Caffeine is a popular psychostimulant that acts as an adenosine receptor antagonist at physiological concentrations. It is the most widely consumed xanthine in the world, consumed daily by more than 70% of New Zealanders in the form of coffee, tea, chocolate and caffeinated soft drinks. It has been reported that adults aged between 20 and 64 years are exposed to an average of 3.5 mg of caffeine/kg body weight/day.14,15

Historical studies suggest some ophthalmologists have long expressed concerns about the affect of caffeine on intraocular pressure (IOP). Although glaucoma patients have been identified as the only treatable risk factor in primary open angle glaucoma (POAG), the most common type of glaucoma. Thus, establishing the link between caffeine and IOP is of great importance for improving the management of POAG.

Effect of caffeine on IOP

A number of clinical trials have investigated the immediate effect of caffeine on IOP. The effect of caffeine has been regarded as controversial due to inconsistencies amongst study findings. These inconsistencies can be attributed to variable study protocols, such as sources and doses of caffeine, methods of tonometry and time of IOP measurement. Additionally, participant characteristics and severity of glaucoma were often not documented in some studies. Nonetheless, a careful review of the literature reveals a common trend. In young and healthy volunteers without history of ocular diseases, no significant changes in IOP were detected up to four hours following ingestion of caffeine at doses up to 400 mg.16

One study however, demonstrated a post-coffee increase in IOP of 2-3 mmHg in healthy volunteers aged between 20 and 29 and this increase was maintained for three hours.17 However, the volunteers drank a litre of coffee in this study and the authors did not delineate the effects of volume overload and high dose caffeine.

Several randomised controlled trials and subsequent meta-analyses of those studies reported IOP changes in patients with glaucoma or ocular hypertension following caffeine ingestion. There was a statistically significant increase in IOP when the patients were exposed to 180 mg of caffeine in coffee, equivalent to approximately one double shot espresso18 (see Table 1). The meta-analysis showed the weighted mean IOP difference between patients and controls was 1.19 mmHg in patients with glaucoma or ocular hypertension: 0.347 at 20 and 29 and this increase was maintained for three hours.19 In young and healthy volunteers, 200mg of oral caffeine led to significant retinal vasoconstriction one hour post ingestion20. This was negatively correlated with mean arterial pressure, suggesting an auto-regulatory response to increased blood pressure. Another study demonstrated that ingestion of 300 mg of caffeine caused an increase in the resistive index of retrobulbar arteries in young and healthy volunteers.21 Hypothetically, the increase in systemic blood pressure will increase pressure within the ciliary arteries, which in turn will increase ultrafiltration and aqueous production, thereby elevating IOP. Increased arterial pressure can also increase venous pressure and reduce aqueous clearance, thereby contributing to elevated IOP. Caffeine-induced vasoconstriction was however not associated with high IOP in the young and healthy, suggesting the presence of an unknown homeostatic mechanism to maintain the IOP.

Consequently, more questions arise as to why caffeine elevates IOP in only glaucoma patients. Several researchers postulate there may be an inherent susceptibility to the effect of caffeine in glaucomatous eyes. There is mounting evidence that vascular and autonomic dysfunction is a key pathological process in glaucoma (for a comprehensive review, see reference 14). Doppler ultrasound imaging studies demonstrated that POAG patients failed to auto-regulate central retinal artery blood flow during postural change. Gene expression studies identified impairment of nitric oxide-mediated smooth muscle cell relaxation and excessive plasma levels of endothelin, a potent vasoconstrictor, in response to physiological perturbations in POAG patients. Polymorphisms of nitric oxide synthase and caveolin, which lead to impaired vasodilatation, have been associated with POAG. Genetic dysautonomic conditions such as familial dysautonomia and nail-patella syndrome are associated with subtypes of POAG. Moreover, examination of the nail bed capillary network revealed abnormal peripheral microvascular circulation in glaucoma patients. It is possible that caffeine produces a pathologic haemodynamic response and consequent IOP change in glaucoma patients with structurally and functionally impaired microvascularity.

The debate continues...

Based on the evidence accumulated to date, glaucoma patients may be advised to avoid caffeine intake for 90 minutes before IOP measurement, in order to obtain a more accurate reading of IOP. There is however, no known clinical benefit of avoiding caffeine in the long-term management of POAG and without clear evidence we might want to cause unnecessary anxiety associated with caffeine consumption. A few crucial questions remain to be answered before clinicians can make evidence-based recommendations on caffeine consumption.

- If caffeine transiently elevates IOP does frequent coffee drinking lead to sustained elevation in IOP? What is the effect of repetitive caffeine intake?
- Vasoconstriction was observed in healthy eyes following caffeine administration, but the mechanism of response to caffeine is yet to be explored in glaucoma patients.
- The link between chronic caffeine exposure and severity of glaucoma has been established. Is chronic caffeine exposure associated with more advanced POAG? Does caffeine consumption provide any benefit in terms of progression?
- These questions need to be addressed in large scale studies, which establish evidence and recommendations. In the meantime, it would be reasonable to advise patients to avoid excessive caffeine intake in the first instance, even a small reduction in IOP has been shown to reduce the risk of glaucoma progression.

References


About the authors

Dr Jinny Yoon is a neuro-ophthalmology research fellow at the University of Auckland and graduated with a PhD after completing basic medical training in Auckland. She followed her passion for eye health and joined the Department of Ophthalmology.

Professor Helen Danesh-Meyer is an international authority on neuro-ophthalmology and chair of the Department of Ophthalmology. She was one of the first authors of this journal article and is a renowned international journal editor.

Table 1. Average IOP before and after caffeine ingestion in patients with normo-tension glaucoma and ocular hypertension

<table>
<thead>
<tr>
<th>Normo-tension glaucoma</th>
<th>Baseline IOP (mmHg)</th>
<th>IOP difference 30 min after caffeine</th>
<th>IOP difference 60 min after caffeine</th>
<th>IOP difference 90 min after caffeine</th>
</tr>
</thead>
<tbody>
<tr>
<td>IOP difference 30 min after caffeine</td>
<td>14 ± 2.6</td>
<td>0.9 ± 0.5</td>
<td>3.6 ± 1.1</td>
<td>2.3 ± 0.6</td>
</tr>
<tr>
<td>IOP difference 60 min after caffeine</td>
<td>22.7 ± 1.5</td>
<td>1.1 ± 0.7</td>
<td>3.4 ± 1.0</td>
<td>3.0 ± 2.7</td>
</tr>
</tbody>
</table>

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Professor Helen Danesh-Meyer

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BY DR JINNY YOON AND PROFESSOR HELEN DANESHMeyer

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