

## OnabotulinumtoxinA Injections for Patients with Chronic Migraine During the COVID-19 Pandemic

Samer Narouze MD PhD\*<sup>1</sup>, Alexander Feoktistov MD PhD<sup>2</sup>

<sup>1</sup> Professor and Chairman, Center for Pain Medicine, Western Reserve Hospital, Cuyahoga Falls, OH

<sup>2</sup> Diamond Headache Clinic, Chicago, IL, USA

**\*Corresponding Author:** Samer Narouze, MD, PhD

**Address:** Professor and Chairman, Center for Pain Medicine, Western Reserve Hospital, 1900 23rd St, Cuyahoga Falls, OH 44223, USA

**Email:** [narouzs@hotmail.com](mailto:narouzs@hotmail.com)

**Twitter:** @NarouzeMD

**Keywords:** COVID-19, OnabotulinumtoxinA, Migraine, Headache, Coronavirus

### Article Information

**DOI:** [10.30756/ahmj.2020.02.06](https://doi.org/10.30756/ahmj.2020.02.06)

**Article Type:** Editorial

**Issue:** 02.06

**Manuscript ID:** 2020013

**Received:** April 22, 2020

**Revised:** April 22, 2020

**Accepted:** April 23, 2020

**Published:** April 28, 2020

**Recommended Citation:** Narouze S, Feoktistov A. OnabotulinumtoxinA Injections for Patients with Chronic Migraine During the COVID-19 Pandemic. *Ann Head Med.* 2020;02:06.

Headaches are among the top prevalent conditions that physicians encounter in their daily practice. Migraine headaches affect nearly 15% of the United States population (approximately 45 million).<sup>1,2</sup> Over 50% of all patients with migraine report significant or severe impairment and disability.<sup>2</sup> Migraine is the leading cause of years lived with disability among patients between ages 15 and 49 years old – the most productive years.<sup>3</sup>

According to the World Health Organization headache report, up to 4% of the world's population experience chronic migraine (headaches occurring on at least 15 days per month with at least 8 of these headaches meeting migraine criteria).<sup>4</sup>

Approximately, 65% of patients with episodic migraine and 75% of patients with chronic migraine have missed family events and activities in the past month due to migraine-related impairment.<sup>5</sup> Migraine also significantly impacts work-related activities. It has been estimated that 11% of patients with chronic migraine have been missing at least 1 day of work per week in the past 2 weeks.<sup>6</sup> Based on migraine attack frequency and related disability,

headache experts suggest offering prophylactic treatment options to patients with four migraine attacks per month or more.<sup>7</sup> Nevertheless, it has been estimated that only 26-29% of patients continue to adhere to their prophylactic treatment regimen at 6 months and only 17-20% continue to use their oral preventive medications at 12 months.<sup>8,9</sup> OnabotulinumtoxinA injection is an established FDA-approved therapy for chronic migraine prevention.

### The COVID Pandemic and OnabotulinumtoxinA Injection

Novel Coronavirus-2019 (COVID-19) infection can cause severe acute respiratory syndrome (SARS-CoV-2). Older patients, as well as patients with significant comorbidities (e.g. immunosuppression, cardiovascular disease, chronic respiratory disease, diabetes, cancer) are at risk to develop serious illness. On March 11, 2020, the WHO declared it a pandemic.<sup>10</sup> Currently, as of April 2020, there have been over 2,300,000 confirmed cases around the globe, including over 150,000 deaths.<sup>11</sup>

The virus is highly contagious as the reproductive number ( $R_0$ ), which represents the number of secondary infections resulting from an infected individual, is reported to be 2.6.<sup>12</sup> Globally, healthcare systems across the world have been faced with unique challenges for controlling the spread of infection. To limit the spread of infection and to preserve limited health care resources, elective surgeries have been canceled or postponed, including pain procedures.<sup>13</sup> This has negatively impacted the care of headache patients with complex needs and lead to the interruption of injection of onabotulinumtoxinA for chronic migraine prevention.

Lack of adequate prophylactic therapy may result in frequent ER visits and hospitalizations. Therefore, stable and effective therapy is warranted to improve patients' quality of life and minimize the utilization of healthcare resources. Although most of the routine visits could be performed using various telemedicine platforms or over the phone, the injections of onabotulinumtoxinA requires in-person procedure visit. OnabotulinumtoxinA injection is an established standard of care prophylactic treatment modality that requires injections to be repeated every 90 days and ideally should not be interrupted.<sup>14,15</sup>

There are special considerations for using onabotulinumtoxinA during COVID-19 pandemic. SARS-CoV-2 presentation varies dramatically, but usually, patients present with fever and cough. There are asymptomatic and there are severe cases. Several cases of new-onset Guillain-Barré syndrome have also been described in patients recently diagnosed with SARS-CoV.<sup>16, 17, 18</sup> Guillain-Barré syndrome is a contraindication for onabotulinumtoxinA injection, and therefore, risks and benefits, and alternative treatment options should be carefully weighed and discussed with the patient.<sup>19, 20, 21</sup>

### **The Challenges in Identifying the Patient's COVID-19 Status**

Experts advocate for screening all surgical patients to determine their COVID-19 status (e.g. COVID-19 positive, suspected positive (under investigation)).<sup>22</sup> However, testing capabilities are not widely

available yet. If the community spread of COVID-19 infection is significant and in the absence of universal testing, all asymptomatic patients should be presumed to be COVID-19 positive.<sup>23</sup> On the other hand, if the community spread is low and a patient is asymptomatic or if tested COVID-19 negative, then the procedure may be performed following usual established guidelines. However; based on recent evidence, The CDC updated their interim guidance on April 12, 2020 This Interim Guidance was updated and archived on April 12, 2020 to reflect new recommendations for community-related exposure to COVID-19, which changed the period of exposure risk from "onset of symptoms" to "48 hours before symptom onset".<sup>24</sup>

Approximately 80% of infected individuals present with no or mild symptoms.<sup>25</sup> Accordingly, clinical screening to identify infected patients is not reliable. This emphasizes the need for universal testing. To complicate the challenging clinical situation even further, there is significant variability in the accuracy of different available diagnostic testing modalities with high false-negative rates.<sup>26</sup> High index of suspicion should be exercised and maintain safety precautions. The infection attack rate is estimated to be 50–80% of the population, so all patients should be presumed to have COVID-19 positive.<sup>27</sup>

### **Personal Protective Equipment (PPE)**

Personal protective equipment is usually classified into three categories: contact precautions, droplet precautions and airborne precautions.<sup>28</sup> Generally, appropriate level of PPE is determined by the medical procedure and the proximity of healthcare provider to the patient.

Botox procedures are not considered aerosol-generating procedure (AGP), and therefore droplets precautions are recommended as a minimum.<sup>29</sup> However, airborne precautions are preferable as the physician is in remarkable proximity to the patient's face (unexpected coughing or sneezing). The patient should wear surgical facemask to restrict droplet spread and prevent transmission of COVID-19.<sup>30</sup>

<b>Procedural Recommendations for OnabotulinumtoxinA Injection During COVID-19</b>	
<b>Risk stratification</b>	<ul style="list-style-type: none"><li>• The risks of exacerbations of migraine headaches and possible ER/hospital admissions should be carefully weighed against continuing onabotulinumtoxinA injections.</li><li>• Switching to other preventive therapies, including calcitonin gene-related peptide (CGRP) modulating drugs, may be discussed with the patient.</li></ul>
<b>COVID-19 infected patients</b>	<ul style="list-style-type: none"><li>• OnabotulinumtoxinA injection should be avoided in symptomatic COVID-19 infected patients.</li></ul>
<b>Guillain–Barré Syndrome</b>	<ul style="list-style-type: none"><li>• All patients with recent febrile symptoms and who have recovered completely (regardless of known COVID-19 status) should be screened for any evidence for Guillain–Barré syndrome or neuromuscular disorders, and, if positive or suspicious, referred to an appropriate specialist, and the procedure should be avoided.</li></ul>
<b>Determining the patient's COVID-19 status</b>	<ul style="list-style-type: none"><li>• Universal testing should be considered.</li><li>• However, due to the current significant testing limitations, all asymptomatic patients should be presumed to be COVID-19 positive.</li></ul>
<b>Procedure room</b>	<ul style="list-style-type: none"><li>• The procedure should be performed in a procedure room.</li><li>• The use of common office areas should be avoided to reduce the risk of cross-infection.</li></ul>
<b>Modifying the environment</b>	<ul style="list-style-type: none"><li>• Educating and training the staff to limit unnecessary staff exposure to the patient.</li><li>• The number of personnel present during the procedure should be kept to the minimum.</li></ul>
<b>Appropriate personal protective equipment (PPE)</b>	<ul style="list-style-type: none"><li>• <u>Droplet precautions</u> are recommended as a minimum. Gloves, face shield or goggles, fluid resistant surgical face mask and gown.</li><li>• <u>Airborne precautions</u> are preferable (close contact with the patient face). Gloves, face shield or goggles, respirator mask (e.g. N95 mask) and gown.</li><li>• The patient should wear surgical facemask.</li></ul>

## Acknowledgement

None

## Disclosures

Dr. Samer Narouze is the current EIC for Annals of Headache Medicine. Dr Dmitri Souza was the acting EIC handling this manuscript.

*Conflicts of interest:* In compliance with the ICMJE uniform disclosure form, all authors declare the

following: *Payment/services info:* All authors have declared that no financial support was received from any organization for the submitted work. *Financial relationships:* All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. *Other relationships:* All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

## References

1. Burch R, Rizzoli P, Loder E. The Prevalence and Impact of Migraine and Severe Headache in the United States: Figures and Trends From Government Health Studies. *Headache*. 2018 Apr;58(4):496-505. [PubMed](#) [CrossRef](#)
2. Lipton RB, Bigal ME, Diamond M, et al. Migraine prevalence, disease burden, and the need for preventive therapy. *Neurology*. 2007 Jan 30;68(5):343-349. [PubMed](#) [CrossRef](#)
3. Vos T, Abajobir AA, Abate KH, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet*. 2017 Sep 16;390(10100):1211-1259. [PubMed](#) [CrossRef](#)
4. World Health Organization. Headache disorders. [who.int/mediacentre/factsheets/fs277/en/](http://who.int/mediacentre/factsheets/fs277/en/)
5. Buse DC, Scher AI, Dodick DW, Reed ML, et al. Impact of Migraine on the Family: Perspectives of People With Migraine and Their Spouse/Domestic Partner in the CaMEO Study. *Mayo Clin Proc*. 2016;91:596-611. [PubMed](#) [CrossRef](#)
6. Stewart WF, Wood GC, Manack A, et al. Employment and work impact of chronic migraine and episodic migraine. *J Occup Environ Med*. 2010 Jan;52(1):8-14. [PubMed](#) [CrossRef](#)
7. The American Headache Society Position Statement On Integrating New Migraine Treatments Into Clinical Practice. *Headache*. 2019;59:1-18. [PubMed](#) [CrossRef](#)
8. Hepp Z, Dodick DW, Varon SF, Chia J, et al. Persistence and switching patterns of oral migraine prophylactic medications among patients with chronic migraine: A retrospective claims analysis. *Cephalalgia*. 2017;37:470-485. [PubMed](#) [CrossRef](#)
9. Hepp Z, Dodick DW, Varon SF, Gillard P, et al. Adherence to oral migraine-preventive medications among patients with chronic migraine. *Cephalalgia*. 2015;35:478-488. [PubMed](#) [CrossRef](#)
10. WHO Director-General's opening remarks at the media briefing on COVID-19. World Health Organization. <https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020>. Published Mar 11, 2020. Accessed Apr 20, 2020.
11. WHO COVID-19 Dashboard. World Health Organization (WHO). <https://covid19.who.int/>. Accessed Apr 20, 2020.
12. Imai N, Cori A, Dorigatti I, et al. Report 3: Transmissibility of 2019-nCoV. *Imperial College London*. Jan 25, 2020. [PDF](#) [CrossRef](#)
13. Shanthanna H, Strand NH, Provenzano DA, et al. Caring for patients with pain during the COVID-19 pandemic: Consensus recommendations from an international expert panel. *Anaesthesia*. 2020 Apr 7. [PubMed](#) [CrossRef](#)
14. Aurora SK, Dodick DW, Turkel CC, et al. OnabotulinumtoxinA for treatment of chronic migraine: Results from the double-blind, randomized, placebo-controlled phase of the PREEMPT 1 trial. *Cephalalgia*. 2010 Jul;30(7):793-803. [PubMed](#) [CrossRef](#)
15. Blumenfeld AM, Stark RJ, Freeman MC, et al. Long-term study of the efficacy and safety of OnabotulinumtoxinA for the prevention of chronic migraine: COMPEL study. *J Headache Pain*. 2018 Feb 5;19(1):13. [PubMed](#) [CrossRef](#)
16. Toscano G, Palmerini F, Ravaglia S, et al. Guillain-Barré Syndrome Associated with SARS-CoV-2. *N Engl J Med*. 2020 Apr 17. [PubMed](#) [CrossRef](#)
17. Helms J, Kremer S, Merdji H, et al. Neurologic Features in Severe SARS-CoV-2 Infection. *N Engl J Med*. 2020 Apr 15. [PubMed](#) [CrossRef](#)
18. Mao L, Jin H, Wang M, et al. Neurologic Manifestations of Hospitalized Patients With Coronavirus Disease 2019 in Wuhan, China. *JAMA Neurol*. 2020 Apr 10. [PubMed](#) [CrossRef](#)
19. Omprakash Hm, Rajendran Sc. Botulinum Toxin Deaths: What is the Fact?. *J Cutan Aesthet Surg*. 2008 Jul;1(2):95-97. [PubMed](#) [CrossRef](#)
20. Nigam PK, Nigam A. Botulinum toxin. *Indian J Dermatol*. 2010;55(1):8-14. [PubMed](#) [CrossRef](#)
21. BOTOX (OnabotulinumtoxinA) for injection, for intramuscular, intradetrusor, or intradermal use. [https://www.accessdata.fda.gov/drugsatfda\\_docs/lab/el/2017/103000s5302lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/lab/el/2017/103000s5302lbl.pdf). Published 1989. Revised Apr 2017. Accessed Apr 21, 2020.
22. Wong J, Goh QY, Tan Z, et al. Preparing for a COVID-19 pandemic: a review of operating room outbreak response measures in a large tertiary hospital in Singapore. *Can J Anaesth*. 2020 Mar 11. [PubMed](#) [CrossRef](#)
23. Landau R, Bernstein K, Mhyre J. Lessons learned from first COVID-19 cases in the United States. *Anesth Analg*. 2020 Mar 31. [PubMed](#) [CrossRef](#)
24. Interim U.S. Guidance for Risk Assessment and Public Health Management of Healthcare Personnel with Potential Exposure in a Healthcare Setting to Patients with Coronavirus Disease 2019 (COVID-19). Centers for Disease Control and Prevention. <https://www.cdc.gov/coronavirus/2019-ncov/hcp/guidance-risk-assessment-hcp.html>. Published Apr 15, 2020. Accessed Apr 21, 2020.
25. The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. The Epidemiological Characteristics of an Outbreak of 2019 Novel Coronavirus Diseases (COVID-19). *Chinese Journal of Epidemiology*. 2020 Feb 17;41(2):145-151. [PubMed](#) [CrossRef](#)

26. Wang W, Xu Y, Gao R, et al. Detection of SARS-CoV-2 in Different Types of Clinical Specimens. *JAMA*. 2020 Mar 11. [PubMed](#) [CrossRef](#)
27. Verity R, Okell LC, Dorigatti I, et al. Estimates of the severity of coronavirus disease 2019: a model-based analysis. *Lancet Infect Dis*. 2020 Mar 30. pii: S1473-3099(20)30243-7. [PubMed](#) [CrossRef](#)
28. Cook TM. Personal protective equipment during the COVID-19 pandemic - a narrative review. *Anaesthesia*. 2020 Apr 4. [PubMed](#) [CrossRef](#)
29. Updated guidance on Personal Protective Equipment (PPE) for clinicians. Association of Anaesthetists (AAGBI). <https://icmanaestheticsacovid-19.org/personal-protective-equipment-ppe-for-clinicians>. Published Apr 11, 2020. Accessed April 21, 2020.
30. Rational use of personal protective equipment for coronavirus disease 2019 (COVID-19). World Health Organization (WHO). [https://apps.who.int/iris/bitstream/handle/10665/331215/WHO-2019-nCov-IPCPPE\\_use-2020.1-eng.pdf](https://apps.who.int/iris/bitstream/handle/10665/331215/WHO-2019-nCov-IPCPPE_use-2020.1-eng.pdf). Published Feb 27, 2020. Accessed Apr 21, 2020.