

Involvement of the Toxic AGEs (TAGE)-RAGE System in the Pathogenesis of Diabetic Vascular Complications: A Novel Therapeutic Strategy.

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Diabetic vascular complications are leading causes of acquired blindness, end-stage renal failure, a variety of neuropathies, and accelerated atherosclerosis, which may be involved in the disabilities and high mortality rates suffered by diabetic patients. Continuous hyperglycemia is involved in the pathogenesis of diabetic micro- and macrovascular complications via various metabolic pathways, and numerous hyperglycemia-induced metabolic and hemodynamic conditions exist, including increased generation of various types of advanced glycation end-products (AGEs). Recently, we demonstrated that glyceraldehyde-derived AGEs (Glycer-AGEs), the predominant components of toxic AGEs (TAGE), play an important role in the pathogenesis of angiopathy in diabetic patients. Moreover, a growing body of evidence suggests that the interaction of TAGE with the receptor for AGEs (RAGE) alters intracellular signaling, gene expression, and the release of pro-inflammatory molecules and elicits oxidative stress generation in numerous types of cells, all of which may contribute to the pathological changes observed in diabetic vascular complications. Therefore, the inhibition of TAGE formation, blockade of TAGE-RAGE interaction, and the suppression of RAGE expression or its downstream pathways are promising targets for therapeutic interventions against diabetic vascular complications. In this review, we discuss the pathophysiological role of the TAGE-RAGE-oxidative stress system and related therapeutic interventions for preventing the development and progression of diabetic vascular complications.

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