SPECIAL ARTICLE LEVEL OF RECOMMENDATION

Practice guideline update summary: Acute treatment of migraine in children and adolescents

Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the American Headache Society

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Neurology® 2019;93:487-499. doi:10.1212/WNL.0000000000008095

Abstract

Objective

To provide evidence-based recommendations for the acute symptomatic treatment of children and adolescents with migraine.

Methods

We performed a systematic review of the literature and rated risk of bias of included studies according to the American Academy of Neurology classification of evidence criteria. A multidisciplinary panel developed practice recommendations, integrating findings from the systematic review and following an Institute of Medicine–compliant process to ensure transparency and patient engagement. Recommendations were supported by structured rationales, integrating evidence from the systematic review, related evidence, principles of care, and inferences from evidence.

Results

There is evidence to support the efficacy of the use of ibuprofen, acetaminophen (in children and adolescents), and triptans (mainly in adolescents) for the relief of migraine pain, although confidence in the evidence varies between agents. There is high confidence that adolescents receiving oral sumatriptan/naproxen and zolmitriptan nasal spray are more likely to be headache-free at 2 hours than those receiving placebo. No acute treatments were effective for migraine-related nausea or vomiting; some triptans were effective for migraine-related phonophobia and photophobia.

Recommendations

Recommendations for the treatment of acute migraine in children and adolescents focus on the importance of early treatment, choosing the route of administration best suited to the characteristics of the individual migraine attack, and providing counseling on lifestyle factors that can exacerbate migraine, including trigger avoidance and medication overuse.

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Go to Neurology.org/N for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.

Approved by the American Academy of Neurology (AAN) Guideline Development, Dissemination, and Implementation Subcommittee on October 20, 2018; by the AAN Practice Committee on March 29, 2019; by the AAN Institute Board of Directors on April 10, 2019; and by the American Headache Society Board of Directors on May 1, 2019.

This guideline was endorsed by the Child Neurology Society on February 9, 2019 and The American Academy of Pediatrics on April 8, 2019.

Glossary

AAN = American Academy of Neurology; **CI** = confidence interval; **FDA** = Food and Drug Administration; **NS** = nasal spray; **NSAID** = nonsteroidal anti-inflammatory drug; **ODT** = oral disintegrating tablet; **OS** = oral solution; **OT** = oral tablet; **RCT** = randomized controlled trial; **RR** = relative risk.

This article summarizes the findings of a systematic review and practice recommendations for the acute treatment of migraine in children and adolescents. The complete practice guideline, including the risk of bias assessment for each study, meta-analysis, methods for analysis of the evidence, and confidence in evidence determinations, is available at https://www.aan.com/Guidelines/home/GetGuidelineContent/977.

Diagnosis of primary headache disorders is based on clinical criteria specified in the International Classification of Headache Disorders.[1] Management of migraine includes acute and preventive therapies as well as behavioral and lifestyle changes. Acute treatments must be carefully selected and individually tailored to a patient's headache pattern, severity, and disability as well as their expectations, needs, and goals of treatment.

The purpose of this guideline is to systematically assess all randomized controlled trials (RCTs) that evaluated acute migraine treatments in children and adolescents. The guideline seeks to answer the following clinical question:

In children and adolescents with migraine, do acute self-administered treatments, compared with placebo, reduce headache pain and associated symptoms (nausea, vomiting, photophobia, and phonophobia) and maintain headache freedom?

Description of the analytic process

The Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology (AAN) convened a multidisciplinary panel consisting of 12 AAN physician members and 3 patient representative members to develop this guideline according to the process described in the 2011 AAN guideline development process manual,[2] as amended. The authors included RCTs on the acute pharmacologic treatment of migraine in children (individuals younger than 12 years) and adolescents (individuals aged 12–17 years). The authors considered studies published in English and in other languages. Trials of medications administered IV in the emergency department or in an infusion center setting were not included. The outcomes evaluated were reduction of headache pain and associated symptoms at specific time points. For headache pain, the most commonly reported outcomes were headache pain improvement, usually termed "headache pain response" and typically quantified as an improvement in intensity from moderate to severe pain to mild or no pain, and headache pain freedom, at specific time points after intervention (typically from 30 minutes to 2 hours). The most commonly reported associated symptoms were freedom from photophobia, phonophobia, nausea, or vomiting at specific time points after intervention.

This guideline updates a previous guideline published in 2004 on the treatment of migraine in children. The panel performed a literature search of articles published between December 1, 2003, and August 25, 2017. Two authors independently reviewed all abstracts and full-text articles for relevance. Articles were included if (1) at least 90% of study participants were aged 0–18 years, (2) the study included a diagnosis of migraine, (3) the study had at least 20 participants, and (4) treatment was compared with placebo.

The authors found 2,482 abstracts relevant to acute or preventive therapy for pediatric migraine. The authors reviewed 313 full-text articles and identified 10 new studies of acute therapy to be included in the guideline. Of the 10 acute treatment studies included in the 2004 guideline on treatment of migraine in children, 6 were included in the current guideline; the other 4 studies were excluded because they were either Class IV (3 studies) or included fewer than 20 participants (1 study).

A modified Grading of Recommendations Assessment, Development and Evaluation process[3] was used to develop conclusions. The confidence in the evidence (high, moderate, low, or very low) was anchored to the error domain—class of evidence, indirectness of evidence, and precision of effect estimate—with the highest risk of error. This confidence was upgraded or downgraded by a maximum of one level based on several other domains.

The panel formulated practice recommendations based on the strength of evidence and other factors, including axiomatic principles of care, the magnitude of anticipated health benefits relative to harms, financial burden, availability of interventions, and patient preferences. The panel assigned levels of obligation (A, B, C, U, R) to the recommendations, using a modified Delphi process.[2]

Analysis of evidence

Conclusions to the analysis of evidence are listed as follows. These conclusions are also summarized in tables 1–3.

Outcome: Pain response at 30 minutes

Low confidence in the evidence

Adolescents receiving sumatriptan nasal spray (NS) 20 mg are possibly more likely than those receiving placebo to have a headache pain response at 30 minutes (relative risk [RR] 1.27; 95% confidence interval [CI], 1.01–1.60; 1 Class I[4] study).

Very low confidence in the evidence

There is insufficient evidence to determine whether adolescents receiving sumatriptan NS 5 mg are more or less likely than those receiving placebo to have a headache pain response at 30 minutes (RR 1.03; 95% CI 0.80–1.32; 1 Class I[4] study).

There is insufficient evidence to determine whether children and adolescents receiving the following treatments are more or less likely than those receiving placebo to have a headache pain response at 30 minutes:

- Sumatriptan oral tablet (OT) 25 mg (RR 0.35; 95% CI 0.03–4.14; 1 Class I[5] study)
- Sumatriptan OT 50 mg (RR 2.27; 95% CI 0.58–8.90; 1 Class I[5] study)

Outcome: Pain response at 1 hour

Moderate confidence in the evidence

Adolescents receiving sumatriptan NS 5 mg are probably no more likely than those receiving placebo to have a headache pain response at 1 hour (RR 1.05; 95% CI 0.91–1.21; 1 Class I[4] and 1 Class II[6] study).

Low confidence in the evidence

Children and adolescents receiving the following treatments are possibly more likely than those receiving placebo to have a headache pain response at 1 hour:

- Sumatriptan NS 10 mg (RR 1.55; 95% CI 1.08–2.23; 2 Class II studies[6,7])

Table 1 Pain outcomes and confidence in evidence

Outcome	High confidence (more likely than placebo)	Moderate confidence (probably more likely than placebo)	Low confidence (possibly more likely than placebo)	Moderate confidence (probably no more likely than placebo)	Low confidence (possibly no more likely than placebo)	Very low confidence (insufficient evidence)
Pain response at 30 minutes			Sumatriptan NS 20 mg			Sumatriptan NS 5 mg Sumatriptan OT 25 mg Sumatriptan OT 50 mg
Pain response at 1 hour			Zolmitriptan NS 5 mg Sumatriptan NS 10 mg Sumatriptan NS 20 mg	Sumatriptan NS 5 mg		Sumatriptan OT 25 mg Sumatriptan OT 50 mg
Pain response at 2 hours			Ibuprofen OS 7.5–10 mg/kg Acetaminophen OS 15 mg/kg Almotriptan OT 6.25 mg Almotriptan OT 12.5 mg Sumatriptan NS 20 mg Zolmitriptan NS 5 mg	Rizatriptan ODT 5 or 10 mg	Eletriptan OT 40 mg	Almotriptan OT 25 mg Sumatriptan NS 5 mg Sumatriptan NS 10 mg Sumatriptan OT 25 mg Sumatriptan OT 50 mg
Pain-free at 1 hour		Zolmitriptan NS 5 mg				
Pain-free at 2 hours	Sumatriptan naproxen OT 10/60 mg Sumatriptan/naproxen OT 30/180 mg Sumatriptan/naproxen OT 85/500 mg Zolmitriptan NS 5 mg	Ibuprofen OS 7.5–10 mg/kg Sumatriptan NS 20 mg	Rizatriptan ODT 5 or 10 mg		Almotriptan OT 12.5 mg	Acetaminophen OS 15 mg/kg Almotriptan OT 6.25 mg Almotriptan OT 25 mg Eletriptan OT 40 mg Sumatriptan OT 25 mg Sumatriptan OT 50 mg

Abbreviations: NS = nasal spray; ODT = oral disintegrating tablet; OS = oral solution; OT = oral tablet.

Table 2 Associated symptom outcomes and confidence in evidence

Outcome	High confidence (more likely than placebo)	Moderate confidence (probably more likely than placebo)	Low confidence (possibly more likely than placebo)	Moderate confidence (probably no more likely than placebo)	Low confidence (possibly no more likely than placebo)	Very low confidence (insufficient evidence)
Relief of nausea at 2 hours				Sumatriptan NS 5 mg Sumatriptan NS 20 mg Sumatriptan/ naproxen OT 85/500 mg	Eletriptan OT 40 mg	Ibuprofen OS 7.5–10 mg/kg Sumatriptan NS 10 mg Sumatriptan/ naproxen OT 10/60 mg Sumatriptan/ naproxen OT 30/180 mg Rizatriptan ODT 5 or 10 mg
Relief of vomiting at 2 hours				Sumatriptan NS 5 mg Sumatriptan NS 20 mg	Sumatriptan NS 10 mg Rizatriptan ODT 5 or 10 mg	
Relief of photophobia at 30 minutes		Zolmitriptan NS 5 mg				
Relief of photophobia at 2 hours		Sumatriptan/ naproxen OT 10/60 mg Sumatriptan/ naproxen OT 85/500 mg	Zolmitriptan NS 5 mg		Eletriptan OT 40 mg	Sumatriptan NS 10 mg Sumatriptan/ naproxen OT 30/180 mg Rizatriptan ODT 5 or 10 mg
Relief of phonophobia at 30 minutes		Zolmitriptan NS 5 mg				
Relief of phonophobia at 2 hours		Sumatriptan/ naproxen OT 10/60 mg Sumatriptan/ naproxen OT 85/500 mg	Sumatriptan NS 5 mg Sumatriptan NS 20 mg Sumatriptan/ naproxen OT 30/ 180 mg	Rizatriptan ODT 5 or 10 mg	Eletriptan OT 40 mg	Sumatriptan NS 10 mg Zolmitriptan NS 5 mg

Abbreviations: NS = nasal spray; ODT = oral disintegrating tablet; OS = oral solution; OT = oral tablet.

- Sumatriptan NS 20 mg (RR 1.27; 95% CI 1.09–1.49; 1 Class I[4] and 2 Class II studies[6,7])

Adolescents receiving zolmitriptan NS 5 mg are possibly more likely than those receiving placebo to have a headache pain response at 1 hour (RR 1.34; 95% CI 1.05–1.71; 1 Class II study[8]).

Very low confidence in the evidence

There is insufficient evidence to determine whether children and adolescents receiving the following treatments are more or less likely than those receiving placebo to have a headache pain response at 1 hour:

- Sumatriptan OT 25 mg (RR 0.49; 95% CI 0.16–1.48; 1 Class I study[5])
- Sumatriptan OT 50 mg (RR 0.39; 95% CI 0.13–1.19; 1 Class I study[5])

Outcome: Pain response at 2 hours

Moderate confidence in the evidence

Children and adolescents receiving 5 or 10 mg of rizatriptan oral disintegrating tablets (ODT) are probably no more likely than those receiving placebo to have a headache pain response at 2 hours (RR 1.07; 95% CI 0.97–1.17; 3 Class II studies[9–11]).

Low confidence in the evidence

Children and adolescents receiving the following treatments are possibly more likely than those receiving placebo to have a headache pain response at 2 hours:

- Ibuprofen oral solution (OS) 7.5–10 mg/kg (RR 1.54; 95% CI 1.18–2.01; 1 Class II[12] and 1 Class III[13] study)
- Acetaminophen OS 15 mg/kg (RR 1.46; 95% CI 1.02–2.09; 1 Class II study[12])
- Sumatriptan NS 20 mg (RR 1.32; 95% CI 1.04–1.68; 1 Class I[4] and 2 Class II[6,7] studies)

Table 3 Confidence in evidence by drug and outcome

	Pain response at 30 minutes	Pain response at 1 hour	Pain response at 2 hours	Pain-free at 1 hour	Pain-free at 2 hours	Relief of nausea at 2 hours	Relief of vomiting at 2 hours	Relief of photophobia at 2 hours	Relief of phonophobia at 2 hours
Ibuprofen OS 7.5–10 mg/kg			Low		Moderate	Very low			
Acetaminophen OS 15 mg/kg			Low		Very low				
Sumatriptan OT 25 mg	Very low	Very low	Very low		Very low				
Sumatriptan OT 50 mg	Very low	Very low	Very low		Very low				
Sumatriptan NS 5 mg	Very low	Moderate: probably no more likely than placebo	Very low			Moderate: probably no more likely than placebo	Moderate: probably no more likely than placebo	Very low	Low
Sumatriptan NS 10 mg		Low	Very low			Very low	Low: possibly no more likely than placebo	Very low	Very low
Sumatriptan NS 20 mg	Low	Low	Low		Moderate	Moderate: probably no more likely than placebo	Moderate: probably no more likely than placebo	Very low	Low
Sumatriptan/ naproxen OT 10/ 60 mg					High	Very low		Moderate	Moderate
Sumatriptan/ naproxen OT 30/ 180 mg					High	Very low		Very low	Low
Sumatriptan/ naproxen OT 85/ 500 mg					High	Moderate: probably no more likely than placebo		Moderate	Moderate
Rizatriptan ODT 5 or 10 mg			Moderate: probably no more likely than placebo		Low	Very low	Low: possibly no more likely than placebo	Very low	Moderate: probably no more likely than placebo
Eletriptan OT 40 mg			Low: possibly no more likely than placebo		Very low	Low: possibly no more likely than placebo		Low: possibly no more likely than placebo	Low: possibly no more likely than placebo
Zolmitriptan NS		Low	Low	Moderate	High			Low	Very low
Almotriptan OT 6.25 mg			Low		Very low				
Almotriptan OT 12.5 mg			Low		Low: possibly no more likely than placebo				
Almotriptan OT 25 mg			Very low		Very low				

Abbreviations: NS = nasal spray; ODT = oral disintegrating tablet; OS = oral solution; OT = oral tablet.

Adolescents receiving the following treatments are possibly more likely than those receiving placebo to have a headache pain response at 2 hours:

- Almotriptan OT 6.25 mg (RR 1.30; 95% CI 1.10–1.53; 1 Class II study[14])
- Almotriptan OT 12.5 mg (RR 1.31; 95% CI 1.11–1.54; 1 Class II study[14])
- Zolmitriptan NS 5 mg (RR 1.29; 95% CI 1.06–1.58; 1 Class I study[15])

Adolescents receiving eletriptan OT 40 mg are possibly no more likely than those receiving placebo to have a headache pain response at 2 hours (RR 0.99; 95% CI 0.81–1.21; 1 Class II study[16]).

Very low confidence in the evidence

There is insufficient evidence to determine whether adolescents receiving the following treatments are more or less likely than those receiving placebo to have a headache pain response at 2 hours:

- Sumatriptan NS 5 mg (RR 1.14; 95% CI 1.01–1.30; 1 Class I[4] and 1 Class II[6] study)
- Almotriptan OT 25 mg (RR 1.21; 95% CI 1.02–1.43; 1 Class II study[14])

There is insufficient evidence to determine whether children and adolescents receiving the following treatments are more or less likely than those receiving placebo to have a headache pain response at 2 hours:

- Sumatriptan NS 10 mg (RR 1.50; 95% CI 0.93–2.41; 2 Class II studies[6,7])
- Sumatriptan OT 25 mg (RR 0.86; 95% CI 0.48–1.46; 1 Class I study[5])
- Sumatriptan OT 50 mg (RR 0.76; 95% CI 0.44–1.32; 1 Class I study[5])

Outcome: Pain-free at 1 hour

Moderate confidence in the evidence

Adolescents receiving zolmitriptan NS 5 mg are probably more likely than those receiving placebo to be free of headache pain at 1 hour (RR 2.71; 95% CI 1.54–4.78; 1 Class II study[8]).

Outcome: Pain-free at 2 hours

High confidence in the evidence

Adolescents receiving the following treatments are more likely than those receiving placebo to be free of headache pain at 2 hours:

- Sumatriptan/naproxen OT 10/60 mg (RR 2.95; 95% CI 1.65–5.27; 1 Class I study[17])
- Sumatriptan/naproxen OT 30/180 mg (RR 2.72; 95% CI 1.51–4.89; 1 Class I study[17])
- Sumatriptan/naproxen OT 85/500 mg (RR 2.17; 95% CI 1.49–3.16; 1 Class I[17] and 1 Class II[18] study)
- Zolmitriptan NS 5 mg (RR 1.90; 95% CI 1.47–2.46; 1 Class I study[15] and 1 Class II study[8])

Moderate confidence in the evidence

Children and adolescents receiving the following treatments are probably more likely than those receiving placebo to be free of headache pain at 2 hours:

- Ibuprofen OS 7.5–10 mg/kg (RR 2.15; 95% CI 1.28–3.71, 1 Class II study[12])
- Sumatriptan NS 20 mg (RR 1.46; 95% CI 1.21–1.77; 1 Class I[4] and 2 Class II studies[6,7])

Low confidence in the evidence

Children and adolescents receiving rizatriptan ODT 5 or 10 mg are possibly more likely than those receiving placebo to be free of headache pain at 2 hours (RR 1.28; 95% CI 1.10–1.48; 3 Class II studies[9–11]).

Adolescents receiving almotriptan OT 12.5 mg are possibly no more likely than those receiving placebo to be free of headache pain at 2 hours (RR 1.20; 95% CI 0.91–1.58; 1 Class II study[14]).

Very low confidence in the evidence

There is insufficient evidence to determine whether children and adolescents receiving the following treatments are more or less likely than those receiving placebo to be free of headache pain at 2 hours:

- Acetaminophen OS 15 mg/kg (RR 1.40; 95% CI 0.77–2.56, 1 Class II study[12])
- Sumatriptan OT 25 mg (RR 0.85; 95% CI 0.42–1.46; 1 Class I study[5])
- Sumatriptan OT 50 mg (RR 0.68; 95% CI 0.34–1.38; 1 Class I study[5])

There is insufficient evidence to determine whether adolescents receiving the following treatments are more or less likely than those receiving placebo to be free of headache pain at 2 hours:

- Almotriptan OT 6.25 mg (RR 1.04; 95% CI 0.78–1.39; 1 Class II study[14])
- Almotriptan OT 25 mg (RR 1.18; 95% CI 0.90–1.55; 1 Class II study[14])
- Eletriptan OT 40 mg (RR 1.46; 95% CI 0.88–2.42; 1 Class II study[16])

Outcome: Relief of nausea at 2 hours

Moderate confidence in the evidence

Adolescents receiving the following treatments are probably no more likely than those receiving placebo to have relief of nausea at 2 hours:

- Sumatriptan NS 5 mg (RR 1.03; 95% CI 0.96–1.11; 1 Class I[4] and 1 Class II[6] study)
- Sumatriptan NS 20 mg (RR 1.02; 95% CI 0.94–1.11; 1 Class I study[4])

Adolescents receiving sumatriptan/naproxen OT 85/500 mg are probably no more likely than those receiving placebo to be nausea-free at 2 hours (RR 1.00; 95% CI 0.86–1.16; 1 Class I study[17]).

Low confidence in the evidence

Adolescents receiving eletriptan ODT 40 mg are possibly no more likely than those receiving placebo to be free of nausea at 2 hours (RR 0.96; 95% CI 0.84–1.10; 1 Class II study[16]).

Very low confidence in the evidence

There is insufficient evidence to determine whether children receiving ibuprofen OS 7.5–10 mg/kg are more or less likely than those receiving placebo to be free of nausea at 2 hours (RR 1.40; 95% CI 1.00–1.96; 1 Class III study[13])

There is insufficient evidence to determine whether children and adolescents receiving rizatriptan ODT 5 or 10 mg are more or less likely than those receiving placebo to be free of nausea at 2 hours (RR 1.11; 95% CI 1.04–1.18; 1 Class II study[10]).

There is insufficient evidence to determine whether adolescents receiving the following treatments are more or less likely than those receiving placebo to be free of nausea at 2 hours:

- Sumatriptan NS 5 mg (RR 1.19; 95% CI 0.96 to 1.48; 1 Class II study)
- Sumatriptan NS 10 mg (RR 1.11; 95% CI 0.97–1.27; 1 Class II study[6])
- Sumatriptan/naproxen OT 10/60 mg (RR 1.17; 95% CI 1.01–1.35; 1 Class I study[17])
- Sumatriptan/naproxen OT 30/180 mg (RR 1.10; 95% CI 0.94–1.28; 1 Class I study[17])

Outcome: Relief of vomiting at 2 hours

Moderate confidence in the evidence

Adolescents receiving the following treatments are probably no more likely than those receiving placebo to have relief of vomiting at 2 hours:

- Sumatriptan NS 5 mg (RR 1.01; 95% CI 0.98–1.05; 1 Class I[4] and 1 Class II[6] study)
- Sumatriptan NS 20 mg (RR 1.02, 95% CI 0.99–1.05; 1 Class I study[4])

Low confidence in the evidence

Children and adolescents receiving the following treatments are possibly no more likely than those receiving placebo to have resolution of vomiting at 2 hours:

- Sumatriptan NS 10 mg (RR 1.00; 95% CI 0.94–1.07; 1 Class II study[6])
- Rizatriptan ODT 5 or 10 mg (RR 1.02; 95% CI 0.99–1.05; 1 Class II study[10])

Outcome: Relief of photophobia at 30 minutes

Moderate confidence in the evidence

Adolescents receiving zolmitriptan NS 5 mg are probably more likely than those receiving placebo to be free of photophobia at 30 minutes (RR 1.66; 95% CI 1.03–2.68; 1 Class II study[8]).

Outcome: Relief of photophobia at 2 hours

Moderate confidence in the evidence

Adolescents receiving the following treatments are probably more likely than those receiving placebo to be free of photophobia at 2 hours:

- Sumatriptan/naproxen OT 10/60 mg (RR 1.45; 95% CI 1.12–1.87; 1 Class I study[17])
- Sumatriptan/naproxen OT 85/500 mg (RR 1.44; 95% CI 1.14–1.82; 1 Class I study[17])

Low confidence in the evidence

Adolescents receiving zolmitriptan NS 5 mg are possibly more likely than those receiving placebo to be free of photophobia at 2 hours (RR 1.26; 95% CI 1.05–1.51, 1 Class I study[15]).

Adolescents receiving eletriptan OT 40 mg are possibly no more likely than those receiving placebo to be free of photophobia at 2 hours (RR 0.97; 95% CI 0.85–1.10; 1 Class II study[16]).

Very low confidence in the evidence

There is insufficient evidence to determine whether adolescents receiving the following treatments are more or less likely than those receiving placebo to have resolution of photophobia at 2 hours:

- Sumatriptan NS 5 mg (RR 1.19; 95% CI 0.96–1.48; 1 Class II study[6])
- Sumatriptan NS 10 mg (RR 1.10; 95% CI 0.88–1.37; 1 Class II study[6])
- Sumatriptan NS 20 mg (RR 1.24; 95% CI 1.00–1.54; 1 Class II study[6])

There is insufficient evidence to determine whether children and adolescents receiving the rizatriptan ODT 5 or 10 mg are more or less likely than those receiving placebo to have resolution of photophobia at 2 hours (RR 1.11; 95% CI 0.98–1.25; 1 Class II study[10]).

There is insufficient evidence to determine whether adolescents receiving sumatriptan/naproxen OT 30/180 mg are more or less likely than those receiving placebo to be free of

photophobia at 2 hours (RR 1.19; 95% CI 0.90–1.58; 1 Class I study[17]).

Outcome: Relief of phonophobia at 30 minutes

Moderate confidence in the evidence

Adolescents receiving zolmitriptan NS 5 mg are probably more likely than those receiving placebo to be free of phonophobia at 30 minutes (RR 1.68; 95% CI 1.03–2.74; 1 Class II study[8]).

Outcome: Relief of phonophobia at 2 hours

Moderate confidence in the evidence

Adolescents receiving the following treatments are probably more likely than those receiving placebo to be free of phonophobia at 2 hours:

- Sumatriptan/naproxen OT 10/60 mg (RR 1.45; 95% CI 1.13–1.87; 1 Class I study[17])
- Sumatriptan/naproxen OT 85/500 mg (RR 1.43; 95% CI 1.14–1.80; 1 Class I study[17])

Children and adolescents receiving the rizatriptan ODT 5 or 10 mg are probably no more likely than those receiving placebo to be free of phonophobia at 2 hours (RR 1.07; 95% CI 0.97–1.18; 2 Class II studies[10,11]).

Low confidence in the evidence

Adolescents receiving sumatriptan/naproxen OT 30/180 are possibly more likely than those receiving placebo to be free of phonophobia at 2 hours (RR 1.38; 95% CI 1.07–1.78; 1 Class I study[17]).

Adolescents receiving the following treatments are possibly more likely than those receiving placebo to be free of phonophobia at 2 hours:

- Sumatriptan NS 5 mg (RR 1.29; 95% CI 1.07–1.56; 1 Class II study[6])
- Sumatriptan NS 20 mg (RR 1.34; 95% CI 1.11–1.62; 1 Class II study[6])

Adolescents receiving eletriptan OT 40 mg are possibly no more likely than those receiving placebo to be free of phonophobia at 2 hours (RR 1.05; 95% CI 0.89–1.24; 1 Class II study[16]).

Very low confidence in the evidence

There is insufficient evidence to determine whether adolescents receiving the following treatments are more or less likely than those receiving placebo to have resolution of phonophobia at 2 hours:

- Sumatriptan NS 10 mg (RR 1.20; 95% CI 0.99–1.46; 1 Class II study[6])
- Zolmitriptan NS 5 mg (RR 1.21; 95% CI 1.02–1.44; 1 Class I study[15])

Practice recommendations

Establish a specific headache diagnosis

Recommendation 1 rationale

The appropriate care of a patient with headaches requires establishing a correct diagnosis. This affects our diagnostic approach, treatment, and prognosis. Patients with signs and symptoms of secondary headache, such as sudden change in headache, papilledema, focal deficits, and the additional presence of seizures, require further evaluation beyond a thorough history and physical examination. When migraine is diagnosed, tailored treatments may be considered that can result in improved outcomes.[19] Diagnostic criteria for pediatric migraine include at least 5 headaches over the last year that last 2–72 hours when untreated, with 2 of 4 additional features (pulsatile quality, unilateral, worsening with activity or limiting activity, moderate to severe in intensity), and association with at least nausea, vomiting, photophobia, or phonophobia. These associated symptoms can be inferred by family report of the child's activities. The time a child sleeps can be considered part of the headache duration. Auras typically occur in about one third of older children and adolescents and precede the headache by 5–60 minutes.[1]

Statement 1a

When evaluating children and adolescents with headache, clinicians should diagnose a specific headache type (primary, secondary, or other headache syndrome) (Level B).

Statement 1b

When evaluating children and adolescents with headache, clinicians should ask about premonitory and aura symptoms, headache semiology (onset, location, quality, severity, frequency, duration, and aggravating and alleviating factors), associated symptoms (nausea, vomiting, phonophobia, and photophobia), and pain-related disability in order to improve diagnostic accuracy for migraine and appropriately counsel the patient (Level B).

Acute migraine treatment

Recommendation 2 rationale

Migraine treatment should aim to achieve fast, complete pain relief, with minimum side effects. Associated symptoms like nausea, vomiting, photophobia, and phonophobia should also be addressed. In adults, early treatment of migraine (within less than 1 hour of headache onset) improves pain-free rates.[20] Improved efficacy with early treatment is likely to be seen in children and adolescents as well. Many children and adolescents use and benefit from nonprescription oral analgesics like acetaminophen, ibuprofen, and naproxen.[21] Triptans are less commonly prescribed in children than in adults, and only almotriptan (for patients aged 12 years and older), rizatriptan (for patients aged 6–17 years), sumatriptan/naproxen (for patients aged 12 years and older), and zolmitriptan NS (for patients aged 12 years and older) are approved by the Food and Drug Administration (FDA) for use in children. Ergots and oral naproxen alone have not been studied in children.

Statement 2a

Clinicians should counsel that acute migraine treatments are more likely to be effective when used earlier in the migraine attack, when pain is still mild (Level B).

Statement 2b

Clinicians should prescribe ibuprofen OS (10 mg/kg) as an initial treatment option to reduce pain in children and adolescents with migraine (Level B)

Statement 2c

For adolescents with migraine, clinicians should prescribe sumatriptan/naproxen OT (10/60, 30/180, 85/500 mg), zolmitriptan NS (5 mg), sumatriptan NS (20 mg), rizatriptan ODT (5 or 10 mg), or almotriptan OT (6.25 or 12.5 mg) to reduce headache pain (Level B).

Recommendation 3 rationale

Patients respond differently to the same medication. In adults, failure to respond to 1 triptan does not preclude response to an alternate triptan.[22] In adults who respond to a triptan but have recurrence of their headache within 24 hours, taking a second dose is effective.[23] Children might have the same experience, but product monograph daily maximum doses must be followed. Migraine features (severity, associated symptoms, disability, and most bothersome symptoms) differ among individuals and among different attacks in the same individual.[24] Intranasal sumatriptan and zolmitriptan are absorbed more quickly than the oral form[25,26] and have a faster onset of action.[27,28] For migraines that rapidly peak in severity or are associated with nausea and vomiting, nonoral forms of treatment may be more effective. Thus, children with migraine may benefit from more than 1 acute treatment choice and different delivery routes, depending on their individual headache characteristics.

Statement 3a

Clinicians should counsel patients and families that a series of medications may need to be used to find treatments that most benefit the patient (Level B).

Statement 3b

Clinicians should instruct patients and families to use the medication that best treats the characteristics of each migraine to provide the best balance of efficacy, side effects, and patient preference (Level B).

Statement 3c

Clinicians should offer an alternate triptan, if 1 triptan fails to provide pain relief, to find the most effective agent to reduce migraine symptoms (Level B).

Statement 3d

Clinicians may prescribe a nonoral route when headache peaks in severity quickly, is accompanied by nausea or vomiting, or oral formulations fail to provide pain relief (Level C).

Statement 3e

Clinicians should counsel patients and families that if their headache is successfully treated by their acute migraine medication but headache recurs within 24 hours of their initial treatment, taking a second dose of acute migraine medication can treat the recurrent headache (Level B).

Recommendation 4 rationale

Sumatriptan/naproxen OT (10/60, 30/180, and 85/500 mg) is more likely than placebo to result in headache pain-free status at 2 hours. Sumatriptan and naproxen have different pharmacokinetic profiles targeted to aid in migraine relief.[29] In adults, the sumatriptan/naproxen combination OT is more effective than monotherapy with either component.[30] Because of cost and insurance issues, not all patients have access to all available formulations of medications. Given the distinct mechanisms of action among medications in the triptan class and the nonsteroidal anti-inflammatory drug (NSAID) class, the addition of an NSAID to a triptan may improve rates of pain response and pain-free status.

Statement 4

In adolescents whose migraine is incompletely responsive to a triptan, clinicians should offer ibuprofen or naproxen in addition to a triptan to improve migraine relief (Level B).

Treatment of associated symptoms

Recommendation 5 rationale

Migraine is typically accompanied by other symptoms (nausea, vomiting, photophobia, phonophobia) in addition to head pain. Antiemetics are often prescribed along with specific (triptan) and nonspecific (NSAID) migraine treatments to address nausea and vomiting and to speed the rate of medication absorption. In pediatric migraine trials, the treatment effects on migraine-associated symptoms were less pronounced than the treatment effects on pain. While photophobia and phonophobia were responsive to zolmitriptan NS and sumatriptan/naproxen, none of the treatments studied had demonstrated effectiveness against nausea or vomiting. Antiemetics are available to treat nausea and vomiting related to other pediatric conditions (acute gastroenteritis, postoperative state, chemotherapy)[31,32] and may be of benefit for migraine-associated nausea, although no clinical trials specifically evaluating antiemetics for pediatric migraine-associated nausea have been performed. NS formulations of zolmitriptan and sumatriptan may be easier to administer in adolescents with migraine with prominent nausea or vomiting.

Statement 5

For children and adolescents with migraine who experience prominent nausea or vomiting, clinicians should offer additional antiemetic treatments (Level B).

Counseling

Recommendation 6 rationale

Patient education can improve patient safety and adherence to interventions. It is important to learn about the behavioral

aspects of self-care that might improve migraine, including healthy habits with lifestyle modification, potential migraine triggers/aggravating factors, and the risk of overusing medication. Maintaining a headache diary is helpful to track response to any new therapy. Patients and families will benefit from understanding the limitations of current available treatments. Overuse of medication to treat acute attacks has been associated with medication overuse headache in adults[33] but has not been well-studied in children. Methods to prevent medication overuse headache are included in adult treatment plans.

Statement 6a

Clinicians should counsel children and adolescents with migraine and their families about migraine-healthy habits, including lifestyle modification, identification/disproof/resolution of migraine triggers/aggravating factors, and avoidance of medication overuse (Level B).

Statement 6b

Clinicians should make collaborative agreements with children and adolescents with migraine and their families on treatment goals that are individualized to the patient (Level B).

Statement 6c

Clinicians may counsel children and adolescents with migraine and their families to maintain a headache diary to monitor their response to treatments (Level C).

Statement 6d

Clinicians should counsel patients and families to use no more than 14 days of ibuprofen or acetaminophen per month, no more than 9 days of triptans per month, and no more than 9 days per month of any combination of triptans, analgesics, or opioids for more than 3 months to avoid medication overuse headache (Level B). (There is no evidence to support the use of opioids in children with migraine. Opioids are included in this statement to be consistent with the International Classification of Headache Disorders[1] regarding medication overuse.)

Contraindications and precautions to triptan use

Recommendation 7 rationale

According to the FDA, triptans are contraindicated in patients with a history of cardiovascular disease, including stroke, TIA, myocardial infarction, severe peripheral vascular disease, ischemic bowel disease, and coronary vasospasm, including Prinzmetal angina. Triptans are also contraindicated in patients with cardiac accessory conduction pathway disorders, including Wolff-Parkinson-White syndrome. Although the 2004 American Headache Society consensus statement does not consider these as absolute contraindications,[34] these contraindications are based on the known pharmacology of the triptans[35] and triptan effects on vascular muscle.[36] While these medical contraindications are less prevalent in the pediatric population, they are important to consider.

Statement 7

Clinicians must not prescribe triptans to those with a history of ischemic vascular disease or accessory conduction pathway disorders to avoid the morbidity and mortality associated with aggravating these conditions (Level A).

Recommendation 8 rationale

In adults who have migraine with typical aura, there is evidence that it is safe to take triptans during the aura, although the triptan may be more effective if taken at the onset of pain.[37,38] The use of triptans during the aura phase is of concern because of potential difficulties differentiating early stroke symptoms from migraine aura. While this is unlikely a problem in those with established migraine with visual aura, caution is warranted in those with more complex aura presentations. According to the FDA, triptans are contraindicated in those with a history of hemiplegic aura or migraine with brainstem aura. This contraindication was based on a view of migraine pathophysiology that is no longer considered current.

Statement 8a

Clinicians should counsel adolescent patients with migraine with aura that taking their triptan during a typical aura is safe, but that the triptan may be more effective if taken at the onset of head pain (Level B).

Statement 8b

Clinicians may consider referral of children and adolescents with hemiplegic migraine or migraine with brainstem aura who do not respond to other treatments to a headache specialist to find effective treatment (Level C).

Suggestions for future research

Most adults with migraine have onset in childhood or adolescence. Accurate diagnosis and treatment in childhood and adolescence can prevent migraine-related disability and significantly improve quality of life.[19] Lifestyle modifications and acute pharmacologic treatments are the mainstay of management. Although the pathophysiology of migraine is presumed to be the same as in adults, a higher placebo response is observed in children and adolescents, with a lower therapeutic gain measured in clinical trials.[39] Patterns of migraine presentation and associated symptoms in children and adolescents evolve into the adult patterns and their shortest headaches may be shorter in duration.[1] These factors should be considered when designing clinical trials. The fact that all acute treatment trials in children and adolescents are performed after proven efficacy in adults may be a contributor to the expectation response adding to the placebo effect. This expectation response is widely seen in pain studies and may explain why so few trials of acute migraine therapy in children and adolescents have shown positive results.

Although there is a growing body of evidence to support recommendations for the acute treatment of pediatric

migraine, challenges remain. Many children and adolescents do not respond to treatment at home with NSAIDs and triptans and seek pain relief at an emergency department or infusion center.[40] Trials of refractory headache treatment in children and adolescents have been conducted[41] but therapeutic approaches in these circumstances vary.[42] Studies are also needed of alternate delivery routes for acute treatments such as transdermal patches because oral medications are poorly absorbed in children and adolescents with nausea and vomiting. Regardless of the strategy chosen for acute migraine therapy, treatment plans should be individually tailored to the patient and family and include education about migraine prevention strategies.

Author contributions

Dr. Oskoui: study concept and design, acquisition of data, analysis or interpretation of data, drafting/revising the manuscript, critical revision of the manuscript for important intellectual content, study supervision. Dr. Holler-Managan: study concept and design, acquisition of data, analysis or interpretation of data, revising the manuscript. Dr. Pringsheim: study concept and design, acquisition of data, analysis or interpretation of data, drafting/revising the manuscript, critical revision of the manuscript for important intellectual content, study supervision. Dr. Potrebic: study concept and design, acquisition of data, analysis or interpretation of data, drafting/revising the manuscript, critical revision of the manuscript for important intellectual content, study supervision. Dr. Billinghurst: analysis or interpretation of data, drafting/revising the manuscript, critical revision of the manuscript for important intellectual content, study supervision. Dr. Gloss: study concept and design, acquisition of data, analysis or interpretation of data, drafting/revising the manuscript. Dr. Hershey: study concept and design, interpretation of data, drafting/revising the manuscript, critical revision of the manuscript for important intellectual content. Dr. Licking: acquisition of data, interpretation of data, revising the manuscript. Dr. Sowell: interpretation of data revising the manuscript. Dr. Victorio: interpretation of data, revising the manuscript. E.M. Gersz: study concept, interpretation of data, revising the manuscript. E. Leininger: study concept, interpretation of data, revising the manuscript. H. Zanitsch: study concept, interpretation of data, revising the manuscript. Dr. Yonker: study concept, interpretation of data, revising the manuscript. Dr. Mack: study design and concept, interpretation of data, drafting/revising the manuscript, critical revision of manuscript for important intellectual content.

Study funding

This practice guideline was developed with financial support from the AAN. Authors who serve or have served as AAN subcommittee members or as methodologists (M.O., Y.H.M., T.P., S.P., L.B., D.G., and N.L.) were reimbursed by the AAN for expenses related to travel to subcommittee meetings where drafts of manuscripts were reviewed. All authors on the panel were reimbursed by the AAN for expenses related to travel to in-person meetings.

Disclosure

M. Oskoui reports no disclosures relevant to the manuscript. Y. Holler-Managan serves on the editorial advisory board for *Neurology Now*. T. Pringsheim reports no disclosures relevant to the manuscript. S. Potrebic has received funding from the AAN for travel to biennial Guidelines International Network meetings by the AAN; has received an honorarium and funding for travel to serve as an expert from the Center for Diagnostic Imaging and Insight Imaging (CDI) Quality Institute for work on Appropriate Use Criteria for headache imaging; and has received an honorarium from the California Technology Assessment Forum for participation as expert reviewer of the Institute for Clinical and Economic Review Calcitonin Gene-Related Peptide (CGRP) Inhibitors as Preventive Treatments for Patients with Episodic or Chronic Migraine: Effectiveness and Value Final Evidence Report. L. Billinghurst and D. Gloss report no disclosures relevant to the manuscript. A. Hershey has served on a scientific advisory board for Allergan, XOC Pharma, and Amgen; served as an editor for *Headache*, *Cephalalgia*, and the *Journal of Headache and Pain*; has received compensation from Allergan and MAP Pharma and currently receives compensation from Alder, Amgen, Avanir, Curelator, Depomed, Impax, Lilly, Supernus, and Upsher-Smith for serving on speakers' bureaus and as a medical consultant; has received research support from GlaxoSmithKline for serving as a Local Site PI on a study on pediatric migraine treatment, from the Migraine Research Foundation and Curelator, Inc. for serving as a principal investigator on studies on migraine genomics and diagnosis, and from the National Headache Foundation for serving as a coinvestigator on a study on migraine prognosis; has received grants from the National Institutes of Health/National Institute of Neurologic Disorders and Stroke (NINDS) for serving as a coinvestigator on a study on migraine management, studies on treatment, prognosis, and diagnosis of pediatric chronic migraine and headache, and for serving as a dual principal investigator on a study on amitriptyline and topiramate in the prevention of childhood migraine; and serves as a board member of the American Headache Society. N. Licking has no relevant disclosures for this guideline. M. Sowell has received compensation for serving on a speakers' bureau for Amgen/Novartis Pharmaceuticals; has served as manuscript editor for the journal *Headache* and the *Journal of Child Neurology*, on a speakers' bureau for Allergan, and as an interviewer for *Neurology* podcasts; served as site principal investigator for the CHAMP (Childhood and Adolescent Migraine Prevention) study, for which he received research support from NINDS; and receives research support from Impax Pharmaceuticals. M.C. Victorio is the site primary investigator for a childhood and adolescent migraine prevention study funded by the NIH and site investigator for a pediatric migraine treatment study funded by Impax Laboratories (both studies were contracted through Akron Children's Hospital); has received funding for travel to meetings of the

Registry Committee and Quality and Safety Subcommittee by the AAN; has received honoraria for authoring and coauthoring chapters in the *Merck Manual* and for authoring an article in *Pediatric Annals*; and performs the following clinical procedures in her practice: onabotulinumtoxinA injection for chronic migraine (2%) and peripheral nerve block injections (2%). E. Gersz and E. Leininger report no disclosures relevant to the manuscript. H. Zanitsch has received financial compensation from the Patient-Centered Outcomes Research Institute and Peer Reviewed Medical Research Program and serves as a volunteer advocate for the National Headache Foundation. M. Yonker has served on a scientific advisory board for AMGEN and for Upsher-Smith Pharmaceuticals; has served as a reviewer for *Cephalalgia, Headache, Pediatrics,* and the *Journal of the Child Neurology Society*; has received research support as a primary investigator from AstraZeneca, Allergan, Avanir, and NINDS; has received funding for travel from the American Headache Society for serving as a presenter at the Scottsdale Headache Symposium; and serves as a consultant to Impax. Dr. Kenneth Mack has served as an advisor for AMGEN; receives publishing royalties from UpToDate; performs botulinum toxin injections for headache treatment as 5% of his clinical effort; and serves as a member of the *Neurology*® editorial board. Go to Neurology.org/N for full disclosures.

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The AAN is committed to producing independent, critical, and truthful clinical practice guidelines (CPGs). Significant efforts are made to minimize the potential for conflicts of interest to influence the recommendations of this CPG. To the extent possible, the AAN keeps separate those who have a financial stake in the success or failure of the products appraised in the CPGs and the developers of the guidelines. Conflict of interest forms were obtained from all authors and reviewed by an oversight committee prior to project initiation. AAN limits the participation of authors with substantial conflicts of interest. The AAN forbids commercial participation in, or funding of, guideline projects. Drafts of the guideline have been reviewed by at least 3 AAN committees, a network of neurologists, *Neurology* peer reviewers, and representatives from related fields. The AAN Guideline Author Conflict of Interest Policy can be viewed at aan.com. For complete information on this process, access the 2011 AAN process manual, as amended.[2]

Publication history

Received by *Neurology* December 17, 2018. Accepted in final form May 14, 2019.

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