Abstract

Cataracts are a significant and common cause of reversible blindness, for which definitive management is by surgical removal. However, a lack of ophthalmologists and funding means many do not have access to such procedures worldwide. Therefore a less invasive and cheaper alternative is desirable. This paper aims to provide a brief overview of the physiology and risk factors of cataract formation, as well as discussing current evidence regarding prevention and management of cataracts non-surgically. This review finds there are numerous promising prevention strategies to reduce the likelihood of a cataract developing. These include aldose reductase inhibitors, non-steroidal anti-inflammatory drugs (NSAIDs), and vitamin supplementation. However, further large-scale human trials are required for definitive medical prevention strategies. There is also almost no data on alternative management of established cataract as opposed to prevention of cataract development. This identifies a key gap in the literature requiring further investigation.

Review

Cataracts continue to be a significant cause of blindness worldwide, despite technological advancements. The gold standard treatment for hundreds of years has been surgical removal of the opacified lens. Modern cataract surgery is not without its costs and risks. Complications occur in 1–5% of patients and the worldwide burden of cataract surgery is upwards of several billion dollars per year. There is also a 10–20% chance of posterior capsule opacification with each cataract operation, although this is easily fixed. In addition, the demand for surgery far exceeds supply, particularly in developing countries, with the associated issue of inequitable access. Cataract surgery can also present significant challenges in certain circumstances, such as patients with additional ocular pathology, small pupils, unstable lenses, or diabetic retinopathy. A cheaper, non-invasive, and accessible alternative to surgery would be welcome.

There is extensive literature regarding strategies for medical prevention of cataracts, but almost no research has been conducted on the medical treatment of an established cataract. Do any of these hypotheses actually reduce the risk of cataract prevention, and will there ever be a viable medical alternative to cataract surgery?

A cataract is an opacification of the lens, the aetiology of which is complex and multifactorial. Patients typically present with blurred vision and glare (reduced vision in the presence of oncoming light). Cataracts can broadly be classified based on cause: age-related, paediatric, or secondary. Age-related cataracts are the most common, and can be categorised as nuclear, cortical, and posterior subcapsular based on the location of opacification within the lens. Risk factors for cataracts include age, female sex, Asian ethnicity, certain genetic patterns, low education level, and myopia. Systemic illnesses such as diabetes mellitus and hypertension also contribute. Environmental factors such as lifetime exposure to ultra violet (UV) light and other sources of oxidative stress also contribute to gradual damage to lens proteins. There is an increased incidence of cataracts in countries with higher UV exposure. It is also thought that the lens contains a substantial amount of protective antioxidants which are degenerated by time and smoking. Almost any ocular pathology such as trauma, inflammation, glaucoma, vitrectomy, or any other intraocular surgery contribute to cataract formation, as well as corticosteroid exposure which is the treatment for many conditions. Therefore, there are a multitude of potential targets for cataract intervention.

Diabetic cataracts are thought to be a result of increased glucose causing overflow from the glycolysis pathway into alternative metabolic pathways. When glycolysis is overloaded in hyperglycaemia, the nicotinamide adenine dinucleotide phosphate (NAPDH)-dependent aldose reductase enzyme is activated, producing sorbitol. Sorbitol increases osmotic pressure and draws water into the lens, and these fluid shifts cause refractive changes and opacification. Sorbitol is also converted to fructose via this pathway resulting in ongoing hyperglycaemia and oxidative stress. Hence one of the oldest proposed medical methods for inhibiting cataracts is the use of aldose reductase inhibitors. One such drug, sorbinil, showed promising effects in both preventing and slowing the development of cataracts in diabetic rats. A recent trial demonstrated the use of Vitamin K1 as an aldose reductase inhibitor and was shown to significantly reduce sorbitol and drop blood glucose levels by 65% at 90 days. However, despite encouraging results in rats and clinical trials in humans several decades ago, aldose reductase inhibitors are still not found in clinical practice. There is one new aldose reductase inhibitor called Epalrestat which is commercially available in Japan, but apart from this, they are virtually non-existent in clinical ophthalmology. There have been no human clinical trials investigating aldose reductase inhibitors in cataract development published within the last five years. It is unclear why this is, but for now it remains a possible avenue to be further investigated.

Another potential medical solution to cataract formation is the use of antioxidants and vitamins to reduce the impact of oxidative stress and UV damage to the lens. It was found that pyruvate and ascorbate significantly prevented photosensitive damage in the eyes of rats and mice. Caffeine was also found to be efficacious in inhibiting cataracts induced by galactose in rat and mice lens organ cultures. Caffeine is believed to prevent oxidative stress in the tissue. In a major prospective cohort, multivitamins such as CentrumTM were associated with reduced incidence of nuclear cataracts. Other vitamins also seemed promising, but a large meta-analysis involving 117,272 patients found no difference in incidence or progression of cataract with supplemental beta-carotene, Vitamin C, or Vitamin E. It is suggested that different areas of the lens have individual metabolic pathways for antioxidants and thus the...
issue is not the antioxidants themselves but the uptake into the lens structure. A randomised placebo-controlled trial would be required to demonstrate any preventive benefit, but would be expensive and prolonged and may not reveal a strong effect. Vitamin and caffeine supplements are cheap and readily accessible, and thus could be widely implemented in lower socioeconomic areas.

There has also been significant debate over the role of aspirin and other non-steroidal anti-inflammatories (NSAIDs) in cataract formation. An early case control study showed a strongly protective effect, with up to a 50% reduction in cataract development with these analgesics in human participants. However, a large cohort study and a cross-sectional study showed no association or even an increased risk of cataract surgery with NSAID use. A challenge to testing this idea is that cataract is a gradual pathology and so trials would be expensive and prolonged. The majority of data comes from cross sectional population based studies or cohort studies. Hence, it is challenging to be certain around the outcomes of NSAIDs in cataract prophylaxis.

Reduction in modifiable risk factors is the most substantiated method of preventing cataracts to date. Quitting or reducing smoking has a close-response relationship in terms of cortical cataract risk, with a hazard ratio of 1.4 in the smokers compared with non-smokers. Exposure to UV can also be vastly reduced by sun protection and wearing sunglasses outdoors, but sun protection behaviour across a lifetime is difficult to measure, and has not been shown to affect cataract incidence. Maintaining good glycaemic control is imperative to protect against cataract development in diabetics. Reducing alcohol intake would likely be preventative, as would eating a diet rich in fruits and vegetables.

The author could find no clinical studies testing whether a cataract could be reversed or treated with medication. One barrier to testing these medications might be that participants would be required to delay cataract surgery while trying the medication, and long periods of treatment may be required.

As cataracts remain a prevalent and pressing cause of vision loss, and surgical access remains inadequate in many areas, there would seem to be a need for medical treatment. Barriers to testing potentially promising strategies, such as aldose reductase inhibitors, certain vitamins, and NSAIDs, are that controlled trials are long and expensive for a gradual disease process. Few companies are motivated to invest in these trials when the medications are cheap and not patent protected. Currently, the only preventive treatment for cataracts is reducing modifiable risk factors. Therefore, with our current knowledge, the best way to prevent cataracts is the best way to prevent every other pathology: a healthy lifestyle.

References


About the author

Natalie Allen is a final-year medical student at the University of Auckland with a keen interest in ophthalmology.

Correspondence
Natalie Allen: nall562@aucklanduni.ac.nz