Focus

Andropause: fact or fiction?

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Introduction

Androgen deficiency in the ageing male, or andropause, is being diagnosed with increased frequency.
A growing body of literature supports the view that a true testosterone decrease develops in some men around the age of 45 which can be associated with a broad spectrum of deficiency symptoms.
The measurement of serum bioavailable testosterone appears to be a relative reliable indicator of androgen deficiency in the ageing male. However, many of the clinical manifestations of andropause may be ascribed to a decrease in the production of other hormones such as human growth hormone and insulin-like growth factor, as well as dehydroepiandrosterone.
The level of bioavailable testosterone may be decreased primarily from Leydig cell impairment, and/or a reduced cell number correlating with age.
Pituitary tumours and deficiencies specific for LH and FSH also lower the levels of bioavailable testosterone.
Binding of circulating testosterone to sex hormone binding globulin also increases with age because of the increased aroma-tisation of testosterone to oestrogens.

Manifestations associated with andro-pause relate to:

(a) Vasomotor/nervous system

- episodes of sweating
- hot flushes
- insomnia
- nervousness

(b) Masculinity

- decreased vigour and physical energy
- diminished muscle mass and strength
- abdominal obesity
- loss of lean muscle mass

(c) Sexuality

- decreased libido
- reduced sexual activity

KEY POINTS

- A true testosterone decrease develops in some men around 45 years which can be associated with a broad spectrum of deficiency symptoms
- Measurement of serum testosterone appears to be a relative reliable indicator of androgen deficiency
- A number of studies have demonstrated that testosterone minimises several important risk factors for heart attack
- Prominent manifestations of andropause are mood disorders and decreased libido
- Male hormone therapy is dramatically effective in relieving

- poor erectile function
- limited quality of orgasm
- reduced volume of ejaculate
- weakness of ejaculation.

symptoms and restoring drive, health, potency and a sense of renewed vitality

It is obvious that testosterone affects many body systems, including male sexual development, sexual behaviour, sexual and erectile function, bone mineralisation, lipid and carbohydrate metabolism, muscle mass, muscle strength and hematopoiesis.

Cardiovascular disease

The belief that androgen replacement poses a danger in altering lipid metabolism and therefore increases the risk of developing cardiovascular pathology persists. This theory is based on conclusions derived from differences in life expectancy between the sexes and the abnormal balances between androgens and oestrogens in women suffering from polycystic ovarian disease.
The evidence of long term studies with follow-up periods of six to 12 years proves the contrary. These studies have shown that neither coronary events nor cardiovascular mortality were correlated with plasma levels of testosterone, free testosterone or oestrogens. In fact, several studies in the past decade suggest that low endogenous testos-terone levels could be associated with an increased cardiovascular risk. In this context, several researchers have concluded that maintenance of physiological levels of testosterone does not, or only slightly, affects the lipid profile in both young and aged men.

A number of studies have demonstrated that testosterone minimises several important risk factors for heart attack including:

- reducing cholesterol and triglycerides
- reducing blood glucose levels
- decreasing visceral fat mass
- normalising blood clotting.

Of these, the two that have probably received the most study are the effects on blood clotting and cholesterol levels.
There might be a biological point of no return where the normal balance between testosterone and oestradiol starts tilting towards oestradiol. When this happens, the suppressive effects of oestradiol on testosterone production (via decreased LH release) begin to predominate, causing testosterone levels to drop to a lower level of equilibrium.

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In one Norwegian study researchers analysed the blood of 42 middle-aged men judged to be at risk for coronary artery disease. They found a highly significant correlation between a low testosterone:oestradiol ratio and impaired fibrinolytic capacity.

Behavioural changes

Prominent among the manifestations of andropause are mood disorders and decreased libido. Androgen administration renders men more vigorous when the hypogonadal state is

corrected. The increased sense of wellbeing experienced by these patients can be dramatic. Self-reported changes include: more relaxed feelings, improved sleep pattern, decreased fear and/or sadness, renewed sexual desire, increased sexual interest, partial correction in sexual dysfunction and a decline in lethargic episodes.
Dr Malcolm Carruthers, author of Beyond Viagra: Testosterone and Sildenafil in treating sexual dysfunction (available on audio-cassette) has found that in most men combining the above treatment regimens will lead to a decrease in sexual/erectile dysfunction.
In my practice, I make use of the following hormonal score sheet to ask patients to grade their symptoms. I repeat the procedure after a course of androgen administration and have found without exception an improvement of two points in most of the categories.

Hormonal score sheet:
Rate the following as they apply to you; use numbers one to four,with one being rare and four being frequent or severe.

1. Fatigue, tiredness, loss of energy
2. Decrease in physical stamina
3. Feelings of depression
4. Decreased sex drive
5. Erection and/or potency problems
6. Loss of morning erections
7. Dry skin on face or hands
8. Increase in waist size
9. Loss of motivation
10. Increase in aches in joints and muscles
11. Frequent use of alcohol – now or in past
12. Decrease in muscle mass
13. The age you are?
14. The age you feel?

The prostate

Current opinion on the development of benign prostatic hypertrophy (BPH) is that it is mediated by intracellular events resulting from the action of 5-alpha dihydro-testosterone with very likely participation by oestrogens. The volume of the prostate increases with age in normal men, but not in untreated hypogonodal men. When the latter are treated, the prostate volume increases, but only to the size expected for eugonodal men of the same age, and there is only mild reduction in urine flow.
Much speculation exists regarding serum levels of testosterone and cancer of the prostate. Only the fact that testosterone promotes growth of an established adenocarcinoma is firmly established. The evidence of testosterone causing prostate cancers points to the contrary but is still insufficient to rule out a causal risk.
We do know this: the serum levels of the sex hormones carry no relation to the development of prostate cancer.

THERAPEUTIC PROTOCOL FOR ANDROPAUSE

Male hormone therapy has been shown to be dramatically effective in relieving symptoms and restoring drive, health, potency and a sense of renewed vitality.
This includes careful monitoring of testosterone and oestrogens and supplementary therapy so a healthy balance can be regained. An imbalance

can occur either because of a decrease in testosterone levels, increase in oestrogen levels or a combination of both.
These levels can be accurately measured.

- Reduce oestradiol levels and increase testosterone levels through dieting, exercise and nutritional supplements such as zinc and vitamin C. Testosterone is converted to oestradiol through the aromatase enzyme. Oestrogen is stored in fatty tissue and speeds up aromatase activity, therefore diet and exercise are important. A weight-loss programme can cut down oestradiol build-up.
- Zinc supplementation in amounts of 100mg per day is believed to decrease testosterone conversion to oestrogen, possibly by affecting the number of androgen receptor sites.
- Vitamin C has been used also to decrease aromatase activity in doses of 1–3g per day.

This is a conservative approach which may be useful in a man with borderline results and symptoms, or someone who wishes to forestall the onset of andropause.

- Another approach is more appropriate when laboratory values and symptoms are more definitive and, in such men, increasing testosterone levels is more clearly a major goal.

The testes may be fully intact, but are not receiving proper signals to secrete testosterone. This is secondary hypogonadism, in which the signal hormones LH and FSH may be below normal.

- Chorionic gonadotrophin is very similar in structure to LH, and an injection of HCG can often reactivate the testicular secretion of testosterone. Dosage requirements can vary from patient to patient, with some responding to a single injection and others requiring injections several times a week until testosterone levels are increased to healthier levels.

Testosterone replacement therapy

Testosterone replacement is an important and highly effective means of addressing andropause. It is extremely important that a clinical examination should be done before initiation of treatment. Values should be measured for cholesterol, FBC, haematocrit, PSA, testosterone, oestradiol, LH and FSH.
There are several efficient ways to administer testosterone and several inefficient (and possibly unhealthy) ways.

Testosterone replacement is an important and highly effective means of addressing andropause

a. Oral preparations
This is an inefficient way of dosing because of the high first pass effect, which largely converts testosterone to inactive metabolites. Most researchers and clinicians do not use testosterone orally.
Note: Methyltestosterone is more bioavailable for oral administration, but is not recommended because of its adverse liver profile.

b. Intramuscular injection therapy
This is by far the most common way, and for some men it seems to work well. A serious drawback is its erratic ratio of release. Many men will experience the intramuscular injection as a bolus dose; primarily achieving high testosterone levels in the first week, with noticeable declining levels

beyond that.

c. Implanted pellets
This is a simple office procedure and offers a major compliance advantage. Effectiveness can last from three to five months.

d. Topical preparations
A normal healthy male secretes between eight and 15mg of testosterone per day. Effective topical doses can range from 10–40mg per day.

CONCLUSION

Patients receiving supplemental testosterone therapy should have clear indications based on clinical symptoms and/or physical manifestations.
Proper laboratory assessment is mandatory.
Patients affected by androgen deficiency usually require testosterone administration on a long term basis.
Patients with suspected secondary hypogonadism should not receive testosterone replacement until their endocrine investigation has been completed.
Testosterone replacement may result in increased oestrogen levels and is therefore contraindicated in men with breast cancer. Known prostate cancer is a contraindication for testosterone treatment. Known existence of sleep apnoea remains a contraindication for androgen administration.
Initially patients should be followed on a three-monthly basis. At these visits the following should be undertaken:

- clinical assessment of response to therapy
- PSA if the patient is older than 40 years of age.

Any patient whose PSA exceeds 4 ng/ml should be examined by a urologist.
Patients who remain stable may subsequently be followed every six months, at which time a lipid profile, haemoglobin and haematocrit may also be considered.
Serum levels in treated patients will fluctuate considerably, particular if testosterone is given by intramuscular injection. Regardless of serum levels, clinical response is a better guide to the dose required.
Andropause and testosterone replacement therapy can be complicated, and it wise to refer these patients to an endocrinologist, urologist or medical practitioner with sufficient experience and knowledge.