General

Guideline Title


Bibliographic Source(s)


Guideline Status

This is the current release of the guideline.


The American Academy of Neurology reaffirmed the currency of this guideline in November 2016.

This guideline meets NGC’s 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

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

Acute Inflammatory Demyelinating Polyneuropathy (AIDP)/Guillain-Barré Syndrome (GBS)

Conclusions

On the basis of consistent findings from Class I studies, plasmapheresis is established as effective for the treatment of AIDP/GBS severe enough to impair the ability to walk independently or severe enough to require mechanical ventilation. For milder AIDP/GBS, in which ambulation is preserved, plasmapheresis is probably effective, based on a single Class I study.

Recommendations

Plasmapheresis should be offered in the treatment of AIDP/GBS severe enough to impair independent walking or to require mechanical ventilation (Level A). Plasmapheresis should be considered in the treatment of milder clinical presentations of AIDP/GBS (Level B).
Clinical Context

Intravenous immunoglobulin (IVIg) is an alternative treatment used in patients with AIDP/GBS. There is insufficient evidence to demonstrate the superiority of one treatment over the other.

Chronic Inflammatory Demyelinating Neuropathy (CIDP)

Conclusions

Based on 2 Class I studies, plasmapheresis is established as effective in the short-term treatment of CIDP; both studies showed the beneficial effect is not sustained, with worsening beginning 1–5 weeks after last plasmapheresis treatment.

Recommendation

Plasmapheresis should be offered as a short-term treatment for patients with CIDP (Level A).

Clinical Context

Steroids, IVIg, and immunosuppressants have also been used in the treatment of CIDP.

Dysimmune Neuropathies

Conclusions

Plasmapheresis is probably effective in immunoglobulin A (IgA)- and immunoglobulin G (IgG)-monoclonal gammopathy of undetermined significance (MGUS)-associated polyneuropathy, based on one Class I study. On the basis of one Class I and one Class III study, plasmapheresis is probably not effective in polyneuropathy associated with immunoglobulin M (IgM) MGUS.

Recommendations

Plasmapheresis should be considered in polyneuropathy associated with IgA and IgG MGUS (Level B). Plasmapheresis should not be considered in the treatment of polyneuropathy associated with IgM MGUS (Level B).

Myasthenia Gravis (MG)

Conclusions

There are inadequate data to evaluate the use of plasmapheresis in the treatment of myasthenic crisis or in the treatment of MG prethymectomy.

Recommendation

Because of the lack of randomized controlled studies with masked outcomes, there is insufficient evidence to support or refute the efficacy of plasmapheresis in the treatment of myasthenic crisis (Level U) or MG prethymectomy (Level U).

Clinical Context

Despite the fact that the use of plasmapheresis in myasthenic crisis and MG prethymectomy receives a Level U recommendation, plasmapheresis is used at many medical centers for these indications.

Central Nervous System (CNS) Demyelinating Disease

Conclusions

Plasmapheresis as adjunctive therapy is probably effective for management of exacerbations in relapsing forms of multiple sclerosis (MS), based on a single Class I study. Based on a single Class II study, plasmapheresis is possibly effective for acute fulminant CNS demyelinating diseases (including MS, acute disseminated encephalomyelitis, neuromyelitis optica, and transverse myelitis) that fail to respond to high-dose corticosteroid treatment. Because the study included subgroups of patients with demyelinating diseases, it is not possible to determine if plasmapheresis is more or less effective in patients with different demyelinating diseases. For chronic progressive or secondary progressive MS, plasmapheresis is established as ineffective based on consistent Class I evidence. (Note that the term chronic progressive MS is no longer used, but previously included patients are now described as having either primary progressive MS or secondary progressive MS.)

Recommendations

Plasmapheresis should be considered for the adjunctive treatment of exacerbations in relapsing forms of MS (Level B). Plasmapheresis may be
considered in the treatment of fulminant CNS demyelinating diseases that fail to respond to high-dose corticosteroid treatment (Level C). Plasmapheresis should not be offered for chronic progressive or secondary progressive MS (Level A).

Clinical Context

No studies on the efficacy of plasmapheresis compared to other treatment options in MS are available.

Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infection (PANDAS)

Conclusions

There are inadequate data to determine the efficacy of plasmapheresis in the treatment of acute obsessive-compulsive disorder (OCD) and tic symptoms in the setting of PANDAS (one Class III study).

Recommendation

There is insufficient evidence to support or refute the use of plasmapheresis in the treatment of acute OCD and tic symptoms in the setting of PANDAS (Level U).

Sydenham Chorea

Conclusions

There are inadequate data to determine the efficacy of plasmapheresis in Sydenham chorea (one Class III study).

Recommendation

There is insufficient evidence to support or refute the use of plasmapheresis in the treatment of Sydenham chorea (Level U).

Definitions:

Classification of Recommendations

The strength of practice recommendations is linked directly to the level of evidence:

Level A = Established as effective, ineffective or harmful (or established as useful/predictive or not useful/predictive) for the given condition in the specified population. (Level A rating requires at least two consistent Class I studies.*)

Level B = Probably effective, ineffective or harmful (or probably useful/predictive or not useful/predictive) for the given condition in the specified population. (Level B rating requires at least one Class I study or two consistent Class II studies.)

Level C = Possibly effective, ineffective or harmful (or possibly useful/predictive or not useful/predictive) for the given condition in the specified population. (Level C rating requires at least one Class II study or two consistent Class III studies.)

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

*In exceptional cases, one convincing Class I study may suffice for an "A" recommendation if 1) all criteria are met, 2) the magnitude of effect is large (relative rate improved outcome >5 and the lower limit of the confidence interval is >2).

Classification of Evidence for Therapeutic Intervention

Class I: A randomized, controlled clinical trial of the intervention of interest with masked or objective outcome assessment, in a representative population. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences.

The following are also required:

a. Concealed allocation
b. Primary outcome(s) clearly defined
c. Exclusion/inclusion criteria clearly defined
d. Adequate accounting for drop-outs (with at least 80% of enrolled subjects completing the study) and crossovers with numbers sufficiently low to have minimal potential for bias.

e. For non-inferiority or equivalence trials claiming to prove efficacy for one or both drugs, the following are also required*:

1. The authors explicitly state the clinically meaningful difference to be excluded by defining the threshold for equivalence or non-
The standard treatment used in the study is substantially similar to that used in previous studies establishing efficacy of the standard treatment (e.g., for a drug, the mode of administration, dose and dosage adjustments are similar to those previously shown to be effective).

3. The inclusion and exclusion criteria for patient selection and the outcomes of patients on the standard treatment are comparable to those of previous studies establishing efficacy of the standard treatment.

4. The interpretation of the results of the study is based upon a per protocol analysis that takes into account dropouts or crossovers.

Class II: A randomized controlled clinical trial of the intervention of interest in a representative population with masked or objective outcome assessment that lacks one criteria a-e above or a prospective matched cohort study with masked or objective outcome assessment in a representative population that meets b-e above. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences.

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: Studies not meeting Class I, II or III criteria including consensus or expert opinion.

*Note that numbers 1-3 in Class Ie are required for Class II in equivalence trials. If any one of the three are missing, the class is automatically downgraded to Class III.

**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

Scope

Disease/Condition(s)

Neurologic disorders including:

- Acute inflammatory demyelinating polyneuropathy (AIDP)/Guillain-Barré syndrome (GBS)
- Chronic inflammatory demyelinating polyneuropathy (CIDP)
- Chronic or secondary progressive multiple sclerosis (MS)
- Dysimmune neuropathies: neuropathy associated with immunoglobulin A (IgA), immunoglobulin G (IgG), and immunoglobulin M (IgM) gammopathy
- Acute fulminant demyelinating central nervous system (CNS) disease
- Myasthenia gravis
- Pediatric autoimmune neuropsychiatric disorders associated with streptococcus infection (PANDAS)
- Sydenham chorea

Guideline Category

Technology Assessment

Treatment

Clinical Specialty

Family Practice

Internal Medicine
Intended Users
Advanced Practice Nurses
Physician Assistants
Physicians

Guideline Objective(s)
To reassess the role of plasmapheresis in the treatment of neurologic disorders

Target Population
Patients with neurologic disorders

Interventions and Practices Considered
Plasmapheresis (plasma exchange)

Major Outcomes Considered
- Effectiveness of plasmapheresis for neurologic disorders
- Disease specific:
  - Severe acute inflammatory demyelinating polyneuropathy (AIDP)/Guillain-Barré syndrome (GBS)
    - Patient's ability to walk
    - Time to motor recovery
  - Chronic inflammatory demyelinating polyneuropathy/dysimmune neuropathies
    - Change on the Neuropathy Disability Scale (NDS)
    - Clinical grade and grip strength measurement
    - Electrophysiologic measures
  - Myasthenia gravis (MG)
    - Change in respiratory measures
    - Occurrence of myasthenic crisis
  - Central nervous system (CNS) demyelinating disease
    - Occurrence and severity of multiple sclerosis (MS) exacerbations
    - Changes on standardized clinical scales for the targeted neurologic deficits
  - Pediatric autoimmune neuropsychiatric disorders associated with streptococcus infection (PANDAS)
    - Change in obsessive-compulsive disorder (OCD) symptoms, anxiety, overall functioning, and tics
  - Sydenham chorea
    - Chorea severity
    - Ability to perform selected activities of daily living (ADL)

Methodology

Methods Used to Collect/Select the Evidence
Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

2011 Guideline

The MEDLINE, Cochrane Library, Web of Science, and EMBASE databases were searched from 1995 to September 2009 using the terms "plasmapheresis" and "neurologic disease (exploded)" and key text words and index words for plasmapheresis, plasma exchange, immunoadsorption, and double filtration plasmapheresis. The search was limited to reports in humans and abstracts available in English. Standard search procedures were used, and subheadings were applied as appropriate. The initial search yielded 2,263 articles. This list was refined by reviewing the abstracts and including only articles reporting results from controlled clinical trials in humans.

2016 Reaffirmation

The guideline developer searched Medline for studies published between January 2013 to January 2016, using the following search strategy: "plasmapheresis" and "neurologic disease" and key text words and index words for plasmapheresis, plasma exchange, immunoadsorption, and double filtration plasmapheresis. Inclusion criteria were RCTs, humans only, relevant to clinical questions; exclusion criteria used to screen search results were the same as described in the 2011 published guideline.

Number of Source Documents

Fifty-nine articles considered relevant to the guideline were reviewed in their entirety.

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

Classification of Evidence for Therapeutic Intervention

Class I: A randomized, controlled clinical trial of the intervention of interest with masked or objective outcome assessment, in a representative population. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences.

The following are also required:

a. Concealed allocation
b. Primary outcome(s) clearly defined
c. Exclusion/inclusion criteria clearly defined
d. Adequate accounting for drop-outs (with at least 80% of enrolled subjects completing the study) and crossovers with numbers sufficiently low to have minimal potential for bias.
e. For non-inferiority or equivalence trials claiming to prove efficacy for one or both drugs, the following are also required*:
   1. The authors explicitly state the clinically meaningful difference to be excluded by defining the threshold for equivalence or non-inferiority.
   2. The standard treatment used in the study is substantially similar to that used in previous studies establishing efficacy of the standard treatment (e.g., for a drug, the mode of administration, dose and dosage adjustments are similar to those previously shown to be effective).
   3. The inclusion and exclusion criteria for patient selection and the outcomes of patients on the standard treatment are comparable to those of previous studies establishing efficacy of the standard treatment.
   4. The interpretation of the results of the study is based upon a per protocol analysis that takes into account dropouts or crossovers.

Class II: A randomized controlled clinical trial of the intervention of interest in a representative population with masked or objective outcome assessment that lacks one criteria a-e above or a prospective matched cohort study with masked or objective outcome assessment in a
representative population that meets b-e above. Relevant baseline characteristics are presented and substantially equivalent among treatment
groups or there is appropriate statistical adjustment for differences.

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: Studies not meeting Class I, II or III criteria including consensus or expert opinion.

*Note that numbers 1-3 in Class Ie are required for Class II in equivalence trials. If any one of the three are missing, the class is automatically downgraded to Class III.

**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

Description of the Methods Used to Analyze the Evidence

The evidence was rated according to the American Academy of Neurology (AAN) criteria for the classification of therapeutic articles, and
recommendations were linked to the strength of the evidence. In addition, due to revision of the definitions of classification of evidence since 1996,
the evidence cited in the previous AAN assessment was reviewed and reclassified accordingly.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

2011 Guideline

The Therapeutics and Technology Assessment (TTA) subcommittee of the American Academy of Neurology (AAN) appointed panel members
for this assessment based on their expertise in the neurologic disorders under discussion, their familiarity with the guideline process, or both.

The strength of the practice recommendations was directly linked to the class of evidence using the scheme described in the "Rating Scheme for the
Strength of the Evidence" field.

2016 Reaffirmation

A Guideline Development, Dissemination, and Implementation (GDDI) Subcommittee member who had expertise in autoimmune and movement
disorders conducted a targeted literature search for high quality studies using the same criteria as presented in the original guideline. The GDDI
reviewer and the subcommittee reviewed the new evidence and determined that the following three criteria were met: 1. There is no new evidence
that would alter conclusions or recommendations in the guideline since the last literature search, 2. Guideline methodology is sound and current
methodology is not substantially different, and 3. No significant practice variation relevant to the guideline currently exists.

Rating Scheme for the Strength of the Recommendations

Classification of Recommendations

Level A = Established as effective, ineffective or harmful (or established as useful/predictive or not useful/predictive) for the given condition in the
specified population. (Level A rating requires at least two consistent Class I studies.)*

Level B = Probably effective, ineffective or harmful (or probably useful/predictive or not useful/predictive) for the given condition in the specified
population. (Level B rating requires at least one Class I study or two consistent Class II studies.)

Level C = Possibly effective, ineffective or harmful (or possibly useful/predictive or not useful/predictive) for the given condition in the specified
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

Drafts of the guideline have been reviewed by at least 3 American Academy of Neurology (AAN) committees, a network of neurologists, Neurology® peer reviewers, and representatives from related fields.

This guideline was approved by the Therapeutics and Technology Assessment Subcommittee on February 6, 2010; by the Practice Committee on June 28, 2010; and by the AAN Board of Directors on October 18, 2010.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

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

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Appropriate utilization of plasmapheresis in treating neurologic conditions
- Improved clinical outcome of patients with neurologic conditions, such as acute inflammatory demyelinating polyneuropathy (AIDP)/Guillain-Barré syndrome (GBS), due to effective plasmapheresis

Potential Harms

In one reported study, rebound worsening of symptoms occurred in 8 of 15 patients (66%) with chronic inflammatory demyelinating polyneuropathy following plasmapheresis.

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
Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Patient Resources
Pocket Guide/Reference Cards
Quick Reference Guides/Physician Guides
Resources
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
Living with Illness

IOM Domain
Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

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

Date Released
2011 Jan 18 (reaffirmed 2016 Nov 22)

Guideline Developer(s)
American Academy of Neurology - Medical Specialty Society

Source(s) of Funding
American Academy of Neurology (AAN)

Guideline Committee
Therapeutics and Technology Assessment Subcommittee

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

*Disclosure*

Dr. Cortese reports no disclosures. Dr. Chaudhry serves on the editorial board of *Neurologist*; is an inventor on patent(s) re: Total Neuropathy Score (TNS)—a score for evaluating peripheral neuropathies, for which he receives technology royalties from Abbott, Johnson & Johnson, and sanofi-aventis; receives publishing royalties for *Harrison’s Principles of Internal Medicine, 17th ed.* (McGraw Hill Companies, Inc., 2008); estimates that 40% of his clinical effort is spent on nerve conduction studies; has given expert testimony for the Department of Health and Human Services Vaccine Injury Compensation program and receives research support from the Neuropathy Association, Nutricia, and Insmed Inc. Dr. So receives publishing royalties for *Occupational & Environmental Medicine* (Appleton & Lange, 2007) and contributions to UpToDate; receives research support from the NIH (NIEHS, NINDS) and holds stock in Sartorius, Inc. Dr. Cantor has received honoraria from Elsevier and research support from NINDS Intramural Research Funds. Dr. Cornblath has served on a scientific advisory board or as a consultant for Merck Serono, Sun Pharmaceutical Industries Ltd., DP Clinical, Inc., Geron Corporation, Schwarz Biosciences, Avigen, Inc., Pfizer Inc, Johnson & Johnson, GlaxoSmithKline, Abbott, Acorda Therapeutics Inc., Alexion Pharmaceuticals, Inc., Astellas Pharma Inc., Baxter International Inc., Bionevia Pharmaceuticals Inc., Bristol-Myers Squibb, Celix Incorporated, CSL Behring, Eisai Inc., Exelixis Inc., FoldRx Pharmaceuticals, Genzyme Corporation, Neryx Biopharmaceuticals, Inc., Mitsubishi Tanabe Pharma Corporation, Octapharma AG, Sangamo BioSciences, sanofi-aventis, and Talecris Biotherapeutics; is an inventor on patent(s) re: Total Neuropathy Score (TNS)—a score for evaluating peripheral neuropathies, for which he receives technology royalties from Abbott, Johnson & Johnson, and sanofi-aventis; receives publishing royalties for *Diagnosis and Management of Peripheral Nerve Disorders* (Oxford University Press, 2001); and has given expert testimony, prepared affidavits, and acted as a witness or consult with regard to legal proceedings. Dr. Rae-Grant has received speaker honoraria from Biogen Idec, Teva Pharmaceutical Industries Ltd., and EMD Serono, Inc.; receives publishing royalties for *Handbook of Multiple Sclerosis* (Springer Healthcare, 2010); and has served on the speakers’ bureau for Biogen Idec

*Conflict of Interest*
The American Academy of Neurology 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 www.aan.com.

Guideline Endorser(s)

National Multiple Sclerosis Society - Disease Specific Society

Guideline Status

This is the current release of the guideline.


The American Academy of Neurology reaffirmed the currency of this guideline in November 2016.

This guideline meets NGC’s 2013 (revised) inclusion criteria.

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, 201 Chicago Avenue South, Minneapolis, MN 55415.

Availability of Companion Documents

The following are available:


In addition, Continuing Medical Education (CME) material for this guideline is available at the AAN Web site.
Patient Resources

The following is available:


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 December 1, 1998. The information was verified by the guideline developer as of February 12, 1999. This NGC summary was updated by ECRI Institute on April 7, 2011. The currency of the guideline was reaffirmed by the developer in November 2016 and this summary was updated by ECRI Institute on January 30, 2017.

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