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Review Article

OXIDATIVE STRESS AND INFLAMMATORY PATHWAYS IN THE PATHOGENESIS OF DIABETIC RETINOPATHY: A REVIEW

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ABSTRACT

Diabetic retinopathy (DR) is a prevalent microvascular consequence of diabetes mellitus and continues to be a primary cause of preventable blindness globally. Even though there have been improvements in how diabetes is managed and eye care, the number of people with DR keeps going up. This shows that we need to learn more about how it works at the molecular level. There is more and more proof that oxidative stress and long-term inflammation are major causes of retinal impairment in diabetes. Chronic hyperglycemia stimulates the overproduction of reactive oxygen species (ROS), which subsequently activates inflammatory signalling pathways, compromises the blood-retinal barrier, and causes neuronal and vascular dysfunction. This study critically analyses the molecular processes connecting oxidative stress and inflammatory pathways in diabetic retinopathy, focussing on the functions of NF-κB signalling, the NLRP3 inflammasome, mitochondrial failure, and pro-inflammatory cytokines. Moreover, novel treatment approaches addressing oxidative stress and inflammation, such as antioxidant and combination therapy, are examined.

KEYTERMS: Diabetic retinopathy; oxidative stress; inflammation; reactive oxygen species.

INTRODUCTION

Diabetic retinopathy (DR) is a long-term, worsening microvascular problem that happens when diabetes mellitus damages the retinal blood vessels and nerve tissue. This can lead to vision problems or perhaps blindness. It is one of the most common reasons for vision loss that could have been avoided in working-age adults around the world, and it costs a lot of money in terms of lost productivity. Around 30% of people with diabetes worldwide have diabetic retinopathy (DR), and the number of people with DR is rising along with the number of people with type 1 and type 2 diabetes mellitus.[1] Even though there have been improvements in glycaemic control, antihypertensive medication, lipid management, and the start of eye screening programs, diabetic retinopathy is still a big public health problem, especially in low- and middle-income countries where diabetes care and early detection are hard to get.

The retina is a highly specialised brain tissue with an extraordinarily high metabolic demand, rendering it particularly susceptible to metabolic abnormalities linked to chronic hyperglycemia. The pathophysiology of diabetic retinopathy (DR) is intricate and multifaceted, encompassing interconnected metabolic, vascular, neuronal, and inflammatory mechanisms. Traditionally, diabetic retinopathy (DR) was viewed mainly as a microvascular condition; however, mounting data suggests that neurodegeneration and persistent low-grade inflammation manifest early in the disease process, frequently preceding clinically observable vascular lesions. This changing understanding has changed the way we think about DR from a microvascular illness to a neurovascular and inflammatory disease of the retina.

Chronic hyperglycemia is the primary catalyst in the onset of diabetic retinopathy (DR). Extended elevation of blood glucose levels triggers various metabolic pathways in retinal cells, such as the polyol pathway, protein kinase C (PKC)

activation, enhanced flux through the hexosamine pathway, and the synthesis of advanced glycation end products (AGEs). These mechanisms converge on a singular outcome: the excessive generation of reactive oxygen species (ROS). Mitochondrial malfunction, especially in retinal endothelial cells, pericytes, and neurones, is a major cause of ROS overproduction. In physiological settings, reactive oxygen species (ROS) are strictly controlled and play a role in normal cellular signalling. In diabetes, however, too many ROS are generated, which overwhelms the body's own antioxidant defence systems including superoxide dismutase, catalase, and glutathione peroxidase. This leads to a condition of constant oxidative stress.

Oxidative stress causes a lot of damage to the cells of the retina, including lipids, proteins, and nucleic acids. Lipid peroxidation damages cell membranes, protein oxidation changes the activity and structure of enzymes, and DNA damage causes cells to stop working and die. Oxidative damage is especially harmful to retinal endothelial cells. This damage breaks down the inner blood-retinal barrier, makes blood vessels more permeable, and causes capillaries to bleed. The loss of pericytes, which is a common early sign of DR, is also strongly linked to oxidative stress and makes capillaries less stable and microaneurysms more likely to occur. Oxidative damage to retinal neurones and glial cells also plays a role in early neurodegenerative alterations, such as ganglion cell death and problems with vision.

Oxidative stress is not an isolated phenomenon; it is intricately associated with the activation of inflammatory pathways that worsen retinal damage. Excess reactive oxygen species (ROS) act as powerful signalling molecules that turn on redox-sensitive transcription factors, the most important of which is nuclear factor kappa B (NF-κB). When NF-κB is turned on, it makes a lot of pro-inflammatory genes, such as cytokines (including tumour necrosis factor-α, interleukin-1β, and interleukin-6), chemokines, adhesion molecules, and enzymes that are involved in inflammatory reactions. These mediators enhance leukostasis, endothelial dysfunction, and increased vascular permeability in the retinal microvasculature.

The activation of the NLRP3 inflammasome, a multiprotein complex that is very important for innate immunity, is another important inflammatory process involved in DR. Oxidative stress and mitochondrial dysfunction caused by high blood sugar levels are two of the main things that cause the NLRP3 inflammasome to become active in retinal cells. When the inflammasome is turned on, it causes pro-inflammatory cytokines like interleukin-1β and interleukin-18 to split and mature, which makes local inflammatory reactions stronger. Continual activation of the inflammasome leads to long-term inflammation of the retina, blood vessel leakage, and damage to neurones, which speeds up the course of DR.

Oxidative stress and inflammation work together to make a vicious cycle in the diabetic retina that keeps going on its own. Oxidative stress triggers inflammatory pathways, and inflammatory mediators exacerbate ROS generation by activating NADPH oxidases and disrupting mitochondrial function. This reciprocal relationship maintains chronic retinal injury, even with enhanced glycaemic control, a phenomenon commonly termed “metabolic memory.” Metabolic memory elucidates why individuals with a history of inadequate glycaemic control continue to face an elevated risk of diabetic retinopathy progression, despite subsequent improvements in blood glucose levels.

As diabetic retinopathy progresses, these molecular and cellular disruptions result in the distinctive clinical phases of the condition. In non-proliferative diabetic retinopathy, microaneurysms, intraretinal haemorrhages, hard exudates, and capillary non-perfusion indicate early vascular injury caused by oxidative stress and inflammation. In later phases, retinal hypoxia causes angiogenic factors to be made more, especially vascular endothelial growth factor (VEGF). Both oxidative stress and inflammatory signalling pathways have a big effect on VEGF expression. High levels of VEGF make blood vessels more permeable and cause abnormal new blood vessels to grow, which is what happens in proliferative diabetic retinopathy and can lead to vitreous haemorrhage and tractional retinal detachment.

Comprehending the pivotal functions of oxidative stress and inflammation in the pathophysiology of diabetic retinopathy (DR) carries significant therapeutic ramifications. Current treatments, including laser photocoagulation, intravitreal anti-VEGF medicines, and corticosteroids, focus on late-stage vascular problems but do not directly target the metabolic and inflammatory pathways that cause the disease to start and develop worse. New treatments are trying to change oxidative stress and inflammatory pathways by using antioxidants, anti-inflammatory drugs, drugs that stop NF-κB and NLRP3 inflammasome activation, and drugs that make mitochondria work better. These strategies show promise for halting or reducing the advancement of diabetic retinopathy, especially when implemented early in the disease trajectory.

Diabetic retinopathy is a complex, progressive retinal disease characterised by persistent hyperglycemia-induced oxidative stress and inflammation, which play crucial and interrelated roles. Excessive production of reactive oxygen species (ROS) and compromised antioxidant defences precipitate oxidative damage, whereas the activation of inflammatory signalling pathways, including NF-κB and the NLRP3 inflammasome, exacerbates vascular dysfunction, neuronal death, and pathological angiogenesis.[2,3] Understanding the intricate molecular linkages between oxidative stress and inflammation is crucial for the advancement of innovative, mechanism-driven therapeutics and for enhancing long-term visual outcomes in individuals with diabetes.

Oxidative Stress in Diabetic Retinopathy

Oxidative stress occurs when there is too much ROS and not enough antioxidant defence systems to deal with it. In diabetes, chronic hyperglycemia significantly increases the production of reactive oxygen species (ROS) via multiple interconnected metabolic pathways, including the activation of the polyol pathway, protein kinase C (PKC) signalling, the creation of advanced glycation end products (AGEs), and mitochondrial dysfunction.[4]

Superoxide anion (O_2^-), hydrogen peroxide (H_2O_2), and hydroxyl radicals (•OH) are the main ROS that are involved in DR. These reactive chemicals harm lipids, proteins, and nucleic acids in retinal capillary endothelial cells, pericytes, and photoreceptors. When the mitochondrial electron transport chain doesn't work right, it makes more ROS, which kills retinal neurones and vascular endothelial cells and speeds up retinal degeneration.[5]

Oxidative stress is a major cause of the breakdown of the blood-retinal barrier (BRB), which is a major sign of diabetic retinopathy. Too many ROS change the expression and structure of tight junction proteins such occludin and claudin-5, which makes the endothelium more permeable.[6] This disruption allows plasma to flow into the retina, which causes macular oedema and early microvascular dysfunction.

Weakening of Antioxidant Defence Mechanisms

Individuals with diabetes demonstrate considerable dysfunction of endogenous antioxidant mechanisms. Enzymatic antioxidants, such as superoxide dismutase (SOD), catalase, and glutathione peroxidase (GPx), are frequently diminished, and non-enzymatic antioxidants, including vitamins C and E, are decreased.[7] This diminished antioxidant capacity worsens oxidative damage, which in turn increases inflammation and damage to the retina.

Diabetic Retinopathy's Inflammatory Pathways

Diabetic retinopathy is increasingly acknowledged as a persistent, low-grade inflammatory disorder. Hyperglycaemia-induced oxidative stress activates redox-sensitive transcription factors, particularly NF-κB, leading to the upregulation of pro-inflammatory cytokines such as tumour necrosis factor-α (TNF-α), interleukin-1β (IL-1β), and interleukin-6 (IL-6), as well as adhesion molecules including ICAM-1 and VCAM-1.[8] These mediators facilitate leukocyte adherence to the retinal endothelium (leukostasis), capillary blockage, and localised ischaemia, thereby expediting microvascular damage and neovascularisation.

The NLRP3 Inflammasome

Recent evidence underscores the critical function of the NLRP3 inflammasome in the pathophysiology of diabetic retinopathy. Hyperglycemia, mitochondrial reactive oxygen species (ROS), and advanced glycation end-products (AGEs) activate the NLRP3 complex, resulting in the caspase-1-mediated cleavage of pro-IL-1β and pro-IL-18 into their active inflammatory forms.[9] The activation of the NLRP3 inflammasome creates a direct relationship between oxidative stress and inflammation, which makes the damage to the retina worse by creating a loop that keeps going.

The Function of Microglia and Retinal Cells

In a diabetic environment, resident retinal immune cells, especially microglia, become active and generate pro-inflammatory cytokines and reactive oxygen species (ROS), which damage the nerves and blood vessels. Müller glial cells and retinal pigment epithelium (RPE) cells also play a role in the inflammatory response by releasing vascular endothelial growth factor (VEGF) and other inflammatory mediators that encourage angiogenesis and BRB breakdown.[3]

The Relationship Between Oxidative Stress and Inflammation

Oxidative stress and inflammation are closely linked factors in the development of diabetic retinopathy. Reactive oxygen species (ROS) not only directly harm cellular macromolecules but also serve as secondary messengers that initiate inflammatory signalling pathways. On the other hand, pro-inflammatory cytokines cause more ROS to be made by turning on enzymes like NADPH oxidase. This keeps the cycle of oxidative and inflammatory harm going.[2] This two-way communication increases vascular permeability, leukostasis, neuronal death, and progressive retinal degeneration.

Implications for treatment

Antioxidant Treatment

Numerous antioxidant substances, such as α-lipoic acid, resveratrol, and curcumin, have exhibited protective benefits in experimental models of diabetic retinopathy by mitigating oxidative stress and inhibiting inflammatory signaling.[5] Vitamin D supplementation has been documented to provide antioxidant and anti-inflammatory effects, indicating possible supplementary advantages in the therapy of diabetic retinopathy.

Anti-Inflammatory Drugs

Using non-steroidal anti-inflammatory medications (NSAIDs), corticosteroids, and specific NF-κB inhibitors to stop inflammatory mediators from working has had mixed results in the clinic. New treatments that focus on certain inflammatory pathways, including NLRP3 inflammasome inhibitors (like MCC950) and cytokine-specific medicines (like IL-1β inhibitors), are being studied right now and could be useful in the future.[3,9]

Therapeutic Approaches in Combination

Because oxidative stress and inflammation are so closely linked, combination treatments that target both pathways may work better in the clinic. Anti-VEGF drugs like ranibizumab and aflibercept not only stop bad angiogenesis, but they also lower inflammation levels in a roundabout way. These treatments may provide better

protection against retinal damage when used alongside antioxidant supplements.[1]

CONCLUSION

Oxidative stress and inflammation are key, linked processes that cause diabetic retinopathy. Hyperglycemia-induced ROS production triggers inflammatory pathways that undermine retinal vascular integrity and neuronal function. Focussing on these molecular pathways could lead to new approaches to prevent and treat diabetic retinopathy. To create effective treatments for this devastating consequence of diabetes, we need to keep doing translational research and well-planned clinical trials. These treatments should address both oxidative and inflammatory aspects of the condition.

REFERENCE

1. Ciorba AL, Saber S, Abdelhamid AL, Keshk N, Elmorsy EA, Abu-khudir R, et al. Diabetic retinopathy in focus: Update on treatment advances, pharmaceutical approaches, and new technologies. **Eur J Pharm Sci.,** 2025; 214: 107307.
2. Hussain A, Ashique S, Afzal O, Altamimi MA, Malik A, Kumar S, et al. Correlation between oxidative stress and diabetic retinopathy: An updated review. **Exp Eye Res.,** 2023; 236: 109650.
3. Yang Y, Jiang G, Liu Y, Chang X, Fu S. Targeting the NLRP3 inflammasome in diabetic retinopathy. **Biochem Pharmacol,** 2023; 212: 115569.
4. Li H, Liu X, Zhong H, Fang J, Li X, Shi R, et al. Research progress on the pathogenesis of diabetic retinopathy. **BMC Ophthalmol,** 2023; 23(1): 372.
5. Mimura T, Noma H. Oxidative stress in diabetic retinopathy: A comprehensive review of mechanisms, biomarkers, and therapeutic perspectives. **Antioxidants (Basel),** 2025; 14(10): 1204.
6. Dia X, Hui X, Xi-Ming X. Critical factors driving diabetic retinopathy pathogenesis and promising interventional strategies. **Biomed Pharmacother,** 2025; 189: 118106.
7. Petkova-Parlapanska K, Draganova V, Georgieva G, Goycheva P, Nikolova G, Karamalakova Y. Systemic inflammation and oxidative stress elevation in diabetic retinopathy and diabetic patients with macular oedema. **Int J Mol Sci.,** 2025; 26(8): 3810.
8. Gómez-Jiménez V, Matas RB, Ortega AL. Modulation of oxidative stress in diabetic retinopathy: Therapeutic role of natural polyphenols. **Antioxidants (Basel),** 2025; 14(7): 875.
9. Jiao X, Tian G. Role of the NLRP3 inflammasome in diabetes and its complications. **Mol Med Rep.,** 2025; 32(5): 292.