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PATHOGENESIS OF MICROCIRCULATION DISORDERS IN DIABETIC PATIENTS AND THERAPEUTIC APPROACHES

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Annotation

This thesis examines microcirculation disorders in diabetes mellitus and modern strategies to correct them. It reviews molecular, cellular, and hemodynamic changes in diabetic microangiopathy, focusing on endothelial dysfunction, basement membrane thickening, and impaired autoregulation. Key factors include hyperglycemia-induced oxidative stress, advanced glycation products, and inflammation. Therapies like glycemic control, antioxidants, and targeted drugs show potential for restoring microcirculation. The study offers a clear framework for understanding and managing diabetic microvascular complications.

Keywords: diabetes mellitus, microcirculation disorders, diabetic microangiopathy, endothelial dysfunction, advanced glycation end products, oxidative stress, basement membrane thickening, autoregulation impairment, therapeutic intervention

Today, diabetes mellitus is one of the most pressing global health challenges, affecting over 537 million adults and projected to reach 783 million by 2045. Its impact extends beyond glycemic control, causing microvascular complications that impair tissue perfusion and metabolism at the capillary level. These disorders underlie diabetic nephropathy, retinopathy, and neuropathy — leading causes of renal failure, blindness, and nerve damage in developed countries. Over recent decades, our understanding of diabetic microangiopathy has advanced, uncovering how chronic hyperglycemia and metabolic dysfunction remodel the microvasculature. Key mechanisms include endothelial dysfunction, basement membrane thickening, pericyte loss, and failed autoregulation. These changes disrupt oxygen delivery, nutrient transport, and waste removal, driving progressive organ damage and irreversible complications.

The pathogenesis of microcirculation disorders in diabetic patients involves a sophisticated interplay of biochemical, cellular, and hemodynamic mechanisms that collectively transform the microvascular environment through multiple interconnected pathways. Chronic hyperglycemia initiates the pathogenetic cascade through the polyol pathway activation, where aldose reductase enzyme converts excessive glucose to sorbitol, creating osmotic stress within endothelial cells and pericytes while depleting essential cofactors such as nicotinamide adenine dinucleotide phosphate. This metabolic disturbance compromises cellular antioxidant capacity and enhances susceptibility to oxidative injury, establishing the foundation for progressive microvascular damage. Advanced glycation end products formation constitutes another critical pathogenetic mechanism, wherein chronic hyperglycemia promotes non-enzymatic protein glycation, creating irreversibly modified macromolecules that accumulate within vessel walls and basement membranes. These glycated proteins exhibit altered structural properties, increased cross-linking tendency, and enhanced inflammatory potential through receptor for advanced glycation end products activation, leading to basement membrane thickening and reduced permeability selectivity that impairs normal diffusion processes. Oxidative stress plays a central role in diabetic microangiopathy, resulting from mitochondrial dysfunction, activation of nicotinamide adenine dinucleotide phosphate oxidase, and weakened antioxidant defenses. Excess reactive oxygen species damage lipids, proteins, and deoxyribonucleic acid, reduce nitric oxide availability, and impair microvascular autoregulation. Inflammation worsens the condition through activation of the nuclear factor kappa light chain enhancer of activated B cells pathway, increasing cytokines, adhesion molecules, and complement system activity. Elevated tumor necrosis factor alpha, interleukin six, and C-reactive protein increase endothelial permeability, leukocyte adhesion, and thrombosis. Therapy focuses on controlling blood glucose with insulin, medications, and monitoring, alongside angiotensin-converting enzyme inhibitors or angiotensin receptor blockers to protect endothelium and improve microcirculation. Antioxidants such as alpha-lipoic acid, vitamin E, and glutathione precursors also help reduce oxidative stress and support endothelial function.

In diabetes, microcirculation disorders result from metabolic, oxidative, and inflammatory mechanisms that damage vascular function. Targeted therapies and good glycemic control help restore microcirculation. Future research should focus on personalized treatments, new targets, and early detection to prevent complications.

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