Complete Summary

GUIDELINE TITLE

Guidelines for the management of severe traumatic brain injury. Antiseizure prophylaxis.

BIBLIOGRAPHIC SOURCE(S)

Brain Trauma Foundation, American Association of Neurological Surgeons, Congress of Neurological Surgeons. Guidelines for the management of severe traumatic brain injury. Antiseizure prophylaxis. J Neurotrauma 2007;24(Suppl 1):S83-S86. [13 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates previous versions: Brain Trauma Foundation, American Association of Neurological Surgeons, Congress of Neurological Surgeons, Joint Section on Neurotrauma and Critical Care. Guidelines for the management of severe traumatic brain injury: cerebral perfusion pressure. New York (NY): Brain Trauma Foundation, Inc.; 2003 Mar 14. 14 p.

Brain Trauma Foundation, Inc, American Association of Neurological Surgeons. Part 1: guidelines for the management of severe traumatic brain injury. New York (NY): Brain Trauma Foundation, Inc.; 2000. 165 p.

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SCOPE

DISEASE/CONDITION(S)

Posttraumatic seizures associated with severe traumatic brain injury

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Management
Prevention
Treatment

CLINICAL SPECIALTY

Critical Care
Emergency Medicine
Neurological Surgery
Neurology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

- To offer the possibility for uniformity of traumatic brain injury care, and conformity with the best standards of clinical practice
- To evaluate the efficacy and overall benefit, as well as potential harms, of anticonvulsants used for the prevention of posttraumatic seizures

TARGET POPULATION

Adults with severe traumatic brain injury (Glasgow Coma Scale score 3-8)

INTERVENTIONS AND PRACTICES CONSIDERED

Antiseizure prophylaxis with anticonvulsants (phenytoin, valproate)

MAJOR OUTCOMES CONSIDERED

- Incidence of early and late posttraumatic seizures
- Incidence of drug-related side effects (e.g., hypersensitivity reactions, neuropsychological performance)
- Morbidity and mortality

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

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

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

General Search Strategy

Center staff worked with a doctoral level research librarian to construct electronic search strategies for each topic (see Appendix B of the original guideline document). For new topics, the literature was searched from 1966 to 2004, and for previous topics from 1996 to 2004. Strategies with the highest likelihood of capturing most of the targeted literature were used, which resulted in the acquisition of a large proportion of non-relevant citations. Two authors were assigned to the topic, and a set of abstracts was sent to each. Blinded to each others' work, they read the abstracts and eliminated citations using the pre-determined inclusion/exclusion criteria.

Inclusion Criteria

- Human subjects
- Traumatic brain injury (TBI)
- English language
- Adults (age $\geq$18 years)
- In-hospital (e.g., no studies from the prehospital setting)
- $\geq$25 subjects
- Randomized controlled trials (RCTs), cohort studies, case-control studies, case series, databases, registries

Exclusion Criteria

- Sample contained >15% of pediatric patients or >15% of patients with pathologies other than TBI, and the data were not reported separately (see Appendix C of the original protocol document)
- Wrong independent variable (e.g., the intervention was not specific to the topic)
- Wrong dependent variable (e.g., outcomes were not mortality or morbidity, or did not associate with clinical outcomes)
- Case studies, editorials, comments, letters

Center staff compared the selections, and identified and resolved discrepancies either through consensus or through use of a third reviewer. A set of full-text publications was then sent to each author. Again blinded to each others' work, they read the publications and selected those that met the inclusion criteria.

Results of the electronic searches were supplemented by recommendations of peers and by reading reference lists of included studies. A second search was conducted from 2004 through April 2006 to capture any relevant Class I or II literature (see "Rating Scheme for the Strength of the Evidence") that might have been published since the first literature search in 2004. Relevant publications were added to those from the original search, constituting the final library of studies that were used as evidence in this document. The yield of literature from each phase of the search is presented in Appendix D of the original guideline document.

Specific Strategy for This Topic

For this update, Medline was searched from 1996 through April of 2006 (see Appendix B of the original guideline document for search strategy), and results were supplemented with literature recommended by peers or identified from reference lists. Of 10 potentially relevant studies, one was added to the existing table and used as evidence for this question (see Evidence Table I in the original guideline document).

NUMBER OF SOURCE DOCUMENTS

5

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

Class I: Good quality randomized controlled trial (RCT)

Class II: Moderate quality RCT, good quality cohort, or good quality case-control

Class III: Poor quality RCT; moderate or poor quality cohort; moderate or poor case-control; case series, databases, or registries

Additional detail on quality criteria for each category is available in the original guideline document.

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Data Abstraction and Synthesis

Two authors independently abstracted data from each publication using an evidence table template (see Appendix E in the original guideline document). They compared results of their data abstraction and through consensus finalized the data tables. Due to methodological heterogeneity of studies within topics, and to the lack of literature of adequate quality, data were not combined for this topic.

Quality Assessment and Classification of Evidence for Treatment Topics

In April of 2004, the Brain Trauma Foundation established a collaboration with the Evidence-Based Practice Center (EPC) from Oregon Health & Science University (OHSU). Center staff worked with two EPC epidemiologists to develop criteria and procedures for the quality assessment of the literature. Criteria for classification of evidence based on study design and quality are derived from criteria developed by the U.S. Preventive Services Task Force, the National Health Service Centre for

Reviews and Dissemination (U.K.), and the Cochrane Collaboration (see "Rating Scheme for the Strength of the Evidence in this summary" and Table 1 in the original guideline document).

Two investigators independently read the studies included in the Evidence Tables (both new studies and those maintained from the previous edition) and classified them as Class I, II, or III, based on the design and quality criteria. Discrepancies were resolved through consensus, or through a third person's review.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

In 2004, the Brain Trauma Foundation (BTF) called a meeting of all the Traumatic Brain Injury (TBI) Guidelines contributing authors for the purpose of formalizing a collaborative process of Guidelines updates, publication, and implementation shared by those with a stake in acute TBI care. A partnership of interested professional associations was formed to review, endorse and implement editions of the Guidelines. The mission of this TBI Partnership is to improve the outcome of TBI through collaboration and the promotion of evidence-based medicine.

For these and future Guidelines projects, contributing authors agreed to establish a Center for Guidelines Management (Center), which would be responsible for generating new guidelines as well as updating those that exist. The participants endorsed the BTF proposal to establish the Center to be located at Oregon Health & Sciences University (OHSU). A collaboration was established between the Center and the Oregon Evidence-based Practice Center (EPC). The Oregon EPC conducts systematic reviews of various healthcare topics for federal and state agencies and private foundations. These reviews report the evidence from clinical research studies, and the quality of that evidence, for use by policy makers in decisions about guidelines and coverage issues. The collaboration made the expertise and personnel of the EPC available to the Center.

The TBI partnership further agreed to adopt and explicitly adhere to a systematic process and set of criteria for reviewing, assessing, and synthesizing the scientific literature. The process and criteria are derived from work by the U.S. Preventive Services Task Force, the National Health Service Centre for Reviews and Dissemination (U.K.), and the Cochrane Collaboration. The goal was to establish a process for *Guidelines* development that was scientifically rigorous, consistent across all topics, and independent of the interests and biases of contributing authors.

Authors drafted manuscripts for each topic. The entire team gathered for a 2-day work session to discuss the literature base and to achieve consensus on classification of evidence and level of recommendations. Manuscripts were revised. Virtual meetings were held with a subset of the co-authors to complete the editing and consensus processes. The final draft manuscript was circulated to the peer review panel.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Levels of recommendation are Level I, II, and III, derived from Class I, II, and III evidence, respectively.

- **Level I** recommendations are based on the strongest evidence for effectiveness, and represent principles of patient management that reflect a high degree of clinical certainty.
- **Level II** recommendations reflect a moderate degree of clinical certainty.
- For **Level III** recommendations, the degree of clinical certainty is not established.

To determine the recommendation level derived from a meta-analysis, three criteria were considered:

- Were all included studies of the same quality class?
- Were the findings of the studies in the same or contradictory directions?
- What were the results of analyses that examine potential confounding factors?

Thus, a meta-analysis containing only Class II studies may have been used to make a Level III recommendation if the answers to the above questions render uncertainty in the confidence of the overall findings.

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

A partnership of interested professional associations was formed to review, endorse and implement editions of the Guidelines. The mission of this Traumatic Brain Injury (TBI) Partnership is to improve the outcome of TBI through collaboration and the promotion of evidence-based medicine.

The partnership also recommended appointing a Review Committee to consist of a small number of individuals who would serve as liaison between the guidelines development process and the key medical societies related to TBI. These representatives of neurosurgery, trauma, neurointensive care, pediatrics, emergency medicine, and prehospital care, as well as international organizations, were standing members of the Committee across all Guidelines updates. The current members of this Committee reviewed this edition of the Guidelines (the names of reviewers are listed at the front of the original guideline document).

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The grades of evidence (I-III) and levels of recommendations (I-III) are defined at the end of the "Major Recommendations" field.

Level I

There are insufficient data to support a Level I recommendation for this topic.

Level II

Prophylactic use of phenytoin or valproate is not recommended for preventing late posttraumatic seizures (PTS).

Anticonvulsants are indicated to decrease the incidence of early PTS (within 7 days of injury). However, early PTS is not associated with worse outcomes.

Summary

The majority of studies do not support the use of the prophylactic anticonvulsants evaluated thus far for the prevention of late PTS. Routine seizure prophylaxis later than 1 week following traumatic brain injury (TBI) is, therefore, not recommended. If late PTS occurs, patients should be managed in accordance with standard approaches to patients with new onset seizures. Phenytoin has been shown to reduce the incidence of early PTS. Valproate may also have a comparable effect to phenytoin on reducing early PTS but may also be associated with a higher mortality.

Definitions:

Grades of Evidence

Class I - Good quality randomized controlled trial (RCT)

Class II - Moderate quality RCT, good quality cohort, or good quality case-control

Class III - Poor quality RCT; moderate or poor quality cohort; moderate or poor case-control; or case series, databases, or registries

Levels of Recommendation

Levels of recommendation are Level I, II, and III, derived from Class I, II, and III evidence, respectively.

Level I - Recommendations are based on the strongest evidence for effectiveness, and represent principles of patient management that reflect a high degree of clinical certainty.

Level II - Recommendations reflect a moderate degree of clinical certainty.

Level III - Recommendations for which the degree of clinical certainty is not established.

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 the "Major Recommendations" field).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Reduction in early posttraumatic seizures

POTENTIAL HARMS

- Anticonvulsants have been associated with adverse side effects including rashes, Stevens-Johnson syndrome, hematologic abnormalities, ataxia, and neurobehavioral side effects.
- There was a trend toward higher mortality in patients treated with valproate.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- The information contained in this guideline reflects the current state of knowledge at the time of publication. The Brain Trauma Foundation (BTF), American Association of Neurological Surgeons (AANS), Congress of Neurological Surgeons (CNS), and other collaborating organizations are not engaged in rendering professional medical services and assume no responsibility for patient outcomes resulting from application of these general recommendations in specific patient circumstances. Accordingly, the BTF, AANS, and CNS consider adherence to these clinical practice guidelines will not necessarily assure a successful medical outcome. The information contained in these guidelines reflects published scientific evidence at the time of completion of the guidelines and cannot anticipate subsequent findings and/or additional evidence, and therefore should not be considered inclusive of all proper procedures and tests or exclusive of other procedures and tests that are reasonably directed to obtaining the same result. Medical advice and decisions are appropriately made only by a competent and licensed physician who must make decisions in light of all the facts and circumstances in each

individual and particular case and on the basis of availability of resources and expertise. Guidelines are not intended to supplant physician judgment with respect to particular patients or special clinical situations and are not a substitute for physician-patient consultation. Accordingly, the BTF, AANS, and CNS consider adherence to these guidelines to be voluntary, with the ultimate determination regarding their application to be made by the physician in light of each patient's individual circumstances.

- As with the previous guidelines for traumatic brain injury, the reader must be aware of the limitations and restricted scope of the guidelines. The guidelines reflect only what is contained in the existing human-based literature. They do not reflect pathomechanistic information from animal studies, nor *in vitro* or mathematical modeling studies.
- As in all areas of clinical medicine, the optimal plan of management for an individual patient may not fall exactly within the recommendations of these guidelines. This is because all patients, and in particular, neurotrauma patients, have heterogeneous injuries, and optimal management depends on a synthesis of the established knowledge based upon *Guidelines*, and then applied to the clinical findings in the individual patient, and refined by the clinical judgment of the treating physician.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Brain Trauma Foundation, American Association of Neurological Surgeons, Congress of Neurological Surgeons. Guidelines for the management of severe traumatic brain injury. Antiseizure prophylaxis. J Neurotrauma 2007;24(Suppl 1):S83-S86. [13 references]

ADAPTATION

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

DATE RELEASED

2000 (revised 2007)

GUIDELINE DEVELOPER(S)

Brain Trauma Foundation - Disease Specific Society

SOURCE(S) OF FUNDING

Brain Trauma Foundation

GUIDELINE COMMITTEE

Not stated

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

ENDORSER(S)

Congress of Neurological Surgeons - Professional Association

GUIDELINE STATUS

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Brain Trauma Foundation, Inc, American Association of Neurological Surgeons. Part 1: guidelines for the management of severe traumatic brain injury. New York (NY): Brain Trauma Foundation, Inc.; 2000. 165 p.

GUIDELINE AVAILABILITY

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

Print copies: Available from the Brain Trauma Foundation, 708 Third Avenue, New York, NY 10017, E-mail: info@braintrauma.org

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI Institute on August 15, 2007. The information was verified by the guideline developer on January 28, 2008.

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