Complete Summary

GUIDELINE TITLE

EFNS task force - therapy of nystagmus and oscillopsia.

BIBLIOGRAPHIC SOURCE(S)

Straube A, Leigh RJ, Bronstein A, Heide W, Riordan-Eva P, Tijssen CC, Dehaene I, Straumann D. EFNS task force--therapy of nystagmus and oscillopsia. Eur J Neurol 2004 Feb;11(2):83-9. [75 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 and/or warning information has been released.

- December 12, 2007, Carbamazepine: The U.S. Food and Drug Administration (FDA) has provided recommendations for screening that should be performed on specific patient populations before starting treatment with carbamazepine.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Nystagmus and oscillopsia

GUIDELINE CATEGORY

Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Neurology
Ophthalmology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To summarize all published treatment options for nystagmus and oscillopsia as well as to provide a short overview of the definition and pathophysiology of certain distinct ocular motor syndromes

TARGET POPULATION

Patients presenting with nystagmus and oscillopsia

INTERVENTIONS AND PRACTICES CONSIDERED

1. *Downbeat nystagmus*: clonazepam, baclofen, gabapentin, anticholinergic drugs, 3,4-diaminopyridine, surgical decompression in isolated patients, base-down prisms
2. *Upbeat nystagmus*: baclofen
3. *Seesaw nystagmus*: alcohol, clonazepam, gabapentin
4. *Periodic alternating nystagmus*: baclofen, phenothiazine, barbiturates
5. *Acquired pendular nystagmus*: memantine, gabapentin, benzodiazepines (e.g., clonazepam), scopolamine patches, trihexyphenidyl
6. *Opsoclonus and ocular flutter*: therapy for any underlying process, immunoglobulins, prednisolone, valproic acid, propranolol, nitrazepam, clonazepam, intravenous thiamine
7. *Superior oblique myokymia*: carbamazepine, phenytoin, gabapentin, beta-blockers, tenotomy of the superior oblique muscle, surgical decompression of the IVth nerve
8. *Paroxysmal vestibular episodes*: carbamazepine (slow release formulation), phenytoin, lamotrigine, surgical approach

MAJOR OUTCOMES CONSIDERED

Effectiveness of treatment

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

One member of the Task Force Panel searched through all available published information using the database Med-Line (last search March 2003). The search was restricted to papers published in English, French, or German. The key words used for the search included the following sequences: "nystagmus and therapy," "treatment of ocular motor disorders," and "treatment of double vision." All published papers were included, as only a limited number of controlled studies are available.

NUMBER OF SOURCE DOCUMENTS

Not stated

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 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

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The members of the task force read the first draft of the recommendation and discussed changes (informative consensus approach)

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Rating of Recommendations

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.

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 (Hughes RAC, Barnes MP, Baron J, Brainin M [2001]. Guidance for the preparation of neurological management guidelines by EFNS scientific task forces. *Eur J Neurol* 8:549-550).

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

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

All treatment recommendations available in the literature are classified as **Class C** only.

Supranuclear Ocular Motor Disorders

Central Vestibular Disorders

Downbeat Nystagmus

No studies on the natural course of downbeat nystagmus are available. In non-placebo-controlled studies with a limited number of patients, administration of the gamma-aminobutyric acid-A (GABA-A) agonist clonazepam (0.5 mg orally [p.o.] three times daily), the GABA-B agonist baclofen (10 mg p.o. three times daily), and gabapentin (probably calcium channel blocker) had positive effects and reduced downbeat nystagmus. Intravenous injection of the cholinergic drug physostigmine (Ach-esterase inhibitor) worsened downbeat nystagmus in five patients. This effect was partially reversed in one patient by the anticholinergic drug biperiden, suggesting that anticholinergic drugs might be beneficial, as was shown in a double-blind study on intravenous scopolamine. In isolated patients with a craniocervical anomaly, a surgical decompression by removal of part of the occipital bone in the region of the foramen magnum was beneficial. Recent placebo-controlled studies have suggested that the potassium channel blocker 3, 4-diaminopyridine may be effective in downbeat nystagmus. As downbeat nystagmus is generally less pronounced in upward gaze, base-down prisms sometimes help to reduce oscillopsia during reading.

Upbeat Nystagmus

Treatment with baclofen (5 to 10 mg p.o. three times daily) resulted in an improvement in several patients.

Seesaw Nystagmus

Alcohol had a beneficial effect (1.2 g/kg body weight) in two patients, as was clonazepam. Recently, one study reported on three patients with a seesaw component to their pendular nystagmus, who improved on gabapentin.

Periodic Alternating Nystagmus

In general, periodic alternating nystagmus does not improve spontaneously. Several case reports describe a positive effect of baclofen, a GABA-B agonist, in a dose of 5–10 mg p.o. three times daily. Furthermore, phenothiazine and barbiturates have been found to be effective in single cases. Periodic alternating nystagmus due to bilateral visual loss resolves if vision is restored.

Non-Vestibular Supranuclear Ocular Motor Disorders

Acquired Pendular Nystagmus

Most reports (case reports or case series) state that anticholinergic treatment with trihexyphenidyl (20 to 40 mg p.o. daily) is effective, but in a double-blind study only one of six patients showed improvement from this oral treatment, whereas three patients showed a decrease in nystagmus and improvement of visual acuity during treatment with tridihexethyl chloride (a quaternary anticholinergic that does not cross the blood-brain barrier). In contrast, other authors found in a double-blind trial that scopolamine (0.4 mg intravenously [i.v.]) decreased the nystagmus in all five tested patients with acquired pendular nystagmus. However, there are even observations that scopolamine may make the pendular nystagmus worse in some patients. In three other patients the combination with lidocaine (100 mg i.v.) decreased nystagmus. Recently, an improvement was reported in three of 10 patients who received a scopolamine patch (containing 1.5 mg scopolamine, released at a rate of 0.5 mg per day). The same authors failed to observe further improvement when scopolamine and mexiletine (400 to 600 mg p.o. daily) were given in combination. The most effective substance in their study was memantine, a glutamate antagonist, which significantly improved the nystagmus in all nine tested patients (15 to 60 mg p.o. daily). Two patients responded to clonazepam (3 x 0.5 to 1.0 mg p.o. daily), a GABA-A agonist. Two other groups have reported benefit with GABA-ergic drugs. One study showed improvement in one of three patients with acquired pendular nystagmus (APN) and cerebellar ataxia due to multiple sclerosis (MS) when treated with isoniazid (800 to 1000 mg p.o. daily) and glasses with prisms that induced convergence. This observation was not confirmed by other investigators. Gabapentin substantially improved the nystagmus (and visual acuity) in 10 of 15 patients in another study. Gabapentin was superior to vigabatrin in a small series of patients. Interestingly, a study described two patients who benefited from intake of alcohol but not from other substances. The necessary blood levels were 20 to 35 mmol/L. Recently, a beneficial effect of cannabis was also reported.

Practically, treatment should start with memantine in a dosage of 15 to 60 mg p.o. or alternatively 300 to 400 mg gabapentin three times daily. If there is no or only a small effect, benzodiazepines like clonazepam (0.5 to 1.0 mg p.o. three times daily) can be tried. Further possibilities are scopolamine patches or trihexyphenidyl. However, side effects are a major limitation of anticholinergic therapy.

Opsoclonus and Ocular Flutter

In addition to therapy for any underlying process such as tumor or encephalitis, treatment with immunoglobulins or prednisolone may be occasionally effective.

Four of five patients with square-wave oscillations, probably a related fixation disturbance, showed an improvement on therapy with valproic acid. In single cases an improvement has been observed during treatment with propranolol (40 to 80 mg p.o. three times daily), nitrazepam (15 to 30 mg p.o. daily), and clonazepam (0.5 to 2.0 mg p.o. three times daily). One study reported a dramatic improvement in one patient after the administration of 200 mg thiamine i.v.; no further descriptions of the patient are given in the paper.

Nuclear and Infranuclear Ocular Disorders

Superior Oblique Myokymia

Spontaneous remissions, which can last for days up to years, are typical of superior oblique myokymia but there are several reports that anticonvulsants, especially carbamazepine, have a therapeutic effect. Carbamazepine (200 to 400 mg p.o. three or four times daily) or, less often, phenytoin (250 to 400 mg p.o. daily) are recommended. Gabapentin has also been reported to be effective. Long-term studies on the continued effectiveness of these drugs are not available. One study described a decrease in the efficacy of the treatment after a month in some patients. Beta-blockers, even topically, have been reported to be effective.

In chronic cases that did not improve with anticonvulsants, tenotomy of the superior oblique muscle has been performed, but usually it necessitates inferior oblique surgery as well. Surgical decompression of the IVth nerve has also been reported to be beneficial but may result in superior oblique palsy.

Practically, treatment should be started with carbamazepine (200 to 400 mg p.o. three to four times daily) or phenytoin (250 to 400 mg p.o. daily). The side effects and the risk of such therapy are the same as when used to treat trigeminal neuralgia.

Paroxysmal Vestibular Episodes

As initial therapy, an anticonvulsant [carbamazepine (slow release formulation) 2 x 200 to 800 mg p.o. daily; phenytoin 250 to 400 mg p.o. daily, lamotrigine 100 to 400 mg p.o. daily] should be given. In general, a positive response to antiepileptic drugs can be achieved with low dosages. If the symptoms do not cease, a surgical approach may be considered. There are no satisfactory follow-up studies, and the diagnostic criteria have not yet been fully established.

Definitions:

Evidence Classification Scheme for a Therapeutic Intervention

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a. Randomization concealment

b. Primary outcome(s) is/are clearly defined
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Class IV: Evidence from uncontrolled studies, case series, case reports, or expert opinion

Rating of Recommendations

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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.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Only a few controlled trials have been published in recent years, and they were all based on a small number of subjects, and not all patients respond positively to the treatment. Thus, all treatment recommendations have to be classified as *class C*.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate therapy of nystagmus and oscillopsia

POTENTIAL HARMS

- Side effects are a major limitation of anticholinergic therapy.
- Side effects and risks of anticonvulsants are the same as when used to treat trigeminal neuralgia.
- Surgical decompression of the IVth nerve for treatment of superior oblique myokymia may result in superior oblique palsy.

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.
- Treatment options for abnormal eye movements remain fairly limited. Most drug treatments are based on case reports. Only a few controlled trials have been published in recent years, and they were all based on a small number of subjects, and not all patients respond positively to the treatment. Thus, all treatment recommendations have to be classified as class C.

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

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Straube A, Leigh RJ, Bronstein A, Heide W, Riordan-Eva P, Tijssen CC, Dehaene I, Straumann D. EFNS task force--therapy of nystagmus and oscillopsia. Eur J Neurol 2004 Feb;11(2):83-9. [75 references] PubMed

ADAPTATION

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

DATE RELEASED

2004 Feb

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

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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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 A. Straube, Department of Neurology, Klinikum Grosshadern, Marchioninistrasse 15, 81377 Munich, Germany; E-mail: astraube@brain.nefo.med.unimuenchen.de

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 questions available from the European Journal of Neurology Web site.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on December 4, 2006. The information was verified by the guideline developer on December 29, 2006. This summary was updated by ECRI Institute on January 10, 2008, following the U.S. Food and Drug Administration advisory on Carbamazepine.

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