Complete Summary

GUIDELINE TITLE

Practice parameter: pharmacological treatment of migraine headache in children and adolescents: report of the American Academy of Neurology Quality Standards Subcommittee and the Practice Committee of the Child Neurology Society.

BIBLIOGRAPHIC SOURCE(S)

Lewis D, Ashwal S, Hershey A, Hirtz D, Yonker M, Silberstein S. Practice parameter: pharmacological treatment of migraine headache in children and adolescents: report of the American Academy of Neurology Quality Standards Subcommittee and the Practice Committee of the Child Neurology Society. Neurology 2004 Dec 28;63(12):2215-24. [46 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

*** * REGULATORY ALERT * ***

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory information has been released.

- On July 19, 2006, the FDA notified healthcare professionals and consumers of new safety information regarding taking medications used to treat migraine headaches (triptans) together with certain types of antidepressant and mood disorder medications, selective serotonin reuptake inhibitors (SSRIs) and selective serotonin/norepinephrine reuptake inhibitors (SNRIs). A life-threatening condition called serotonin syndrome may occur when triptans are used together with a SSRI or a SNRI. See the FDA Web site for more information.
- On April 7, 2005, after concluding that the overall risk versus benefit profile is unfavorable, the FDA requested that Pfizer, Inc voluntarily withdraw Bextra (valdecoxib) from the market. The FDA also asked manufacturers of all marketed prescription nonsteroidal anti-inflammatory drugs (NSAIDs), including Celebrex (celecoxib), a COX-2 selective NSAID, to revise the labeling (package insert) for their products to include a boxed warning and a Medication Guide. Finally, FDA asked manufacturers of non-prescription (over the counter [OTC]) NSAIDs to revise their labeling to include more specific information about the potential gastrointestinal (GI) and cardiovascular (CV) risks, and information to assist consumers in the safe use of the drug. See the FDA Web site for more information.

COMPLETE SUMMARY CONTENT

** REGULATORY ALERT **
SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
EVIDENCE SUPPORTING THE RECOMMENDATIONS
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
QUALIFYING STATEMENTS
IMPLEMENTATION OF THE GUIDELINE
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES
IDENTIFYING INFORMATION AND AVAILABILITY
DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

Migraine headache

GUIDELINE CATEGORY

Prevention
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Neurology
Pediatrics

INTENDED USERS

Health Plans
Hospitals
Managed Care Organizations
Pharmacists
Physicians
Students
Utilization Management

GUIDELINE OBJECTIVE(S)

- To review evidence on the pharmacologic treatment of the child with migraine headache
- To answer the following questions with regard to acute treatments:
    - How safe and tolerable are acute migraine medications in children and adolescents?

    - What are the effects on acute headache pain of medications taken during the attack?
- To answer the following questions with regard to preventive treatments:
    - What are the effects on the frequency and/or severity of migraine attacks of medications taken on a daily basis for prevention of migraine?
    - How safe and tolerable are preventive migraine medications in children and adolescents?
    - How do the efficacy and tolerability of preventive medications for migraine compare to those for placebo?

TARGET POPULATION

Children and adolescents (aged 3 to 18 years) with migraine headache

INTERVENTIONS AND PRACTICES CONSIDERED

Acute Treatment

1. Sumatriptan nasal spray
2. Subcutaneous and oral sumatriptan*
3. Nonsteroidal anti-inflammatory drugs (NSAIDs) including ibuprofen
4. Acetaminophen
5. Rizatriptan*
6. Zolmitriptan*

Preventive Therapy

1. Flunarizine
2. Cyproheptadine*
3. Amitriptyline*
4. Divalproex sodium*
5. Topiramate*
6. Levetiracetam*
7. Propranolol*
8. Trazodone*
9. Pizotifen*
10. Nimodipine*
11. Clonidine*

*Considered, but not recommended

MAJOR OUTCOMES CONSIDERED

- Resolution of headache and nausea
- Resolution of photophobia and phonophobia
- Pain score
- Frequency of adverse effects of migraine medications
- Headache frequency
- Headache severity
- Headache duration

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Computer-assisted literature searches were conducted with the help of the American Academy of Neurology (AAN) and the University of Minnesota Biomedical Information Services Research Librarian for relevant articles published from 1980 through December 2003. Databases searched included Medline and Current Contents using the following key words: headache, migraine, children and adolescents, and treatment. The age qualifier of 3 years to 18 years was selected, as this is the age group, based on previous literature, when most children are seen for pediatric or neurologic evaluation. Searches included titles from English and non-English language journals. Only those articles reporting studies with $\geq$10 patients were included. Relevant position papers from professional organizations were also reviewed.

Individual committee members reviewed titles and abstracts for content and relevance. Those articles dealing with aspects of treatment of pediatric headache were selected for further detailed review. Bibliographies of the articles cited were checked for additional pertinent references.

NUMBER OF SOURCE DOCUMENTS

166

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Rating of a Therapeutic Article

Class I: Prospective, randomized, controlled clinical trial with masked outcome assessment, in a representative population. The following are required:

a. Primary outcome(s) is/are clearly defined.
b. Exclusion/inclusion criteria are clearly defined.
c. Adequate accounting for dropouts and crossovers with numbers sufficiently low to have minimal potential for bias.
d. Relevant baseline characteristics are presented and substantially equivalent among treatment groups, or there is appropriate statistical adjustment for differences.

Class II: Prospective matched group cohort study in a representative population with masked outcome assessment that meets a-d above OR a randomized, controlled trial in a representative population that lacks one criterion a-d

Class III: All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome is independently assessed, or independently derived by objective outcome measurement**

Class IV: Evidence from uncontrolled studies, case series, case reports, or expert opinion

**Objective outcome measurement - an outcome measure that is unlikely to be affected by an observer's (patient, treating physician, investigator) expectation or bias (e.g., blood tests, administrative outcome data).

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Each of the selected articles was reviewed, abstracted, and classified by at least two committee members. Abstracted data included the number of patients, age, sex, nature of subject selection, case-finding methods (prospective, retrospective, or referral), inclusion and exclusion criteria, headache type and characteristics, and study design and statistical analysis employed.

A four-tiered classification scheme for therapeutic evidence approved by the Quality Standards Subcommittee was utilized (see "Rating Scheme for the Strength of the Evidence" field). Depending on the strength of this evidence it was decided whether specific recommendations could be made, and if so, the strength of these recommendations (see below "Rating Scheme for the Strength of the Recommendations" field). Evidence pertinent to treatment with the committee's evidence-based recommendations is presented.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Other

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

When formulating the recommendations the guideline developers considered the magnitude of the effect (benefit or harm of therapy, accuracy of tests, yield of studies) and the relative value of various outcomes. Under most circumstances, there is a direct link between the level of evidence used to formulate conclusions and the strength of the recommendation. Thus, an "established as" (two class I) conclusion supports a "should be done" (level A) recommendation; a "probably effective" (two class II) conclusion supports a "should be considered" (level B) recommendation; a "possibly effective" (two class III) conclusion supports a "may

be considered" recommendation. In those circumstances where the evidence indicates that the intervention is not effective or useful, wording was modified. For example, if multiple adequately powered class I studies demonstrated that an intervention is not effective, the recommendation read, "should not be done."

There are important exceptions to the rule of having a direct linkage between the level of evidence and the strength of recommendations. Some situations where it may be necessary to break this linkage are listed below:

- A statistically significant but marginally important benefit of the intervention is observed
- The intervention is exorbitantly costly
- Superior and established alternative interventions are available
- There are competing outcomes (both beneficial and harmful) that cannot be reconciled

Under such circumstances the guideline developers may have downgraded the level of the recommendation.

Edlund W, Gronseth G, So Y, Franklin G. Clinical practice guideline process manual. St. Paul (MN): American Academy of Neurology (AAN); 2004. 49 p.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Rating of Recommendation

A = Established as effective, ineffective, or harmful (or established as useful/predictive or not useful/predictive) for the given condition in the specified population

B = Probably effective, ineffective, or harmful (or probably useful/predictive or not useful/predictive) for the given condition in the specified population

C = Possibly effective, ineffective, or harmful (or possibly useful/predictive) for the given condition in the specified population

U = Data inadequate or conflicting. Given current knowledge, treatment (test, predictor) is unproven.

Translation of Evidence to Recommendations

Level A rating requires at least two consistent class I studies.*

Level B rating requires at least one class I study or two consistent class II studies.

Level C rating requires at least one class II study or two consistent class III studies.

Level U rating for studies not meeting criteria for class I-class III

* In exceptional cases, one convincing class I study may suffice for an "A" recommendation if 1) all criteria met, 2) magnitude of effect ≥5, and 3) narrow confidence intervals (lower limit >2).

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The guidelines were approved by the Quality Standards Subcommittee on April 27, 2004, by the Practice Committee on August 7, 2004, and by the American Academy of Neurology (AAN) Board of Directors on October 16, 2004.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions of the strength of the recommendations (A, B, C, U) and classification of the evidence (Class I through Class IV) are provided at the end of the "Major Recommendations" field.

Recommendations for the Acute Treatment of Migraine in Children and Adolescents

1. Ibuprofen is effective and should be considered for the acute treatment of migraine in children (Level A).
2. Acetaminophen is probably effective and should be considered for the acute treatment of migraine in children (Level B).
3. Sumatriptan nasal spray is effective and should be considered for the acute treatment of migraine in adolescents (Level A).
4. There are no data to support or refute use of any oral triptan preparations in children or adolescents (Level U).
5. There are inadequate data to make a judgment on the efficacy of subcutaneous sumatriptan (Level U).

Recommendations for Preventive Therapy of Migraine in Children and Adolescents

1. Flunarizine is probably effective for preventive therapy and can be considered for this purpose but is not available in the United States (Level B).
2. There is insufficient evidence to make any recommendations concerning the use of cyproheptadine, amitriptyline, divalproex sodium, topiramate, or levetiracetam (Level U).

3. Recommendations cannot be made concerning propranolol or trazodone for preventive therapy as the evidence is conflicting (Level U).
4. Pizotifen and nimodipine (Level B) and clonidine (Level B) did not show efficacy and are not recommended.

Definitions:

Rating of Recommendation

A = Established as effective, ineffective, or harmful (or established as useful/predictive or not useful/predictive) for the given condition in the specified population

B = Probably effective, ineffective, or harmful (or probably useful/predictive or not useful/predictive) for the given condition in the specified population

C = Possibly effective, ineffective, or harmful (or possibly useful/predictive) for the given condition in the specified population

U = Data inadequate or conflicting. Given current knowledge, treatment (test, predictor) is unproven.

Translation of Evidence to Recommendations

Level A rating requires at least two consistent class I studies.*

Level B rating requires at least one class I study or two consistent class II studies.

Level C rating requires at least one class II study or two consistent class III studies.

Level U rating for studies not meeting criteria for class I-class III

* In exceptional cases, one convincing class I study may suffice for an "A" recommendation if 1) all criteria met, 2) magnitude of effect $\geq$5, and 3) narrow confidence intervals (lower limit >2).

Rating of a Therapeutic Article

Class I: Prospective, randomized, controlled clinical trial with masked outcome assessment, in a representative population. The following are required:

a. Primary outcome(s) is/are clearly defined.
b. Exclusion/inclusion criteria are clearly defined.
c. Adequate accounting for dropouts and crossovers with numbers sufficiently low to have minimal potential for bias
d. Relevant baseline characteristics are presented and substantially equivalent among treatment groups, or there is appropriate statistical adjustment for differences.

Class II: Prospective matched group cohort study in a representative population with masked outcome assessment that meets a-d above OR a randomized, controlled trial in a representative population that lacks one criterion a-d

Class III: All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome is independently assessed, or independently derived by objective outcome measurement**

Class IV: Evidence from uncontrolled studies, case series, case reports, or expert opinion

** Objective outcome measurement - an outcome measure that is unlikely to be affected by an observer's (patient, treating physician, investigator) expectation or bias (e.g., blood tests, administrative outcome data).

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate pharmacological prevention and treatment of migraine headache in children and adolescents

POTENTIAL HARMS

Adverse effects of the various treatments

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- This statement is provided as an educational service of the American Academy of Neurology (AAN). It is based on an assessment of current scientific and clinical information. It is not intended to include all possible proper methods of care for a particular neurologic problem or all legitimate criteria for choosing to use a specific procedure. Neither is it intended to exclude any reasonable alternative methodologies. The American Academy of Neurology recognizes that specific patient care decisions are the prerogative

of the patient and the physician caring for the patient, based on all of the circumstances involved.
- Failure of an agent for acute or preventive therapy to demonstrate efficacy to a statistically significant degree does not imply that these medications have no role in the pediatric population and their use must be based upon good clinical judgment.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Clinical Algorithm
Patient Resources
Personal Digital Assistant (PDA) Downloads
Quick Reference Guides/Physician Guides
Slide Presentation
Staff Training/Competency Material

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Lewis D, Ashwal S, Hershey A, Hirtz D, Yonker M, Silberstein S. Practice parameter: pharmacological treatment of migraine headache in children and adolescents: report of the American Academy of Neurology Quality Standards Subcommittee and the Practice Committee of the Child Neurology Society. Neurology 2004 Dec 28;63(12):2215-24. [46 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2004 Dec

GUIDELINE DEVELOPER(S)

American Academy of Neurology - Medical Specialty Society

SOURCE(S) OF FUNDING

American Academy of Neurology (AAN)

GUIDELINE COMMITTEE

Quality Standards Subcommittee
Practice Committee of the Child Neurology Society

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Quality Standards Subcommittee Members: Gary Franklin, MD, MPH (co-chair); Gary Gronseth, MD (co-chair); Charles E. Argoff, MD; Steven A. Ashwal, MD (ex-officio); Christopher Bever, Jr., MD; Jody Corey-Bloom, MD, PhD; John D. England, MD; Jacqueline French, MD (ex-officio); Gary H. Friday, MD; Michael J. Glantz, MD; Deborah Hirtz, MD; Donald J. Iverson, MD; David J. Thurman, MD; Samuel Wiebe, MD; William J. Weiner, MD; Catherine Zahn, MD (ex-officio)

CNS Practice Committee Members: Carmela Tardo, MD (chair); Bruce Cohen, MD (vice-chair); Elias Chalhub, MD; Roy Elterman, MD; Murray Engel, MD; Bhuwan P. Garg, MD; Brian Grabert, MD; Annette Grefe, MD; Michael Goldstein, MD; David Griesemer, MD; Betty Koo, MD; Edward Kovnar, MD; Leslie Anne Morrison, MD; Colette Parker, MD; Ben Renfroe, MD; Anthony Riela, MD; Michael Shevell, MD; Shlomo Shinnar, MD; Herald Silverboard, MD; Russell Snyder, MD; Dean Timmons, MD; Greg Yim, MD; Mary Anne Whelan, MD

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

D.L. has grant funded research grants from Astra-Zeneca, Ortho-McNeil, Merck, American Home Products, GlaxoSmithKline, Abbott Laboratories, and Eli Lilly. A.H. has grant support from MedPointe, Pfizer, and Ortho-McNeil; advisory board for Astra-Zeneca and Ortho-McNeil; grant support from GlaxoSmith-Kline, Ortho-McNeil, and UCB Pharma; pharmaceutical studies sponsored by AstraZeneca, GSK, Ortho-McNeil, Johnson & Johnson, and Abbott Laboratories. M.Y. has grant funded research from Ortho-McNeal and Astra-Zeneca. S.S. is on the advisory panel, speakers bureau, or serves as a consultant for Abbott, Allergan, AstraZeneca, Eli Lilly, GlaxoSmithKline, Johnson & Johnson, Merck, Metis, NPS, Pfizer, Pozen, UCB Pharma, and X-Cel Pharmaceuticals; he receives research support from Abbott, Allergan, AstraZeneca, Eli Lilly, GlaxoSmithKline, Johnson & Johnson, Medtronics, Merck, NPS, Pfizer, Pozen, UCB Pharma, and X-Cel Pharmaceuticals.

ENDORSER(S)

American Academy of Pediatrics - Medical Specialty Society

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: A list of American Academy of Neurology (AAN) guidelines, along with a link to a Portable Document Format (PDF) file for this guideline, is available at the AAN Web site.

Print copies: Available from the AAN Member Services Center, (800) 879-1960, or from AAN, 1080 Montreal Avenue, St. Paul, MN 55116.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Pharmacological treatment of migraine headache in children and adolescents. AAN guideline summary for clinicians. St. Paul (MN): American Academy of Neurology. 2 p. Available in Portable Document Format (PDF) file from the American Academy of Neurology (AAN) Web site.
- Pharmacological treatment of migraine headache in children and adolescents. CME quiz. Available online to subscribers of Neurology at the Neurology Web site.
- Practice parameter: pharmacological treatment of migraine headache in children and adolescents. St. Paul (MN): American Academy of Neurology. 2004. 14 p. Available for personal digital assistant (PDA) download from the AAN Web site.
- Pharmacological treatment of migraine headache in children and adolescents. Slide presentation. St. Paul (MN): American Academy of Neurology. Available as a Power Point file from the AAN Web site.
- AAN encounter kit for dementia: a multi-media, web-based algorithm. Available from the AAN Web site.
- AAN guideline development process [online]. St. Paul (MN): American Academy of Neurology. Available from the AAN Web site.
- Edlund W, Gronseth G, So Y, Franklin G. Clinical practice guideline process manual. St. Paul (MN): American Academy of Neurology (AAN); 2004. 49 p. Electronic copies available in Portable Document Format (PDF) from the AAN Web site.

PATIENT RESOURCES

The following is available:

- Pharmacological treatment of migraine headache in children and adolescents. AAN guideline summary for parents and caregivers. St. Paul (MN): American Academy of Neurology (AAN). 2 p.

Electronic copies: Available in Portable Document Format (PDF) from the AAN Web site.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

This NGC summary was completed by ECRI on February 11, 2005. The information was verified by the guideline developer on March 8, 2005. This summary was most recently updated on May 3, 2005 following the withdrawal of Bextra (valdecoxib) from the market and the release of heightened warnings for Celebrex (celecoxib) and other nonselective nonsteroidal anti-inflammatory drugs (NSAIDs). This summary was updated by ECRI on August 29, 2006, following the U.S. Food and Drug Administration advisory on Triptans, SSRIs, and SNRIs.

COPYRIGHT STATEMENT

This NGC summary is based on the original guideline, which is copyrighted by the American Academy of Neurology.

DISCLAIMER

NGC DISCLAIMER

The National Guideline Clearinghouse™ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria which may be found at http://www.guideline.gov/about/inclusion.aspx.

NGC, AHRQ, and its contractor ECRI make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.

© 1998-2006 National Guideline Clearinghouse

Date Modified: 10/9/2006