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Short Communication

Unlocking A Future of Diabetic Retinopathy Management

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Abstract

Exponentially growing diabetic macular edema (DME) cases due to increased prevalence of diabetes and incidence of diabetic retinopathy (DR), including DME, as the most challenging cause of blindness worldwide, occurring in more than one-third persons with diabetes represent an unresolved medico-social challenge. This obstacle highlights the urgent need for thoughtful interventions. A search for patient- and provider-friendly, financially rewarding pharmacotherapetic options will be extremely attractive.

Keywords: diabetic retinopathy; diabetic macular edema, pharmacotherapy

Introduction

Exponentially growing diabetic macular edema (DME) cases due to increased prevalence of diabetes and incidence of diabetic retinopathy (DR), including DME, as the most challenging cause of blindness worldwide, occurring in more than one-third persons with diabetes represent an unresolved medico-social challenge [1]. This obstacle highlights the urgent need for thoughtful interventions.

DR is classified as Mild Non-Proliferative DR (Mild NPDR), Moderate Non-Proliferate DR (Moderate NPDR), Severe Non-Proliferate DR (Severe NPDR), Proliferative DR (PDR). Any type of DR could be accompanied by DME. Sight-threatening DR was defined as Severe NPDR or higher severity with/without DME. Importantly**,** the latest findings suggest that DME is highly associated with advanced levels of DR, especially proliferative DR [2].

Despite significant advancements in intraocular antiangiogenic therapy of retinal disorders, including DR, half of patients with DME are not responsive, signaling an unmet need even in developed countries [3]. There is still discrepancy between clinical guidelines and routine practice in DME cases [4] and unresolved long-term safety concerns, such as cardiovascular, neurological, nephrological [5] . The last one is more obvious in patients with diabetes and renal vulnerability [6]. Besides, validated algorithm of invasive therapy by vascular endothelial growth factor (VEGF) inhibitors will be chosen for personalized therapy. Healthcare system faces a challenge, taken into account the need for regular endless intravitreal injections by expensive drugs in elderly population accompanied by caregivers, representing an economic burden [7]. With this in mind, it should be considered, that a search for patient- and provider-friendly, financially rewarding pharmacotherapetic options will be extremely attractive. It must be taken into consideration that pathogenesis of DR and DME is multifactorial, representing a cascade of biochemical events starting from neurodegeneration followed by microvascular dysfunction, inflammation,

oxidative stress, and angiogenesis [1]. Recent studies have implicated neurovascular unit (NVU) formed by different neuron cells (horizontal cells, bipolar cells ganglion cells, amacrine cells), glial cells (microglia, astrocytes, Müller cells) and vascular cells (pericytes, endothelial cells) in pathophysiology of DR, suggesting that the cardinal position belongs to primary neurodegeneration manifesting before microvascular abnormalities. VEGF is also involved in the pathogenesis of DR with or without DME as a key regulator of angiogenesis and vascular permeability [8], but it is not a single druggable target. From this point of view research conducted by Pereira et al. [9] deserves special attention, who report for the first randomized, double-blind, placebo-controlled clinical trial upon oral lamivudine in DME. The trial was supported by grants from the National Institutes of Health's National Eye Institute and National Institute on Aging. Lamivudine, initially indicated for HIV, has gone beyond its original purpose, and shown promise in DME.

Twenty-four eligible patients with center-involved DME (CI-DME) were randomly assigned to receive either 150 mg lamivudine orally or placebo twice daily for 8 weeks. At week 4 additional intravitreal injection of vascular endothelial growth factor (VEGF) inhibitor bevacizumab (1.25 mg) was done on all patients. The participants who received lamivudine showed significant vision amelioration in those first 4 weeks before their first eye injections. These patients' reading ability on an eye chart improved by 9.8 letters at 4 weeks. At the same time the patients receiving placebo have shown decreased reading ability by 1.8 letters. Besides, a month later after receiving bevacizumab injections, lamivudine recipients improved by 16.9 letters, with the placebo group increasing by 5.3. Lamivudine blocks the activity of inflammasomes implicated in genesis of DME, and at the same time has an additive effect to anti-VEGF, as was shown in the trial. These findings highlight a good therapeutic potential of lamivudine in combination therapy.

This study emphasizes the need for larger double-blind, placebo-controlled clinical trial with longer follow-up to reconfirm the primary results [9]. These efforts are essential for affordable and a life-changing patients and the healthcare-transforming oral treatment of DME.

Hopefully that promising results of pharmacotherapy by oral lamivudine in DME will open a new avenue in thoughtful management of DR.

Conflict of interest: The author declares that there is no conflict of interest.

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