

Managements for Corneal Neovascularization

To the Editor:

I appreciate Dr. Papathanassiou and colleagues for their meta-analysis on the treatment of corneal neovascularization (CNV).¹ However, there are some points that should be mentioned:

In the title of the manuscript, it is more prudent to change “treatment” to its more logic alternative “management” because, in none of the articles mentioned, was the CNV either “cured” or “treated”; however, its size was decreased. Hence, the term “management” seems to be more appropriate.

The 7 eligible human studies that were mentioned showed the quantitative measurement of the neovascular area and excluded 4 articles that only showed slit-lamp photographs or graphs without values and concluded that both topical and subconjunctival bevacizumab could achieve a significant reduction in the area of the CNV. They claimed that their meta-analysis provided an evidential basis for the new therapeutic concept of treating CNV with antiangiogenic therapy; however, it seems that they partially overlooked the intrastromal injection of bevacizumab as a novel safe and effective modality for the management of CNV^{2,3} in their conclusion, and merely mentioned it as an alternative, perhaps unimportant modality, in the “Discussion.”

We also used to employ subconjunctival injections of bevacizumab; however, because of frequent recurrences of CNV with the application of this technique, we started deep intrastromal injection by making a small deep pass through the vascularized site without any subconjunctival injection. In this method, a 2.5 mg/0.1 mL of bevacizumab is injected deep into the stroma until stromal whitening was visible in the paracentral area of 2 adjacent quadrants of the cornea.

The deeper the intrastromal injection is, the more delayed is the clearance of the drug and the lesser the need for recurrent injections. This will exempt us from subconjunctival administration, which has a more limited half-life. Also, there is no need for postoperative antibiotics to be given because bevacizumab is injected in a sterile condition² (see Video, Supplemental Digital Content 1, <http://links.lww.com/ICO/A12>).

Later on, I performed this technique for a considerable number of cases with CNV, and a great improvement occurred after administering a single injection in miscellaneous causes of CNV such as traumatic, postinfectious (mostly herpetic necrotizing stromal keratitis), autoimmune (graft-versus-host disease), and postanterior lamellar keratoplasty (CNV in the donor–recipient interface).³

They also mentioned that anti-vascular endothelial growth factor (VEGF) therapy is more effective in active rather than in stable CNV and small-sized vessels that had developed, and it occludes new or fresh blood vessels rather than old or stabilized vessels.^{4,5} However, in our practice, the intrastromal route of administration seems to be more effective even in cases of long-lasting stable or recurrent forms of CNV in the context of inflammatory and autoimmune pathologies.^{2,3}

Considering the high cost of administering routine anti-VEGF monoclonal antibodies, such as bevacizumab, and their limited effect on old or stabilized vessels, perhaps because of their limited inhibitory effect on the VEGF-1 receptor, we have started a new era of research on the nanodrug delivery of new anti-VEGF modalities. We hope that the topical route of drug delivery in the form of nanoparticles through the ocular barriers may exempt us from administering intrastromal and intravitreal injections in patients with corneal and choroidal NV, respectively.

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appear in the printed text and are provided in the HTML and PDF versions of this article on the journal’s Web site (www.corneajrnl.com).

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Reply:

We thank Riccardo Vinciguerra, MD, for his comments. We agree with him that corneal cross-linking (CXL) should not be the first and/or only treatment of *Acanthamoeba* keratitis. In our article, we evaluated the efficacy of corneal CXL (riboflavin/ultraviolet-A) as a simple therapy for *Acanthamoeba* keratitis in rabbits. The CXL treatment of *Acanthamoeba* keratitis was not effective in decreasing the intensity and severity of infection in rabbits. We did not perform this in humans. In our article, we wrote, “The present study has some limitations. The concentration of organisms we used appears to be greater than what one would normally find in humans with *Acanthamoeba* keratitis. Perhaps the result of CXL treatment would be different if tested on the usual concentration of organisms. There are some anecdotal case reports of successful treatment of *Acanthamoeba* keratitis by corneal CXL.” For this reason, in