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Editorial

The Dilemma of Difference Between Randomized Control Trials and Real-Life Practice in the Treatment of Retinal Diseases with Intravitreal anti-VEGF Agents

Abdullah Ozkaya, Muhittin Taskapili

University of Health Sciences Beyoglu Eye Training and Research Hospital, Istanbul, Turkey

In recent years, intravitreal anti-vascular endothelial growth factor (VEGF) agents have become the most important adjuncts to the treatment of retinal diseases, such as neovascular age-related macular degeneration (nAMD), diabetic macular edema (DME), and macular edema secondary to retinal vein occlusions (RVO) (1–5).

Pegaptanib was the first intravitreal anti-VEGF agent introduced for the treatment of nAMD, and was followed by bevacizumab, ranibizumab, and aflibercept (1). Previous treatment options were laser photocoagulation, several surgical techniques, and photodynamic therapy, none of which was able to improve vision (1). In the anti-VEGF era, we are now able to achieve significant visual improvement in up to 40% of treated patients (1).

The first treatment regimen used in a randomized controlled study was fixed monthly treatment with ranibizumab, which was quite easy to adapt (1). However, patients were required to present every month for 12 injections a year, which was quite a difficult task. Then, various, more flexible treatment regimens, such as pro re nata and treat and extend, were introduced in order to reduce number of visits and/or injections (1, 5). These treatment regimens were found to be as effective as monthly treatment regimens in prospective studies, with mean number of 7–9 injections (1). Pro re nata regimen quickly gained acceptance in Europe and in Turkey (4). We were able to call our patients for monthly visits and check for activity criteria of decrease in visual acuity, new hemorrhage, persistence of sub/intraretinal fluid etc., and when 1 or more activity criteria were present, injection was administered. However, it was realized that real-life experience was not similar to facts presented in prospective studies (4). Monthly visits were not always observed and injection numbers were dramatically lower. Some precautions were taken to overcome this issue: patients were monitored more closely, and injection schedules were reorganized. We tried to adapt, and implemented some optimizations for our medical retina patients in the retina clinic. In 2013, follow-up and intravitreal treatment procedures for patients who were admitted for the first time were delayed. It took 30 to 50 days before performing first injection and 100 to 150 days for third injection of loading phase. Medical retina patients were being scheduled for retina clinic from general outpatient clinic in 1 to 15 days, then scheduled for fluorescein angiography (FA) evaluation in 15 to 20 days, and finally scheduled for first injection in another 15 to 30 days. Patients were given appointment date for as much as 40 days later due to high clinical admittance. As a result, patient management process was slower than expected and all of the follow-up visits and injections were delayed. Process was then altered such that patients referred from outpatient clinic were seen and evaluated, including FA, on same day in the retina clinic and received first intravitreal injection in maximum of 7 to 21 days, and given an appointment within 28±7

Address for correspondence: Abdullah Ozkaya, MD. Beyoglu Goz Egitim ve Arastirma Hastanesi, Bereketzade Cami Sokak, 34421 Beyoglu, Istanbul, Turkey
Phone: +90 212 251 59 00 **E-mail:** abdozkaya@gmail.com
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day period. These changes allowed us to increase first year ranibizumab injection number in DME patients from 3.1 (in 2013) to 4.6 (in 2015).

In conclusion, it is difficult to follow flexible anti-VEGF treatment regimens for retinal diseases in real life. It is useful to monitor clinical data periodically and assess clinic visit and injection data. This will help determine and improve treatment efficacy of our clinics accordingly.

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