# PROPOSED STRATEGIES FOR INTRAVITREAL INJECTIONS DURING THE COVID-19 PANDEMIC



















Adjusting protocols for a new era in medicine.

BY ASHISH SHARMA, MD; NILESH KUMAR, MD; NIKULAA PARACHURI, MD; ROHINI SHARMA, MDS; BARBARA PAROLINI, MD; SENGUL OZDEK, MD, FEBO; BARUCH D. KUPPERMANN, MD, PHD; FRANCESCO BANDELLO, MD, FEBO; AND ANAT LOEWENSTEIN, MD, MHA

ost of the medical world (except for emergency medicine) has been shuttered during the COVID-19 pandemic, and cases continue to rise. It is expected that this situation may last for many more months until researchers find solutions for containing outbreaks and identify effective treatments.

During this period, we need to find the best possible ways to treat our patients who are at risk of vision loss if they forgo intravitreal injections. Reduction or elimination of anti-VEGF therapy could result in permanent visual disability for these patients.

Global ophthalmic authorities have provided general practice safety recommendations. However, we wish to focus on the best possible approaches in performing one of the most common retinal procedures, intravitreal injections, during this challenging time.

#### **NEED FOR INJECTIONS**

The data tell us how important intravitreal injections are to many retina patients. Approximately 2.6 million intravitreal injections of ranibizumab (Lucentis, Genentech) and aflibercept (Eylea, Regeneron) were administered

in 2016.1 That figure does not include the use of bevacizumab (Avastin, Genentech), a common practice in the United States.

The most common indications for intravitreal injections are cystoid macular edema (CME) secondary to retinal vein

### AT A GLANCE

- ▶ Office visits for intravitreal injections during the COVID-19 pandemic may be necessary to preserve vision in some patients.
- ▶ Physicians must rethink pre-pandemic routines and plan accordingly.
- ► The authors offer measures to keep patients, physicians, and staff safe during the pandemic.

## MILLIONS OF RETINA PATIENTS FROM AROUND THE WORLD WHO ARE AT RISK OF VISION LOSS SHOULD NOT BE FORGOTTEN DURING THE COVID-19 PANDEMIC. ADDITIONALLY, THE WELL-BEING OF HEALTH CARE PROVIDERS IS VERY IMPORTANT.

occlusion (RVO), center-involved diabetic macular edema (CI-DME), and neovascular or wet age-related macular degeneration (AMD).

Among these indications, treatment for wet AMD is most urgent. The natural history of RVO includes spontaneous improvement.<sup>2</sup> CI-DME manifests following systemic disease, and factors affecting diabetes may help to control disease activity. Further, given that diabetic patients have a higher risk of mortality from a COVID-19 infection,<sup>3,4</sup> the need to reduce the risk of exposure may outweigh the need to treat visual symptoms. Untreated wet AMD, however, may cause fibrosis or scarring, which can lead to permanent visual loss.

#### REDUCING RISK FOR PROVIDERS

Retina specialists are rightly concerned about the potential transmission of COVID-19 from patients to physicians and staff. A few strategies may help to reduce this risk.

#### **Patient Selection**

Classify patients by diagnosis. For patients who have been receiving injections for CME secondary to RVO or CI-DME, telephone communication about their general visual function may suffice. If they do not complain about a deterioration in vision since their most recent visit, counsel them that missing one or two injections is not likely to cause permanent harm and that deferring follow-up is safe.

The timing of deferred follow-up will vary based on clinical judgment, local transmission data, and recommendations from local authorities. It is important to remember that deferral may be safe for most patients but not for everyone.

Patients with wet AMD who have been undergoing regular injection schedules such as monthly or treat-and-extend (T&E) regimens should visit the hospital and meet the clinician for evaluation and, if needed, injection. Indeed, a visual acuity-based T&E strategy may be the safest regimen during this time. Monocular patients should receive timely injections irrespective of etiology. A telephone conversation to acquire a health update (eg, presence of flu-like symptoms, contact history with COVID-19 patients in the past 2 weeks, and travel history) should occur before confirming the appointment for injection.

#### **Abbreviated Clinical Routine**

When a patient who needs an intravitreal injection visits the clinic, he or she should enter the clinic alone, and the accompanying person should wait outside unless his or her presence is necessary. Patient reception—from entry to meeting the clinicians to exit—should be as quick as possible. To make this happen, regular evaluations with fundus photography, OCT, and formal detailed vision testing should be avoided. The clinician will have a record of such data from the patient's previous visit.

A dilated examination may also be postponed. Clinicians will receive adequate information about changes to a patient's visual function from a quick conversation with the patient. If anatomic data are needed, a quick, undilated central fundus examination and OCT imaging with a no-touch technique can be performed. However, the patient's visual assessment should be the primary driver for scheduling a follow-up visit.

#### Protection

There is a chance of COVID-19 transmission from an asymptomatic patient to a clinician and vice versa. Patients and clinicians need to wear masks. If possible, clinicians should protect their eyes with protective glasses or face shields. Clinicians can follow their regular injection protocol with standard precautions as long as they wear a mask (and, if possible, eye protection). Complete personal protective equipment (PPE) may not be warranted when managing asymptomatic patients.

The use of an N95 mask in lieu of a surgical mask and use of complete PPE should be weighed against PPE availability. In general, complete PPE should be reserved for managing high-risk patients. If available, an N95 mask may be used by the clinician and a surgical mask may be used by the patient.

A slit-lamp shield should be in place for patients who absolutely require slit-lamp examination during injection visits.

If needed, a quick intravitreal injection with minimal staff interaction can be performed in a dedicated outpatient injection room. This is common in Western nations. However, there are many countries, such as India, where

injections are predominantly given in an OR.<sup>5</sup> We encourage instead the use of a sterile injection room. This obviates the need for patients' change of clothing and minimizes exposure of the OR and staff. Disinfecting a dedicated procedure room is easier than disinfecting an OR. Furthermore, bilateral injections on the same day might be of help during this time.

#### **Exit Instructions**

Patients receiving injections should be instructed to report flu-like symptoms that arise in the ensuing 2 to 3 weeks. This helps with contact tracing if the patient tests positive for COVID-19 and reduces the risk of further transmission in the clinic. Patients with flu-like symptoms should undergo a different protocol, which should include extending treatment during recovery.

#### **HELPING PATIENTS IN A TIME OF CRISIS**

Millions of retina patients from around the world who are at risk of vision loss should not be forgotten during the COVID-19 pandemic. Additionally, the well-being of health care providers is very important.

The strategies suggested in this article are not derived from evidence-based medicine. Rather, they synthesize key points recommended by scientific authorities such as the AAO, the American Society of Retina Specialists, the Royal Academy of Ophthalmologists, and the All India Ophthalmology Society. These recommendations are also based on the experience of clinicians who have been involved in the clinical care of retina patients for many years.

The authors wish to emphasize that the COVID-19 pandemic is a dynamic situation. It is impossible to suggest something right for all situations, and best practices may vary with time and according to region, state, and country. It is of utmost importance to follow regular updates from the authorities and to act upon them.

The exceptional situation we face calls on ophthalmologists to rely on clinical judgment rather than first-level evidence. With the suggestions put forth here, we believe that we are equipped to do just that in the COVID-19 era. <sup>10</sup>

1. Bakri SJ, Thorne JE, Ho AC, et al. Safety and efficacy of anti-vascular endothelial growth factor therapies for neovascular age-related macular degeneration. *Ophthalmology*. 2019;126(1):55-63.

2. Hayreh SS. Retinal vein occlusion. Indian J Ophthalmol. 1994;42(3):109-132.

- 3. CÓVID-19 Surveillance Group. Characteristics of COVID-19 patients dying in Italy: report based on available data on March 20th, 2020. Rome, Italy: Instituto Superiore Di Sanita. March 20, 2020. https://www.epicentro.iss.it/coronavirus/bollettino/Report-COVID-2019\_20\_marzo\_eng.pdf.
- 4. Guan W, Ni Z, Hu Y, et al; China Medical Treatment Expert Group for Covid-19. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020;382(18):1708-1720.
- Narayanan R. Guidelines for intravitreal injections. The Official Newsletter of Vitreo-Retinal Society—India. 2018;7-10.
  American Academy of Ophthalmology. Recommendations for Urgent and Nonurgent Patient Care. March 18, 2020.
  Updated April 17, 2020. https://www.aao.org/headline/new-recommendations-urgent-nonurgent-patient-care.
- 7. The American Society of Retina Specialists. COVID-19: Updates and Resources. Updated May 6, 2020. https://www.asrs. org/practice/asrs-member-alert-regarding-covid-19-pandemic.
- 8. The Royal College of Ophthalmologists. Wet AMD Patients' Injections and Appointments During Coronavirus Pandemic. March 20, 2020. https://www.rcophth.ac.uk/2020/03/wet-amd-patients-injections-and-appointments-during-coronavirus-pandemic/
- 9. Honavar SG, Sharma N, Sachdev M; Governing Council of the All India Ophthalmological Society. AIOS Operational Guidelines for Ophthalmic Practice During COVID 19 Outbreak. March 28, 2020. https://aios.org/pdf/AIOS-Operational-Guidelines-COVID19.pdf.

10. Parrish RK, Stewart MW, Duncan Powers SL. Ophthalmologists are more than eye doctors—in memoriam Li Wenliang. Am J Ophthalmol. 2020;213:A1-A2.

#### CORRESPONDING AUTHOR ASHISH SHARMA, MD

- Lotus Eye Hospital and Institute, Coimbatore, India
- drashish79@hotmail.com
- Financial disclosure: None

#### FRANCESCO BANDELLO, MD, FEBO

- University Vita-Salute, Scientific Institute San Raffaele, Milan, Italy
- Financial disclosure: None

#### NILESH KUMAR, MD

- Lotus Eye Hospital and Institute, Coimbatore, India
- Financial disclosure: None

#### BARUCH D. KUPPERMANN, MD, PHD

- Gavin Herbert Eye Institute, University of California, Irvine
- bkupper@uci.edu
- Financial disclosure: None

#### ANAT LOEWENSTEIN, MD, MHA

- Professor of Ophthalmology and Deputy Dean of the Medical School at the Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel
- Chairman of the Department of Ophthalmology, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel
- anatlow@tasmc.health.gov.il
- Financial disclosure: None

#### SENGUL OZDEK MD, FEBO

- Professor of Ophthalmology, Gazi University, School of Medicine, Ankara, Turkey
- Financial disclosure: None

#### NIKULAA PARACHURI, MD

- Lotus Eye Hospital and Institute, Coimbatore, India
- Financial disclosure: None

#### BARBARA PAROLINI, MD

- Director, Vitreoretinal Service, Eyecare Clinic, Brescia, Italy
- b.parolini@eyecareclinic.it
- Financial disclosure: None

#### ROHINI SHARMA, MDS

- Department of Healthcare, The TIPS Global Institute, Coimbatore, India
- Financial disclosure: None

