Complete Summary

GUIDELINE TITLE

Practice parameter: corticosteroid treatment of Duchenne dystrophy: report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society.

BIBLIOGRAPHIC SOURCE(S)

Moxley RT 3rd, Ashwal S, Pandya S, Connolly A, Florence J, Mathews K, Baumbach L, McDonald C, Sussman M, Wade C. Practice parameter: corticosteroid treatment of Duchenne dystrophy: report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. Neurology 2005 Jan 11;64(1):13-20. [49 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

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SCOPE

DISEASE/CONDITION(S)

Duchenne dystrophy (DD) (also known as Duchenne muscular dystrophy [DMD])

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Management
Treatment

CLINICAL SPECIALTY

Family Practice
Neurology
Pediatrics
Physical Medicine and Rehabilitation

INTENDED USERS

Health Plans
Hospitals
Managed Care Organizations
Pharmacists
Physicians
Students
Utilization Management

GUIDELINE OBJECTIVE(S)

To review available evidence on corticosteroid treatment of boys with Duchenne dystrophy

TARGET POPULATION

Boys with Duchenne muscular dystrophy

INTERVENTIONS AND PRACTICES CONSIDERED

1. Prednisone/prednisolone
    - Daily dosing
    - Reductions in daily dose
    - Alternate day dosing (not recommended)
    - Cyclical dosing (not recommended)
2. Deflazacort (an oxazolone analogue of prednisone)
3. Azathioprine (Imuran) immunosuppressive therapy (not recommended)
4. Ongoing monitoring of the benefits and side effects of corticosteroid therapy
    - Timed function tests
    - Pulmonary function tests (forced vital capacity [FVC])
    - Twenty-four hour urinary excretion of creatine (a surrogate measure of muscle mass)

MAJOR OUTCOMES CONSIDERED

- Effects of corticosteroid treatment on muscle strength, muscle function, functional ability, pulmonary function, 24-hour excretion of creatinine, and progression of weakness
- Side effects of corticosteroids

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Computer-assisted literature searches were conducted with the assistance of the University of Minnesota Biomedical Information Services Research Librarian for relevant articles published from 1966 to 2004. Databases searched included Medline (1966 to 2004) and Current Contents using the search terms Duchenne dystrophy, corticosteroids, steroids, prednisone, deflazacort, and treatment. All search titles and abstracts were analyzed for content. The search included all languages. Articles on therapy, prognosis, and side effects were selected, including original and review articles.

NUMBER OF SOURCE DOCUMENTS

25

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

Evidence Classification Scheme for Therapeutics

Class I: Evidence provided by a 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 drop-outs 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: Evidence provided by a prospective matched group cohort study in a representative population with masked outcome assessment that meets a-d above OR a randomized control trial in a representative population that lacks one criteria 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 assessment is independent of patient treatment

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

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Individual committee members reviewed, abstracted, and classified these articles to assess the quality of data related to study design and treatment effect. Abstracted data included the number of patients, age range, design of study, duration, dosage, outcome measures, response to treatment, and side effects. A four-tiered classification scheme for therapeutic evidence recently approved by the Quality Standards Subcommittee was utilized as part of this assessment (see "Rating Scheme for the Strength of the Evidence"). Depending on the strength of this evidence, it was decided whether specific recommendations could be made and, if so, the strength of these recommendations. Evidence pertinent to each treatment together 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 Recommendations

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

U = Data inadequate or conflicting; given current knowledge, treatment is unproven

Translation of Evidence to Recommendations

Level A rating requires at least one convincing class I study or at least two consistent, convincing class II studies.

Level B rating requires at least one convincing class II study or at least three consistent class III studies.

Level C rating requires at least two convincing and consistent class III studies.

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

Guidelines were approved by the Quality Standards Subcommittee (QSS) on February 13, 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

The classes of evidence (I-IV) and the ratings of recommendations (A-C) are listed at the end of the "Major Recommendations" field.

1. Prednisone has been demonstrated to have a beneficial effect on muscle strength and function in boys with Duchenne dystrophy (DD) and should be offered (at a dose of 0.75 mg/kg/day) as treatment (**Level A**). Maintaining a dosage of 0.75 mg/kg/day is optimal, but if side effects require a decrease in prednisone, a gradual tapering of prednisone (as indicated below) to dosages as low as 0.3 mg/kg/day will give less robust but significant improvement.
2. Benefits and side effects of corticosteroid therapy need to be monitored. Timed function tests, pulmonary function tests, and age at loss of independent ambulation are useful to assess benefits. An offer of treatment with corticosteroids should include a balanced discussion of potential risks. Potential side effects of corticosteroid therapy (weight gain, cushingoid appearance, cataracts, short stature [i.e., a decrease in linear growth], acne, excessive hair growth, gastrointestinal symptoms, and behavioral changes) also need to be assessed. If excessive weight gain occurs (>20% over estimated normal weight for height over a 12-month period), based on available data, it is recommended that the dosage of prednisone be decreased (to 0.5 mg/kg/day with a further decrease after three to four months to 0.3 mg/kg/day if excessive weight gain continues) (**Level A**).
3. Deflazacort (0.9 mg/kg/day) can also be used for the treatment of DD in countries in which it is available (**Level A**). Patients should be monitored for asymptomatic cataracts as well as weight gain during treatment with deflazacort.

Definitions:

Evidence Classification Scheme for Therapeutics

Class I: Evidence provided by a 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 drop-outs 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: Evidence provided by a prospective matched group cohort study in a representative population with masked outcome assessment that meets a-d above OR a randomized control trial in a representative population that lacks one criteria 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 assessment is independent of patient treatment

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

Translation of Evidence to Recommendations

Level A rating requires at least one convincing class I study or at least two consistent, convincing class II studies.

Level B rating requires at least one convincing class II study or at least three consistent class III studies.

Level C rating requires at least two convincing and consistent class III studies.

Rating of Recommendations

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

U = Data inadequate or conflicting; given current knowledge, treatment is unproven

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 use of corticosteroids leads to improvements in muscle strength, timed function tests, the 24-hour urinary excretion of creatinine, and pulmonary function including higher forced vital capacity (FVC) averages.

POTENTIAL HARMS

Side Effects of Corticosteroid Treatment

- Weight gain and increased appetite
- Cushingoid appearance (round face)
- Short stature (decrease in linear growth)
- Hirsutism (excessive hair growth)
- Cataracts
- Acne
- Gastrointestinal symptoms
- Behavioral change (irritability)

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 AAN 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.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

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

Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Moxley RT 3rd, Ashwal S, Pandya S, Connolly A, Florence J, Mathews K, Baumbach L, McDonald C, Sussman M, Wade C. Practice parameter: corticosteroid treatment of Duchenne dystrophy: report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. Neurology 2005 Jan 11;64(1):13-20. [49 references] PubMed

ADAPTATION

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

DATE RELEASED

2005 Jan

GUIDELINE DEVELOPER(S)

American Academy of Neurology - Medical Specialty Society

SOURCE(S) OF FUNDING

American Academy of Neurology (AAN)

GUIDELINE COMMITTEE

Quality Standards Subcommittee of the American Academy of Neurology
Practice Committee of the Child Neurology Society

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

American Academy of Neurology (AAN) Quality Standards Subcommittee Members: Gary Franklin, MD, MPH (*co-chair*); Gary Gronseth, MD (*co-chair*); Charles E. Argoff, MD; Stephen 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, and Catherine Zahn, MD (*ex-officio*)

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

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 is available:

- AAN guideline development process [online]. St. Paul (MN): American Academy of Neurology. Available from the American Academy of Neurology 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
- Practice parameter: corticosteroid treatment of Duchenne dystrophy. AAN summary of evidence-based guidelines for clinicians. St. Paul (MN): American Academy of Neurology. 2 p. Available in Portable Document Format (PDF) from the AAN Web site.
- Practice parameter: corticosteroid treatment of Duchene dystrophy. St. Paul (MN): American Academy of Neurology. 2005. 11 p. Available for personal digital assistant (PDA) download from the AAN Web site.
- Practice parameter: corticosteroid treatment of Duchenne muscular dystrophy. Slide presentation. St. Paul (MN): American Academy of Neurology. 36 p. Available as a PowerPoint file from the AAN Web site.
- Corticosteroid treatment of Duchenne muscular dystrophy. CME quiz. Available online to subscribers of *Neurology* at the *Neurology* Web site.

PATIENT RESOURCES

The following is available:

- Corticosteroids for Duchenne muscular dystrophy. 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

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