been concluded that "coffee consumption may have an acute harmful effect in causing coronary events and growing infarct size in elected patient groups, rather than advancing the expansion of atherosclerosis in the public population" [4]. It is appears that diterpenes in unfiltered coffee elevate risk of coronary heart diseases [48].

Most of the effects of coffee in blood pressure from caffeine, which the effects it is acute that can be concluded effect of coffee on blood pressure is transient and body is tolerated to coffee consumption in the long-term and the effect it on myocardial infraction depends on cyp1A2 genotype. Antagonism of adenosine is a mechanism of caffeine on blood pressure that cause vasoconstriction and increase total peripheral resistance [50]. However, research has shown lower risk of CHD mortality in persons whom drink caffeinated coffee and without moderate or severe hypertension [51].

One study showed that coffee consumption did not increase the long-term risk of coronary heart diseases and habitual moderate coffee consumption associated with a reduced risk of coronary heart diseases in women [52]. The search of long-term follow-up cohort studies did not demonstrate any communication between coffee consumption and CHD [36]. In the cohort studies have been reported that their data do not provide any evidence that coffee consumption increases the risk of CHD in general [35].

In the US Physician's and Nurses' Health Study assessed long-term habitual coffee drinking over 44,000 men and 85,000 women free of CHD to heart disease risk for 16–20 years. There was not seen influence of coffee on risk even at >6 cups/day [53]. Most prospective studies have not shown a positive association, whereas case-control studies in general have reported such a relationship. This difference may be due to bias and confounding in case-control studies [4]. Also, coffee consumption is associated with an unhealthy lifestyle such as smoking [36]. In addition to serum cholesterol increases with boiled coffee and some research suggests that high consumption of coffee is associated with CHD risk [35]. However, in some studies it was recognized that coffee

to be safe and not related with any unpleasant cardiovascular consequences in the short term [54]. Also, moderate caffeine intakes up to 400 mg/d is not related to adverse health effects in healthy adults [55]. In addition to it has been shown consumption of coffee was related to reduced risk of mortality from CVD [56].

In conclusion, results of research in coffee consumption and coronary heart diseases are contradictory but, in general coffee can affect coronary heart diseases and these effects can depend on method of brewing coffee, brewing time, genetics such as genetic polymorphism in cytP450, the homozygous 677TT genotype of the methylenetetrahydrofolate reductase (MTHFR) gene, underlying diseases such as hypertension and amount of coffee consumption. So, some people may be sensitive to coffee consumption and some may be not. Also the other health-related behaviors can affect the association between coffee drinking and coronary heart diseases. It is clear that further research is needed to show the effects of long-term drinking of coffee on the cardiovascular system.

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