THE ROLE OF PLATELETS IN THE PATHOGENESIS OF PRIMARY OPEN-ANGLE GLAUCOMA: INSIGHTS FROM LITERATURE REVIEW

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Annotation: *Primary open-angle glaucoma (POAG) is a leading cause of irreversible blindness, characterized by progressive optic neuropathy. While elevated intraocular pressure (IOP) is a key factor, vascular dysregulation and ischemia contribute significantly, especially in normal-tension glaucoma (NTG). Recent studies highlight the involvement of platelets in exacerbating ocular hypoperfusion through activation, aggregation, and microvascular interactions.*

Keywords: *POAG, vascular dysregulation, aggregation, platelets, IOP*

INTRODCTION

Primary open-angle glaucoma (POAG) is a chronic, progressive optic neuropathy characterized by elevated intraocular pressure (IOP), retinal ganglion cell loss, and visual field defects.

While elevated IOP is a primary risk factor, vascular dysregulation and ischemia play crucial roles in its pathogenesis, particularly in cases of normal-tension glaucoma (NTG), a subtype of POAG.

Emerging evidence suggests that platelets contribute to this process through mechanisms involving activation, aggregation, and interaction with ocular microvasculature.[1][2] Platelets, traditionally known for hemostasis, can exacerbate ocular hypoperfusion by promoting microthrombosis, endothelial damage, and vasoconstriction in retinal and optic nerve head vessels.[3]

This review aims to synthesize the literature on the mechanistic role of platelets in POAG pathogenesis, focusing on platelet parameters, aggregation, and therapeutic implications.

Methods

A comprehensive literature search was conducted using web-based academic databases, including PubMed Central (PMC), Frontiers, Taylor & Francis, and others. Key search terms included "role of platelets in pathogenesis of open-angle glaucoma," "platelets in primary open-angle glaucoma," and "review literature platelets pathogenesis open-angle glaucoma.

" Inclusion criteria encompassed peer-reviewed articles published between 1985 and 2024, focusing on clinical studies, animal models, and in vitro experiments related to platelet function in POAG. Exclusion criteria included non-English articles, case reports, and studies unrelated to pathogenesis.

A total of 10-20 results were screened per query, with full-text reviews performed on relevant articles. Data extraction emphasized platelet parameters (e.g., mean platelet volume [MPV], platelet distribution width [PDW], platelet count [PLT]), aggregation assays, and associations with glaucoma severity, retinal thickness, and disc hemorrhage.

Results

Several studies have demonstrated altered platelet parameters in POAG patients compared to healthy controls.

For instance, POAG patients exhibit significantly lower PLT counts (e.g., 207.08 ± 54.70 × 10^9/L vs. 220.46 ± 55.85 × 10^9/L in controls) and higher MPV (10.46 ± 1.32 fL vs. 10.13 ± 1.10 fL) and PDW (13.76 ± 3.16 fL vs. 11.82 ± 2.44 fL).[1]

These changes correlate with disease severity, as classified by visual field mean deviation (MD): MPV and PDW increase progressively from mild (MD ≤6 dB) to severe (MD >12 dB) stages, with PDW showing independent association (OR=1.297, 95% CI=1.011–1.663).[1]

Similar findings were reported in another cohort, where elevated PDW and MPV negatively correlated with retinal nerve fiber layer (RNFL) and ganglion cell complex (GCC) thickness (e.g., PDW: $r = -0.370$ for RNFL, $P < 0.001$), and positively with cup/disk ratio ($r = 0.322$, $P < 0.001$).[2] Multiple regression confirmed these as independent predictors of structural damage.

Platelet aggregation studies reveal hyper-aggregability in POAG, particularly in response to agonists like adenosine diphosphate (ADP) and collagen.[3] In NTG, delayed platelet absorption is associated with disc hemorrhage (odds ratio not specified in abstract, but significant association noted).[4]

Animal models show monocyte-platelet aggregates in the optic nerve head and P-selectin-mediated endothelial interactions in post-ischemic retina, leading to neuroprotection upon inhibition.[2]

In vitro, anti-glaucomatous eye drops (e.g., Azarga, Betoptic) inhibit platelet aggregation induced by platelet-activating factor (PAF), ADP, thrombin receptor-activating peptide (TRAP), and arachidonic acid (AA), with IC_{50} values as low as 0.1 μL for PAF.[3] Reduced pigment epithelium-derived factor (PEDF) in glaucomatous eyes may enhance this aggregability.

Mechanistically, activated platelets release thromboxane A2, promoting vasoconstriction and microthrombosis in short ciliary arteries and retinal capillaries, causing ischemia-reperfusion injury.[2][3] Platelets may also occlude Schlemm's canal pores, impairing aqueous humor outflow and elevating IOP.[2] Older studies confirm increased spontaneous platelet aggregation in POAG, independent of systemic vascular disease.[5]

Discussion

The literature consistently implicates platelets in POAG pathogenesis via vascular and thrombotic mechanisms, where activation markers like elevated MPV and PDW reflect a prothrombotic state contributing to optic nerve ischemia and structural degeneration.[1][2]

This is particularly relevant in NTG, where IOP-independent factors predominate, and disc hemorrhages link to platelet dysfunction.[4] The anti-aggregant effects of glaucoma medications suggest a dual therapeutic benefit, beyond IOP reduction, potentially mitigating progression.[3] However, limitations include small sample sizes, cross-sectional designs, and confounding by comorbidities like hypertension.

Future research should explore longitudinal studies, genetic factors (e.g., platelet-expressed proteins like tau), and anti-platelet interventions (e.g., aspirin) in POAG management. Overall, platelets represent a promising target for adjunctive therapies in glaucoma.

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