Complete Summary

GUIDELINE TITLE

The role of testosterone therapy in postmenopausal women: position statement of The North American Menopause Society.

BIBLIOGRAPHIC SOURCE(S)

The North American Menopause Society. The role of testosterone therapy in postmenopausal women: position statement of The North American Menopause Society. Menopause 2005 Sep 1;12(5):497-511. [66 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Menopause-associated sexual function disorders, particularly disorders of sexual desire

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Treatment

CLINICAL SPECIALTY

Endocrinology
Family Practice
Internal Medicine
Obstetrics and Gynecology

INTENDED USERS

Health Care Providers
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To provide a review of clinical data relating to efficacy and safety of testosterone therapy and to make recommendations regarding its role in the clinical management of postmenopausal women

TARGET POPULATION

Postmenopausal women with decreased sexual desire associated with personal distress

INTERVENTIONS AND PRACTICES CONSIDERED

Evaluation and Diagnosis

1. Medical, psychosexual and psychosocial history
2. Physical examination
3. Laboratory tests
    - Serum lipids
    - Liver functions tests
    - Others as indicated
4. Measurement of serum testosterone levels
    - Total testosterone
    - Free testosterone (direct or calculated)
    - Bioavailable testosterone

Note: Salivary testing was considered, but not recommended for measuring testosterone levels.

Treatment and Management

1. Testosterone therapy (with concomitant estrogen therapy)
    - Oral
    - Transdermal gel, cream, and ointment
    - Transdermal patch
    - Subcutaneous pellets
    - Intramuscular
    - Sublingual and buccal
2. Therapeutic monitoring
3. Patient counseling regarding benefits/risks

MAJOR OUTCOMES CONSIDERED

- Testosterone-associated improvements in sexual desire, sexual responsiveness, and frequency of sexual activity
- Adverse events associated with testosterone treatment

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases
Searches of Unpublished Data

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

For this position statement, a MEDLINE search of the medical literature was conducted to identify studies presenting data on the efficacy of testosterone therapy to treat postmenopausal women. Priority was given to evidence from randomized, controlled trials as well as to systematic reviews and meta-analyses of such trials.

Recommendations from other evidence based guidelines as well as data from meeting abstracts, US Food and Drug Administration (FDA) committee reviews, and unpublished sources were also reviewed.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review
Review of Published Meta-Analyses

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

An Editorial Board composed of experts from both clinical practice and research was enlisted to review the published data, compile supporting statements and conclusions, and make recommendations. If the evidence was contradictory or inadequate to form a conclusion, a consensus-based opinion was established. Practice parameter standards related to North American Menopause Society (NAMS) position statements have been described in an editorial (previously published).

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

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

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The North American Menopause Society (NAMS) Board of Trustees was responsible for the final review and approval of this document.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Based on the evidence, The North American Menopause Society supports the following recommendations regarding testosterone use in postmenopausal women.

- Postmenopausal women may be candidates for testosterone therapy if they present with symptoms of decreased sexual desire associated with personal distress and have no other identifiable cause for their sexual concerns.
- Testosterone therapy without concomitant estrogen therapy cannot be recommended, because there are no data on the safety and efficacy of testosterone therapy in women not using concomitant estrogen.
- Laboratory testing of testosterone levels should be used only to monitor for supraphysiologic testosterone levels before and during therapy, not to diagnose testosterone insufficiency. Laboratory assays are not accurate for detecting testosterone concentrations at the low values typically found in postmenopausal women, and no testosterone level has been clearly linked to

a clinical syndrome of hypoandrogenism or testosterone insufficiency. Oral methyltestosterone cannot be measured by standard assays.

- Testosterone values vary from laboratory to laboratory. In assessing results of testosterone testing, clinicians should use the reference ranges provided by the testing laboratory.
- The simplest and most readily available clinical estimate of free testosterone is the free testosterone index, calculated from total testosterone and sex hormone-binding globulin (SHBG).
- The Sodergard equation for free testosterone uses total testosterone, SHBG, and albumin. Although it is a more complex formula, it provides a more accurate calculation than the free testosterone index. It is an option to consider if the testing laboratory can provide the calculation.
- Salivary testing is not considered to be a reliable measure of testosterone levels.
- Before initiating testosterone treatment, baseline profiles for serum lipids and liver function tests should be established and retesting at 3 months considered. If stable, annual testing is advised.
- Testosterone therapy should be administered at the lowest dose for the shortest time that meets treatment goals.
- Testosterone transdermal patches and topical gels or creams may be preferred over oral products based on their avoidance of first-pass hepatic effects documented with oral formulations. However, only oral and intramuscular (IM) testosterone products for women are currently government-approved.
- Pellet and IM testosterone formulations have a risk of excessive dosing. Also, administration may be uncomfortable.
- Testosterone products formulated specifically for men provide excessive doses for women and should not be used unless doses are reduced considerably and blood testosterone levels are monitored closely for supraphysiologic levels.
- Custom-compounded testosterone products should be used with caution because the dosing may be more inconsistent than it is with government-approved products.
- There are insufficient data for any conclusions to be made regarding the efficacy and safety of testosterone therapy exceeding 6 months.
- Therapeutic monitoring of testosterone therapy should include subjective assessments of sexual response, desire, and satisfaction as well as evaluation for potential adverse effects.
- If adverse events are observed with testosterone therapy, dose reductions are advised. If the adverse events do not diminish with lower doses, therapy should be discontinued.
- Contraindications of testosterone therapy are focused primarily on those associated with estrogen therapy. However, testosterone therapy should not be initiated in postmenopausal women with breast or uterine cancer or with cardiovascular or liver disease.
- Counseling regarding the potential risks and benefits of testosterone use and the limitations of formulations not government-approved should be provided before initiating therapy.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is not specifically stated for each recommendation. Priority was given to evidence from randomized, controlled trials as well as to systematic reviews and meta-analyses of such trials.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate use of testosterone therapy in postmenopausal women to improve sexual desire disorders and quality of life while minimizing health risks

POTENTIAL HARMS

- Commonly reported adverse effects of testosterone therapy include acne and excess facial hair.
- High testosterone doses causing supraphysiologic levels could result in lowering of the voice (which could be permanent), clitoral enlargement, excess body hair, edema, erythrocytosis, and liver dysfunction.
- Psychological changes (e.g., increased anger or aggression) are potential risks.
- Adverse changes in lipids and liver function tests may occur, particularly with oral testosterone formulations. Prolonged use of high doses of oral testosterone has been associated with liver dysfunction in women, including hepatomas and hepatocellular carcinomas. Oral formulations also reduce high-density lipoprotein (HDL) cholesterol levels and triglycerides in estrogen-treated women.
- With topical testosterone, hair growth or skin irritation may occur at the application site.

CONTRAINDICATIONS

CONTRAINDICATIONS

Testosterone therapy is contraindicated in women with breast or uterine cancer or in those with cardiovascular or liver disease.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

In narrowing the focus of this position statement, several qualifying statements were established:

- Therapeutic recommendations are limited to postmenopausal women. Safety and efficacy data from adequately sized randomized controlled trials in premenopausal and perimenopausal women are lacking.
- Recommendations pertain to women who have experienced either spontaneous or surgically induced menopause. Although surgically induced menopause may cause physiologic symptoms different from those of spontaneous menopause, it is reasonable to assume that the therapeutic results will be similar. However, there have been no adequately powered clinical trials comparing these populations. No data are available for women who experienced induced menopause for reasons other than surgery.
- Clinical evidence presented in this position statement is limited to prescription testosterone products. Custom-compounded testosterone formulations are sometimes used; however, the quality and dosing consistency of these formulations can vary greatly.
- Although the treatment recommendations are relevant internationally, the discussion is limited to prescription therapies available for clinical practice in the United States and Canada.
- A general evaluation of all androgens, including over-the-counter products such as dehydroepiandrosterone (DHEA), is beyond the scope of this position statement. Although some efficacy data on DHEA in women with adrenal insufficiency are encouraging, data in healthy postmenopausal women are not adequate to establish the efficacy of this agent in this population.
- Clinical evidence and management strategies focus primarily on sexual concerns that occur around the time of menopause, as this was the primary end point of most clinical trials. A general discussion of other causes of, and treatments for, sexual health problems is beyond the scope of this position statement.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Patient Resources
Slide Presentation

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)

The North American Menopause Society. The role of testosterone therapy in postmenopausal women: position statement of The North American Menopause Society. Menopause 2005 Sep 1;12(5):497-511. [66 references] PubMed

ADAPTATION

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

DATE RELEASED

2005 Jun 30

GUIDELINE DEVELOPER(S)

The North American Menopause Society - Private Nonprofit Organization

SOURCE(S) OF FUNDING

The development of the guideline document was supported by an unrestricted educational grant from Procter & Gamble Pharmaceuticals.

GUIDELINE COMMITTEE

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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 in Portable Document Format (PDF) from The North American Menopause Society (NAMS) Web site.

Print copies: Available from NAMS, P.O. Box 94527, Cleveland, OH 44101, USA. Order forms are available in Portable Document Format (PDF) from The North American Menopause Society (NAMS) Web site, www.menopause.org.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Key points: NAMS 2005 position statement on testosterone. Slide set. 2005. 17 p. Available from The North American Menopause Society (NAMS) Web site.
- NAMS continuing medical education (CME) activities. Available from The NAMS Web site.
- Boggs PP, Utian WH. The North American Menopause Society develops consensus opinions. Menopause 1998 Summer;5(2):67-8. Available from the NAMS Web site.

PATIENT RESOURCES

The following is available:

- Menopause: a new beginning. Available in English, French, or Spanish from the NAMS Web site.

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 summary was completed by ECRI on October 10, 2005. The information was verified by the guideline developer on December 12, 2005.

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