Complete Summary

GUIDELINE TITLE

Evaluation and treatment of adult growth hormone deficiency: an Endocrine Society clinical practice guideline.

BIBLIOGRAPHIC SOURCE(S)

The Endocrine Society. Evaluation and treatment of adult growth hormone deficiency: an Endocrine Society clinical practice guideline. Chevy Chase (MD): Endocrine Society; 2006. 33 p. [166 references]

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
EVIDENCE SUPPORTING THE RECOMMENDATIONS
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
CONTRAINDICATIONS
QUALIFYING STATEMENTS
IMPLEMENTATION OF THE GUIDELINE
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES
IDENTIFYING INFORMATION AND AVAILABILITY
DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

Adult growth hormone deficiency

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Treatment

CLINICAL SPECIALTY

Endocrinology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To summarize information regarding adult growth hormone deficiency (AGHD) and to provide recommendations related to several specific questions:

- Who are appropriate candidates for growth hormone (GH) therapy?
- What tests should be used to diagnose GHD, and what criteria are necessary to make this diagnosis with the various test?
- What are the benefits of treatment with GH in GH-deficient adults?
- What are the risks of treatment with GH in GH-deficient adults?
- What treatment regimens should be used, and how should these be monitored?

TARGET POPULATION

Adults with growth hormone deficiency

INTERVENTIONS AND PRACTICES CONSIDERED

Evaluation

1. Retesting adult patients who were diagnosed with childhood-onset growth hormone deficiency (GHD)
2. Evaluation for acquired GHD

Diagnosis

1. Insulin tolerance test (ITT)
2. Growth hormone releasing hormone (GHRH)-arginine test
3. Insulin-like growth factor-I (IGF-I) level

Treatment with Growth Hormone (GH)

1. Dosing
    - Weight-based vs. individualized
    - Consideration of age, sex, estrogen status
    - Titration according to clinical response, side effects, and IGF-I levels
2. Monitoring
    - Appropriate monitoring intervals
    - Lipid profile
    - Fasting glucose
    - Bone density
    - Quality of life
    - Assessment of side effects

MAJOR OUTCOMES CONSIDERED

- Accuracy (sensitivity, specificity) of diagnostic tests for growth hormone (GH) deficiency
- Response to GH treatment in terms of body composition, bone health, cardiovascular risk factors, quality of life, and mortality in patients with hypopituitarism.
- Side effects and risks of GH treatment

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

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

Types of Evidence

High: Randomized trial

Low: Observational study (cohort studies, case-control studies, interrupted time series analyses, controlled before and after studies

Very low: Any other evidence

Overall Grades of Evidence

High: Further research is very unlikely to change the confidence in the estimate of effect.

Moderate: Further research is likely to have an important impact on the confidence in the estimate of effect and may change the estimate.

Low: Further research is very likely to have an important impact on the confidence in the estimate of effect and is likely to change the estimate.

Very Low: Any estimate of effect is very uncertain.

Above based on criteria for assigning grade of evidence

Decrease grade if:

- Serious (−1) or very serious (−2) limitation to study quality
- Important inconsistency (−1)
- Some (−1) or major (−2) uncertainty about directness
- Imprecise or sparse data (−1)
- High probability of reporting bias (−1)

Increase grade if:

- Strong evidence of association-significant relative risk of >2 based on consistent evidence from two or more observational studies with no plausible confounders (+1)
- Very strong evidence of association-significant relative risk of >5 based on direct evidence with no major threats to validity (+2)
- Evidence of a dose-response gradient
- All plausible confounders would have reduced the effect (+1)

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 chair of the Task Force was selected by the Clinical Guidelines Subcommittee of The Endocrine Society (TES). The chair selected five other endocrinologists and a medical writer, who were approved by TES Council. One closed meeting of the group was held. There was no corporate funding, and members of the group received no remuneration.

Consensus was achieved through one group meeting and e-mailing of drafts that were written by the group with grammatical/style help from the medical writer.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Recommendation statements in the guideline are defined as 'Do it' or 'Don't do it'—indicating a judgment that most well-informed people would make.

Suggestion statements in the guideline are defined as: 'Probably do it' or 'Probably don't do it'—indicating a judgment that a majority of well-informed people would make but a substantial minority would not.

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 were reviewed successively by the Clinical Guidelines Subcommittee, the Clinical Affairs Committee, and The Endocrine Society (TES) Council, and a version was placed on the TES Web site for comments. At each level, the task force incorporated needed changes.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions for the levels (grades) of evidence (very low, low, moderate, high) and for the difference between a "recommendation" and a "suggestion" are provided at the end of the Major Recommendations field.

Recommendations

- Patients with childhood-onset growth hormone deficiency (GHD) who are appropriate candidates for growth hormone (GH) therapy should be retested for GHD as adults unless they have known mutations, embryopathic lesions, or irreversible structural lesions/damage (level of evidence, high).
- Adult patients with evidence of structural hypothalamic/pituitary disease, surgery or irradiation to these areas, or other pituitary hormone deficiencies should be considered for evaluation for acquired GHD (level of evidence, high).
- The insulin tolerance test (ITT) or the growth hormone releasing hormone (GHRH)-arginine test is the preferred test for establishing the diagnosis of GHD. However, in those with clearly established recent hypothalamic causes of suspected GHD (e.g. irradiation) testing with GHRH-arginine may be misleading (level of evidence, high).
- Because of the irreversible nature of the cause of the GHD in children with structural lesions with multiple hormone deficiencies and those with proven genetic causes, a low insulin-like growth factor I (IGF-I) level at least 1 month off GH therapy is sufficient documentation of persistent GHD without additional provocative testing (level of evidence, moderate).

- GH therapy of GH-deficient adults offers significant clinical benefits in body composition, exercise capacity, skeletal integrity, and quality of life measures (level of evidence, moderate).
- GH treatment is most likely to benefit those patients who have more severe clinical and biochemical abnormalities and should be encouraged in such patients (level of evidence, moderate).
- GH treatment is contraindicated in the presence of an active malignancy (level of evidence, low).
- GH dosing regimens should be individualized rather than weight-based (level of evidence, high).
- GH treatment should start with low doses and be titrated according to clinical response, side effects, and IGF-I levels (level of evidence, high).
- GH dosing should take age, sex, and estrogen status into consideration (level of evidence, high).
- During GH treatment, patients should be monitored at 1- to 2-month intervals during dose titration and semiannually thereafter with a clinical assessment and an evaluation for adverse effects, IGF-I levels, and other parameters of GH response (level of evidence, moderate).

Suggestions

- A normal IGF-I level does not exclude the diagnosis of GHD and, in the context of other pituitary disease, makes provocative testing mandatory to make the diagnosis of GHD (level of evidence, high).
- A low IGF-I level, in the absence of catabolic conditions and liver disease, indicates severe GHD and may be useful in identifying patients who will benefit from treatment (level of evidence, moderate).
- The presence of deficiencies in three or more pituitary axes strongly suggests the presence of GHD, and in this context provocative testing is optional (level of evidence, moderate).
- GH treatment in patients with diabetes mellitus may require adjustments in antidiabetic medications (level of evidence, moderate).

Definitions:

Types of Evidence

High: Randomized trial

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Very low: Any other evidence

Overall Grades of Evidence

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Decrease grade if:

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- High probability of reporting bias (−1)

Increase grade if:

- Strong evidence of association-significant relative risk of >2 based on consistent evidence from two or more observational studies with no plausible confounders (+1)
- Very strong evidence of association-significant relative risk of >5 based on direct evidence with no major threats to validity (+2)
- Evidence of a dose-response gradient
- All plausible confounders would have reduced the effect (+1)

Recommendation: 'Do it' or 'Don't do it'—indicating a judgment that most well-informed people would make

Suggestion: 'Probably do it' or 'Probably don't do it'—indicating a judgment that a majority of well-informed people would make but a substantial minority would not

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting the recommendations is not specifically stated.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Benefits of growth hormone treatment of growth hormone deficient adults have been found in body composition, bone health, cardiovascular risk factors, and quality of life indicators. A full discussion of these benefits can be found in the original guideline document.

POTENTIAL HARMS

Side effects and risks associated with growth hormone therapy include:

- Fluid retention
- Insulin resistance and type 2 diabetes
- Benign intracranial hypertension
- Onset or recurrence of malignancy (theoretical risk only)
- Lowering of serum free thyroxine (T4) level

A full discussion of these risks can be found in the original guideline document.

CONTRAINDICATIONS

CONTRAINDICATIONS

Growth hormone treatment is contraindicated in the presence of an active malignancy.

QUALIFYING STATEMENTS

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- Clinical Practice Guidelines are developed to be of assistance to endocrinologists by providing guidance and recommendations for particular areas of practice. The Guidelines should not be considered inclusive of all proper approaches or methods, or exclusive of others. The Guidelines cannot guarantee any specific outcome, nor do they establish a standard of care. The Guidelines are not intended to dictate the treatment of a particular patient. Treatment decisions must be made based on the independent judgment of healthcare providers and each patient's individual circumstances.
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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

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

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

DATE RELEASED

2006

GUIDELINE DEVELOPER(S)

The Endocrine Society - Disease Specific Society

SOURCE(S) OF FUNDING

The Endocrine Society

GUIDELINE COMMITTEE

Growth Hormone Guideline Task Force

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Task Force Members: Mark E. Molitch; David R. Clemmons; Mary Lee Vance; Saul Malozowski; George R. Merriam; Stephen M. Shalet

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Mark E. Molitch, M.D., Consultant or Adviser: Abbott Laboratories, Novo Nordisk, Novartis, Pfizer, Sanofi-Aventis; Research Support: Eli Lilly & Co., Novartis, Pfizer, Genentech, Amgen, Sanofi-Aventis; David R. Clemmons, M.D., Consultant or Adviser: Eli Lilly & Co., Pfizer; Research Support: Pfizer; Other: reviewed grants for Genentech; Saul Malozowski, M.D., Ph.D., None; George R. Merriam, M.D., Consultant or Adviser: Elixir, Genentech, LG Life Sciences, Theratechnologies, Tokai; Research Support: Genentech, Eli Lilly & Co., LG Life Sciences Pfizer; Stephen M. Shalet, M.D., Consultant or Adviser: Transpharma, Skyepharma; Research Support: Pfizer, Novo Nordisk, Novartis; Mary Lee Vance, M.D., Consultant or Adviser: Genentech, Novartis, Pfizer; Research Support: Eli Lilly & Co., Novartis, Genentech, Pfizer

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from The Endocrine Society.

Print copies: Available from The Endocrine Society, c/o Bank of America, P.O. Box 630721, Baltimore, MD 21263-0736; Phone: (301) 941.0210; Email: Societyservices@endo-society.org

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on July 31, 2006. The information was verified by the guideline developer on August 11, 2006.

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