Original Article

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The Short-term Effects of Coffee and Caffeine on Intraocular Pressure in Healthy Subjects

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Abstract:

Objective: Coffee consumption is a prevalent habit with potential implications for ocular health. This study investigated the short-term effect of caffeine in coffee beverages on healthy subjects' intraocular pressure (IOP).

Material and Methods: Thirty subjects (10 males, 23.40±1.33 years) attended three visits at similar times. During each visit, subjects were asked to ingest either 250 ml of water, 250 ml of caffeinated coffee, or 250 ml of decaffeinated coffee within five minutes. The initial drink set was randomised. IOP was measured before ingestion (baseline) and at 0-, 5-, 10-, 15-, 20-, 30, 45-, and 60 minutes after each beverage consumption. Repeated measures of ANOVA and pairwise analysis were utilised to analyse the IOP difference within and between groups.

Results: Baseline IOP across beverage groups were not significantly different (p-value>0.05). Water and caffeinated coffee groups showed a significant increase in IOP over time (p-value<0.0005), whereas decaffeinated coffee did not (p-value=0.437). The highest IOP values recorded were 16.09±2.41 mmHg for water and 15.22±2.26 mmHg for caffeinated coffee, 10 minutes and 15 minutes post-consumption, respectively. IOP spiked until minute 45 for the caffeinated coffee

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group but only until minute 20 for the water group. IOP in the water and caffeinated coffee groups returned to baseline levels by minute 30 and 60, respectively.

Conclusion: Caffeinated coffee has a prolonged effect on increasing IOP compared to water. Additionally, low doses of caffeine, such as those found in decaffeinated coffee, may protect against IOP spikes. Further study is needed to investigate the long-term effect of coffee and caffeine consumption on ocular health.

Keywords: caffeine, decaffeinated coffee, Intraocular pressure, water

Introduction

Coffee is widely consumed globally, and the potential effects of caffeine in coffee on various aspects of health have been a subject of ongoing research and discussion[1,2]. One particular area of interest is the impact of caffeine consumption on intraocular pressure (IOP), which is a critical factor in the development and progression of various eye conditions, including glaucoma[3]. The regulation of IOP is complex and influenced by various physiological and environmental factors such as diurnal variation, age, gender, race, hormonal changes, and drug and dietary factors[4,5]. Caffeine consumption through beverages such as coffee, tea, and soft drinks is a dietary factor influencing IOP[6–9].

Caffeine, a well-known central nervous system stimulant, has a complex and diverse association with eye health[10–12]. The relationship between caffeine and IOP is not straightforward, as past research has shown mixed results. Some studies have suggested that caffeine can lead to a transient increase in IOP, while others have found no significant impact[3,9,11,13–16]. This discrepancy in findings may be attributed to factors such as individual variation in caffeine sensitivity, baseline ocular health, and the specific form of caffeine consumption. A comprehensive systematic review and meta-analysis by Li and colleagues[14] concluded that while caffeine does not affect IOP in normotensive individuals, it can significantly elevate IOP in patients with glaucoma or ocular hypertension. This intricate relationship underscores the importance of considering baseline ocular health when examining the effects of caffeine on IOP.

Caffeine has varying effects on IOP, which are contingent on each individual's habits. Vera and associates[16] found that caffeine's effect on IOP is subject to tolerance, with low-caffeine consumers experiencing a more pronounced increase in IOP than high-caffeine consumers. This tolerance effect suggests that habitual caffeine intake may modulate the body's response to acute caffeine consumption, influencing its clinical relevance. In addition to caffeine's effect, coffee's overall composition may also play a role in its influence on IOP. Coffee contains various bioactive compounds, such as chlorogenic acids and trigonelline, which may have distinct physiological effects[17–19]. Some studies have reported that decaffeinated coffee, which still contains these non-caffeine compounds, may not have the same hypertensive effect on IOP as caffeinated coffee[8,9,13,20]. This suggests that the non-caffeine components of coffee may mitigate or counteract the IOP-elevating effect of caffeine.

Moreover, the specific form of caffeine consumption, such as caffeinated coffee, has also been scrutinised. Okimi and colleagues[13] demonstrated that caffeinated coffee significantly increases IOP in non-glaucomatous subjects, with elevated pressure maintained for up to three hours. However, Higginbotham and colleagues[15] reported that regular coffee drinking might only slightly elevate IOP in glaucoma patients, an effect deemed clinically insignificant. This disparity underscores the need to explore further the short-term and long-term effects of different caffeine sources on ocular pressure. The potential cumulative

effects and individual variations further complicate the interplay between caffeine consumption and IOP. Studies such as those by Chandrasekaran et al.[21] and Ajayi et al.[22] indicate a potential association between regular coffee consumption and elevated IOP in individuals with open-angle glaucoma, suggesting that habitual intake might influence disease progression. Conversely, research by Chandra and associates[9] implies that caffeine alone may not significantly impact IOP in glaucoma patients, pointing to other components in coffee that could be responsible for the observed effects.

The short-term effects of caffeine on ocular parameters extend beyond IOP. Jiwani and associates[11] found that a single cup of caffeinated coffee could increase IOP and ocular perfusion pressure, though the clinical significance of these changes remains debatable. Additionally, recent findings by Dervişoğulları and colleagues[23] indicated that caffeine intake can significantly decrease choroidal thickness but does not notably affect IOP or ocular pulse amplitude.

The correlation between caffeine intake and IOP is complex and impacted by various elements, such as personal tolerance, consumption habits, and preexisting ocular health conditions. The effect of caffeine on the IOP is unclear, considering the mixed results in the literature. Against this backdrop, the present study investigated the short-term effect of caffeinated coffee and decaffeinated coffee on IOP in healthy individuals.

Material and Methods

This study abides by the Declaration of Helsinki, and the ethical clearance was obtained from the Kulliyyah of Allied Health Sciences Postgraduate and Research Committee (ID No: IIUM/ 310/G/13/4/4-199- KAHS 09). Written consent was obtained from all participants.

Caffeine Concentration Measurement and Coffee Brew Preparation.

The UV/Vis-spectrophotometer was conducted to measure the amount of caffeine in samples of coffee. Three coffee samples were tested, i.e., (i) Sumatra ground coffee (Starbucks, Malaysia), (ii) Espresso ground coffee (Starbucks, Malaysia), and (iii) decaffeinated coffee (Nescafe, Nestle Malaysia). Samples with the highest and lowest caffeine were assigned for the caffeinated and decaffeinated groups, respectively.

In preparing all coffee solutions, 1 g of ground coffee from each coffee sample was weighed using an electronic balance and dissolved in 100 mL of water. The coffee solutions were stirred for 30 minutes using a magnetic stirrer to dissolve the ground coffee. Impurities were filtered, and extraction was used for caffeine measurement.

The extraction of caffeine from the coffee solution was conducted using the liquid-liquid extraction (LLE) method with dichloromethane (Sigma-Aldrich, Germany) as the solvent[24]. It was reported that the efficiency of dichloromethane as the solvent to extract caffeine from coffee beans was 98-99%[25]. The prepared coffee solution was mixed with 25 mL dichloromethane at a 1:1 (v/v) ratio and shaken for several minutes. After resting, the colourless caffeine extract was isolated for caffeine level analysis. Four sets of caffeine extraction were prepared for each coffee sample, and the caffeine level measurements were repeated three times. The concentration of the caffeine in the extraction was obtained by measuring the absorbance of the solution using a UV-Vis spectrophotometer at 272 nm wavelength.

The caffeine level analysis yielded that the Sumatra coffee solution contained 9.138 mg of caffeine, while the Espresso coffee solution contained 5.693 mg of caffeine. Meanwhile, the decaffeinated coffee solution contained 0.888 mg of caffeine. Considering the caffeine levels, the Sumatra ground and decaffeinated coffee were chosen for use in the current study.

In preparing coffee beverages for the subjects, 15 g of ground coffee was dissolved in 250 ml boiling water. The mixture was then stirred for a minute and left to cool for 10 minutes before being given to the subjects. The brewed coffees, by calculation, contained 137.0 mg and 13.3 mg of caffeine in each serving of caffeinated and decaffeinated coffee, respectively. Subjects needed to finish drinking each beverage in less than five minutes before proceeding to IOP measurements. The initial drink set was randomised.

Subjects

A total of 35 healthy subjects were recruited, but five subjects dropped out due to commitment issues. Thirty subjects (10 males, 23.40±1.33-year-old) committed to three visits and completed three experiment conditions, i.e., ingestion of (i) 250 mL water, (ii) 250 mL caffeinated coffee, and (iii) 250 mL decaffeinated coffee. The subjects' inclusion criteria included healthy individuals of emmetropic/low myopic. The strict refractive state aimed to prevent bias of refractive error on IOP[26,27]. Exclusion criteria include being a smoker, having a history of ocular surgery, having active ocular diseases, or taking medication that may affect IOP. Subjects were ensured to cease contact lens wear for at least one week and to abstain from caffeine intake for 10 hours before any visit. No food and water intake were allowed two hours before any visit.

IOP measurement

The study eye was chosen randomly between right and left eyes, and the chosen eye was measured throughout all visits. The Goldmann applanation tonometer (GAT) (Keeler, United Kingdom) was used to measure IOP in conjunction with the GAT protocol[28]. Measurements were taken between 8 am to 12 pm or 2 pm to 5 pm. All visits were attended at similar timings to eliminate diurnal variation bias on IOP[29]. IOP readings were taken before drinking (baseline) and after drinking at minutes -0, -5, -10, -15, -20, -30, -45, and -60.

Statistical analysis

Data were analysed using IBM Statistical Package for Social Sciences (SPSS) version 29.0. The Shapiro-Wilk test confirmed that all data were normally distributed. Repeated measures analysis of variance (RM ANOVA) was used to compare IOPs between beverage groups and between nine time points within each beverage group. The Tukey post hoc test was performed to investigate the significant pairs between beverage groups, and the Bonferroni post hoc test was performed to investigate the significant pairs within time points of each beverage group. Significance was taken at p-value≤0.05, and for the pairwise comparison, a significance level of p-value<0.05 was also applied as the adjustments have been applied automatically via SPSS.

Results

The baseline IOP across beverage groups was not significantly different (p-value=0.426). Ingestion of 250 ml of water and 250 ml of caffeinated coffee causes a significant increase of the IOP over one hour (p-value<0.0005). Interestingly, ingesting 250 mL of decaffeinated coffee causes no change to the IOP over one hour (p-value=0.437). The IOP spiked to a maximum of 16.09±2.41 mmHg from 13.98±1.87 mmHg at minute-10 post ingestion upon 250 ml water ingestion (Bonferroni p-value=0.001). Caffeinated coffee causes IOP increment, which maximised 15.22±2.26 mmHg (13.30±2.31 mmHg) later at minute-15 post-ingestion (Bonferroni p-value=0.008).

Ingestion of both water and caffeinated coffee caused an IOP increment. Nevertheless, the increasing trend in the caffeinated coffee group occurred later than ingesting water, beginning only at minute-5 and remaining until minute-45. Relative to the baseline, the IOP spiked immediately after ingestion and retained its effect until minute-20 in the water group (Table 1).

The effects on IOP between water and caffeinated coffee, and between caffeinated coffee and decaffeinated coffee were not statistically significant (Bonferroni >0.05).

Nevertheless, water's IOP-increasing effect was significantly higher than the decaffeinated coffee ingestion at minute-0, -5, -10, -15, -20, and -30 (Tukey p-value<0.05) (Table 1).

Discussion

Our study aimed to investigate the short-term effects of coffee and caffeine consumption on IOP in healthy subjects. The collected data indicate that ingesting 250ml of caffeinated coffee and 250ml of water significantly increases IOP. In contrast, the same volume of decaffeinated coffee does not produce a significant change. Interestingly, the elevation in IOP following caffeinated coffee consumption is more prolonged than water ingestion, and decaffeinated coffee appears to have no effect on IOP elevation.

These findings are consistent with the literature on the effects of caffeine and coffee on IOP. Specifically, Okimi and associates (1991) demonstrated that caffeinated coffee significantly increases IOP in non-glaucomatous subjects, with elevated pressure maintained for three hours[13]. Their finding aligns with our observation of prolonged IOP elevation after caffeinated coffee consumption. Similarly, Avisar and colleagues (2002) reported that drinking regular coffee may increase IOP in patients with normotensive glaucoma or ocular hypertension, further supporting the potential of caffeine to influence IOP levels[8]. Our observation also supports Tran and colleagues (2014), who noted a higher IOP increase in caffeine tests compared to water-drinking tests in glaucoma patients[30].

Table 1 The mean and standard deviation for the IOP values of 30 subjects at different time points for three types of beverage ingestion. RM ANOVA 1 compares IOP across beverage groups, while RM ANOVA 2 compares IOP between the time points within each beverage group. The italic-bolded IOP values in water and caffeinated coffee groups indicate pairwise significant differences to their baseline values, measured by the Bonferroni post hoc test

Time points	IOP (mmHg)			RM ANOVA 1
	Water	Caffeinated coffee	Decaffeinated coffee	
Baseline	13.98±1.87	13.30±2.31	13.33±2.39	F (2, 87)=0.861 p-value=0.426
0 min post-ingestion	15.37±2.54	13.89±2.36	13.71±2.57	F (2, 87)=4.097 p-value=0.020*
5 min post-ingestion	15.62±2.46	14.39±2.37	13.88±2.57	F (2, 87)=3.884 p-value=0.024*
10 min post-ingestion	16.09±2.41	14.69±2.42	13.87±2.48	F (2, 87)=6.227 p-value=0.003*
15 min post-ingestion	15.81±2.35	15.22±2.26	13.84±2.56	F (2, 87)=5.524 p-value=0.006*
20 min post-ingestion	15.58±2.41	15.21±2.52	13.68±2.48	F (2, 87) = 5.084 p-value=0.008*
30 min post-ingestion	15.18±2.27	14.81±2.26	13.58±2.51	F (2, 87) = 3.818 p-value=0.026*
45 min post-ingestion	14.23±2.27	14.55±2.19	13.70±2.51	F (2, 87)=1.050 p-value=0.354
60 min post-ingestion	13.96±2.32	14.08±2.11	13.82±2.71	F (2, 87)=0.075 p-value=0.928
RM ANOVA 2	F (3.979, 115.382)=11.052, p-value<0.0005	F (4.206, 121.979)=10.614, p-value<0.0005	F (3.177,92.128)=0.925, p-value=0.437	

The asterisks (*) note significant differences in the IOPs between the beverage groups (RM ANOVA 1). The Tukey post hoc test revealed pairwise significance between the water group and decaffeinated coffee group (p-value<0.05) on each significant time point
IOP= intraocular pressure

On the other hand, our results contrast with those of Chandra and colleagues (2011), who found no significant effect of caffeine on IOP in patients with primary open-angle glaucoma[9]. This discrepancy may be attributed to differences in the study population and experimental conditions. Our study focused on healthy subjects, while Chandra et al. examined individuals with glaucoma, suggesting that the effects of caffeine on IOP may vary based on underlying ocular conditions.

No effect of decaffeinated coffee towards IOP elevation was observed in our study, which warrants further investigation. While the exact mechanisms remain unclear, it is possible that other constituents in decaffeinated coffee may counteract the IOP-raising effects of caffeine. This hypothesis is partially supported by the findings of Chandra and associates[9], who suggested that other components in coffee, rather than caffeine alone, may be responsible for the observed effects on IOP. Similarly, Ilechie and Tetteh[31] found an inverse association between caffeine and IOP, which they deduced due to the interaction between caffeine and taurine inside their tested energy drink. They reported a significant reduction in IOP after ingestion of energy drinks. On the other hand, Madeira and associates[32] demonstrated caffeine's neuroprotective effects in reducing retinal ganglion cell loss in an animal model of glaucoma. These findings underscore the complexity of coffee's impact on ocular physiology and suggest the potential benefits of decaffeinated variants in managing IOP.

The presence of other substances in beverages that regulate the activities of caffeine could stimulate future studies. Numerous bioactive substances found in coffee, including trigonelline and chlorogenic acids, may have different physiological effects[17–19]. According to some research, decaffeinated coffee might not have the same hypertensive effect on IOP as caffeinated coffee, even if it still includes these non-caffeine chemicals[8,9,13,20]. This shows that coffee's non-caffeine ingredients may lessen or even reverse the effect of caffeine's elevation in IOP.

Additionally, our study found that ingesting 250ml water also resulted in a more significant increase in IOP, although to a shorter duration than caffeinated coffee. This observation aligns with Tran and colleagues[30] findings, who reported a higher increase in IOP in a caffeine test compared to a water-drinking test in patients with glaucoma. The prolonged elevation of IOP after caffeinated coffee consumption observed in our study is consistent with several previous reports. Ajayi and Ukwade[22] highlighted the impact of caffeine on increasing IOP in Nigerians, emphasising the need for glaucoma screenings. Similarly, Jiwani and associates[11] noted a significant increase in IOP and ocular perfusion pressure after consuming caffeinated coffee, although the clinical significance of these changes remains debatable. The tolerance effect discussed by Vera and colleagues[16] could also play a role in habitual caffeine consumers exhibiting a blunted IOP response compared to non-habitual consumers. This suggests that while caffeine and water can elevate IOP, the mechanisms and magnitude of their effects differ.

The mechanisms of the effects exerted by caffeine on IOP are unclear, but it has been postulated that caffeine can cause elevation by increasing the aqueous formation or inhibiting drainage[11,21-22,33]. Some have postulated that caffeine, being a phosphodiesterase inhibitor, may increase cyclic adenosine monophosphate (cAMP) activities that stimulate the production of aqueous by the ciliary body[22]. Reverberating on the increased IOP by caffeine, increased inhibition of aqueous drainage was postulated as a causal factor that may be due to the closure of trabecular pores and decreased tone of the ciliary body's smooth muscle[22,33]. The increment of IOP due to water ingestion was suggested due to expansions of choroidal volume[34], elevation of episcleral venous pressure, or reduction of aqueous outflow[35].

Several studies have explored caffeine's broader ocular effects, supporting our observations. For instance, Chandrasekaran et al.[21] and Hecht et al.[20] noted that regular coffee consumption is associated with elevated IOP and

potential glaucoma progression. Chandrasekaran et al. found that individuals who consume coffee regularly and have higher caffeine intake are more likely to experience elevated IOP, particularly in those with open-angle glaucoma. Hecht and associates further emphasised that coffee and tea consumption can raise IOP, which could influence the course of glaucoma by increasing retinal vascular resistance and decreasing choroidal thickness. These findings underscore the potential risk of regular caffeine consumption for individuals predisposed to glaucoma.

Conversely, the meta-analysis by Li and colleagues[14] found that caffeine does not significantly affect IOP in normal individuals but does increase it in those with glaucoma or ocular hypertension. Analyzing data from multiple studies showed that IOP response to caffeine depends on the individual's eye condition. In people without preexisting ocular hypertension or glaucoma, caffeine did not significantly change IOP levels. However, in those with glaucoma or ocular hypertension, caffeine consumption led to a noticeable increase in IOP. This suggests that individuals with these conditions should be more cautious with their caffeine intake to avoid worsening their condition. These studies collectively suggest that while caffeine may not pose a significant risk to IOP in the general population, it can have adverse effects on those with specific ocular conditions such as glaucoma or ocular hypertension. This differentiation is crucial for tailoring dietary recommendations and managing glaucoma risk, emphasising the importance of individualised advice based on a person's ocular health status.

Limitations of study

While our study provides valuable insights into the short-term effects of coffee and caffeine on IOP in healthy subjects, it is not without limitations. The sample size of our study was relatively small, which may limit the generalizability of the findings. A larger sample size could provide more robust and reliable results. Our study focused on the short-term effects of coffee and caffeine intake. Long-term effects and potential cumulative impacts on IOP were not assessed. This limits our understanding of how chronic coffee consumption might influence ocular health. The study was conducted on healthy subjects, which may not represent individuals with preexisting ocular conditions such as glaucoma or ocular hypertension. The findings may not be directly applicable to these populations. Individual differences in caffeine metabolism were not accounted for in this study. Genetic variations and habitual caffeine consumption can influence how caffeine affects IOP, leading to response variability.

Given our study's limitations, including its small sample size and short-term focus, future research should explore coffee and caffeine's long-term effects on IOP, consider genetic and metabolic differences among individuals, and conduct studies in real-world settings to better understand the practical implications of these findings. By addressing these areas, future research can contribute to more comprehensive dietary guidelines and potentially identify novel therapeutic strategies for managing IOP and preventing glaucoma progression.

Conclusion

In conclusion, our study demonstrates that ingesting caffeinated coffee and water leads to a significant short-term increase in IOP in healthy subjects. In contrast, decaffeinated coffee shows no significant change and appears to have a protective effect against IOP elevation. These findings underscore the complex impact of different coffee types on ocular health, highlighting the need for careful consideration of caffeine intake, especially for individuals at risk of developing ocular hypertension or glaucoma.

Caffeine's prolonged effect on elevating IOP raises concerns about the habitual consumption of caffeinated beverages. The protective effect observed with decaffeinated coffee points to the possibility that components other than caffeine may play a role in regulating IOP, meriting further investigation.

In light of our findings, healthcare providers should advise patients, particularly those with glaucoma or ocular hypertension, to monitor their caffeine intake and consider the potential benefits of switching to decaffeinated coffee. This personalised approach to dietary recommendations can help mitigate the risk of elevated IOP and promote better ocular health outcomes.

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