



43 year old man with low libido

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Endorama

July 11, 2013

History of Present Illness

- 42 yo man with DM2 x 10 years, ESRD on HD, HTN, and dyslipidemia who is followed in clinic for DM2.
 - Reports low sexual desire and difficulty with erections.
 - Denies any changes in frequency of shaving, muscle weakness, changes in his voice.

Past Medical History

- Past Medical History

- Diabetes mellitus x 10 years
- ESRD on HD
- Hypertension
- Dyslipidemia
- Obesity
- Chronic left great toe ulcer

- Medications:

- Lantus 50 units daily
- Novolog 20 units with meals
- Amlodipine 10 mg daily
- Metoprolol XL 200 mg daily
- Minoxidil 10 mg daily
- Clonidine 0.2 mg QHS
- Pravastatin 10 mg daily
- Sevelamer carbonate 3200 mg with meals
- Ranitidine 75 mg daily

Past Medical History

○ Family History:

- Father with DM2
- One child with DM2 diagnosed at age 16

○ Social History:

- Unemployed.
- Single
- 3 children
- No history of tobacco use.
- No current ETOH use.

ROS

- Constitutional: Weight gain. Fatigue.
- Eyes: Positive for occ. visual disturbance when hypoglycemic.
- Respiratory: Negative for cough and shortness of breath.
- Cardiovascular: Negative for chest pain and palpitations.
- Gastrointestinal: Negative for nausea, vomiting, abdominal pain, and diarrhea.
- Genitourinary: Anuric.
- Musculoskeletal: Negative for myalgias and arthralgias.
- Neurological: Positive for numbness and occ. Headaches.
- Psychiatric/Behavioral: Negative.

Physical Exam

- Vital signs: BP 128/65, pulse 71, height 6'3", weight 305 lbs, BMI 38.1 kg/m²
- Constitutional: Well-developed and well-nourished.
- HENT: Oropharynx is clear and moist. No oropharyngeal exudate. Conjunctivae and EOM are normal. Pupils are equal, round, and reactive to light.
- Neck: Neck supple. No thyromegaly present. No thyroid nodules noted.
- Cardiovascular: Normal rate and regular rhythm. Systolic murmur.
- Pulmonary/Chest: Effort normal and breath sounds normal. No respiratory distress. He has no wheezes. He has no rales.
- Abdominal: Soft. Bowel sounds are normal. He exhibits no distension. There is no tenderness.
- GU: Normal appearing external genitalia. Prostate is not enlarged and not tender. Inferior edge of prostate palpated. No nodules noted in the area.
- Musculoskeletal: He exhibits no edema.
- Neurological: He is alert and oriented to person, place, and time. He has normal reflexes. Decreased sensation to monofilament.
- Skin: Skin is warm and dry. Acanthosis nigricans noted. Chronic ulcer on plantar aspect of L toe.
- Psychiatric: He has a normal mood and affect. His behavior is normal.

Labs

- A1c 6.1%
- Fructosamine 358 mcmol/L (A1c 8-9%, avg glu 200)
- 1PM:
 - Total testosterone 83 ng/dL (240-950)
 - SHBG 19 nmol/L (10-80)
 - Calculated free testosterone 30 pg/mL (90-300)
- 9AM:
 - Total testosterone 94 ng/dL
 - SHBG 20 nmol/L
 - Calculated free testosterone 35 pg/mL
 - LH 3.3 mIU/mL (2-6.8)
 - FSH 2.6 mIU/mL (1.2-8.0)
 - Prolactin 35.33 ng/mL (4-15.2)
- PSA: 0.35 ng/mL (0.0-4.0)

Labs

- DXA:
 - L1-L4 spine Z-score of 3.2, T-score of 4.6
 - Total hip Z-score of 1.0, T-score 2.1

Assessment & Plan

- 42 yo man with DM2 x 10 years, ESRD on HD, HTN, and dyslipidemia who complained of low sexual desire, erectile dysfunction, found to have hypogonadotropic hypogonadism.
 - Medicare did not want to cover topical testosterone but did cover testosterone injections.
 - Received 200 mg IM q 2 weeks x2.
 - Testim 1% gel was approved, started on 5 grams daily.

Follow up

- 2 month follow up: Feels better with more energy. No changes in erection dysfunction but has not had any recent relationships.
 - Given sample of Cialis.
 - Total testosterone 240.
 - Testim increased to 10 grams daily.
- 6 month follow up: Able to achieve erections now.
 - Total testosterone 468, free testosterone 177.



Questions:

- Epidemiology of hypogonadism in diabetes
- Pathogenesis of hypogonadism in diabetes
 - Insulin resistance
- Effects of testosterone replacement

Hypogonadism in DM2

- 25-40% of men with DM2 have hypogonadotropic hypogonadism.
 - Rare in DM1.
- Not related to A1c or duration of diabetes but are associated with age, BMI, very high CRP, and mild anemia.
 - 44% of lean, 44% of overweight, and 50% of obese diabetic patients have HH, compared to 26%, 29%, and 40% in nondiabetic men.

Pathogenesis of Hypogonadism in DM2

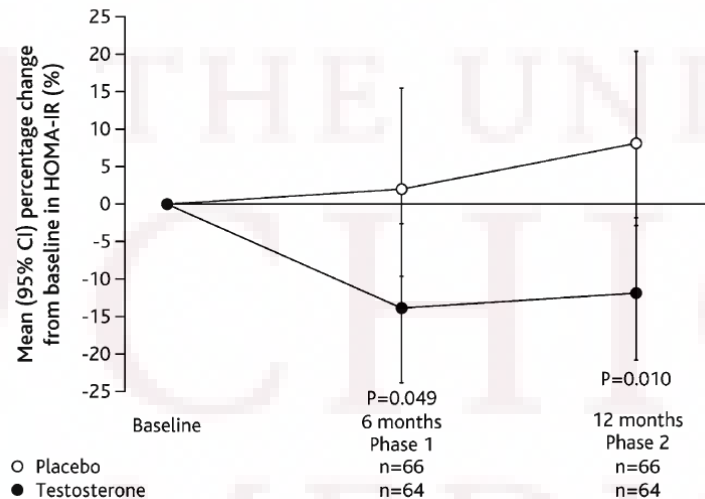
- Obesity: The increase in adipose tissue mass resulting in increased aromatase activity and higher estradiol levels is no longer thought to be the pathogenesis.
 - Actually have lower estradiol levels
- Insulin resistance:
 - Selective deletion of insulin receptor gene from neurons results in systemic insulin resistance and hypogonadotropic hypogonadism in mice.
 - Inflammatory mediators that interfere with insulin signal transduction also suppress HPG axis (TNF α , IL-1).

Hypogonadism in DM2

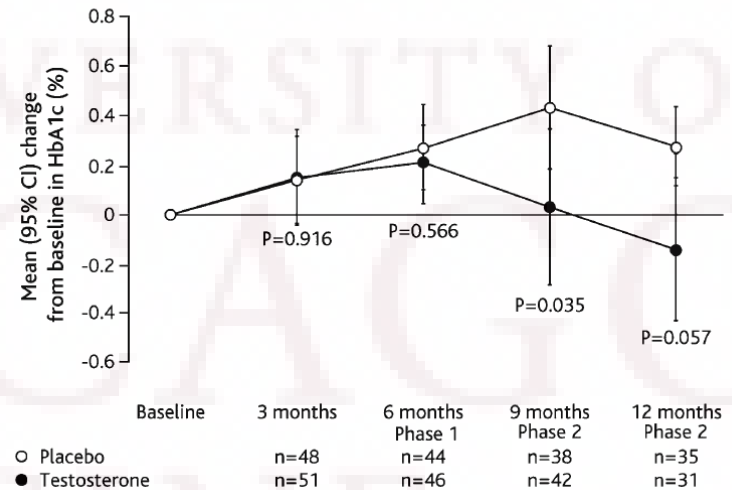
- 2-3 times elevated risk for cardiovascular death.
- Endocrine Society recommends that clinicians consider measuring total testosterone levels in men with DM2.

Testosterone Replacement

B Patients with type 2 diabetes



E Patients with type 2 diabetes



- No sig. difference in lipid parameters.
- No sig. difference in waist circumference, % body fat, BMI, blood pressure.
- Sig. improvement in erectile function, sexual desire.
- No sig. differences in cardiovascular events.

Testosterone Replacement and Cardiovascular Risk

- Meta-analysis showed no change in rates of death, MIs, revascularization procedures.
- Abstract: mortality rate of 9% in eugonadal men, 8.6% in treated hypogonadal men, and 20% in untreated hypogonadal men.



Take Home Points

- Hypogonadism is common in male type 2 diabetics.
- Testosterone deficiency plays a role in insulin resistance.

References

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Testosterone Replacement

- Sexual dysfunction: mainly increases sexual desire, may respond to phosphodiesterase IV inhibitors better
- Body Composition: decreases waist circumference (but not BMI)
- Cardiovascular outcomes: meta-analysis showed no change in rates of death, MIs, revascularization procedures.
 - Abstract: mortality rate of 9% in eugonadal men, 8.6% in treated hypogonadal men, and 20% in untreated hypogonadal men.

Testosterone and Insulin Sensitivity

- Type 2 diabetic patients with hypogonadotropic hypogonadism were treated with placebo v. testosterone therapy.
- Sig. 25% increase in insulin sensitivity after 24 weeks of treatment.
- Slight but sig. improvement in lean mass, total fat, CRP, and free fatty acids.
- No sig. difference in A1c, cholesterol, sexual desire, and satisfaction with erections.