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# Glucagon-like Peptide-1 Receptor Agonist for Diabetic Retinopathy: Friend or Foe?



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#### **Opinion**

Diabetic retinopathy (DR) is a serious complication of diabetes mellitus. In diabetic patients, severe diabetic macular edema or proliferative retinopathy could lead to visual impairment or even blindness. The core pathogenesis of DR is microvascular dysplasia, which includes periretinal cell loss, vascular basement membrane thickening, microaneurysm formation, increased vascular permeability, further retinal capillary occlusion, and neovascularization [1]. Glucagon-like peptide-1 receptor agonist (GLP-1RA) is widely used to treat type 2 diabetes [2]. GLP-1RA has a significant multipotent protective effect on the macrovascular and microvascular complications of diabetes, including DR, as shown in several large randomized controlled clinical trials. The effect of GLP-1RA on DR remains controversial [2,3]. Some observational studies showed a significantly lower risk of DR for diabetic patients treated with GLP-1RA. GLP-1RA has a neutral or beneficial clinical outcome for cardiovascular disease, but recent studies have shown that the incidence of DR events is higher in the GLP-1RA group than in the placebo group. Although the results were not statistically significant, it suggested that GLP-1RA has the potential to increase the risk of developing DR. In addition, studies have shown a higher incidence of serious DR complications with semaglutide, such as vitreous bleeding, diabetes-related blindness, the need for laser photocoagulation, or intravitreal drug therapy. The mechanism is not yet clear [4].

Rapid changes in glucose following GLP-1RA use are thought to raise the chance of possible DR in the short term. Oxidative stress, vascular endothelial growth factor, inflammation, retinal neurodegeneration, and other cytokine influences are other

pathways. However, both studies have their limitations. These include a short follow-up period, absence of DR Classification at baseline and during follow-up, inadequate control of DR severity and hypertension at baseline, and potential sensitivity of some patients to the hypoglycemic effects of GLP-1RA. As a result, conflicting perspectives and evidence exist among studies regarding whether GLP-1RA contributes to an increased risk of DR. Further basic research and clinical trials are imperative to thoroughly elucidate the association between GLP-1RA and the risk of DR [5]. The question of whether GLP-1RA acts as a beneficial agent as a friend or a detriment as a foe in diabetic retinopathy remains contentious. This controversy warrants consideration when selecting diabetes treatment options in the future.

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