Contents available at ScienceDirect

Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres

International Diabetes Federation

Review

Considerations for management of patients with diabetic macular edema: Optimizing treatment outcomes and minimizing safety concerns through interdisciplinary collaboration

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ARTICLE INFO

Article history:
Received 13 November 2016
Accepted 20 January 2017
Available online 29 January 2017

Keywords:
Diabetic macular edema
Diabetes
Anti-VEGF
Safety
Multidisciplinary teams

ABSTRACT

Diabetes is a growing worldwide epidemic and a leading cause of blindness in working-age people around the world. Diabetic retinopathy (DR) and diabetic macular edema (DME) are common causes of visual impairment in people with diabetes and often indicate the presence of diabetes-associated preclinical micro- and macrovascular complications. As such, patients with DR and DME often display complex, highly comorbid profiles. Several treatments are currently available for the treatment of DME, including anti-vascular endothelial growth factor (VEGF) agents, which are administered via intravitreal injection. While the safety profiles of approved ocular anti-VEGF therapies have been reassuring, the high-risk nature of the DME patient population means that treatment must be carefully considered and a holistic approach to disease management should be taken. This requires multidisciplinary, collaborative care involving all relevant specialties to ensure that patients not only receive prompt treatment for DME but also appropriate consideration is taken of any systemic comorbidities to evaluate and minimize potentially serious safety issues.

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http://dx.doi.org/10.1016/j.diabres.2017.01.013
0168-8227/

1. Introduction

Diabetes is one of the leading causes of premature blindness in the world [1–3]. A key contributing factor to this is inadequate glycemic control [4,5]; despite the advent of multiple new agents to treat hyperglycemia, with lower risk of weight gain and hypoglycemia than previous treatments, many people with diabetes are not meeting their glycemic targets [6,7]. This increases the risk of developing serious comorbidities, such as cardiovascular disease, stroke, nephropathy, and neuropathy [2,8,9]. However, the comorbidity most feared by people with diabetes is diabetic retinopathy (DR) [10,11]. This is with good reason; not only can untreated DR progress to diabetic macular edema (DME), one of the most common causes of visual impairment in people with diabetes [12,13], but it often heralds the presence of preclinical micro- and macrovascular complications [4,14–16]. Indeed, the presence of DME is strongly predictive of cardiovascular disease and stroke [17]. Among individuals with diabetes, vision loss is one of the most feared complications [10,11]. Vision is vital for people with diabetes to retain their independence and manage their disease by being able to see well enough to prepare insulin for injection, check blood sugar levels, and take medications [18].

People with diabetes are often primarily under the care of their primary care physician and/or diabetologist [19,20]. Separately, patients may have their disease monitored at retinal photography clinics or by other specialists [20], such as nephrologists or podiatrists. The primary care physician is central in coordinating this care, and in terms of eye care, is responsible for ensuring screening checks and prompt referral to an ophthalmologist, if indicated [21]. However, a recent review by Seidu et al. concluded that, when implementing diabetes care programs, stand-alone interventions, such as primary care physician or nurse education alone, should be avoided [22]. As well as being expensive to deliver, the outcomes were found to be less effective in improving glycemic control than implementation of multifaceted professional interventions on multidisciplinary teams [22]. Continuous quality improvement programs have been essential for ensuring people with diabetes receive adequate and timely care, including the detection of previously undiagnosed comorbidities and complications [23]. Management of risk factors for DR and DME can also help to reduce the risk for other comorbidities associated with diabetes [5,24]. Furthermore, effective treatments for DME that can attenuate and even reverse progression of the disease process are now available [25–28].

2. Pathogenesis of DME

The pathogenesis of DME is multifaceted, complex and not yet fully elucidated [29]. Nevertheless, sustained hyperglycemia and subsequent damage to the microvasculature and breakdown of the blood–retina barrier are thought to be key processes in the development of the disease [29].

Chronic hyperglycemia is thought to promote DME development through oxidative damage, protein kinase C activation and the release of advanced glycation end products [29]. Downstream of these changes, vasoconstriction can lead to altered blood flow to the retina and hypoxia [29]. As a compensatory mechanism, expression of vascular endothelial growth factor (VEGF) is upregulated, contributing to disruption of the blood–retinal barrier by increasing vascular permeability [29]. An accumulation of fluid within the layers of the macular (macular edema) subsequently results from the increased, abnormal flow of fluid into the neurosensory retina [29].

3. Clinical features of DME

Clinical features frequently observed in DME include retinal thickening, cystoid macular edema, serous retinal detachment, vitreomacular traction, and hard exudates [29]. The term ‘clinically significant macular edema’ (CSME) is used in cases where retinal thickening is present at or within 500 μm of the center of the macula or is of at least 1 disk area in size and within 1 disk diameter of the center of the macula, and/or hard exudates are present within 500 μm of the center of the macula with adjacent retinal thickening [29,30]. It is the presence of these features that can cause gradual reduction in visual acuity (VA) [31,32]. CSME is further classified as focal and diffuse DME, based on observations made during clinical investigation [29].