Advanced glycation and retinal pathology during diabetes

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Abstract:
Of all microvascular complications of diabetes mellitus, retinopathy remains the most common. This disease presents major therapeutic problems for the ophthalmologist and despite many decades of intense research it still constitutes a major cause of blindness in the Western world. This review outlines the pathological characteristics of diabetic retinopathy and proposes a link between disease progression with the formation and accumulation of advanced glycation endproducts (AGEs). AGEs form in vivo from the reaction of glucose and/or α-oxoaldehydes leading to chemical modifications on the amino groups of proteins, lipids and DNA. These heterogeneous adducts can modify the structure and function of proteins and lead to intramolecular and intermolecular cross-link formation. As reported in a range of clinical investigations and determined by mechanistic in vitro and in vivo studies, AGEs accumulate in the diabetic retina where they may be effectors of retinal vascular and neural cell dysfunction. Evidence now points towards a pathogenic role for advanced glycation in the initiation and progression of diabetic retinopathy and this review will examine the current state of knowledge of AGE-related pathology in the retina at a cellular and molecular level. It will also describe how ongoing pharmaceutical strategies to inhibit AGE formation and thereby attenuate their pathogenic influence during chronic hyperglycemia may play a significant role in the treatment of diabetic retinopathy.

Key words: advanced glycation endproducts, diabetes, age, retinopathy, eye

Introduction to diabetic retinopathy

Retinopathy is one of the commonest microvascular complications of diabetes and still a major cause of registerable blindness in the working population of many developed countries [20]. With type 1 diabetes of 10 years duration, the prevalence of diabetic retinopathy is around 80% and this increases to ~95% by 20 years [40, 41]. Overall, diabetic retinopathy is slightly less common in type 2 patients but is still the most frequent microvascular complication suffered by this group [40]. There are few preventative measures and sight-threatening diabetic retinopathy can, at present, only be treated or contained to some extent by focal or pan-retinal laser photocoagulation or vitreoretinal surgery but often at the expense of functional retina and visual performance [62].

Diabetic retinopathy is quintessentially a disease of the intra-retinal vasculature, although there is a subtle