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Testosterone Replacement Therapy for Male Aging: ASA Position Statement

Position

The American Society of Andrology suggests that testosterone replacement therapy in aging men is indicated when both clinical symptoms and signs suggestive of androgen deficiency and decreased testosterone levels are present. Testosterone replacement may also be warranted in older men with markedly decreased testosterone levels regardless of symptoms, but signs of androgen deficiency should be present. Based on the data currently available, the measurement of total blood testosterone is the most appropriate and widely available test to confirm hypogonadism. Subject to future research, a total testosterone level of 300 ng/dL measured in the morning, using a reliable assay, may be used as a threshold below which an individual can be considered hypogonadal. The American Society of Andrology recommends periodic monitoring of men receiving testosterone replacement therapy. Subject to individual clinical response, evaluation is recommended at 3 to 6 months after initiation of therapy, and then yearly. A physical examination, including digital rectal examination of the prostate, a prostate-related symptom assessment, prostate-specific antigen (PSA) level, and hematocrit, should be performed at 3, 6, and 12 months, and then annually. Testosterone therapy should be altered or ended if the hematocrit exceeds 52%. Contraindications to therapy include a history of prostate cancer, breast cancer, untreated sleep apnea, and untreated and/or severe congestive heart failure.

Background

The definition of hypogonadism in aging men is controversial. In the absence of agreement, the combination of clinical signs and symptoms and plasma testosterone concentration may be used to determine whether testosterone replacement therapy is indicated. Assays for the measurement of total, free, and bioavailable (free plus albumin-bound) testosterone levels are available from commercial reference laboratories, but local clinical laboratories do not appear to commonly use methods of sufficient accuracy and precision to assess free testosterone. Direct radioimmunoassays of free testosterone should not be used. Replacement therapy includes injectable long-acting testosterone esters, transdermal patches, gel, subcutaneous pellets, and oral testosterone undecanoate (not approved in the United States). Non-injection therapy aims to provide stable and physiologic serum testosterone levels.

Adverse Effects

Testosterone replacement therapy has been associated with increased hematocrit and hemoglobin, oiliness of skin, and acne. Exacerbations of sleep apnea and obstructive uropathy related to benign prostatic hyperplasia are also a concern. Currently available data obtained from relatively small studies support the short-term safety of testosterone replacement therapy with regard to the risk for possible development or stimulation of subclinical prostate cancer, although the long-term risks remain undetermined. The American Society of Andrology encourages adequately powered, long-term, and well-designed studies to assess the clinical benefits and safety (in particular on prostate and cardiovascular disease) of testosterone replacement therapy.

Pretreatment Screening

The American Society of Andrology recognizes that given the possible adverse effects of testosterone therapy in the older man, pretreatment screening for parameters related to potential risks of testosterone therapy is essential. The following program is recommended:

1) Medical history for potential sleep apnea, congestive heart failure, symptoms consistent with lower urinary tract obstruction, and personal or family history of prostate or breast carcinoma. Patients should be informed that testosterone therapy will affect spermatogenesis and their fertility potential during treatment and for some time following cessation of therapy.
2) Physical examination, including a digital rectal examination of the prostate.
3) Laboratory tests, including hematocrit and PSA level.

In cases of abnormal digital rectal examinations and/or consistently elevated PSA levels, a urological evaluation including *trans*-rectal ultrasound and biopsy of the prostate should be performed prior to initiation of testosterone therapy.

Monitoring of Therapy

Periodic follow-up of patients treated with testosterone should take place on a regular basis and should include assessment of symptoms and side effects; physical exam with particular attention to the prostate; and PSA, testosterone, and HCT measurement.

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