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Special Article

Migraine Care in the Era of COVID-19: Clinical Pearls and Plea to Insurers

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Objective.—To outline strategies for the treatment of migraine which do not require in-person visits to clinic or the emergency department, and to describe ways that health insurance companies can remove barriers to quality care for migraine.

Background.—COVID-19 is a global pandemic causing widespread infections and death. To control the spread of infection we are called to observe "social distancing" and we have been asked to postpone any procedures which are not essential. Since procedural therapies are a mainstay of headache care, the inability to do procedures could negatively affect our patients with migraine. In this manuscript we review alternative therapies, with particular attention to those which may be contra-indicated in the setting of COVID-19 infection.

Design/Results.—The manuscript reviews the use of telemedicine visits and acute, bridge, and preventive therapies for migraine. We focus on evidence-based treatment where possible, but also describe "real world" strategies which may be tried. In each section we call out areas where changes to rules from commercial health insurance companies would facilitate better migraine care.

Conclusions.—Our common goal as health care providers is to maximize the health and safety of our patients. Successful management of migraine with avoidance of in-person clinic and emergency department visits further benefits the current urgent societal goal of maintaining social distance to contain the COVID-19 pandemic.

Key words: migraine, COVID-19, treatment, telemedicine

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INTRODUCTION

COVID-19 was declared a global pandemic on March 11, 2020 by the World Health Organization. At the time we write this, there have been more than 700,000 confirmed cases and more than 37,000 deaths, with both of those figures predicted to increase exponentially in the coming weeks. In these unprecedented and uncertain times, headache medicine clinicians are working to keep individuals with migraine out of the Emergency Department (ED) and hospital, while also

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foregoing or at least minimizing face-to-face visits and procedural treatments. This is of critical importance not only in protecting the safety of our patients and limiting their exposure to COVID-19, but also as part of the greater efforts to avoid infection of healthcare workers, and to minimize additional demands on an already oversaturated hospital infrastructure.

This manuscript is focused on 2 audiences. First, we seek to outline strategies which may be helpful to primary care clinicians, neurologists, and headache specialists who are trying to provide the best possible care for patients with migraine despite overwhelming constraints. We will review the use of telehealth for patient communication, and review acute and preventive treatment strategies, with attention to concerns specific to COVID-19.

Second, we call upon health insurance providers, both government-funded and commercial, to remove barriers to quality migraine care. Migraine is highly prevalent, and is the second leading cause of years lost to disability worldwide.[1] In the United States chronic migraine disproportionately affects those of low socioeconomic status,[2] who are also bearing the financial brunt of the COVID-related economic crisis. With this in mind, we applaud the efforts of the federal and state governments and many commercial insurance providers who have quickly altered rules and regulations to facilitate the use of telehealth. **In addition, we call upon insurance providers to eliminate prior authorization and step therapy requirements for migraine therapies, so that patients may have access to appropriate treatments in a time-sensitive manner and without undue administrative encumbrances. Further, given that nearly 1/5 of households in the United States reported a layoff or reduction in work hours related to coronavirus by March 14, 2020,[3] it is imperative that insurance providers minimize or eliminate copays for migraine medications. While it may seem unthinkable to ask insurers to pay additional money for these therapies as other health care costs increase, multiple pharmacoeconomic studies have demonstrated that coverage of expensive migraine medications is actually cost-saving, as it decreases disability and reliance on hospital care**.[4-6]

Telehealth Becomes Mainstream.—Telemedicine, which is real time interactive audio and video remote communication between a patient and a provider, has been practiced for over a decade in the United States. Single clinic studies of telemedicine visits for headache care have demonstrated that patients perceive telemedicine as cost-effective and convenient.[7] Compared to traditional in-person headache visits, telemedicine achieves similar satisfaction rates[8] and outcomes,[9] and recent investigations demonstrated non-inferiority in multiple neurological diseases.[10] However, many factors have precluded its widespread use, including large scale verification of clinical efficacy and safety in comparison to live visits,[11] technological capabilities, patient confidentiality/privacy, licensing restrictions and malpractice, reimbursement, and frank inertia. Federal and state governments have not championed this modality, despite ongoing need to care for patients otherwise unable to reach providers' offices.[12]

In the era of COVID-19, telehealth has become an essential modality for most headache specialists, given the need for providers to take significant precautions for both their patients and themselves,

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limiting touch or close contact.[13] Clinicians have had to rapidly learn local and federal laws, regulations, coding, and reimbursement options that may also change by the day. Qualified providers may now bill fee for service Medicare patients using traditional evaluation and management codes for telemedicine visits, regardless if they are in a Health Professional Shortage Area. However, Medicaid and Medicare Advantage patients are excluded from recent emergency declarations. Parity laws also vary per state, which impacts commercial insurance reimbursements.[14] Furthermore, while federal restraints have been waived to allow qualified providers to practice in any state, state laws may nonetheless continue to prohibit aspects of interstate practice, such as restrictions on new patient consultations or prescribing controlled substances. In some circumstances when telemedicine visits are not permitted or feasible, telephone visits can be performed and billed. As these rules are changing rapidly, the American Academy of Neurology has launched a website which assists with practical details for conducting telehealth visits, coding, and state-by-state coverage (https://www.aan.com/telehealth).

Despite the challenges, telemedicine is long overdue as an effective means to help patients receive care.[15] Patients who live remotely, perhaps hundreds of miles from the nearest headache specialist can now have a clinical encounter via a smart phone. Patients no longer have to miss work, drive long distances, spend money on gas, tolls, and parking lots, and wait prolonged periods in a doctor's office to be seen, where they might also be exposed to communicable diseases. We hope that the widespread use of telehealth will be supported even after the COVID-19 pandemic has resolved.

Acute Therapies.—This is a particularly vulnerable time for individuals with migraine and other disabling headache disorders, with many physical and mental stressors, increased anxiety, and changes in daily routine which may serve as triggering factors for worsening headache. As headache has been reported as an early symptom of COVID-19,[16] patients with worsening or new onset severe headache should be reviewed for exposure risk and any other symptoms which may be consistent with COVID-19 infection.

We note that Non-steroidal anti-inflammatory drugs (NSAIDs), triptans, and neuroleptics may be used in combination therapy when needed. Medications within the same drug category should not be combined. Triptans, Dihydroergotamine (DHE) and lasmiditan should not be co-administered within 24 hours.

1. **Acute treatments for migraine:** The American Headache Society Guideline for acute treatment in 2015 described strong evidence of benefit for several NSAIDs, triptans, and anti-emetics in the acute treatment of migraine headaches.[17] While NSAIDs and triptans remain first line, several additional treatments have received Food and Drug Administration (FDA) approval or clearance for acute treatment of migraine since 2015. These are described below:

Gepants are small-molecule calcitonin gene-related peptide (CGRP) receptor antagonists primarily developed for the acute treatment of migraine. While these medications do have evidence of benefit, there have been significant barriers with insurance providers in accessing these medications, with access typically requiring prior authorization and demonstration of failure of alternate agents. Potentially significant drug-drug interactions may exist; patients should be advised to check for any drug interactions with their prescriber and pharmacist.

- Ubrogepant 50 to 100 mg PO as a single dose; may repeat once based on response and tolerability after ≥2 hours.[18]
- Rimegepant 75 mg PO as a single dose; maximum: 75 mg/24 hours.[19]

Lasmiditan has high affinity and selectivity for 5-HT_{1F} receptors and lacks the vasoconstrictor activity inherent with triptans, thereby making lasmiditan a different class of treatment, designated as a "ditan."[20,21] Lasmitidan can cause significant sedation and dizziness, so patients must wait at least 8 hours between dosing and driving. In addition, lasmitidan should be used with caution in patients who have a history of drug abuse, as there is concern that it may have the potential to be abused.

- Lasmiditan 100 mg; maximum: 1 dose in 24 hours.

Neuromodulation devices have been studied as safe and well-tolerated strategies for the acute treatment of migraine. These devices provide electrical stimulation to extracranial sensory afferent fibers above their depolarization thresholds but below the perceived pain threshold, which activates the central descending inhibitory pathways to inhibit pain. These devices typically require patient payment and need to be obtained from the manufacturer directly.[22]

- Remote electrical neuromodulation (REN) device.[23]
- External trigeminal neurostimulation (eTNS) device.[24]
- Single-pulse transcranial magnetic stimulation (sTMS) device.[25]
- External vagal nerve stimulation (VNS) device.[26]

2. **"Bridge" strategies to help break a severe or continuous pain cycle:** In contrast to the relative depth and breadth of evidence for first line acute migraine treatment, very few therapies have been studied as "bridge" strategies for severe headaches that are unusually prolonged. However, in practice it is common for headache clinicians to recommend strategies for patients to treat refractory symptoms before seeking care in the ED or infusion center. Because there is such a paucity of evidence these strategies are rarely described in the literature. However, given the immediate need to support social distancing and keep patients out of the hospital, we feel there is benefit in trying these agents if deemed clinically appropriate, even if the evidence is not fully established.

Non-steroidal anti-inflammatory drugs (NSAIDs) are frequently used as "bridge" strategies by headache providers. NSAIDs inhibit the neuroinflammatory cascade and prostaglandin synthesis, which are implicated in the pathogenesis of a migraine attack. COX1/COX2 inhibition may also inhibit prostaglandin release in nociceptive neurons in the trigeminal nucleus caudalis (TNC) which is involved in central sensitization in migraine.[27]

Contraindications to NSAID use include a history of GI bleeding, other bleeding risks, and renal impairment. In addition, diclofenac should be avoided in patients with heart failure or previous myocardial infarction.[28]

The World Health Organization initially expressed that NSAIDs may exacerbate COVID-19 symptoms, but then retracted their recommendation to avoid NSAIDs due to lack of evidence for this claim.[29] The FDA issued an advisory on March 19, 2020, that it "*is not aware of scientific evidence connecting the use of NSAIDs, like ibuprofen, with worsening COVID-19 symptoms. The agency is investigating this issue further ….*"[30]

Recommendations may change further as our understanding of COVID-19 evolves. Clinicians should consider these differing viewpoints, the most current guidelines and recommendations, and the needs of their individual patient when deciding to use NSAIDs.

Options include:

- Indomethacin 50 mg PO TID × 7 days.
- Ketorolac 10 mg PO TID × 3 days.
- Naproxen 500 mg PO BID × 5-14 days.
- Nabumetone 500 mg PO BID × 7 days.
- Diclofenac 50 mg BID × 3-5 days (*tablet or powder for oral solution*).
- Mefenamic Acid 250 mg PO TID × 3-5 days.

Neuroleptics.—Dopamine and serotonin (5-HT_3) are thought to be implicated in the pathogenesis of migraine. Neuroleptics act as dopamine antagonists and also have substantial anti-cholinergic, anti-serotonergic, anti-histaminergic, and anti-adrenergic effects.[31,32] Some neuroleptics also have a role as anti-emetics. Side effects may include dizziness, somnolence (especially if taken during daytime, so avoid driving after use), and extra-pyramidal symptoms (especially with prolonged and frequent use). Some of these can prolong the QT interval on EKG, so use caution if the patient has known prolonged QT syndrome or if the patient is taking multiple QT prolonging medications.

Options include:

- Prochlorperazine 5-10 mg PO TID or qhs × 3 days.
  - Also available as 25 mg rectal suppository.[33]
- Promethazine 12.5-50 mg PO TID or qhs × 3 days.
  - Also available as a 25 mg rectal suppository.
- Metoclopramide 5-10 mg PO TID or qHS × 3 days.
- Chlorpromazine 25 mg PO TID or qhs × 3 days.

- Olanzapine 5 mg PO qhs OR BID × 3-5 days.
- Quetiapine 25-50 mg qhs × 7 days.

Triptans.—Long-acting triptan medications can be used as bridge therapies, as is often done in the treatment of menstrually related migraine or in the treatment of medication overuse headache.[34-36] We propose a similar strategy can be trialed as a therapeutic option for refractory or persistent migraine.

Options include:

- Frovatriptan 2.5 mg PO BID × 3 days.
- Naratriptan 1 mg or 2.5 mg PO, BID × 3 days.

Anti-epileptics.—The action of anti-epileptic drugs in migraine likely involves several proposed mechanisms including sodium channel blockade and enhancement of GABA activity in the brain, from increased GABA synthesis and decreased GABA degradation.[37]

Options include:

- Valproic Acid 500-1000 mg PO qhs × 5 days OR 250 mg PO TID × 5-7 days. However, given known teratogenicity, valproic acid should not be used in women of childbearing age.

Corticosteroids.—Although recommendations may evolve as more data become available, currently the Centers for Disease Control (CDC) states in the treatment of COVID-19 "*corticosteroids should be avoided, because of the potential for prolonging viral replication as observed in MERS-CoV patients, unless indicated for other reasons.*"[16] As above, for otherwise healthy, immunocompetent individuals without any infectious symptoms or fever and who are not self-monitoring due to possible COVID-19 exposure, a steroid taper may be considered at the clinician's discretion, weighing potential benefits, and risks.

Steroids should be taken in the morning and with food to avoid gastrointestinal upset.

Options include:

- Methylprednisolone (Medrol Dose Pack), with a taper over 6 days.
- Dexamethasone 6 mg × 3 days, with an option to extend as a taper if not sufficient (4 mg × 3 days, then 2 mg × 3 days.
- Prednisone 60 mg × 2 days, 40 mg × 2 days, 20 mg × 2 days.

3. Other symptom-specific therapies:

- Difficulty sleeping
  - Hydroxyzine 25-50 mg PO qhs × 3-5 days.
  - Amitriptyline 25 mg PO qhs × 7-14 days.
- Neck/Muscle pain
  - Tizanidine 4-8 mg PO qhs × 7 days.
- Aura with migraine
  - Magnesium 500 mg BID × 3-5 days.

4. Other acute/bridge medications:

These medications typically require prior authorization and/or may need to be obtained from a special pharmacy.

- Intranasal Lidocaine (4% lidocaine oral solution with nasal atomizer) one spray in each nostril every 4 hours as needed.[38,39]
- Intranasal Dihydroergotamine (DHE) one spray (0.5 mg) in each nostril, repeat in 15 minutes (2 mg); can also be used BID × 3 days as "bridge" strategy.[40,41]
- Intranasal Ketorolac one spray (15.75 mg) in each nostril (total dose: 31.5 mg).[42]

We encourage providers to avoid the use of opioids and butalbital. Headaches treated with opioids have a high recurrence rate after the initial analgesic effect, and opioids may exert a pro-nociceptive state that may prevent the reversal of central sensitization following a migraine attack. Additionally, both of these classes of medication carry a high risk of habituation and dependency, and over time may contribute to medication overuse headache.[43]

Preventive Therapies.—While the injection of onabotulinumtoxinA is an effective treatment for chronic migraine,[44] the procedure can put the patient and the provider at higher risk of COVID-19 given the close contact encounter. We believe that other migraine preventive treatments should be utilized first when possible. Some patients on onabotulinumtoxinA may have been started on it and stable before newer preventive medication

results have been published/approved. Thus, we urge providers to first consult the American Academy of Neurology/American Headache Society Guidelines (last published in 2012[45]; new ones are currently being produced) and to re-evaluate patients' responses to the medications listed in those guidelines. In addition, therapies which have been demonstrated to be beneficial since the development of that guideline include:

- *CGRP and CGRP receptor antagonist monoclonal antibodies (mAbs)*: In the past 2 years, mAbs against CGRP or the CGRP receptor have been FDA approved for preventive treatment of both episodic and chronic migraine – erenumab-aooe,[46-48] galcanezumab-gnlm,[49-51] fremanezumab-vfrm,[52,53] and eptinezumab-jjmr.[54,55] The first 3 are intended for self-injection at home, with detailed instructions available for each product on its website.
- *Angiotensin-converting enzyme (ACE) inhibitors/angiotensin receptor blockers (ARBs)*: Candesartan[56,57] now has evidence of efficacy and good tolerability in migraine prevention,[58,59] and lisinopril[56,60] was considered "possibly effective" in the 2015 guideline. There has been recent concern in the media about the possibility of these medications interfering with the body's response to COVID-19. However, the Heart Failure Society of America (HFSA)/ American Cardiology Association (ACA)/American Heart Association (AHA) issued a statement, "*Angiotensin converting enzyme 2 (ACE2) receptors have been shown to be the entry point into human cells for SARS-CoV-2, the virus that causes COVID-19 … Currently there are no experimental or clinical data demonstrating beneficial or adverse outcomes with background use of ACE inhibitors, ARBs or other Renin-angiotensin-aldosterone system (RAAS) antagonists in COVID-19 or among COVID-19 patients with a history of cardiovascular disease treated with such agents. The HFSA, ACC, and AHA recommend continuation of RAAS antagonists for those patients who are currently prescribed such agents for indications for which these agents are known to be beneficial, such as heart failure, hypertension, or ischemic heart disease. In the event patients with cardiovascular disease are diagnosed with COVID-19, individualized treatment decisions should be made according to each patient's hemodynamic status and clinical presentation*.[61]" For patients in need of a new preventive therapy, the potential for benefit with an ACE/ARB must be weighed against the theoretical increased risk of infection.
- *Melatonin*: There are also studies indicating melatonin is useful for migraine prevention with few side effects.[62,63]
- *Zonisamide*: Has been found to be effective in cases where people have not had as positive a response to topiramate and/or had side effects to topiramate.[64-66]

First and foremost, migraine preventive prior authorization restrictions need to be lifted for evidence-based, FDA-approved therapies; patients need to be able to access these medications quickly and easily. Patients should not be required to fail older medications (which often have higher rates of side effects and lower evidence for benefit, or even have evidence of ineffectiveness for benefit for chronic migraine[67]) or onabotulinumtoxinA injections (which are not feasible right now) in order to qualify for the anti-CGRP/CGRP receptor mAbs. Similarly, in order to permit the transition of patients from onabotulinumtoxinA to anti-CGRP mAbs, insurers should remove the prohibition against simultaneous coverage of these drug classes.

In addition, insurers should loosen restrictions on the use of acute and preventive medication for adolescents (add reference to PMID: 30324723). The biology of migraine is very similar in adolescents and adults, so we anticipate that the trials of novel therapies will likely have similarly positive results in adolescents. However, ongoing trials of new migraine therapies have been paused in order to prevent spread of COVID-19. During this time when we can not enroll patients into trials, it would be better to use these medications off label to prevent ED visits and hospitalizations.

Medical office staff have an increasing number of responsibilities during the pandemic and many need to be repurposed to other duties. Many are also unable to work due to sickness, childcare issues, etc Thus, we call on the insurance companies to lift restrictions on accessing migraine medications.

CONCLUSIONS

The COVID-19 pandemic highlights significant weaknesses in our health care system and has left clinicians and patients scrambling to find solutions to maintain health that for many may have taken years to achieve. Migraine can worsen during times of stress, so having available options that bypass insurance hurdles and can be administered at home without patient training is imperative. Telehealth provides an important opportunity to continue to care for our vulnerable population and help avoid emergency room and urgent care visits that put patients at risk and burden the overwhelmed healthcare system. The largest at-risk group of established migraine patients are those that depend on procedures to allow them to remain functional and out of the emergency room. The shortage of personal protective equipment has caused an unfortunate break in care for many of these patients. During the current pandemic we, headache specialists, make a plea to insurers to lift cumbersome restrictions to allow patients greater availability of evidence-based treatment options to reduce the burden of their disease. One example would be to allow patients who were being treated with onabotulinumtoxinA to bridge with an anti-CGRP/CGRP-receptor mAb while their procedures may be postponed. Our common goal as health care providers is to maintain the health of our patients while continuing to keep ourselves, our staff, and our families safe. Successful management of migraine with avoidance of in-person patient clinic visits further benefits the current urgent overall societal goal of maintaining social distance to contain the pandemic.

Given that the practice of medicine is changing rapidly during this pandemic, these recommendations may evolve over time, and we will do our best to update the manuscript as the need arises.

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REFERENCES

1. GBD 2016 Headache Collaborators. Global, regional, and national burden of migraine and tension-type headache, 1990-2016: A systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol* 2018;17:954-976.
2. Burch RC, Buse DC, Lipton RB. Migraine: Epidemiology, burden, and comorbidity. *Neurol Clin*. 2019;37:631-649.
3. NewsHour/Marist NP. *Poll Results: Coronavirus* [online]. Available at: http://maristpoll.marist.edu/npr-pbs-newshour-marist-poll-results-coronavirus/#sthash.ANXwf7j1.LqArjlmp.dpbs. Accessed March 25, 2020.
4. Bhambri R, Mardekian J, Liu LZ, Schweizer E, Ramos E. A review of the pharmacoeconomics of eletriptan for the acute treatment of migraine. *Int J Gen Med*. 2015;8:27-36.
5. McCormack PL, Foster RH. Rizatriptan: A pharmacoeconomic review of its use in the acute treatment of migraine. *Pharmacoeconomics*. 2005;23:1283-1298.
6. Sussman M, Benner J, Neumann P, Menzin J. Cost-effectiveness analysis of erenumab for the preventive treatment of episodic and chronic migraine: Results from the US societal and payer perspectives. *Cephalalgia*. 2018;38:1644-1657.
7. Qubty W, Patniyot I, Gelfand A. Telemedicine in a pediatric headache clinic: A prospective survey. *Neurology*. 2018;90:e1702-e1705.
8. Muller KI, Alstadhaug KB, Bekkelund SI. Telemedicine in the management of non-acute headaches: A prospective, open-labelled non-inferiority, randomised clinical trial. *Cephalalgia*. 2017;37:855-863.
9. Muller KI, Alstadhaug KB, Bekkelund SI. A randomized trial of telemedicine efficacy and safety for non-acute headaches. *Neurology*. 2017;89:153-162.
10. Hatcher-Martin JM, Adams JL, Anderson ER, et al. Telemedicine in neurology: Telemedicine Work Group of the American Academy of Neurology update. *Neurology*. 2020;94:30-38.
11. Wootton R. Twenty years of telemedicine in chronic disease management–an evidence synthesis. *J Telemed Telecare*. 2012;18:211-220.
12. Hollander JE, Carr BG. Virtually perfect? Telemedicine for Covid-19. *N Engl J Med*. 2020. doi: 10.1056/NEJMp2003539
13. *Interim US Guidance for Risk Assessment and Public Health Management of Persons with Potential Coronavirus Disease 2019 (COVID-19) Exposures:*

Geographic Risk and Contacts of Laboratory-confirmed Cases [online]. Available at: https://www.cdc.gov/coronavirus/2019-ncov/php/risk-assessment.html. Accessed March 21, 2020.
14. Lacktman NM, Acosta JN, Levine SJ. *50-State Survey of Telehealth Commercial Payer Statutes* [online]. Available at: https://www.foley.com/-/media/files/insights/health-care-law-today/19mc21486-50state-survey-of-telehealth-commercial.pdf.
15. Duffy S, Lee TH. In-person health care as option B. *N Engl J Med*. 2018;378:104-106.
16. *Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease (COVID-19)* [online]. Available at: https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html. Accessed March 20, 2020.
17. Marmura MJ, Silberstein SD, Schwedt TJ. The acute treatment of migraine in adults: The American Headache Society evidence assessment of migraine pharmacotherapies. *Headache*. 2015;55:3-20.
18. Dodick DW, Lipton RB, Ailani J, et al. Ubrogepant for the treatment of migraine. *N Engl J Med*. 2019;381:2230-2241.
19. Lipton RB, Croop R, Stock EG, et al. Rimegepant, an oral calcitonin gene-related peptide receptor antagonist, for migraine. *N Engl J Med*. 2019;381:142-149.
20. Goadsby PJ, Wietecha LA, Dennehy EB, et al. Phase 3 randomized, placebo-controlled, double-blind study of lasmiditan for acute treatment of migraine. *Brain*. 2019;142:1894-1904.
21. Kuca B, Silberstein SD, Wietecha L, Berg PH, Dozier G, Lipton RB. Lasmiditan is an effective acute treatment for migraine: A phase 3 randomized study. *Neurology*. 2018;91:e2222-e2232.
22. Halker Singh RB, Ailani J, Robbins MS. Neuromodulation for the acute and preventive therapy of migraine and cluster headache. *Headache*. 2019;59(Suppl. 2):33-49.
23. Yarnitsky D, Dodick DW, Grosberg BM, et al. Remote electrical neuromodulation (REN) relieves acute migraine: A randomized, double-blind, placebo- controlled, multicenter trial. *Headache*. 2019;59:1240-1252.
24. Chou DE, Shnayderman Yugrakh M, Winegarner D, Rowe V, Kuruvilla D, Schoenen J. Acute migraine therapy with external trigeminal neurostimulation (ACME): A randomized controlled trial. *Cephalalgia*. 2019;39:3-14.
25. Lipton RB, Dodick DW, Silberstein SD, et al. Single-pulse transcranial magnetic stimulation for acute treatment of migraine with aura: A randomised, double-blind, parallel-group, sham-controlled trial. *Lancet Neurol*. 2010;9:373-380.
26. Tassorelli C, Grazzi L, de Tommaso M, et al. Noninvasive vagus nerve stimulation as acute therapy for migraine: The randomized PRESTO study. *Neurology*. 2018;91:e364-e373.
27. Watkins LR, Milligan ED, Maier SF. Glial activation: A driving force for pathological pain. *Trends Neurosci*. 2001;24:450-455.
28. Schmidt M, Sorensen HT, Pedersen L. Diclofenac use and cardiovascular risks: Series of nationwide cohort studies. *BMJ (Clinical research ed)*. 2018;362:k3426.
29. World Health Organization. *Could Ibuprofen Worsen Disease for People With COVID-19?* Geneva: World Health Organization; 2020.
30. Food and Drug Administration. *FDA Advises Patients on Use of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) for COVID-19* [online]. Available at: https://www.fda.gov/drugs/drug-safety-and-availability/fda-advises-patients-use-non-steroidal-anti-inflammatory-drugs-nsaids-covid-19. Accessed March 19, 2020.
31. Kelley NE, Tepper DE. Rescue therapy for acute migraine, part 2: Neuroleptics, antihistamines, and others. *Headache*. 2012;52:292-306.
32. Bigal ME, Bordini CA, Speciali JG. Intravenous chlorpromazine in the emergency department treatment of migraines: A randomized controlled trial. *J Emerg Med*. 2002;23:141-148.
33. Jones EB, Gonzalez ER, Boggs JG, Grillo JA, Elswick RK Jr. Safety and efficacy of rectal prochlorperazine for the treatment of migraine in the emergency department. *Ann Emerg Med*. 1994;24:237-241.
34. Brandes JL, Poole A, Kallela M, et al. Short-term frovatriptan for the prevention of difficult-to-treat menstrual migraine attacks. *Cephalalgia*. 2009;29:1133-1148.
35. Mannix LK, Savani N, Landy S, et al. Efficacy and tolerability of naratriptan for short-term prevention of menstrually related migraine: data from two randomized, double-blind, placebo-controlled studies. *Headache*. 2007;47:1037-1049.
36. Sheftell FD, Rapoport AM, Coddon DR. Naratriptan in the prophylaxis of transformed migraine. *Headache*. 1999;39:506-510.
37. Mathew NT, Saper JR, Silberstein SD, et al. Migraine prophylaxis with divalproex. *Arch Neurol*. 1995;52:281-286.

38. Robbins MS, Robertson CE, Kaplan E, et al. The sphenopalatine ganglion: Anatomy, pathophysiology, and therapeutic targeting in headache. *Headache*. 2016;56:240-258.
39. Maizels M, Geiger AM. Intranasal lidocaine for migraine: A randomized trial and open-label follow-up. *Headache*. 1999;39:543-551.
40. Efficacy, safety, and tolerability of dihydroergotamine nasal spray as monotherapy in the treatment of acute migraine. Dihydroergotamine Nasal Spray Multicenter Investigators. *Headache*. 1995;35:177-184.
41. Szperka CL, Rondinelli MJ. Intranasal dihydroergotamine for headache exacerbations in children and adolescents. American Headache Society 59th Annual Scientific Meeting; 2017; Boston, MA.
42. Rao AS, Gelaye B, Kurth T, Dash PD, Nitchie H, Peterlin BL. A randomized trial of ketorolac vs. sumatripan vs. placebo nasal spray (KSPN) for acute migraine. *Headache*. 2016;56:331-340.
43. Kelley NE, Tepper DE. Rescue therapy for acute migraine, part 3: Opioids, NSAIDs, steroids, and postdischarge medications. *Headache*. 2012;52:467-482.
44. Simpson DM, Hallett M, Ashman EJ, et al. Practice guideline update summary: Botulinum neurotoxin for the treatment of blepharospasm, cervical dystonia, adult spasticity, and headache: Report of the Guideline Development Subcommittee of the American Academy of Neurology. *Neurology*. 2016;86:1818-1826.
45. Silberstein SD, Holland S, Freitag F, Dodick DW, Argoff C, Ashman E. Evidence-based guideline update: Pharmacologic treatment for episodic migraine prevention in adults: Report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society. *Neurology*. 2012;78:1337-1345.
46. Dodick DW, Ashina M, Brandes JL, et al. ARISE: A phase 3 randomized trial of erenumab for episodic migraine. *Cephalalgia*. 2018;38:1026-1037.
47. Tepper S, Ashina M, Reuter U, et al. Safety and efficacy of erenumab for preventive treatment of chronic migraine: A randomised, double-blind, placebo-controlled phase 2 trial. *Lancet Neurol*. 2017;16:425-434.
48. Goadsby PJ, Reuter U, Hallstrom Y, et al. A controlled trial of erenumab for episodic migraine. *N Engl J Med*. 2017;377:2123-2132.
49. Stauffer VL, Dodick DW, Zhang Q, Carter JN, Ailani J, Conley RR. Evaluation of galcanezumab for the prevention of episodic migraine: The EVOLVE-1 randomized clinical trial. *JAMA Neurol*. 2018;75:1080-1088.
50. Detke HC, Goadsby PJ, Wang S, Friedman DI, Selzler KJ, Aurora SK. Galcanezumab in chronic migraine: The randomized, double-blind, placebo-controlled REGAIN study. *Neurology*. 2018;91: e2211-e2221.
51. Skljarevski V, Matharu M, Millen BA, Ossipov MH, Kim BK, Yang JY. Efficacy and safety of galcanezumab for the prevention of episodic migraine: Results of the EVOLVE-2 Phase 3 randomized controlled clinical trial. *Cephalalgia*. 2018;38: 1442-1454.
52. Silberstein SD, Dodick DW, Bigal ME, et al. Fremanezumab for the Preventive Treatment of Chronic Migraine. *N Engl J Med*. 2017;377: 2113-2122.
53. Dodick DW, Silberstein SD, Bigal ME, et al. Effect of fremanezumab compared with placebo for prevention of episodic migraine: A randomized clinical trial. *JAMA*. 2018;319:1999-2008.
54. Dodick DW, Lipton RB, Silberstein S, et al. Eptinezumab for prevention of chronic migraine: A randomized phase 2b clinical trial. *Cephalalgia*. 2019;39:1075-1085.
55. Ashina M, Saper J, Cady R, et al. Eptinezumab in episodic migraine: A randomized, double-blind, placebo-controlled study (PROMISE-1). *Cephalalgia*. 2020;40:241-254.
56. Schrader H, Stovner LJ, Helde G, Sand T, Bovim G. Prophylactic treatment of migraine with angiotensin converting enzyme inhibitor (lisinopril): Randomised, placebo controlled, crossover study. *BMJ*. 2001;322:19-22.
57. Tronvik E, Stovner LJ, Helde G, Sand T, Bovim G. Prophylactic treatment of migraine with an angiotensin II receptor blocker: A randomized controlled trial. *JAMA*. 2003;289:65-69.
58. Halker RB, Starling AJ, Vargas BB, Schwedt TJ. ACE and ARB agents in the prophylactic therapy of migraine-how effective are they? *Curr Treat Options Neurol*. 2016;18:15.
59. Dorosch T, Ganzer CA, Lin M, Seifan A. Efficacy of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers in the preventative treatment of episodic migraine in adults. *Curr Pain Headache Rep*. 2019;23:85.
60. Schuh-Hofer S, Flach U, Meisel A, Israel H, Reuter U, Arnold G. Efficacy of lisinopril in migraine prophylaxis – An open label study. *Eur J Neurol*. 2007;14:701-703.

61. Bozkurt B, Kovacs R, Harrington BB. *HFSA/ACC/AHA Statement Addresses Concerns Re: Using RAAS Antagonists in COVID-19* [online]. Available at: https://www.acc.org/latest-in-cardiology/articles/2020/03/17/08/59/hfsa-acc-aha-statement-addresses-concerns-re-using-raas-antagonists-in-covid-19. Accessed March 24, 2020.
62. Goncalves AL, Martini Ferreira A, Ribeiro RT, Zukerman E, Cipolla-Neto J, Peres MF. Randomised clinical trial comparing melatonin 3 mg, amitriptyline 25 mg and placebo for migraine prevention. *J Neurol Neurosurg Psychiatry*. 2016;87:1127-1132.
63. Ebrahimi-Monfared M, Sharafkhah M, Abdolrazaghnejad A, Mohammadbeigi A, Faraji F. Use of melatonin versus valproic acid in prophylaxis of migraine patients: A double-blind randomized clinical trial. *Restorative neurology and neuroscience*. 2017;35:385-393.
64. Chung JY, Kim MW, Kim M. Efficacy of zonisamide in migraineurs with nonresponse to topiramate. *Biomed Res Int*. 2014;2014:891348.
65. Mohammadianinejad SE, Abbasi V, Sajedi SA, et al. Zonisamide versus topiramate in migraine prophylaxis: A double-blind randomized clinical trial. *Clin Neuropharmacol*. 2011;34:174-177.
66. Bermejo PE, Dorado R. Zonisamide for migraine prophylaxis in patients refractory to topiramate. *Clin Neuropharmacol*. 2009;32:103-106.
67. Jackson JL, Cogbill E, Santana-Davila R, et al. A comparative effectiveness meta-analysis of drugs for the prophylaxis of migraine headache. *PLoS ONE*. 2015;10:e0130733.