Comparative Effectiveness Review Disposition of Comments Report

Research Review Title: *Acute Treatments for Episodic Migraine*

Draft report available for public comment from August 31, 2020 to September 28, 2020.

Citation: VanderPluym JH, Halker Singh RB, Morrow AS, Urtecho M, Nayfeh T, Torres Roldan VD, Farah MH, Hasan B, Saadi S, Shah S, Abd-Rabu R, Daraz L, Prokop LJ, Murad MH, Wang Z. Acute Treatments for Episodic Migraine. Comparative Effectiveness Review No. 239 (Prepared by the Mayo Clinic Evidence-based Practice Center under Contract No. HHSA290201500013I.) Rockville, MD: Agency for Healthcare Research and Quality. December 2020. Available at: www.effectivehealthcare.ahrq.gov/reports/final.cfm.

Comments to Draft Report

The Effective Health Care (EHC) Program encourages the public to participate in the development of its research projects. Each draft report is posted to the EHC Program website or AHRQ website for public comment for a 3- to 4-week period. Comments can be submitted via the website, mail, or email. At the conclusion of the public comment period, authors use the commentators' comments to revise the draft report.

Comments on draft reports and the authors' responses to the comments are posted for public viewing on the website approximately 3 months after the final report is published. Comments are not edited for spelling, grammar, or other content errors. Each comment is listed with the name and affiliation of the commentator, if this information is provided. Commentators are not required to provide their names or affiliations in order to submit suggestions or comments.

This document includes the responses by the authors of the report to comments that were submitted for this draft report. The responses to comments in this disposition report are those of the authors, who are responsible for its contents, and do not necessarily represent the views of the Agency for Healthcare Research and Quality.

Summary of Public Reviewer Comments and Author Response

This systematic review underwent peer review from June 8, 2020, to July 2, 2020, before the draft report was posted for public comment on the EHC website. Peer reviewers emphasized the importance of the topic from a public health and clinical impact perspective. A few limitations of the evidence base were noted, such as the inability to conduct subgroup analyses based on route of administration and study settings (e.g., home, outpatient, emergency room, and inpatient), lack of data on adverse events due to frequent or long-term intermittent use of medications, and harms associated with newer treatments. These limitations were acknowledged in the discussion section of the report. The final report did not provide clinical practice recommendations since making such recommendations requires additional information beyond the comparative effectiveness evidence.

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Commentator & Affiliation	Section	Comment	Response
Public Reviewer #1 – Eugene R. Viscusi, MD (American Society of Regional Anesthesia and Pain Medicine President)	General	ASRA appreciates AHRQ's evaluation of the effectiveness and comparative effectiveness of pharmacologic and non-pharmacologic therapies for the acute treatment of episodic migraine in adults. ASRA would like the working group to consider several options we believe may have been overlooked. **Lidocaine**. Intranasal (IN) lidocaine may improve acute migraine. A meta-analysis that included 6 trials revealed that IN lidocaine reduced pain intensity at 5 minutes and had a lower need for rescue medications than controls (1). In contrast, intravenous (IV) lidocaine does not appear to be effective for acute migraine. A RCT of 25 patients found no difference in pain ratings at 20 minutes after injection between IV lidocaine and placebo groups (2). 1 Chi, Pei-Wen et al. "Intranasal lidocaine for acute migraine: A meta-analysis of randomized controlled trials." PloS one vol. 14,10 e0224285. 23 Oct. 2019, doi:10.1371/journal.pone.0224285 2.Reutens DC, Fatovich DM, Stewart-Wynne EG, Prentice DA: Is intravenous lidocaine clinically effective in acute migraine? Cephalalgia 1991, 11:245–247.	We thank you for the comments and bringing the references to our attention. We already included these two studies in our review. Chi et al, 2019 is a systematic review and was used to identify additional studies. We have updated the discussion with the following information: "Although only studied in one or a few small trials, several other therapies may improve migraine pain compared with placebo, including dexamethasone, dipyrone, flunarizine, lidocaine, magnesium sulfate, octreotide, secobarbital, tezampanel, and tonabersat (low SOE). Evidence was insufficient to draw conclusions about serious adverse events. Although the strength of evidence is low, clinically these interventions are considered if patients do not respond, encounter side effects or have contraindication to the more established treatments and are therefore important to be familiar with as well."

Commentator & Affiliation	Section	Comment	Response
Public Reviewer #1 – Eugene R. Viscusi, MD (American Society of Regional Anesthesia and Pain Medicine President)	General	**Magnesium**. We note useful studies on magnesium (Mg) as an acute migraine pain reliever. A relevant meta-analysis found that IV Mg reduces acute migraine attacks within 15 - 45 minutes, 120 minutes, and 24 hours after the initial infusion and oral magnesium alleviates the frequency and intensity of migraine, concluding that IV and oral magnesium should be adapted as parts of multimodal approach to reduce migraine (3). One RCT also demonstrated efficacy of IV Mg in pts with migraine with aura (4), while another RCT (although single blind) also favored IV Mg (5). 3. Chiu HY, Yeh TH, Huang YC, Chen PY. Effects of Intravenous and Oral Magnesium on Reducing Migraine: A Meta-analysis of Randomized Controlled Trials. Pain Physician. 2016;19(1):E97-E112. 4. Bigal ME, Bordini CA, Tepper SJ, Speciali JG. Intravenous magnesium sulphate in the acute treatment of migraine without aura and migraine with aura. A randomized, double-blind, placebo-controlled study. Cephalalgia. 2002;22(5):345-353. doi:10.1046/j.1468-2982.2002.00364.x 5. Demirkaya S, Vural O, Dora B, Topçuoğlu MA. Efficacy of intravenous magnesium sulfate in the treatment of acute migraine attacks. Headache. 2001;41(2):171-177.	The three studies have been included in this review.

Commentator & Affiliation	Section	Comment	Response
Public Reviewer #1 – Eugene R. Viscusi, MD (American Society of Regional Anesthesia and Pain Medicine President)	General	NSAIDs. Diclofenac potassium and celecoxib oral solution (recently FDA approved) have strong data from RCTs. (6)(7) 6.Joshi, Shivang, and Alan M Rapoport. "Diclofenac potassium for oral solution (CAMBIA®) in the acute management of a migraine attack: clinical evidence and practical experience." Therapeutic advances in neurological disorders vol. 10,4 (2017): 217-226. doi:10.1177/1756285616684494 7. Lipton RB, Munjal S, Serrano D, Ianconangelo C, Tepper SJ, Dodick DW. DFN-15 (Celecoxib Oral Solution, 25 Mg/ml) in the Acute Treatment of Episodic Migraine: Efficacy Results from Two Phase III Randomized, Double-blind, Placebo-controlled Studies. Headache. 2020;60(S1 suppl)	The effectiveness of NSAIDs is well established; thus, we agree overall with the comment. Please note that for NSAIDs, we adopted an umbrella review approach, in which only systematic reviews of NSAIDs were included.
Public Reviewer #1 – Eugene R. Viscusi, MD (American Society of Regional Anesthesia and Pain Medicine President)	General	We encourage AHRQ to consider these additional studies as it modifies its aforementioned report. Further, we encourage AHRQ to work with the pain management community to establish a more comprehensive evidence base around episodic migraine. Conclusion We appreciate the agency's consideration of our comments on the draft report. If you have any questions, comments or concern about our feedback.	We thank you for the comments.