Hypogonadism and Testosterone Replacement in Men with HIV

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Overview

1. Definition and diagnosis of hypogonadism
2. Prevalence among HIV infected men and diagnostic confounders
3. Risks and benefits of testosterone replacement
4. Testosterone delivery and monitoring
Why consider treating male hypogonadism?

Androgen (estrogen) Effects

- **skin**: hair growth, balding, sebum production
- **liver**: synthesis of serum proteins
- **male sexual organs**: penile growth, spermatogenesis
- **prostate growth and function**
- **brain**: libido, mood
- **muscle**: increase in strength and volume
- **kidney**: stimulation of erythropoietin production
- **bone marrow**: stimulation of stem cells
- **bone**: accelerated linear growth, closure of epiphyses
  - increase BMD
• Prevalence of hypogonadism among HIV-infected men pre-HAART 50%, now 13-20%, more common among men with HIV-associated wt. loss

• Among ALL men, incidence of hypogonadism increases with AGE, obesity, and chronic illness

• Endocrine Society 2010 Clinical Practice Guideline for Androgen Deficiency Syndromes: consider screening men with HIV - associated weight loss

Cotter A et al 2011
Signs and Symptoms of Hypogonadism in Adult Men

• Sexual complaints (↓ libido, ED). infertility

• Gynecomastia, ↓ male pattern hair

• ↓ energy, fatigue, moodiness, ↓ muscle mass and strength, increased fat mass

• NON-SPECIFIC: poor overlap with biochemical criteria, most associated with normal aging
Androgen Production and Metabolism: Diagnosing Hypogonadism

#2 Check LH and FSH, free T

Primary: high LH&FSH
Secondary: low LH&FSH
Late Onset Hypogonadism (HIV): low/normal LH

99% TT protein bound (Alb + SHBG): 1% free T

#1 Symptom + Low serum total testosterone AM, fasting, (< 280-300 ng/dl)
Making the Diagnosis of Hypogonadism

• Combination of symptoms + biochemical evidence. Get calculated free T with HIV +

• Primary (high LH): testicular defect

• Secondary (low LH): screen for other Pit hormones, consider MRI, hemochromatosis, anabolic steroids

• Low/normal LH: pit MRI, OPIATES (including methadone), chronic illness, malnutrition, aging
Summary: Risks and benefits of T therapy in men with hypogonadism

• BENEFITS: T therapy will increase lean mass, BMD, libido and HCT and will decrease fat mass. Mild increase in leg strength
  --- Physical performance, ED, and QOL more mixed results, mild improvement overall
  --- improvements in IS, metabolic parameters mixed
  --- benefits generally seen in men with lowest T levels at baseline

• RISKS: unknown. RCT no increase AE.
  - PROSTATE: increases PSA but ? PCa, BPH
  - CVD: lowers HDL, LDL and Total Chol
  - HCT
  - $$$
Testosterone and Mortality

- **No appropriate RCT to evaluate mortality benefit**
- Observational data: multiple large, prospective studies in last 5 years show association between low serum T and earlier mortality (MMAS, VA, Mr. OS)
  - Recent data suggestive of possible treatment benefit (no harm)
RCT of HIV-infected men treated with Testosterone

Limitations

- ALL SMALL (n <100) and short (24 weeks max)
- all done with men with HIV-associated wt. loss
- all but one in pre-HAART era
- LBM not functional outcome

Corona et al 2013 Best Prac Res Clin Endo Metab 27:557-79
Testosterone as an Anabolic agent in HIV

- 3x supraphysiologic T given to HIV+ men with unintentional wt. loss
- NO INCREASE vs. PLACEBO in strength, mood, stair climb
- No adverse events
Options for testosterone replacement therapy

- Depot formulations
  - Intramuscular (q2week)
  - Subcutaneous implant
- Daily dosing
  - Transdermal ($$)
  - Buccal
  - Oral
- Follow-up (3-6 months)
  - HCT
  - PSA (if have baseline)
Summary

- Incidence of hypogonadism may be slightly higher in HIV infected men than HIV- but main RF is age

- Diagnosis based on low T levels + sx, check free T, LH and FSH (or refer based on low T)

- Consider use of anabolic steroids, opiates, and concomitant illness when making the diagnosis

- T therapy will increase LBM, BMD, libido and HCT. Effect on strength likely positive. QOL effects unclear. Risks not known ($$$). Monitor for benefit