Complete Summary

GUIDELINE TITLE

A systematic review on the diagnosis and treatment of primary (idiopathic) dystonia and dystonia plus syndromes: report of an EFNS/MDS-ES Task Force.

BIBLIOGRAPHIC SOURCE(S)

Albanese A, Barnes MP, Bhatia KP, Fernandez-Alvarez E, Filippini G, Gasser T, Krauss JK, Newton A, Rektor I, Savoiardo M, Valls-Sole J. A systematic review on the diagnosis and treatment of primary (idiopathic) dystonia and dystonia plus syndromes: report of an EFNS/MDS-ES Task Force. Eur J Neurol 2006 May;13(5):433-44. [111 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

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SCOPE

DISEASE/CONDITION(S)

Primary (idiopathic) dystonia and dystonia plus syndromes

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Medical Genetics
Neurology
Pediatrics

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To review the literature on diagnosis and treatment of primary dystonia and dystonia plus to provide evidence-based recommendations for diagnosis and treatment

TARGET POPULATION

Patients with primary (idiopathic) dystonia and dystonia plus syndromes

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis

1. Expert observation and neurological examination
2. Classification of dystonia (by cause, age at onset, and distribution)
3. Diagnostic testing (for DYT-1 and DYT-11 genes) and genetic counseling
4. Neurophysiological tests in selected cases
5. Diagnostic levodopa trial
6. Magnetic resonance imaging (MRI) for screening of secondary dystonia (or computed tomography when brain calcifications are suspected)

Treatment

1. Botulinum toxin (BoNT)
2. Levodopa
3. Neurosurgical procedures
    - Pallidal deep brain stimulation (DBS)
    - Selective peripheral denervation and myectomy
    - Intrathecal baclofen

Note: The following interventions were considered but not recommended because of lack of evidence or inefficacy:

- Diagnostic testing in selected patients (see the "Major Recommendations" field for details)
- Routine neurophysiological tests
- Routine structural brain imaging
- Anticholinergic, antiepileptic, and anti-dopaminergic drugs
- Radiofrequency ablations
- Intradural rhizotomy

- Microvascular decompression

MAJOR OUTCOMES CONSIDERED

- Utility and diagnostic accuracy of genetic testing
- Effectiveness of treatment in terms of severity and disability improvement and pain relief

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Computerized MEDLINE and EMBASE searches (1966 to February 2005) were conducted using a combination of text words and MeSH terms 'dystonia', 'blepharospasm', 'torticollis', 'writer's cramp', 'Meige Syndrome', 'dysphonia' and 'sensitivity and specificity' or 'diagnosis', and 'clinical trial' or 'random allocation' or 'therapeutic use' limited to human studies. The Cochrane Library and the reference lists of all known primary and review articles were searched for relevant citations. No language restrictions were applied.

NUMBER OF SOURCE DOCUMENTS

- Consensus agreements – two articles
- Workshops or taskforces – two articles
- Primary studies on clinically based diagnosis – 69 articles
- Primary studies on the diagnostic accuracy of different laboratory tests – 292

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 a Diagnostic Measure

Class I: A prospective study in a broad spectrum of persons with the suspected condition, using a "gold standard" for case definition, where the test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy

Class II: A prospective study of a narrow spectrum of persons with the suspected condition, or a well-designed retrospective study of a broad spectrum of persons with an established condition (by "gold standard") compared to a broad spectrum of controls, where test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy

Class III: Evidence provided by a retrospective study where either persons with the established condition or controls are of a narrow spectrum, and where test is applied in a blinded evaluation

Class IV: Any design where test is not applied in blinded evaluation OR evidence provided by expert opinion alone or in descriptive case series (without controls)

Evidence Classification Scheme for a Therapeutic Intervention

Class I: An adequately powered prospective, randomized, controlled clinical trial with masked outcome assessment in a representative population or an adequately powered systematic review of prospective randomized controlled clinical trials with masked outcome assessment in representative populations. The following are required:

a. Randomization concealment
b. Primary outcome(s) is/are clearly defined
c. Exclusion/inclusion criteria are clearly defined
d. Adequate accounting for dropouts and crossovers with numbers sufficiently low to have minimal potential for bias
e. 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–e above or a randomized, controlled trial in a representative population that lacks one criteria a–e

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

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Studies of diagnosis, diagnostic test, and various treatments for patients suffering from dystonia were considered and rated as level A to C according to the recommendations for European Federation of Neurological Societies (EFNS) scientific task forces (See the "Rating Scheme for the Strength of the Recommendations" field and "Availability of Companion Documents" field in this summary).

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Consensus Development Conference)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The results of the literature searches were circulated by email to the task force members for comments. The task force chairman prepared a first draft of the manuscript based on the results of the literature review, data synthesis and comments from the task force members. The draft and the recommendations were discussed during a conference held in Milan on 11–12 February 2005, until consensus was reached within the task force.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Rating of Recommendations for a Diagnostic Measure

Level A rating (established as useful/predictive or not useful/predictive) requires at least one convincing class I study or at least two consistent, convincing class II studies.

Level B rating (established as probably useful/predictive or not useful/predictive) requires at least one convincing class II study or overwhelming class III evidence.

Level C rating (established as possibly useful/predictive or not useful/predictive) requires at least two convincing class III studies.

Rating of Recommendations for a Therapeutic Intervention

Level A rating (established as effective, ineffective, or harmful) requires at least one convincing class I study or at least two consistent, convincing class II studies.

Level B rating (probably effective, ineffective, or harmful) requires at least one convincing class II study or overwhelming class III evidence.

Level C rating (possibly effective, ineffective, or harmful) requires at least two convincing class III studies.

Good practice point Where only class IV evidence was available but consensus could be achieved the Task Force has proposed good practice points.

COST ANALYSIS

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

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The guidelines were validated according to the European Federation of Neurological Societies (EFNS) criteria (See "Availability of Companion Documents" field in this summary).

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The levels of evidence (class I-IV) supporting the recommendations and ratings of recommendations (A-C, Good practice point) are defined at the end of the "Major Recommendations" field.

Diagnosis and Classification

1. Diagnosis and classification of dystonia are highly relevant for providing appropriate management, prognostic information, genetic counseling and treatment **(good practice point)**. (Refer to Table 1 in the original guideline documentation)
2. Based on the lack of specific diagnostic tests, expert observation is recommended. Referral to a movement disorder's expert increases the diagnostic accuracy **(good practice point)**.
3. Neurological examination alone allows the clinical identification of primary dystonia and dystonia plus, but not the distinction amongst different aetiological forms of heredo-degenerative and secondary dystonias **(good practice point)**.

Use of Genetic Test in Diagnosis and Counseling

1. Diagnostic DYT-1 testing in conjunction with genetic counseling is recommended for patients with primary dystonia with onset before age 30 years (**level B**; Klein et al., 1999).
2. Diagnostic DYT-1 testing in patients with onset after age 30 years may also be warranted in those having an affected relative with early onset (**level B**; Klein et al., 1999; Bressman et al., 2000).
3. Diagnostic DYT-1 testing is not recommended in patients with onset of symptoms after age 30 years who either have focal cranial-cervical dystonia or have no affected relative with early onset dystonia (**level B**: Klein et al., 1999; Bressman et al., 2000).
4. Diagnostic DYT-1 testing is not recommended in asymptomatic individuals, including those under the age of 18, who are relatives of familial dystonia patients. Positive genetic testing for dystonia (e.g. DYT-1) is not sufficient to make a diagnosis of dystonia unless clinical features show dystonia (**level B**; Klein et al., 1999; "Points to consider: ethical, legal, and psychosocial," 1995).
5. A diagnostic levodopa trial is warranted in every patient with early onset dystonia without an alternative diagnosis (**good practice point**; Robinson et al., 1999).
6. Individuals with myoclonus affecting the arms or neck, particularly if positive for autosomal dominant inheritance, should be tested for the DYT-11 gene (**good practice point**; Valente et al., 2005).

7. Diagnostic testing for the paroxysmal non-kinesigenic form of dystonia (PNKD) gene (DYT- 8) is not widely available, but this may become possible in the near future **(good practice point)**.

Use of Neurophysiology in the Diagnosis and Classification of Dystonia

1. Neurophysiological tests are not routinely recommended for the diagnosis or classification of dystonia; however, the observation of abnormalities typical of dystonia is an additional diagnostic tool in cases where the clinical features are considered insufficient to the diagnosis (**good practice point**; Hughes & McLellan, 1985; Deuschl et al., 1992).

Use of Brain Imaging in the Diagnosis of Dystonia

1. Structural brain imaging is not routinely required when there is a confident diagnosis of primary dystonia in adult patients, because a normal study is expected in primary dystonia (**good practice point**; Rutledge et al., 1988).
2. Structural brain imaging is necessary for screening of secondary forms of dystonia, particularly in the paediatric population due to the more widespread spectrum of dystonia at this age (**good practice point**; Meunier et al., 2003).
3. Magnetic resonance imaging (MRI) is preferable to computed tomography (CT), except when brain calcifications are suspected (**good practice point**).
4. There is no evidence that more sophisticated imaging techniques (e.g. voxel-based morphometry, diffusion-weighted imaging, functional MRI [fMRI]) are currently of any value in either the diagnosis or the classification of dystonia **(good practice point)**.

Treatment

Botulinum Toxins (BoNT)

1. BoNT-A (or type B if there is resistance to type A) can be regarded as first line treatment for primary cranial (excluding oromandibular) or cervical dystonia (**level A**; Costa et al., 2005; American Academy of Ophthalmology, 1989).
2. Due to the large number of patients who require BoNT injections, the burden of performing treatment could be shared with properly trained nurse specialists, except in complex dystonia or where electromyography (EMG) guidance is required (**level B**; Whitaker et al., 2001).
3. BoNT-A may be considered in patients with writing dystonia (**level C**; Balash & Giladi, 2004).

Anticholinergic Drugs

The absolute and comparative efficacy and tolerability of anticholinergic agents in dystonia is poorly documented in children and there is no proof of efficacy in adults; therefore, no recommendations can be made to guide prescribing **(good practice point)**.

Antiepileptic Drugs

There is lack of evidence to give recommendations for this type of treatment **(good practice point)**.

Anti-dopaminergic Drugs

There is lack of evidence to give recommendations for this type of treatment **(good practice point)**.

Dopaminergic Drugs

Following a positive diagnostic trial with levodopa, chronic treatment with levodopa should be initiated and adjusted according to the clinical response (**good practice point**; Hwang et al., 2001).

Neurosurgical Procedures

Deep Brain Stimulation (DBS)

Pallidal DBS is considered a good option, particularly for generalized or cervical dystonia, after medication or BoNT have failed to provide adequate improvement. Whilst it can be considered second-line treatment in patients with generalized dystonia, this is not the case in cervical dystonia since there are other surgical options available (see below). This procedure requires a specialized expertise, and is not without side effects (**good practice point**; Vidailhet et al., 2005; Eltahawy et al., 2004).

Selective Peripheral Denervation and Myectomy

Selective peripheral denervation is a safe procedure with infrequent and minimal side effects that is indicated exclusively in cervical dystonia. This procedure requires a specialized expertise (**level C**; The National Institute for Clinical Excellence, 2004).

Intrathecal Baclofen

There is insufficient evidence to use this treatment in primary dystonia; the procedure can be indicated in patients where secondary dystonia is combined with spasticity (**good practice point**; Albright et al., 2001).

Radiofrequency Lesions

Radiofrequency ablations are currently discouraged for bilateral surgery because of the relatively high risk of side effects (**good practice point**). The focus of treatment has currently shifted to DBS because of its lower risk for bilateral procedures.

Rare, Uncommon or Obsolete Procedures

1. Intradural rhizotomy has been replaced by selective ramisectomy and peripheral denervation or myotomy. These procedures are no longer recommended.

2. Microvascular decompression is not recommended for treatment of cervical dystonia.

Definitions:

Evidence Classification Scheme for a Diagnostic Measure

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Rating of Recommendations for a Therapeutic Intervention

Level A rating (established as effective, ineffective, or harmful) requires at least one convincing class I study or at least two consistent, convincing class II studies.

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Level C rating (possibly effective, ineffective, or harmful) requires at least two convincing class III studies.

Good practice point Where only class IV evidence was available but consensus could be achieved the Task Force has proposed good practice points.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

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

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate diagnosis and treatment of primary (idiopathic) dystonia and dystonia plus syndromes

POTENTIAL HARMS

- *Botulinum toxin (BoNT)*. The most frequently reported treatment-related adverse events were dysphagia, neck weakness, local pain at injection site, and sore throat/dry mouth. Most of the adverse events in patients receiving BoNT-A were mild or moderate.
- *Pallidal deep brain stimulation (DBS)*. Chronic stimulation uses both higher pulse width and voltage than in Parkinson disease (PD), which results in much higher energy consumption and earlier battery depletion. Batteries must be replaced sometimes every 2 years or even more often. Sudden battery depletion may induce acute recurrence of dystonia, sometimes resulting in a medical emergency. Three safety aspects have to be considered: surgery-related complications, stimulation-induced side effects and hardware-related problems.
- *Selective peripheral denervation and meyctomy*. Denervation of C2 invariably involves numbness in the territory of the greater occipital nerve in the early post-operative period. Patients should be informed about the invariable procedure-related numbness; neuropathic pain can develop rarely. Swallowing difficulties have been noted in some studies. In about 1 to 2% of patients the procedure causes weakness in non-dystonic muscles, in particular in the trapezius. Re-innervation can occur and may require further surgery.
- *Intrathecal baclofen*. The surgical risk is low, but the method is burdened by medication-related side effects, infections and long-term hardware-related problems. Intrathecal baclofen for treatment of dystonia requires frequent pump refills and follow-up visits.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- This guideline provides the view of an expert task force appointed by the Scientific Committee of the European Federation of Neurological Societies (EFNS). It represents a peer-reviewed statement of minimum desirable standards for the guidance of practice based on the best available evidence. It is not intended to have legally binding implications in individual cases.
- The absolute and comparative efficacy and tolerability of drugs in dystonia, including anticholinergic and anti-dopaminergic drugs, is poorly documented and no evidence-based recommendations can be made to guide prescribing.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

The European Federation of Neurological Societies has a mailing list and all guideline papers go to national societies, national ministries of health, World Health Organisation, European Union, and a number of other destinations. Corporate support is recruited to buy large numbers of reprints of the guideline

papers and permission is given to sponsoring companies to distribute the guideline papers from their commercial channels, provided there is no advertising attached.

IMPLEMENTATION TOOLS

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

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Albanese A, Barnes MP, Bhatia KP, Fernandez-Alvarez E, Filippini G, Gasser T, Krauss JK, Newton A, Rektor I, Savoiardo M, Valls-Sole J. A systematic review on the diagnosis and treatment of primary (idiopathic) dystonia and dystonia plus syndromes: report of an EFNS/MDS-ES Task Force. Eur J Neurol 2006 May;13(5):433-44. [111 references] PubMed

ADAPTATION

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

DATE RELEASED

2006 May

GUIDELINE DEVELOPER(S)

European Federation of Neurological Societies - Medical Specialty Society

SOURCE(S) OF FUNDING

European Federation of Neurological Societies

GUIDELINE COMMITTEE

European Federation of Neurological Societies Task Force/ MDS-ES Task Force

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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: Available to registered users from the European Federation of Neurological Societies Web site.

Print copies: Available from Alberto Albanese, Istituto Neurologica Besta, Milano, Italy; Phone: +39 02 2394 2552; Fax: +39 02 2394 2539; E-mail: alberto.albanese@unicatt.it

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Brainin M, Barnes M, Baron JC, Gilhus NE, Hughes R, Selmaj K, Waldemar G; Guideline Standards Subcommittee of the EFNS Scientific Committee. Guidance for the preparation of neurological management guidelines by EFNS scientific task forces – revised recommendations 2004. Eur J Neurol. 2004 Sep;11(9):577-81. Electronic copies: Available in Portable Document Format (PDF) from the European Federation of Neurological Societies Web site.
- Guideline papers. European Federation of Neurological Societies. Electronic copies: Available from the European Federation of Neurological Societies Web site.
- Continuing Medical Education available from the European Journal of Neurology Web site.

PATIENT RESOURCES

None available

NGC STATUS

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