Global Diabetes 2021: Carbamylation of LDL as a posttranslational modification relevant in diabetes mellitus

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Carbamylation of LDL is a nonenzymatic posttranslational modification of LDL resulting from addition of urea-derived cyanate to either the N-terminus or ε-amino group of lysine residues in apolipoprotein B. Carbamylated LDL (cLDL) has been recently shown to manifest all of the biological effects relevant to atherosclerosis, including endothelial dysfunction, expression of adhesion molecules and vascular smooth muscle cell proliferation. In addition, cLDL binds to macrophage scavenger receptors inducing cholesterol accumulation, foam cell formation as well as enhanced oxidant generation. Despite the discovery of an alternative urea-independent myeloperoxidase-mediated mechanism for carbamylation, cLDL has been studied only in subjects with end stage renal disease. Elevated circulating and intraintimal cLDL levels have been associated with increased cardiovascular risk in those patients. However, other carbamylation products have been delineated as independent risk markers for cardiovascular disease even in the absence of uremia. Although diabetes mellitus is characterized by an increased atherosclerotic risk, chronic low grade inflammation and increased levels of myeloperoxidase, the data on cLDL in diabetes are scarce.

Therefore, the present review reveals the main molecular mechanisms involved in the carbamylation of LDL in diabetes mellitus and briefly describes the atherogenic effects of cLDL. The possibility of using the high levels of cLDLs as a predictive tool for cardiovascular risk in diabetes-related pathologies is also discussed.

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