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The impact of eating disorders on glaucoma

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Abstract

Review of current knowledge on the impact of selected food products on the risk of glaucoma. Materials and Methods: Review and summary of research studies available in open-source format on Google Scholar, PubMed.
Conclusions: There is ample evidence confirming the impact of food products on the risk of developing glaucoma or exacerbating its symptoms. However, further research is necessary to determine the extent of their interference with this disease entity.

Keywords: glaucoma, nicotinamide adenine dinucleotide, lactic acid, caffeine, polyphenols, catechin, ketogenic diet, alcohol, Mediterranean diet, antioxidants.

Introduction and Purpose of the Study

Glaucoma is a group of progressive neuropathies of the optic nerve leading to the destruction of retinal ganglion cells and their axons. It is the leading cause of irreversible blindness worldwide, affecting over 70 million people residing in various geographical regions. This disease ranks second among the causes of blindness in patients. Up to 40% of them lose their vision within the first year of diagnosis.(1) The most common type of glaucoma affecting ophthalmic patients is open-angle glaucoma, in which the iridocorneal angle is not pathologically altered, but there is an elevation of intraocular pressure due to abnormal fluid flow within the eye. The main cause of this disease is obstruction of aqueous humor outflow from the eye and its excessive production. Although the exact mechanism of glaucoma is not fully understood yet, several risk factors have been identified, including high intraocular pressure (IOP), age, and genetics.

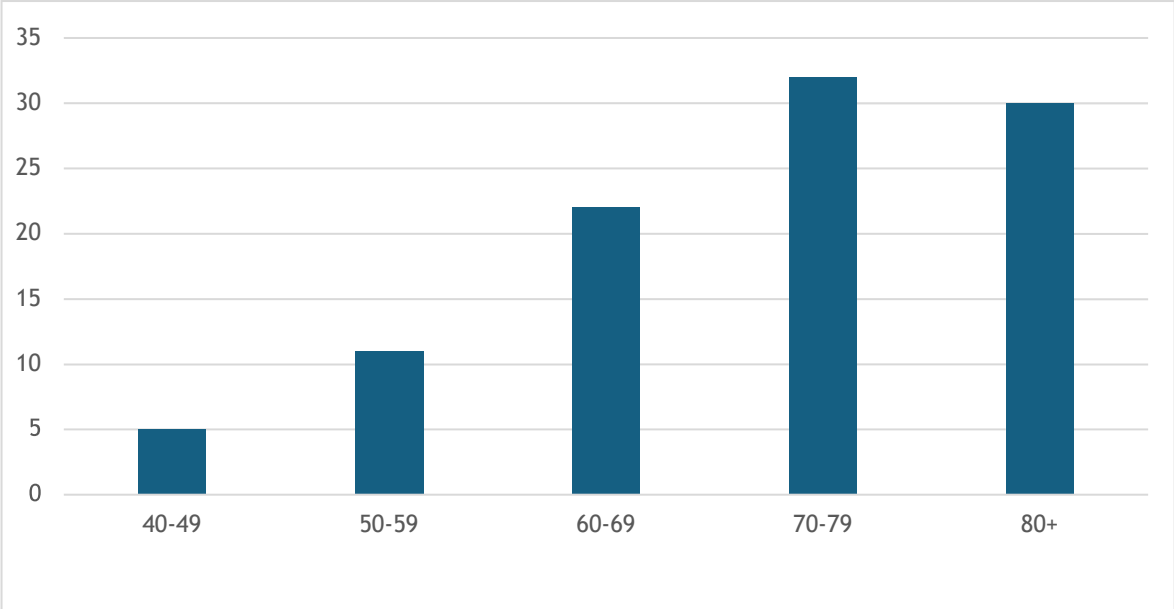

Chart 1. Percentage distribution of open-angle glaucoma patients in different age groups in 2050.(2)

Introduction and Objective:
Recent evidence suggests that diet may play a significant role in the development and management of glaucoma. As this phenomenon has been studied, two main mechanisms have emerged - the influence of specific diets on lowering intraocular pressure and their neuroprotective properties. The diagnosis of this disease primarily consists of two factors:
changes in the optic nerve head and visual field defects. However, the following tests are conducted to confirm the diagnosis:

- Fundus examination with simultaneous assessment of the optic nerve head
- Optic nerve evaluation in imaging studies
- Visual field assessment
- Intraocular pressure measurement
- Angle examination
- Anterior segment optical coherence tomography

Although some nutrients have been proven to have a positive impact on glaucoma, such as antioxidants, omega-3 fatty acids, and others, there are still inconsistencies in the evidence. There is also no summary of current knowledge in the form of specific dietary recommendations.
The aim of this systematic review is to summarize the available evidence on the role of diet in glaucoma, leading to clear and effective guidelines for patients with glaucoma.

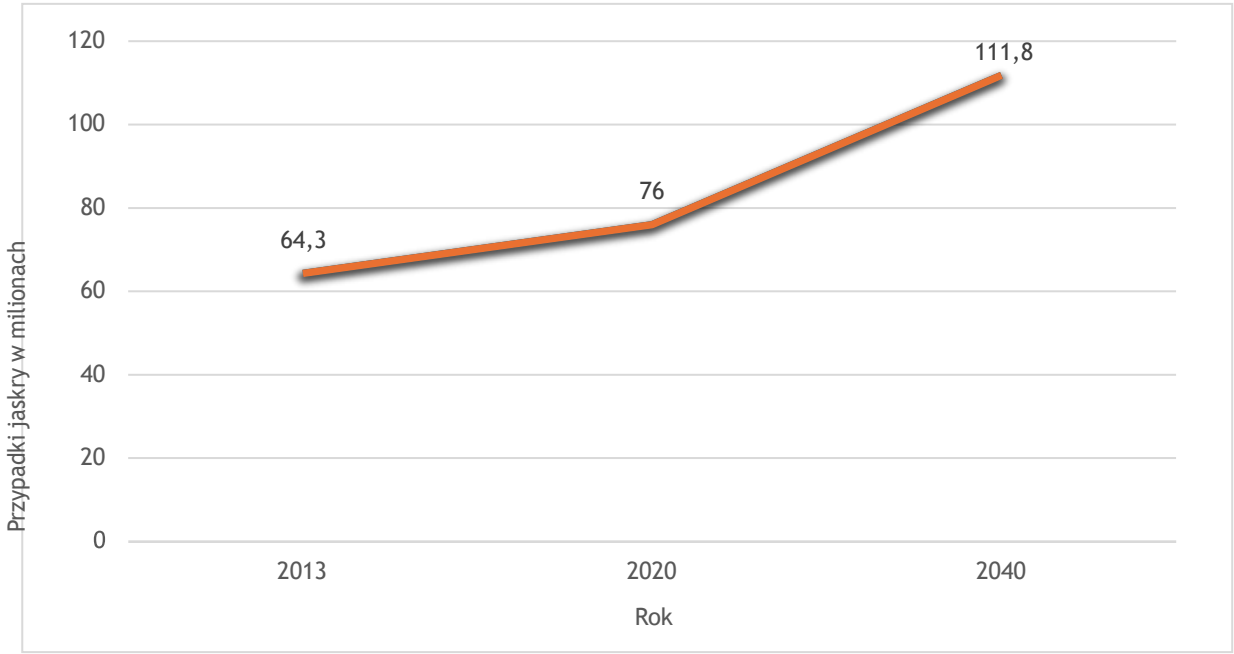

Chart 2. Number of glaucoma cases in individual years.(2)

Review of Current Knowledge
Glaucoma is an optical system disease characterized by gradual atrophy of the optic nerve.
This atrophy is irreversible and without appropriate treatment can even lead to complete vision loss. Therefore, early prevention aiming to reduce the risk of glaucoma is crucial. One of its pillars is diet, which is a significant factor in the occurrence of optic nerve atrophic changes, while being a modifiable component subject to change in daily life and over which each patient has full control. Diets and substances influencing neurodegeneration and the risk of developing glaucoma include: nicotinamide adenine dinucleotide (NAD), lactic acid, caffeine, the

ketogenic diet, alcohol, the Mediterranean diet, and antioxidants. Additionally, caloric restriction is an important factor in preventing neurodegenerative changes in the optic nerve.

Nicotinamide adenine dinucleotide (NAD)

Nicotinamide adenine dinucleotide (NAD) is a chemical compound classified as an organic compound, which plays a significant role in cellular respiration processes. It exists in both reduced (NADH) and oxidized (NAD+) forms. Its components include nicotinamide nucleotide and adenosine 5'-monophosphate, connected by a dehydration bond. NAD participates in REDOX reactions and serves as a substrate for protein synthesis in the body.

(1) With aging, the concentration of NAD naturally decreases in the body, which may lead to disrupted homeostasis resulting in diseases such as glaucoma, Alzheimer's disease, and Parkinson's disease. In mammals, three pathways for NAD synthesis are distinguished: the kynurenine pathway, the Preiss-Handler pathway, and the salvage pathway. Neurons mainly synthesize NAD through the salvage pathway, which involves the conversion of nicotinamide to nicotinamide nucleotide, a substrate for generating nicotinamide adenine dinucleotide with the involvement of NMATs enzyme. There are three types of NMATs enzymes that differ in their cellular localization. The presence of NAD and NMATs significantly affects the degree of neurodegeneration in the human body due to their involvement in the process of protein synthesis necessary for neuronal survival. (1) Therefore, the proper selection of nutrients in the patient's diet is important to ensure the supply of substrates for the synthesis of these chemical compounds is not disrupted. Patients with primary angle-closure glaucoma have been found to have reduced levels of NAD. Precursors of NAD include nicotinic acid, nicotinamide riboside, NMN, NAM, and nicotinamide. Clinical studies have shown that supplementation with NAM (3g/day) in patients significantly improves retinal function.

Nicotinamide used at a dose of approximately 2.5g/day prevented the loss of retinal ganglion cells and reduced significant factors contributing to glaucoma such as intraocular pressure. (1) Retinal ganglion cells are adapted for rapid absorption of nicotinamide to produce NAD and maintain the body's homeostasis of this compound. It has also been shown that nicotinamide supplementation does not significantly affect other metabolic processes in the human body, which is evidence of the lack of adverse effects associated with exogenous administration of this compound to the body. Therefore, nicotinamide supplementation is the easiest way to maintain an adequate level of NAD in the body. The main sources of nicotinamide in the diet are meat products, mainly liver, cereals, eggs, fish, and peanuts.

Lactic Acid

Lactates serve as an important energy substrate for neuronal cells in mammals. The concentration of lactates in the retina significantly exceeds their concentration in serum. At first glance, it may seem that these compounds are produced as a by-product of cellular muscle oxygen deprivation. However, numerous studies indicate the importance of the L- lactic acid enantiomer as a substrate in the gluconeogenesis process and its involvement in signaling in endocrinological processes. It is undeniable, however, that lactic acid serves as a significant source of energy for neurons in the central nervous system. Retinal ganglion cells mainly utilize glucose and lactic acid for energy processes. (1) Photoreceptor cells demonstrate the ability to convert pyruvate to lactate, indicating their ability to supply energy substrates to other neuronal cells of the optic system. (3) Clinical research results suggest disturbances in lactate homeostasis in patients with open-angle glaucoma. Injury to the ocular apparatus, such as optic nerve crush, may induce reduced expression of lactate transporters, resulting in decreased lactate concentration in the retina. (3) This leads to compensatory increases in glucose concentration in this area, which also serves as an energy substrate for neuronal cells.

Caffeine/Polyphenols/Catechin

The most effective preventive measure to reduce the risk of glaucoma is to lower intraocular pressure. Caffeine, commonly found in coffee and tea, can have extremely different effects on the risk of glaucoma. Caffeine, through its vasoconstrictive effect on blood vessels, contributes to increased pressure in the optic system of the eye.(1) It has been shown that after coffee consumption in patients with glaucoma, intraocular pressure periodically increases by up to 2 mmHg within two hours.(1) This effect is associated with the action of caffeine as a phosphodiesterase inhibitor, which disrupts the formation of aqueous humor and blocks adenosine receptors, leading to increased activity of the nervous system, resulting in elevated blood pressure.(1) However, the degree of correlation between caffeine and increased intraocular pressure depends largely on individual factors.

Another product containing relatively large amounts of caffeine is tea. Surprisingly, despite its caffeine-rich composition, tea has a positive effect on the body and intraocular pressure.

Although the mechanisms of this effect are not fully understood, it is believed that the presence of polyphenols/flavonoids, minerals, and vitamins in tea may be significant. Polyphenols potentially may influence the regulation of intraocular pressure, the diameter of blood vessels, and their mechanism of action may be antioxidant in nature. However, their impact remains under investigation, and at present, the exact mechanism leading to the aforementioned effects cannot be determined. Polyphenols from the flavonoid group are abundant in green tea. Flavonoid - catechin acts as an antioxidant, alleviates inflammation, and binds iron ions. For this reason, it is a specific neuroprotective agent and reduces the risk of glaucoma. Catechin is a chemical compound found in large quantities in green tea. It acts as an antioxidant, alleviates inflammation, and binds iron ions. For this reason, it is a specific neuroprotective agent and reduces the risk of glaucoma.

Ketogenic Diet

There is increasing evidence in the scientific literature of the neuroprotective effects of ketogenic diets. (4) The main reason for this is the stimulation of energy metabolism, the GABA system, glutaminergic metabolism, antioxidative effects, influence on programmed cell death, alleviation of inflammation, and stimulation of kynureninic acid production, which acts as an antagonist to NMDA receptors and has neuroprotective effects.(5) Glaucoma is a disease associated with impaired mitochondrial function in cells. Regular adherence to ketogenic dietary recommendations significantly stimulates mitochondrial biogenesis, ATP production, and increases the concentration of phosphocreatine in the brain, thereby significantly increasing the rate of brain metabolism. (1)The ketogenic diet also increases mitochondrial glutathione levels.(5) Individual ketone bodies also act as specific energy
substrates for neuronal cells. (5)These mechanisms clearly indicate the neuroprotective effect of the ketogenic diet, which undoubtedly reduces the risk of glaucoma.

Alcohol

Ethanol, by participating in many biochemical processes (including, among others, the inhibition of vasopressin action), contributes to a temporary decrease in intraocular pressure.
(6) These values fluctuate around 4 mmHg per hour.(1) According to the latest clinical studies, alcohol consumption, even within recommended limits (below 112 g/week according to UK guidelines), significantly increased the risk of developing glaucoma and exacerbated symptoms in already affected patients, leading to the occurrence of coexisting conditions such as diabetes and obesity.(7) Individuals consuming alcohol, besides having higher intraocular pressure, also had a thinner inner layer of retinal ganglion cells and a smaller thickness of nerve fibers. (8) A stronger negative impact of alcohol on glaucoma was observed in individuals genetically

predisposed to this disease. Alcohol is oxidized to acetaldehyde. This process is accompanied by the formation of reactive oxygen species (ROS). Therefore, alcohol consumption can exacerbate oxidative stress, which has degenerative effects on the central nervous system. Acetaldehyde formed binds to proteins and leads to impaired functioning of individual organs. (8) Alcohol metabolism primarily occurs in the liver and partly in the brain. Therefore, visual neurons located in the central nervous system are also subject to damage. Interestingly, the degree of alcohol interference in relation to the risk of developing glaucoma is not dependent on the patient's gender.

Mediterranean Diet

It is widely known that the Mediterranean diet brings many benefits for maintaining overall organism homeostasis. (9) According to scientific studies, consuming products included in the Mediterranean diet significantly lowers the risk of developing glaucoma or exacerbating its symptoms.(10) Glaucoma is one of the consequences of diabetes, a disease based on oxidative reactions leading to the formation of reactive oxygen species (ROS), which contribute to gradual loss of vision. (11) As studies show, the eyes are the most vulnerable to the action of ROS. The Mediterranean diet is a beneficial habit for diabetics. Thanks to the presence of antioxidant components in the vegetables and fruits included in it, the amount of generated reactive oxygen species decreases. Quercetin, present in yellow onions, plays a particularly important role as it inhibits the apoptosis process of retinal pigment epithelial cells induced by the presence of ROS.(4) One piece of evidence from scientific literature is the higher prevalence of glaucoma in countries not following the Mediterranean diet. The presence of cabbage, beans, squash, and bananas in the diet plays a significant role in reducing the risk.
(4) This is mainly due to the presence of antioxidants in these products. Antioxidant compounds are also present in olive oil and red wine. Therefore, the influence of the Mediterranean diet on glaucoma is correlated with the impact of this eating style mainly on the risk of developing eye diseases as a consequence of the progression of the disease in diabetic patients.

Antioxidants

As mentioned in the above text, glaucoma is a disease that can be caused by oxidative stress. This is a state of excessive burden on cells by reactive oxygen species (ROS), which leads, among other things, to the degeneration of DNA, proteins, and lipids, resulting in cell and tissue damage.(12) It is therefore obvious that one of the behaviors to prevent glaucoma can be the intake of antioxidant substances, commonly known as antioxidants. (13) A review of scientific studies clearly indicates a decrease in antioxidant levels in patients with glaucoma.
(13) Antioxidants significantly contribute to controlling intraocular pressure and protect retinal ganglion cells from ROS.(14) However, clinical studies still do not provide unequivocal confirmation of the preventive action of antioxidants against glaucoma. It should also be remembered that the effective dose of antioxidants taken may vary significantly depending on the patient's gender, metabolism, and genetic predisposition.(15) One effective approach is to combine several antioxidant substances to better influence the patient's body.
The issue of using these substances in glaucoma prevention remains uncertain due to their impact on the processes of protein, enzyme, and lipid formation, which can lead to many side effects. Antioxidants are widely present in everyday food items that are part of almost everyone's diet. Such products include beta-carotene found, for example, in tomatoes, carrots, and peaches, vitamin C present in parsley, peppers, black currants, and citrus fruits, coenzyme Q10, which can be found in broccoli, fish, and peanuts, and polyphenols present in grapes, red vegetables, and teas. These substances contribute to inhibiting the neurodegeneration process of retinal ganglion cells, leading to a reduced risk of developing glaucoma.(13) One study has

demonstrated the effect of oral antioxidant supplementation on increasing peak systolic and diastolic blood velocity and reducing vascular resistance in vessels surrounding the eyeball. (16) This directly contributes to better blood supply to eye structures and prevents their degeneration and the formation of pathological changes in this area.

Discussion

Glaucoma undoubtedly becomes an increasingly global problem in the context of ocular diseases. The reason for this state of affairs is undoubtedly the growing number of people suffering from diabetes and cardiovascular diseases, which contribute to an increased risk of developing glaucoma. One of the easiest ways to prevent this disease seems to be appropriate dietary behaviors, mainly focused on enriching one's diet with the compounds discussed earlier. This is certainly one of the easier and most accessible ways to protect oneself from contracting it. However, simply adhering to dietary recommendations is not enough to protect us from the risk of developing glaucoma. Other factors also influence it, such as genetics, age, eye injuries, and coexisting diseases. As shown in the above review, scientific studies do not confirm the preventive effectiveness of the discussed dietary components, but emphasize their positive impact on the body and structures within the ocular system, which can be directly associated with the occurrence of glaucoma. Further scientific research is therefore needed to confirm the discussed thesis. Nevertheless, we see great potential in using diet in the prevention and treatment of glaucoma.

Conclusions

Currently, scientific literature provides evidence of the positive impact of certain substances on the risk of developing glaucoma. However, further scientific research is needed to confirm the discussed thesis. It is difficult to determine unequivocally whether a particular compound contained in food, which is part of a diet aimed at preventing the disease, has fully positive effects on the body, or whether it carries negative consequences. However, if we carefully analyze the impact of individual food components on glaucoma, we can conclude that regular intake or cessation of intake of the discussed substances constitutes a positive element of our diet in terms of glaucoma prevention. Therefore, in our opinion, patients at risk and those suffering from this condition should be advised to adhere to a diet rich in these components and to abstain completely from alcohol consumption.

Author’s Contribution

Conceptualization: J.Kawka ; Methodology: N. Zalewska; Software: A. Baranowska; Check: J. Kawka; Formal Analysis: ; Investigation: J. Kawka, K. Filipek, N. Zalewska, F. Czyżewski, W. Mrugała, S. Mrugała, B. Skierkowski, M. Muciek, K. Baranowska; Resources: J. Kawka, K. Filipek, N. Zalewska, F. Czyżewski, W. Mrugała, S. Mrugała, B. Skierkowski, M. Muciek, K. Baranowska; Writing – Rough Preparation: J. Kawka, K. Baranowska, N. Zalewska, K. Filipek; Writing – Review and Editing: J. Kawka; Visualization: J. Kawka, A. Baranowska, F. Czyżewski, M. Muciek, ; Supervision: B. Skierkowski, W. Mrugała, S. Mrugała, M. Muciek; Project Administrator: J. Kawka.
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