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Short Communication

Inflammatory Mechanisms Involved in Chronic Venous Disease

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DESCRIPTION

Prevalent vascular disorder characterized by impaired venous return, valvular incompetence and progressive structural and functional alterations in the venous system. While hemodynamic factors such as venous hypertension and reflux play a central role in the pathophysiology, mounting evidence highlights the critical contribution of inflammatory mechanisms in initiating and propagating venous dysfunction. Inflammation not only drives structural changes in the venous wall but also mediates microvascular alterations, tissue remodeling and clinical manifestations such as edema, skin changes and ulceration. Understanding these inflammatory pathways is essential for developing targeted therapies and improving clinical outcomes in patients with CVD [1].

At the cellular level, endothelial cells serve as the primary interface between blood flow and venous wall integrity. Venous hypertension induces endothelial activation, leading to increased expression of adhesion molecules such as Intercellular Adhesion Molecule-1 (ICAM-1) and Vascular Cell Adhesion Molecule-1 (VCAM-1). These molecules facilitate the recruitment and adhesion of leukocytes, including neutrophils and monocytes, which infiltrate the venous intima and perivenous tissues. Activated leukocytes release pro-inflammatory cytokines such as Tumor Necrosis Factor-Alpha (TNF-α), Interleukin-6 (IL-6) and Interleukin-1β (IL-1β), amplifying local inflammation and promoting venous wall remodeling. This endothelial-leukocyte interaction establishes a self-perpetuating cycle of inflammation and structural deterioration that underlies disease progression [2-3].

Oxidative stress is a key mediator in the inflammatory cascade of CVD. Mechanical stress and stasis in the venous system increase the production of Reactive Oxygen Species (ROS), which damage endothelial cells and extracellular matrix components. ROS also activate Nuclear Factor-Kappa B (NF-κB), a transcription factor that upregulates pro-inflammatory gene expression, further enhancing leukocyte recruitment and cytokine release. The combination of oxidative stress and sustained inflammation contributes to venous dilation, valve incompetence and disruption of normal venous hemodynamics. These molecular alterations correlate with clinical manifestations, including varicosities, edema and leg discomfort [4]. Matrix remodeling represents another critical consequence of inflammation in CVD. Activated leukocytes and resident fibroblasts release matrix metalloproteinases (MMPs), enzymes that degrade collagen and elastin fibers in the venous wall. This enzymatic activity weakens structural support, promoting venous dilatation, valve dysfunction and tortuosity of superficial and deep veins. Concurrent deposition of fibrotic tissue in response to chronic inflammation leads to lipodermatosclerosis, a hallmark of advanced disease characterized by skin thickening, induration and pigmentation changes. Inflammatory signaling also impairs microcirculatory function, contributing to localized hypoxia, edema and ulcer formation [5-6].

Inflammation in CVD is influenced by both systemic and local factors. Genetic predisposition affecting connective tissue composition, lifestyle factors such as obesity and physical inactivity and repeated venous trauma all exacerbate inflammatory responses. Episodes of thrombophlebitis or deep vein thrombosis further trigger endothelial activation and leukocyte infiltration, accelerating venous wall damage. Additionally, hormonal changes, particularly during pregnancy or menopause, may modulate inflammatory pathways and increase susceptibility to venous dysfunction. These interactions highlight the multifactorial nature of CVD, where inflammation serves as a central mediator linking hemodynamic stress to tissue pathology [7-8].

Therapeutic strategies targeting inflammation are increasingly recognized as essential in managing CVD. Compression therapy, by improving venous return and reducing venous pressure, attenuates endothelial stress and leukocyte activation. Pharmacological interventions, including venoactive drugs such as flavonoids, diosmin and rutosides, exhibit anti-inflammatory properties that reduce leukocyte adhesion, cytokine release and oxidative stress, thereby improving microcirculation and venous tone. Emerging therapies under investigation focus on modulation of specific inflammatory pathways, including inhibition of activity, with the goal of limiting structural venous damage and preventing disease progression [9-10].

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CONCLUSION

In conclusion, chronic venous disease is fundamentally driven by an interplay between hemodynamic stress and inflammatory mechanisms. Endothelial activation, leukocyte recruitment, oxidative stress and matrix remodeling collectively contribute to venous wall damage, valve incompetence and microcirculatory dysfunction. These biological processes underlie the clinical spectrum of CVD, from early varicosities to advanced skin changes and ulceration. Recognizing the central role of inflammation in disease progression informs both preventive and therapeutic strategies, emphasizing the importance of targeted interventions aimed at reducing endothelial stress, modulating immune responses and preserving venous structure and function. Continued research into the inflammatory pathways of CVD promises to improve patient outcomes and advance the development of precision therapies in venous medicine.

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