International Journal of Clinical Nutrition, 2015, Vol. 3, No. 1, 7-11
Available online at http://pubs.sciepub.com/ijcn/3/1/2

DOI:10.12691/ijcn-3-1-2

Coffee Intake and Progression of Glaucoma

Nor Azimah Abdul Aziz, Ahmad Nurfahmi Akhtar Ali, Mohd Najib Kamarudin, Nur Atiqah Shaari, Wan Hazabbah Wan Hitam, Azhany Yaakub, Rohana Abdul Jalil, Liza-Sharmini Ahmad Tajudin*

Department of Ophthalmology, School of Medical Sciences, Universiti Sains Malaysia, Health Campus, Kota Bharu, Kelantan, Malaysia
*Corresponding author: liza@usm.my

Received April 04, 2015; Revised April 21, 2015; Accepted April 26, 2015

Abstract **Introduction:** Glaucoma is a second cause of blindness worldwide. Diet may potentially contribute to the disease progression. Coffee which contains caffeine is widely consumed globally. The aim of this study was to determine the association between coffee intakes and progression of glaucoma. **Method:** A cross sectional study was conducted on 91 primary glaucoma patients who were on topical antiglaucoma drugs. Direct face to face questionnaire on the frequency of coffee intake was conducted between December 2011 and May 2012. Ocular examination was performed including intraocular pressure (IOP) measurement and fundus examination. Two consecutive reliable Humphrey visual field (HVF) 24-2 standard analysis was obtained at the recruitment period. Severity and progression was based Hoddap- Parrish- Anderson (HPA) criteria. The progression of primary glaucoma was based on the difference of HVF at the diagnosis and the recruitment. **Results**: 63 (69%) were coffee drinkers with 68% of them drink coffee daily. 42 of primary glaucoma patients who consumed coffee in their diet developed progression of their disease after 6.6 (SD 4.4) years of follow up. Mean IOP at initial presentation (22.9 SD 8.1mmHg) and at current recruitment period (15.5 SD 2.3mmHg) was slightly lower among coffee drinkers but without significant difference (p=0.538, 0.454 respectively). There was no significant association between coffee drinking and severity of glaucoma (p=0.863). In spite of negative association between coffee drinking and progression of glaucoma (p=0.250), the frequency of coffee drinking was significantly associated (p=0.001) with progression glaucoma. Daily coffee drinking increased the risk of progression 8.1 folds (95% CI 2.5, 26.9) based on multivariate analysis. **Conclusion:** Drinking coffee daily was associated with glaucoma progression in this small study. Perhaps, glaucoma patient should minimize or avoid coffee intake.

Keywords: *glaucoma, coffee, caffeine, intraocular pressure (iop), progression*

Cite This Article: Nor Azimah Abdul Aziz, Ahmad Nurfahmi Akhtar Ali, Mohd Najib Kamarudin, Nur Atiqah Shaari, Wan Hazabbah Wan Hitam, Azhany Yaakub, Rohana Abdul Jalil, and Liza-Sharmini Ahmad Tajudin, "Coffee Intake and Progression of Glaucoma." *International Journal of Clinical Nutrition*, vol. 3, no. 1 (2015): 7-11. doi: 10.12691/ijcn-3-1-2.

1. Introduction

Glaucoma is a leading cause of irreversible blindness worldwide [1]. It is characterized by progressive optic neuropathy due to loss of retinal ganglion cells and damage to the optic nerve head [2]. The estimated number of people with glaucoma is 60.5 million people in 2010, and increasing to 79.6 million by 2020 [1]. An important modifiable risk factor for the progression of glaucoma is elevated intraocular pressure (IOP) [3,4,5,6]. IOP levels may be modulated by lifestyle including dietary habit [7,8]. Coffee is a widely consumed non-alcoholic beverage, which contains a bioactive ingredient; caffeine. Caffeine is a methylxanthine alkaloid, the most widely added ingredients in several popular beverages consumed worldwide [9,10]. Caffeine is metabolized into paraxanthine, theophylline and theobromine [11]. In general, a cup of coffee contains 135-150mg of caffeine [12].

Caffeine exerts pharmacological effect on human body due to antagonism on adenosine receptor that present in various body systems, including central nervous system(CNS), renal, heart, and kidney [11,13,14,15,16]. Caffeine acts as a stimulant on the central nervous system by reduces fatigue, improves concentration, increases alertness and enhances cognitive performance [17,18,19]. The effect on other systems includes cardiac excitation, relaxation of bronchial and vascular smooth muscles, and promotion of diuresis and intestinal motility [15,20]**.** Caffeine is a competitive antagonist of adenosine receptor, which inhibits the degradation of cyclic adenosine monosphosphate (cAMP) by phosphodiesterases and further increase the intracellular cAMP level [18]. Interestingly, caffeine's metabolites; paraxanthine and theophylline also exert similar biological effect as potent as caffeine on adenosine receptor [11,21].

Caffeine ingestion from drinks such as coffee causes transient elevation in IOP [4,5,6,7,8]. Caffeine causes elevation of IOP from 1-2mmHg [22]. Therefore, many clinicians advised patients with glaucoma to avoid or minimise coffee intake. Perhaps, a slight fluctuation of IOP in advanced or severe glaucoma may accelerate the glaucomatous neuropathy. However, the actual caffeine effect on glaucoma patients is not known. The aim of this

study was to determine the relationship between coffee intakes with the severity and progression of glaucoma

2. Materials and Method

A cross sectional study was conducted involving 91 patients diagnosed with primary glaucoma in Hospital Universiti Sains Malaysia, Kelantan between December 2011 and May 2012. This study received approval from research ethics committee, School of Medical Sciences, Universiti Sains Malaysia and was conducted in accordance to Declaration of Helsinki for human research.

Patients with primary open angle glaucoma (POAG) (n=80) and primary angle closure glaucoma (PACG) (n=11) were included in this study. Only patients with good compliance to topical pressure lowering medications were recruited. Exclusion criteria included secondary glaucoma, glaucoma suspect, those with strong family history of glaucoma, optic neuropathy other than glaucoma, stroke or any intracranial pathology and prolonged corticosteroid treatment. Patients with media opacities especially cataract more than grade 2 of LOCS II grading, vitreous haemorrhage and corneal opacities were excluded. Those with retina pathology such as retinitis pigmentosa and diabetic retinopathy were also excluded. Those with history of surgical intervention especially filtering surgery were also excluded except for cataract surgery. In addition, glaucoma patients who were still actively smoking were also excluded.

Ocular examination was performed during the recruitment period including intraocular pressure (IOP) measurement using standard Goldman applanation tonometer and fundus examination. Visual field test was performed using Humphrey Statpac_2 pattern deviation probability map of 24-2, SITA Standard, using a 31.5-apostilb background with a white Goldmann size III (0.43°) stimulus, (Carl Zeiss Meditec, Dublin, CA, USA). Humphrey visual field (HVF) analysis was taken at the recruitment period and compared with the baseline HVF during the first presentation. The baseline HVF was retrieved from patient's medical record. Only patients who were able to produce a two consecutive reliable (false negative and false positive less than 33%, fixation loss less than 20%) and reproducible Humphrey visual field analysis (HVF) were recruited.

A questionnaire on dietary recall of the intake of coffee was designed and validated. The questionnaire was piloted on 10 glaucoma patients. A direct face to face interview was conducted by ophthalmologist in training (NAAA and ANFA) and postgraduate student (NAS). Patients who have problem in remembering their coffee intake were excluded. Those who drank coffee daily were categorised as frequent drinker and those who claimed to drink coffee less than 8 times per month were considered as infrequent drinker. Quantification of coffee per day was not included in the questionnaire.

The Hoddap-Parrish-Anderson (H-P-A) criteria were used to evaluate the severity of glaucoma based on mean deviation (MD). A MD value less than -6 dB is categorized as early defect, MD less than -12 dB is moderate and MD more than -12 dB is severe defect [23]. The severity and progression of glaucoma was determined by glaucoma specialists (LS and AY). In this study, progression was defined as the changes of HPA category at the initial diagnosis and at the recruitment process. Changes of more than -4 MD from baseline was considered significant and defined as progression of glaucoma.

Data were analysed using SPSS Version 20. Association between clinical parameters and coffee intake was determined using Fisher's exact test. Multiple logistic regression was applied to determine associated factors of coffee intake with glaucoma progression. Model fitness for final model was checked by using the Hosmer-Lemershaw test. Significance level was set at α=0.05.

3. Result

Mean age of the recruited primary glaucoma patients was 66.4 (SD 10.1) years old with more than two-third were Malays (n=66, 77.5%) with almost equal distribution of male (50.5%) and female (49.5%) patients (Table 1). Based on HPA classification, two-third of glaucoma patients were at moderate to severe stage of the disease. A total of 57 patients showed progression of the disease (progression group) and 34 were categorised as non-progression (non-progression group) after 6.6 (SD 4.4) years of follow up (Table 1).

Table 1. Demographic characteristic coffee study

Variable	n (%)
Sex	
Male	46 (50.5)
Female	45 (49.5)
Race	
Malay	66(72.5)
Chinese	25(27.5)
Age in years	
Mean (SD)	66.4 (10.14)
Diagnosis	
POAG	80 (87.9)
PACG	11 (12.1)
Severity grading at recruitment	
Mild	23 (25.3)
Moderate	29 (31.9)
Severe	39(42.9)
Duration of follow up in years	
Mean (SD)	6.9 (4.4)
Systemic Comorbidity	
Diabetes Mellitus	44 (48.4)
Hypertension	64 (70.3)
Hyperlipidemia	23 (25.3)
Ischaemic heart disease	15(16.5)
Asthma	4 (4.4)
IOP at initial presentation(mmHg)	
Mean (SD)	23.8(9.3)
IOP at recruitment (mmHg)	
Mean (SD)	16.2(2.9)
HVF at initial presentation (mean, SD)	
Mean deviation	-10.12(8.20)
Pattern standard deviation	5.69 (3.66)
HVF at recruitment (mean, SD)	
Mean deviation	-12.60(9.54)
Pattern standard deviation	6.40(3.73)

SD=standard deviation; IOP=intraocular pressure.

Based on the questionnaire, 63 (69%) of our glaucoma patients were coffee drinker. For the purpose of analysis, they were divided according to coffee and non-coffee drinker groups (Table 2). Coffee drinkers were older (Table 2). However, among the younger age group less than 60 years of age, a higher percentage of coffee drinker was observed compare to non coffee drinker (n=19, 79.2% and 5, 20.8%; respectively). Mean IOP at recruitment and at the initial diagnosis was noted to be slight higher in non-coffee drinker group but without statistically significant difference even after controlling for the type of primary glaucoma (p=0.449). As expected mean IOP for PACG patients at initial diagnosis were higher (Mean=29.9, SD 18.3) compared to POAG (Mean=22.9, SD 7.05). However it was not statistically significant (p=0.238). Among the coffee drinkers, majority drank coffee daily (43, 68.3%). Most of them drank coffee 1-2 times per day except for four patients who drank 3-4 times a day. Nearly a quarter drank coffee once per week (14, 22.2%). Only six (9.5%) glaucoma patients claimed drinking coffee infrequently.

Table 2. Clinical parameters and coffee drinker

Variable	Coffee drinker n=63	Non coffee drinker n=28	P value
Age in years			
<60	19 (30.2)	5(17.9)	0.304[a]
60 and above	44 (69.8)	23 (82.1)	
Sex			
Male	36 (57.1)	10(35.7)	
Female	27(42.9)	18(64.3)	0.072[b]
Race			
Malay	45 (71.4)	21(75.0)	0.803[b]
Chinese	18 (28.6)	7 (25.0)	
IOP at initial presentation			
Mean (SD)	22.9 (8.1)	25.7(11.4)	0.186[a]
IOP at recruitment			
Mean (SD)	15.5(3.2)	16.0(2.9)	0.449[a]
HVF at initial presentation(mean,SD)			
Mean deviation			
Pattern standard deviation	-10.13(8.19)	-10.10(8.37)	0.989[a]
HVF at recruitment (mean,SD)			
Mean deviation			
Pattern standard deviation	- 12.51(9.75)	-12.81(9.36)	0.858[a]
Glaucoma severity at recruitment			
Mild	15 (23.8)	8 (28.6)	
Moderate	20 (31.7)	9 (32.1)	0.863[b]
Severe	28 (44.4)	11(39.3)	

SD=standard deviation; IOP=intraocular pressure
[a]Independent t-test, [b]Chi square test.

Table 3. Comparison of clinical presentation between progression and non-progression group

Variable	Non-progression n=34	Progression n=57	p- value
Type of glaucoma			
POAG	32(40.0%)	48(60.0%)	0.200[c]
PACG	2(18.2%)	9(81.8)	
IOP at initial presentation (mmHg)			
Mean(SD)	22.8(8.4)	24.4(9.8)	0.423[a]
IOP at recruitment (mmHg)			
Mean(SD)	15.0(3.4)	16.2(2.9)	0.123[a]
HVF at initial presentation			
MD, Mean (SD)	-7.17(6.55)	-11.84(8.62)	**0.006**[a]
PSD, Mean (SD)	3.98 (2.46)	6.20(3.83)	**0.020**[a]
HVF at recruitment			
MD, Mean (SD)	-6.64(6.82)	-16.10(9.21)	**<0.001**[a]
PSD, Mean (SD)	4.11(2.26)	7.34(3.81)	**<0.001**[a]
Number of topical pressure lowering			
1	14 (46.7)	16 (53.3)	
2	13(34.2)	25(65.8)	0.418[b]
More than 2	7(30.4)	16(69.6)	
Coffee drinkers			
No	13 (46.4)	15(53.6)	0.250[b]
Yes	21(23.5)	42(66.7)	
Frequency of intake	n=21	n=42	
Infrequent	4(66.7)	2(33.3)	**0.002**[b]
Weekly	9(64.3)	5(35.7)	
Daily	8(15.4)	35(84.6)	

[a]Independent t-test, [b] Chi square test, Fisher exact test.

Table 4. Factors associated with glaucoma progression

Variable	Regression coefficient (b)	Adjusted OR (95% CI)	Wald statistic	p-value
Glaucoma severityat recruitment				
Moderate	-0.20	0.82(0.12,5.60)	0.04	0.838
Severe	5.11	165.5(8.00,34.28)	10.92	**0.001**
Duration of follow up (years)	0.47	1.60(1.13,2.26)	7.16	**0.007**
Frequency of coffee intake				
Daily	2.10	8.13(2.45,26.91)	11.76	**0.001**

Backward LR Multiple Logistic Regression was applied.
Multicolinearity and interaction term were checked and not found.
Hosmer-Lemeshow test (p>0.05) was applied to check the model fitness.

More than two-third of coffee drinkers (42, 66.7%) showed evidence of visual field progression (Table 3). There was no significant association between coffee intake and severity of glaucoma (Table 2). There was a significant association between the frequency of coffee intake and glaucoma progression among coffee drinkers (p=0.001). Those drinking coffee daily have 8.1 times (95% CI; 2.5, 9.6) risk of visual field progression in glaucoma patients (Table 4).

4. Discussion

In the current study, slightly more than two-third of our primary glaucoma patients were coffee drinkers. It was found that coffee in general may not increase the risk of susceptible to glaucoma [24,25]. However, there are studies that found the effect of coffee (particularly caffeine) on IOP [22,26,17] and frequent coffee consumption increase risk of developing glaucoma [24]. It was found that caffeine in the coffee caused transient elevation of IOP for nearly 90 minutes [8,17].

Interestingly, higher IOP was found in non-coffee drinker among primary glaucoma patients at initial diagnosis and at the recruitment period in this study. Perhaps, this is due to the smaller number of non-coffee drinker that may cause biasness.

Caffeine is postulated to cause inhibition of phosphodiesterase resulting in high intracellular levels of cyclic adenosine monophosphate (cAMP) of the ciliary body and greater formation of aqueous humor responsible in elevation of IOP [17,27]. In addition, caffeine intake may cause reduction of aqueous outflow by decreasing the tone of smooth muscle and closure of trabecular pores [17,26,28]. Caffeine has been shown to decrease blood flow to macula, optic nerve head and choroid [10]. Avisar et al., (2002) recommended that patients with normotensive glaucoma and ocular hypertension to avoid drinking caffeinated coffee and other beverages contained ≥180 mg of caffeine [26]. Thus, perhaps frequent transient IOP elevation induced by coffee may further compromised glaucomatous optic neuropathy.

Based on multivariate analysis in the current study, daily coffee intake was significantly associated with glaucoma progression. Daily coffee intake increased the risk of glaucoma progression 8.1 folds (95% CI 2.5, 26.9). On contrary, based on both univariate and multivariate analysis, there was no significant association between coffee drinker and glaucoma progression. Most probably, this is due to the rather small sample size that may not be a true reflection of the effect of coffee on progression of glaucoma. In fact the large confident interval of glaucoma progression with daily coffee intake may further demonstrate the effect of small sample size in this study. Nevertheless, this study provides the potential effect of daily coffee intake on glaucoma progression. A future study with bigger number of primary glaucoma patients especially with equal number of progress and non-progress patients is recommended.

Moreover, in this study, the actual amount and concentration of coffee intake was not quantified; e.g. cup, glass or mug. Perhaps, daily drinking of larger volume of caffeinated coffee (e.g. in the mug versus cup) will have more deleterious effect on glaucomatous optic nerve head [24]. Furthermore, caffeine and polyphenolic level in coffee may also influenced by type and variety of coffee bean and preparation of coffee bean; roast or grind [15,25,29,30]. Preparation of the coffee for drinking such as brewing method may also affect the concentration of caffeine and polyphenol content in coffee. Based on a laboratory study, the amount of bioactive constituent was significantly affected by brewing technique in preparation of coffee [30]. To the best of our knowledge, there is no study conducted on the concentration of caffeine in locally roasted coffee. We assumed that most of our patients in this study consumed locally roasted coffee. Although the specific type of coffee was not included in our questionnaire.

In this study, the dietary recall was exclusively on coffee consumption. Other food that contains caffeine such as chocolate, nuts and other caffeinated beverages were not included. Caffeine in these types of food may also cause similar effect as drinking coffee [17]. Furthermore, in this cross sectional study, other lifestyle risk factors such as physical activities were not included. However, glaucoma patients with strong family history of glaucoma, active smokers and poor compliance to medications were already excluded. Unfortunately, passive smokers and ex-smokers were not assessed.

Glaucoma progression in this study was based on the difference of HVF at the recruitment and initial diagnosis using Hodapp, Parrish and Anderson (HPA) criteria. Despite being clinically useful and feasible, there is disadvantage of using HPA criteria as less objective compared the Advanced Glaucoma Intervention Study (AGIS) score [23]. However, AGIS scoring conducted pattern deviation plot that easily affected by media opacities [31,32].

The current study provides initial information on the effect of coffee on glaucoma progression. A larger sample size and more detail questionnaire are needed to further verify the potential effect of coffee on glaucoma progression. Perhaps, avoidance or minimal intake of coffee should be emphasized to glaucoma patients.

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