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THE ASSOCIATION OF OXIDATIVE STRESS STATUS AND GLAUCOMA: SYSTEMATIC REVIEW

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Abstract

At this point in time, we do not have a full understanding of the pathogenic processes that might lead to glaucoma. Other concurrent variables, such as elevated glutamate levels, changes in nutritional status, abnormalities in vascular parameters, malfunction of the immune system, and oxidative stress, may also play key roles in the genesis and pathophysiology of the condition. However, the levels of antioxidant enzymes such as superoxide dismutase (SOD), glutathione peroxidase (GPX), and catalase (CAT) were found to be enhanced in the aqueous humors of the open-angle glaucoma (OAG) group. The outcomes of the study indicated that the blood TAS was lower in the OAG group than in the control group. OAG is a complicated illness, and a number of different variables, including age, genetics, inflammation, and oxidative stress, have the potential to all play a role in its progression. In individuals who have priamry open-angle glaucoma (POAG), however, damage to the optic nerve and loss of vision can result from intraocular pressure readings that are within the normal range. One of the most important variables that might lead to POAG is having an intraocular pressure that is too high. It would indicate that oxidative stress plays a part in the evolution of glaucomatous optic nerve damage; nonetheless, the causes of open angle glaucoma are still a mystery. The age-related disorder known as exfoliation glaucoma (EXG) is the factor responsible for secondary OAG the majority of the time. The abnormal synthesis and deposition of extracellular fibrillar material are the defining characteristics of this condition. Although the specific processes that underlie the development of exfoliative syndrome and the subsequent transition from exfoliative syndrome to EXG remain unknown, it has been shown that exfoliative syndrome can lead to EXG.

Keyword: *Eye; Glaucoma; Oxidative Stress; Superoxide Dismutase*

INTRODUCTION

Glaucoma is a collection of disorders that are characterized by visual impairment and optic neuropathy. It is one of the leading causes of irreversible blindness around the world.[1] It has been projected that the number of people around the world who are affected by glaucoma (aged 40–80 years) was 64.3 million in 2013, and that figure is expected to increase to 76.0 million in 2020 and 111.8 million in 2040. The frequency of glaucoma has been steadily growing over the past many years due to the fast increase in the number of elderly people around the world.[2]

The pathogenic pathways that lead to glaucoma are not completely understood at this time. Other concomitant factors may also play important roles in the etiology and pathology of the disease, including high glutamate levels, alterations in nutritional status, vascular factors, dysfunction of the immune system, and oxidative stress.[3] Although high intraocular pressure is considered to be the most important risk factor for glaucoma, other concomitant factors may also play important roles in the etiology and pathology Evidence obtained from clinical and experimental studies over the past decade strongly suggested the involvement of oxidative stress in the degeneration of retinal ganglion cells (RGCs) in glaucoma.[4,5]

This involvement was strongly suggested by growing evidence obtained over the course of the last decade. Damage to the structure of the trabecular meshwork and an increase in resistance to the outflow of aqueous humor can be caused by oxidative stress, which in turn puts the retina at danger of suffering from ocular hypertension and neurological damage. Progressive injury to the nervous system is followed by the death of retinal ganglion cells (RGCs) and axon atrophy, which ultimately result in irreversible vision loss. The presence of oxidative stress is an indication that the body's levels of pro-oxidants and antioxidants are out of whack. An antioxidant defense, such as SOD (superoxide dismutase), GPX (glutathione peroxidase), and CAT (catalase), prevents the production of reactive oxygen species (ROS), which can be harmful, under settings that are considered to be normal (catalase).[6,7]

In the case of glaucoma, it has been hypothesized that antioxidants will not be able to eradicate the presence of excessive ROS in an efficient manner. Therefore, reactive oxygen species have the potential to cause damage to ocular tissues and produce a large number of small molecules that are detectable in both the serum and the aqueous humor. The examination of general markers of oxidative stress in various forms of glaucoma has been assessed in a number of studies, but the results are debatable and the samples used in the studies were all rather small.[8,9] This article investigate association of oxidative stress status and glaucoma.

METHOD

SProtocol

This review was carried out in compliance with the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 criteria. These components formed the basis for the regulations that were established.

Eligibility Criteria

This literature review on association "oxidative stress" and "glaucoma" was prepared to analyze the existing research on these two topics. These are the main points that were made in the research under consideration. If you want your work to be considered, you'll need to meet the following conditions: 1) To be accepted for publication, articles must be written in English and address the benefits of tranexamic acid for primary postpartum hemorrhage. (2) Papers were considered if they were published after 2011 but before this systematic review was conducted. No submissions in the following genres will be considered for publication in the anthology: Editorials, submissions without a DOI, reviews of already published articles, and submissions that are substantially similar to those already published in the journal are not considered original research.

Search Strategy

The search for studies to be included in the systematic review was carried out from January, 7nd 2023 using the PubMed and SagePub databases by inputting the words: “oxidative stress status” and “glaucoma". Where *("oxidative stress"[MeSH Terms] OR ("oxidative"[All Fields] AND "stress"[All Fields]) OR "oxidative stress"[All Fields]) AND "status"[All Fields] AND ("glaucoma"[MeSH Terms] OR "glaucoma"[All Fields] OR "glaucomas"[All Fields])* is used as search keywords.

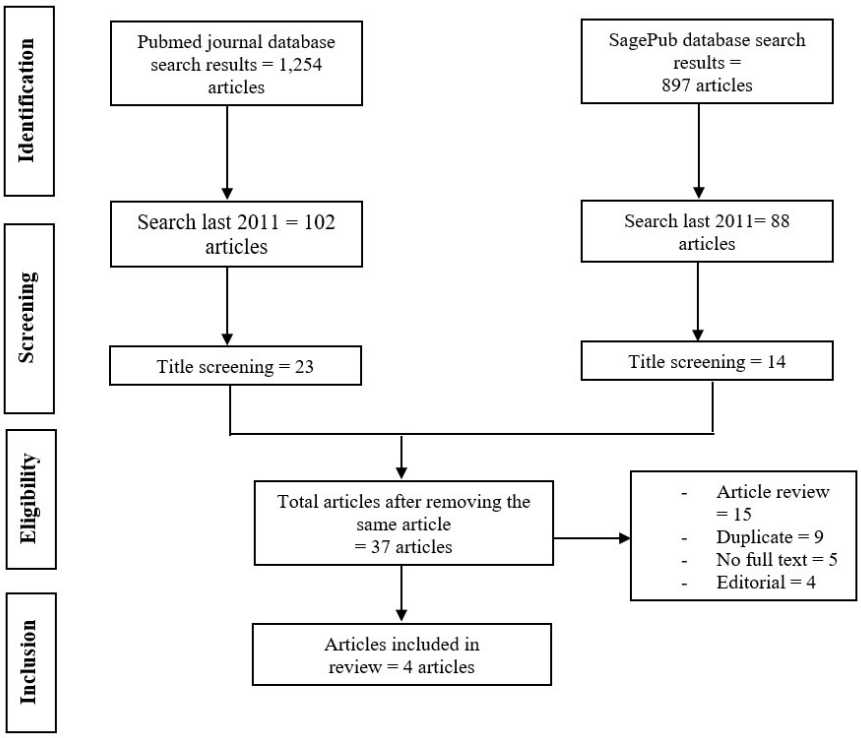

Figure 1. Article search flowchart

Data retrieval

After doing a literature review and reading the titles and abstracts of previously published studies, the study's author changed the criteria for what was included and what wasn't. You can find the updated criteria in the extra materials that come with the study. This was done so that the scope of the problem could be narrowed and it could be seen which areas needed more research. The author came to this conclusion after looking at other research that had been done and published with similar results. During the process of putting together the systematic review, it was decided that only studies that met all of the inclusion criteria should be included.

This meant that we could only consider research proposals that met all of the requirements. This was done to make sure that the evaluation was as complete as it could be. The goal of this project was to gather information about each study, such as its title, author, publication date, place where the study was done, research study design, and research parameters. It is possible to learn about these things. Here are some different kinds of information sources that could be used: You can get this information in a number of ways, depending on what kind of presentation you like.

Quality Assessment and Data Synthesis

The authors did their own independent evaluations of some of the research described in the titles and abstracts of the papers so that they could choose which publications should be evaluated. Then, the full texts of the papers that meet the criteria for inclusion in the systematic review will be looked at to decide which papers will be included in the review. This will be done so that the review can choose which publications to include. This is done in response to the question, "Which studies are good enough to be considered for the review?"

RESULT

Erdurmus[7] did a study in which he used spectrophotometry to measure the serum levels of total antioxidant capacity (TAC) and superoxide dismutase (SOD) as indicators of antioxidant status and total oxidant status (TOS), nitric oxide (NO), protein carbonyl (PC), and malondialdehyde (MDA) as indicators of oxidative stress in the blood of people with POAG (n = 23), PEG (n = 24), and healthy control subjects (n = 19) by spectrophotometry. Mean TAC level was 0.6 ± 0.1 mmol/L in the POAG group; 0.5 ± 0.1 mmol/L in the PEG group and 1.2 ± 0.3 mmol/L in the control group (p = 0.001). Mean SOD level was 13 ± 0.5 mg/L in the POAG group, 11.6 ± 0.2 mg/L in the PEG group and 9.4 ± 0.6 mg/L in the control group (p = 0.001).

Mean TOS level was 19.6 ± 2.6 µmol/L in the POAG group, 21.2 ± 4.2 µmol/L in the PEG group and 15.1 ± 7 µmol/L in the control group (p = 0.001). Mean NO level was 74.3 ± 14.4 µmol/L in the POAG group, 66.1 ± 8.1 µmol/L in the PEG group and 62.3 ± 13.5 µmol/L in the control group (p = 0.005). Mean PC level was 641.5 ± 102.5 nmol/mg in the POAG group, 988.3 ± 214.7 nmol/mg in the PEG group and 654.4 ± 150.7 nmol/mg in the control group (p = 0.001). Mean MDA level was 1.9 ± 0.2 µmol/L in the POAG group, 1.7 ± 0.4 µmol/L in the PEG group and 1.1 ± 0.2 µmol/L in the control group (p = 0.001).[7]

Other study showed biological antioxidant potential (BAP) was shown to have any correlation to (corneal hysteresis) CH or corneal resistance factor (CRF). There was a correlation between BAP and CH and CRF in the female OAG patients who were older than 57 years (r = 0.51 and P = 0.003 respectively; r = 0.49 and P = 0.004), while there was no correlation in the female OAG patients who were younger than 57 years. According to the findings of multiple regression analyses, BAP was found to independently contribute to CH (P = 0.025) and CRF (P = 0.015) in the population of older female OAG patients. In individuals with older age-related corneal opacities and systemic oxidative stress, the cornea's viscoelasticity may be considerably affected. Confirmation from further research is required to establish whether or whether a poor systemic antioxidative status and a low corneal hysteresis are factors in the development of glaucoma.[10]

Table 1. The litelature include in this study

Author	Origin	Method	Sample Size	Result
Erdurmus, 2011[7]	Turkey	Cross sectional	65	TAC levels in the POAG, PEG, and control groups were 0.6, 0.5, and 1.2 mmol/L, respectively (p = 0.001). The POAG group had 13 ± 0.5 mg/L SOD, the PEG group 11.6 ± 0.2, and the control group 9.4 ± 0.6 (p = 0.001). The POAG group had 19.6 ± 2.6 µmol/L TOS, the PEG group 21.2 ± 4.2, and the control group 15.1 ± 7 (p = 0.001). POAG had 74.3 ± 14.4 µmol/L, PEG 66.1 ± 8.1, and control 62.3 ± 13.5 (p = 0.005). The POAG group had 641.5 ± 102.5 nmol/mg, the PEG group 988.3 ± 214.7, and the control group 654.4 ± 150.7 (p = 0.001). The POAG group had 1.9 ± 0.2 µmol/L MDA, the PEG group 1.7 ± 0.4, and the control group 1.1 ± 0.2 (p = 0.001).
Uchida, 2020[10]	Japan	Retrospective study	103	BAP was unrelated to CH or CRF in male and female OAG patients. BAP was associated to CH and CRF in female OAG patients older than 57 years (r = 0.51, P = 0.003; r = 0.49, P = 0.004) but uncorrelated in younger patients. Multiple regression analysis showed that BAP independently caused CH (P = 0.025) and CRF (P = 0.015) in older female OAG patients. Systemic oxidative stress may dramatically impair cornea viscoelasticity in older female OAG patients. Low systemic antioxidant status and corneal hysteresis may cause glaucoma. More research is needed.
Ozkan, 2023[11]	Turkey	Cross sectional	80	The control and POAG groups had greater TAS averages than the PES and PEG groups (p = 0.0001). p > 0.05). The control and POAG groups had lower TOS averages than the PES and PEG groups (p = 0.003, p = 0.0001; p = 0.01, p = 0.001). No other groups differed statistically (p > 0.05). The control and POAG groups had lower OSI means than the PES and PEG groups (p = 0.001, p = 0.0001; p = 0.002, p = 0.0001). The remaining groups did not vary statistically (p > 0.05).
Rokicki, 2017[12]	Poland	Cross sectional	55	When glaucoma patients were compared to healthy controls, a significant increase in the levels of LPS (p = 0.0002) and MDA (p = 0.005) was found in the glaucoma patients. The blood level of manganese superoxide dismutase (Mn-SOD) was considerably lower in glaucoma patients (p = 0.048), although the serum level of copper and zinc superoxide dismutase (Cu,Zn-SOD) was not significantly lower in glaucoma patients. Patients with glaucoma had a significantly higher than average TOS (p = 0.016). Both groups showed a TAC that was comparable to one another.

Study by Ozkan showed the control and POAG group were found to have TAS averages that were statistically considerably greater than those of the PES and PEG groups (p = 0.0001 and p = 0.0001, respectively). It was determined that there was not a significant difference (p > 0.05) between the other groups. It was discovered that the TOS averages of the control and POAG groups were statistically considerably lower than those of the PES and PEG groups (p = 0.003, p = 0.0001; p = 0.01, p = 0.001), but there was not a statistically significant difference identified between any of the other groups (p > 0.05). It was discovered that the OSI mean of the control and POAG groups was considerably lower than that of the PES and PEG groups (p = 0.001, p = 0.0001; p = 0.002, p = 0.0001), but there was not a statistically significant difference identified between any of the other groups (p > 0.05).[11]

Rokicki, et al (2017) showed a significant increase in the levels of LPS (p = 0.0002) and MDA (p = 0.005) was found in glaucoma patients when they compare glaucoma patients to healthy controls. The blood level of manganese superoxide dismutase (Mn-SOD) was considerably lower in glaucoma patients (p = 0.048), although the serum level of copper and zinc superoxide dismutase (Cu,Zn-SOD) was not significantly lower in glaucoma patients. Patients with glaucoma had a significantly higher than average TOS (p = 0.016). Both groups showed a TAC that was comparable to one another.[12]

DISCUSSION

Glaucoma is a chronic optic neuropathy characterized by excavation of the head of the optic nerve and loss of visual field. This loss of vision is caused by gradual destruction to retinal ganglion cells. High intraocular pressure (IOP) is regarded to be the most important risk factor for glaucoma. Primary open-angle glaucoma, also known as POAG, is the most

frequent form of the eye disease found in people over the age of 40. It is also responsible for nearly half of all glaucoma diagnoses.[13]

The pathogenic mechanisms that are associated with OAG and EXG are quite distinct from one another, which suggests that their respective pathogeneses may likewise be distinctive. In spite of the fact that oxidative stress is implicated in both OAG and EXG, the question of whether or not it is involved in other kinds of glaucoma has not yet been answered. In this work, we evaluated all studies that reported the level of oxidative and antioxidative markers in the aqueous humor or serum samples of glaucoma patients.[14–16]

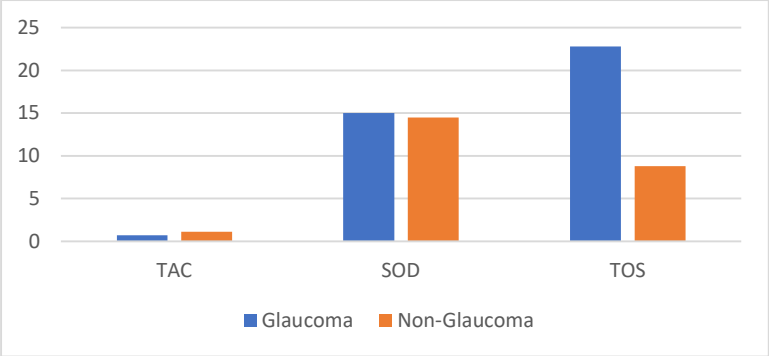

Figure 2. Comparison of TAC, SOD, and TOS patient with and without glaucoma

Study findings showed that the blood TAS was lower in the OAG group than in the control group, but that the levels of antioxidant enzymes such as SOD, GPX, and CAT were increased in the aqueous humors of the OAG group.[16] The same time, we discovered that the blood TAS was lower in the EXG group compared to the control group, but there was no difference between the blood TOS and the aqueous humor TAS and TOS in the EXG group. This was another finding that we made simultaneously.[14,17,18]

OAG is a complex disease, and factors such as aging, genetics, inflammation, and oxidative stress all have the potential to play a part in its development. However, even normal intraocular pressure can cause damage to the optic nerve and loss of vision in patients who have POAG. A high intraocular pressure is one of the most significant risk factors for POAG. Oxidative stress appears to play a role in the progression of glaucomatous optic nerve injury, however the origins of open angle glaucoma are unknown.[7,18]

Meta-analysis of OAG patients showed there was a drop in the blood TAS, which suggested that the equilibrium between the ROS generation and clearance systems had been disrupted. It has been revealed that the death of RGCs most likely occurs through an apoptotic mechanism, which ultimately results in glaucomatous optic neuropathy. It is common knowledge that apoptotic processes include oxidative stress. As a result, we came to the conclusion that oxidative stress was likely the cause of the degeneration of RGCs. Study discovered that the activity of SOD, GPX, and CAT increased in the aqueous humors of OAG patients. They found that this rise occurred in OAG patients.[19,20]

Despite serving a variety of distinct activities, each of these enzymes is capable of producing antioxidant effects. The oxidation / reduction conversion of superoxide radicals to molecular oxygen and hydrogen peroxide can be catalyzed by SOD. Catalase enzyme is yet another important antioxidant enzyme that defends against the damaging effects of peroxide by converting hydrogen peroxide into water and oxygen, thereby reducing the peroxide's toxicity. As a component of a defensive mechanism against ROS, GPX is responsible for catalyzing the reduction of hydrogen peroxide by two molecules of glutathione.[21]

As a result, levels of antioxidant enzymes rose as a defense mechanism against the elevated amounts of ROS present in the aqueous humor.[16] This would prevent the ROS from causing damage to the trabecular meshwork or RGCs. However, there was a substantial amount of variation amongst the several studies that were incorporated into our meta-analysis. It's possible that the causes are due to the fact that the study population was different, and even though the same methodologies were employed to discover indications, the regents or procedures were different.[21]

EXG is the age-related condition that most commonly causes secondary OAG. It is characterized by aberrant production and deposition of extracellular fibrillar material. Although the precise mechanisms underlying the development of exfoliative syndrome and the subsequent progression from exfoliative syndrome to EXG remain unclear, a number of studies in the last decade suggest that increased oxidative stress, which leads to exfoliation-induced tissue damage and pathological alterations of the extracellular matrix, is involved in the pathobiology of EXG.[22]
This is because increased oxidative stress causes exfoliation-induced tissue damage and pathological alterations of the extra According to the findings of our meta-analysis, the TAS of the EXG group was lower than that of the control group, which is in line with the findings that had been previously published.[22] It has been demonstrated that oxidative damage in connective tissues including collagen and elastin can lead to the deposition of extracellular fibrillar, which may be the

etiology of extracellular granuloma. However, we did not detect any significant variations in the TOS of the blood, the TAS of the aqueous humor, or the TOS of the aqueous humor.[16] There is continuing disagreement on the findings of other research that explored TAS or TOS in aqueous humors. It's possible that the discrepancy is due to the fact that the research populations and detection methodologies were different.[23,24]

CONCLUSION

There is a marked difference between the total oxidative stress of patients with glaucoma and without glaucoma. Meanwhile, SOD and TAC are not consistent.

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