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Research Article

Nephrovigilance in Pharmacotherapy of Diabetic Retinopathy

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Abstract

Objective Vascular Endothelial Growth Factor inhibitors (anti-VEGF), such as ranibizumab, aflibercept and bevacizumab delivered intraocularly, reinvigorate ocular pharmacotherapy in general, and diabetic retinopathy (DR) therapy in particular. At present long-term therapy with endless intravitreal injections of anti-VEGF in aging population, especially in persons with diabetes suffering from multimorbidity, causes safety concerns, highlighting a need for evaluating the evidence on nephrotoxicity, based on the currently available findings.

Method A literature search was conducted using PubMed, Web of Science, and Google Scholar databases for studies published up to December 2025. Studies were queried using the following keywords in various combinations: intravitreal pharmacotherapy by anti-VEGF in diabetic retinopathy, systemic adverse effects, nephrotoxicity, bevacizumab, ranibizumab, aflibercept.

Result and conclusion Nephrotoxicity in intraocular pharmacotherapy by anti-VEGF deserves a special attention in people with diabetes taking into account renal vulnerability. Clinical suspicion of renal systemic complications associated with intravitreal injections of anti-VEGF agents should be borne in mind. Early identification and prompt management of such patients can help achieve earlier resolution and positive outcomes.

Keywords: Angiogenesis Inhibitors / therapeutic use, Diabetes Mellitus, Diabetic Retinopathy / drug therapy

Key Points

1. Vascular Endothelial Growth Factor inhibitors (anti-VEGF), such as ranibizumab, aflibercept and bevacizumab delivered intraocularly, reinvigorate ocular pharmacotherapy in general, and diabetic retinopathy (DR) therapy in particular.
2. Currently DR as a most common visually disabling neurovascular complication of diabetes poses a great challenge for healthcare, to overcome which is required to provide comprehensive and evidence-based care for patients in order to prevent discernible vision loss.
3. At present long-term therapy with endless intravitreal injections of anti-VEGF in aging population, especially in persons with diabetes suffering from multimorbidity, causes safety concerns.
4. Nephrotoxicity in intraocular pharmacotherapy by anti-VEGF deserves a special attention in people with diabetes taking into account renal vulnerability.
5. Clinical suspicion of renal systemic complications associated with intravitreal injections of anti-VEGF agents should be borne in mind. Early identification and prompt management of such patients can help achieve earlier resolution and positive outcomes.

Introduction

Vascular Endothelial Growth Factor inhibitors (anti-VEGF), such as ranibizumab, aflibercept and bevacizumab delivered intraocularly, reinvigorate ocular pharmacotherapy in general [1], and diabetic retinopathy (DR) therapy in particular.

Currently DR as a most common visually disabling neurovascular complication of diabetes poses a great challenge for healthcare [2], to overcome which is required to provide comprehensive and evidence-based care for patients in order to prevent discernible vision loss.

Pathogenesis of DR is multifactorial, including vascular permeability, tissue hypoxia and angiogenesis with a cardinal role of VEGF [3] making it an attractive druggable target [4].

Multiple influential trials have evidenced therapeutic potential of such anti-VEGF agents, as ranibizumab, aflibercept, and recently brolicizumab, conbercept in management of DR with or without diabetic macular edema (DME). However, real-word experience underscores a need for in-depth evaluation of undesirable effects accompanying the therapy [5-9]. It is noteworthy that at present long-term therapy with endless intravitreal injections of anti-VEGF in aging population, especially in persons with diabetes suffering from multimorbidity, causes safety concerns.

It is well-known that not only DR, but also Diabetic nephropathy (DN) is a microvascular complication of diabetes, which directly correlates with the severity of retinopathy [10].

Importantly, one of the most common causes of chronic kidney disease (CKD) and renal disorders, manifesting as urinary alterations, proteinuria or kidney failure, is diabetes [11]. Approximately 80% of patients with DR suffer from diabetic renal disease [12].

The review by Hanna and colleagues [13] cover a significant amount of works that evaluate impact of intravitreal injections of anti-VEGF on systemic renal effects, including also patients with DR and DME. The authors highlighted that accumulating evidence has suggested that systemic absorbtion of antiangiogenics could cause or accelerate proteinuria, glomerulonephritis, decreased estimated glomerular filtration rate (eGFR) and concluded that clinicians should be aware of "the potential for adverse renal risks" in such pharmacotherapy.

Further supportive data for this notion were obtained by Fang et al. [14] where it was shown a persistent decline in eGFR in DME patients documented in cohort study within the 2-year of treatment. Their results reveal that poor baseline eGFR correlates with a need for renal replacement therapy. Another large cohort study of patients with DR reports kidney malfunction in cases with a baseline eGFR above 30 ml/min/1.73 m^2.

The recent case-control study conducted by Rivero et al. [12] evaluated the effect of anti-VEGF agents on renal function in patients with diabetes and with or without CKD. This study adds more to the body of knowledge about anti-VEGF-related nephrotoxicity highlighting that ophthalmopharmacotherapy by antiangiogenics is a risk factor for CKD and fast development of end-stage kidney disease in patients suffering from CKD.

Recently Cai et al. [15] have evidenced the same risk of kidney failure in bevacizumab, ranibizumab and aflibercept injections respectively. This impact is more prominent in patients with diabetes.

The latest population-based retrospective cohort study was conducted by Lee et al. [16] to assess the risk of adverse renal events of aflibercept comparing to ranibizumab in cases of DME. It was documented the incidence rate of adverse renal events per 1000 person-years equal to 138.7 and 102.2 for aflibercept and ranibizumab, respectively. Researchers have evidenced the significantly increased risk of acute kidney injury and hospitalisation due to renal events in patients treated by aflibercept and concluded that obtained findings "provide a solid foundation for future studies to validate these results further".

In conclusion, nephrotoxicity in intraocular pharmacotherapy by anti-VEGF deserves a special attention in people with diabetes taking into account renal vulnerability. Multidisciplinary approach with pharmacovigilance in antiangiogenic therapy is required. It is advisable that ophthalmologists should collect current medical history, and general practitioners should collect current ocular history. Clinical suspicion of renal systemic complications associated with intravitreal injections of anti-VEGF agents should be borne in mind. Early identification and prompt management of such patients can help achieve earlier resolution and positive outcomes.

Transparency & Ethical requirements

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