



BESINS HEALTHCARE SCIENTIFIC LITERATURE REVIEW – August 2021

Must Read Articles in Men’s Health

Association between low testosterone and anemia: Analysis of the National Health and Nutrition Examination Survey (NHANES)

Valancy D et al

Andrologia 2021:

Pubmed Link: DOI: 10.1111/and.14210

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How Would You Manage This Male Patient with Hypogonadism? Grand Rounds Discussion from Beth Israel Deaconess Medical Center.

Libman et al

Annals of Internal Medicine 2021

PubMed link: doi:10.7326/M21-2524

Other Articles of Interest - Men’s Health

Cognitive response to testosterone replacement (TRT) added to intensive lifestyle intervention in older men with obesity and hypogonadism: prespecified secondary analyses of a randomized clinical trial	<i>Gregori et al</i> Am J Clin Nutr 2021; 0:1-10	A secondary analysis of the LITROS trial exploring if TRT could improve cognitive function when added to intensive lifestyle intervention in frail old men with obesity and hypogonadism. The results suggest that TRT add to intensive a lifestyle intervention (weight management and
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		exercise training) may further improve cognitive function.
Serum Total Testosterone and Premature Mortality Among Men in the USA	Fantus R <i>et al</i> European Urology Open Science 2021:29: 89-92	Data from the NHANE Survey was analyzed to explore the association between serum testosterone and premature mortality using contemporary guidelines and testosterone measurements. Low testosterone levels were associated with both premature death and related diseases such as obesity, which can be treated initially with both diet and exercise

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Title	Authors	Journal and Issue	Article Type
Association between low testosterone and anemia: Analysis of the National Health and Nutrition Examination Survey	Valancy D <i>et al</i>	Andrologia 2021:	Retrospective analysis

Background:

- Anemia in men is typically diagnosed when hemoglobin levels are <13.5 g/ dl.
- 11% of men over the age of 65 were found to have anemia in the third National Health and Nutrition Examination Survey (NHANES III).
- It has been postulated that the increased prevalence of anemia seen in older men could be due to declining testosterone levels due to aging.

Aim:

The aim of this study was to determine the association of total serum testosterone and hemoglobin concentrations in the general American male population using a nationally representative sample.

Methods:

- Men between the age of 18 to 80 years of age who met the inclusion/exclusion criteria were analyzed.
- Anemia was defined as serum hemoglobin less than ≤ 13.5 ng/dl and low serum testosterone as ≤ 300 ng/dl.

Results:

- 591/ 5888 (10%) men who met the inclusion criteria had anemia.
- Compared to men without anemia, those with anemia had the following characteristics:
 - generally older (40[29-55] versus 58[43-69] p<0.001)
 - lower BMI (27.5kg/m² versus 26.9kg/m² p<0.001)
 - lower testosterone (368.7ng/dl versus 401ng/dl)
 - a higher prevalence of low testosterone (≤300ng/dl) 24.1% versus 32.3% p<0.001).

Discussion:

- Men with low total testosterone of less than or equal to 300 ng/dl are 1.44 times more likely to have anemia compared to men with normal or high total testosterone.
- Lower than normal hemoglobin in elderly individuals is associated with multiple adverse outcomes such as cognitive decline, frailty, longer hospital stays and increase mortality.

Practice Points:

Large cross-sectional study from American NHANES III database produces more confirming evidence about the correlation between low testosterone levels and anaemia.

Title	Authors	Journal and Issue	Article Type
How Would You Manage This Male Patient with Hypogonadism? Grand Rounds Discussion from Beth Israel Deaconess Medical Center.	Libman H	Annals of Internal Medicine 2021	Grand Rounds Discussion

What this discussion between two experts brings:**Background:**

- In 2020 the American College of Physicians published a clinical guideline for the use of Testosterone Replacement Therapy (TRT) in adult men.
- Included in the guideline was a recommendation for clinicians to discuss whether to initiate testosterone treatment in men with age related low testosterone with sexual dysfunction who want to improve sexual function and not initiate testosterone treatment in men with age related low testosterone to improve energy, vitality, physical function or cognition.
- Two clinicians, a generalist and an endocrinologist debate the management of a patient with sexual symptoms and a low serum testosterone level.

Clinical Case:

- A male 40 years old presented in 2016 with lethargy, decreased libido and erectile dysfunction.

- Underlying conditions included hypertension, diabetes mellitus, atrial fibrillation, congestive heart failure, gout, obstructive sleep apnea, severe obesity, vitamin D insufficiency and hyperlipidemia.
- Serum testosterone levels were tested and found to be low.
- The patient began once weekly testosterone cypionate injections intramuscularly.
- Mild improvement was seen initially with libido and erectile function.
- The patient developed mild erythrocytosis.
- He stopped therapy in 2019 due to a “fear of needles” but symptoms reoccurred.
- He returned to the clinic in the hope of restarting treatment.

Patient Management – Clinical Opinion 1 – Dr Marc Cohen - Generalist

- Repeat serum testosterone testing levels with morning samples to confirm the patient’s hypogonadism.
- Free Testosterone levels should be checked in addition to Total Testosterone levels in patients with co-morbid conditions.
- A weight loss attempt should be made and supported through either pharmacotherapy or surgical intervention as obesity has a clear association with hypogonadism.
- Switch the patient from injection therapy to transdermal gel and provide appropriate training on avoidance of skin contact with other members of the family.
- Gels are generally better tolerated than patches, given the high rates of skin irritation with patches (up to 60% of patients, with 5% to 10% discontinuing use).
- The potential time burden for clinicians, particularly those without a nurse or pharmacist on site, to provide teaching about needle and syringe assembly, injection technique, and appropriate needle disposal may be considerable.
- Due to the patient’s multiple cardiovascular risks and greater likelihood of erythrocytosis on injection therapy, transdermal testosterone gel may provide a better benefit-risk ratio.

Patient Management – Clinical Opinion 2 – Dr Michael S. Irwig - Endocrinologist

- Restart testosterone replacement therapy as the patient has had several low testosterone level measurements and recurrent sexual symptoms.
- Short acting testosterone esters administered intramuscularly or subcutaneously are recommended based on American ACP 2020 guidelines for the patient as they are the most cost-effective option.
- Uncertainty exists with regards to whether TRT will improve the patient sexual symptoms. It is likely that his erectile dysfunction is multifactorial related to aging, vascular disease and side effects from antihypertensive medication.
- It is possible that TRT could improve the patient's anemia and maintain bone health.

Practice Points:

- Please review the useful diagnosis algorithm within this paper and the guidance on monitoring testosterone levels post treatment.

- Also review the answers regarding risk for prostate cancer and how to counsel patients about this and the questions about raised haematocrit.
- Review the Table 2 on the characteristics of the different formulations and considerations from the US context.
- Very interesting points made about the newer formulations of nasal, subcutaneous pellets and the buccal tablets and the lack of convenience that these new formulations are seen to provide plus the prohibitive cost.