Dear Editor,

We read with great interest the article by Dutra Medeiros et al. [1] entitled ‘Dexamethasone intravitreal implant for treatment of patients with persistent diabetic macular edema’ published in the March 2014 issue of Ophthalmologica. The authors shared their experience on intravitreal dexamethasone implantation for the treatment of patients with persistent diabetic macular edema (DME). Although there was no clear consensus about the optimal treatment of those patients, we have some important concerns and believe that some key aspects should be emphasized.

First, in the study by Dutra Medeiros et al. [1], there was an incomplete responsiveness and recurrence of macular edema (ME) at 3 months [foveal thickness (FT) >300 μm]; therefore, these patients might need additional treatments. However, the authors preferred to observe them in spite of any intervention. Consequently, the patients with FT >300 μm were left undertreated 3 months after implantation. Besides patient observation, repeated injections can be administered from 3 to 6 months depending on the patients’ individual clinical course.

Second, the patients were followed up only at 3 and 6 months. We believe that this time period is too long. An increase in FT might be seen in some eyes between the third and sixth month, and some eyes might need retreatment before the sixth month. As a result, the evaluation for retreatment should occur <6 months.

Currently, there are no established protocols for the retreatment of ME in DME. In addition, present Ozurdex studies have not directly addressed the question of the optimum retreatment interval in DME [2]. Although DME patients were not included, some recent studies evaluated the role of retreatment with Ozurdex in branch retinal vein occlusion [3, 4]. In the study by Coscas et al. [4], the decision to retreatment was reported to be based on both functional and morphologic criteria, and the authors suggested that retreatment should be considered when visual acuity (VA) deteriorates or if persistent or recurrent ME is documented by optical coherence tomography (OCT).

In the light of those data, the time course and the magnitude of the response to Ozurdex treatment suggest that some eyes are undertreated and that physicians may want to evaluate their patients for retreatment before 6 months. Today, in our clinical practice, many patients are being retreated before 6 months depending on their individual clinical course.

In conclusion, while the findings by Dutra Medeiros et al. [1] are important, some key points should also be emphasized. A complete examination including VA and OCT imaging should be performed 3 months after an Ozurdex injection. According to the findings of the examination, other medical and/or laser treatments should be performed if ME is still present or if VA has decreased. With this strategy, repeated injections can be administered from 3 to 6 months depending on the patients’ individual clinical course.

References
Dear Editor,

We appreciate the comments made by Arıkan Yorgun and Toklu regarding our article [1]. We agree with the authors that there was a partial responsiveness as well as recurrence of macular edema (ME) after 3 months in 32 patients [foveal thickness (FT) >300 μm, and in 18 patients, FT was >350 μm]. In fact, these patients may require additional treatments, depending on other variables such as visual acuity (VA) and effective metabolic control.

Similarly, we should take into account the baseline FT values and the clinical features of the patients included (all patients with refractory ME and a mean FT value of 543 at baseline which decreased to 341 μm after 3 months). On the other hand, we achieved a significant functional improvement over this period. In fact, the BCVA data improved to 0.52 and 0.44 logMAR after 1 and 3 months, respectively, from the baseline value of 0.66 logMAR.

Currently, information regarding the response to multiple treatments, the suitable retreatment interval and long-term follow-up is lacking concerning diabetic ME (DME). In fact, almost all published studies on Ozurdex focused on its short-term efficacy and safety, conducting a follow-up for 6 or 12 months only. Two studies carried out by Coscas et al. [2] and Moisseiev et al. [3] evaluated the role of retreatment with Ozurdex in branch retinal vein occlusion, as Arıkan Yorgun and Toklu correctly mentioned.

Similarly, from a clinical point of view, the cutoff to retreat DME should be based on both functional (VA) and morphologic (optical coherence tomography, OCT) criteria. In line, the suggested retreatment algorithm should be considered when VA deteriorates or if persistent ME is documented by OCT.

Given the wide therapeutic armamentarium available to approach DME, it can be difficult to individualize treatment options, especially when attempting to minimize costs and simplify retreatment cycles (the number of injections) concerning a disease which is chronic and recurrent. Concerning pharmacokinetics, the dexamethasone implant features a bimodal profile, which has a rapid and incise effect on the macula for about 10 weeks followed by a sustained modest effect up to week 26. The optimal retreatment time period is expected to last from week 16 until week 30.

According to our clinical experience, which includes one of the largest series of patients treated with Ozurdex in Europe, repeated Ozurdex injections should be performed with FT ≥300 μm or evidence of residual edema on OCT, seen as intraretinal cysts or regions of retinal thickening within or outside the central subfield combined with a VA impairment.

The imperative of regular assessments and the objective analysis of the therapy progress provide a basis for clinical decision support. On that basis, any further reinjection as well as other medical and laser-boosting treatment can be specifically tailored according to the patient demands.

Furthermore, clinical trials such as the MEAD study [4] may just partially answer this issue, since all patients who met retreatment eligibility criteria could be retreated only every 6 months.

Nonetheless, the time course and magnitude of the response to Ozurdex suggest that some eyes are undertreated and that physicians should evaluate their patients for retreatment earlier (before 6 months) than the current major studies indicate.

Our clinical practice documents several cases that have been tailored to a reinjection procedure after 6 months, according to the patients’ unique clinical course. Despite this, one should emphasize that indications and protocols for re-injections have not yet been accomplished. Hence, it is crucial to achieve a broad consensus regarding this matter.

Moreover, large-scale, randomized, controlled trials addressing and comparing the long-term safety and efficacy of Ozurdex with other treatment modalities are also required to better define accurate therapeutic algorithms [5]. Such treatment options will play an important role in the complex management of DME.

References


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