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Should we be prescribing testosterone to perimenopausal and menopausal women?

A guide to prescribing testosterone for women in primary care

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INTRODUCTION

Testosterone is one of the sex hormones that women produce, yet it is often overlooked. Women actually produce three times as much testosterone as oestrogen before the menopause. Levels of testosterone gradually decline because of increasing age or they reduce abruptly following oophorectomy.

The most commonly described symptoms of androgen insufficiency include dysphoric mood, unexplained fatigue, change in sexual function including reduced libido, changes in cognition, vasomotor symptoms, bone loss, and decreased muscle strength.[1]

Reduced or lack of libido is very common in menopausal women. The National Institute for Health and Care Excellence (NICE) guidelines state that testosterone supplementation can be considered for menopausal women with low sexual desire if hormone replacement therapy (HRT) alone is not effective.[2] The British Menopause Society (BMS) 2016 recommendations advise that this indication could be extended to include menopausal women with low sexual desire and tiredness.[3]

Testosterone can be important in women for bone density and muscle mass, cognitive function, mood, sexual function, and energy.[1] Adequate levels of testosterone are important for the maintenance of musculoskeletal health and possibly vascular and brain function.

EVIDENCE TO SUPPORT TESTOSTERONE USE IN WOMEN

Numerous studies have shown that adding testosterone to hormonal therapy can improve sexual function and general wellbeing among women during their menopause. A recent systematic review and meta-analysis of testosterone treatment in women has provided robust support for a trial of testosterone in women when clinically indicated. In postmenopausal women, testosterone supplementation improved several domains of sexual response, including sexual desire, pleasure, arousal, orgasm, and self-image.[4]

It has also been shown to have additional benefits including the improvement of urogenital, psychological, and somatic symptoms, an increase in bone density, and enhancement of cognitive performance when combined with oestrogen as part of HRT. Many women notice that taking testosterone improves their mood, concentration, motivation, and energy levels.

A significant problem with prescribing testosterone is that there are currently no available licensed preparations for women in the UK. The BMS has recently released some guidance on testosterone prescribing which suggests some of the products that can be used and their doses (Box 1).[5] General Medical Council guidance on the prescription of unlicensed medication should be consulted when prescribing. It is important to ensure that women are adequately oestrogenised before adding in testosterone; this is usually the case when they are no longer experiencing vasomotor symptoms or vaginal dryness.

The normal range of testosterone is difficult to define as most of the available

Box 1. Commonly used testosterone replacement in menopause[5]

- Testogel® [[Besins Healthcare UK Ltd] 1% testosterone gel in 5.0 g sachets containing 50 mg testosterone): starting dose 1/10 of a sachet/day = 5 mg/day, that is, each sachet should last 10 days.
- Tostran® [[Kyowa Kirin Ltd] 2% testosterone gel in a canister containing 60 g): starting dose 1 metered pump of 0.5–10 mg on alternate days — each canister should last 240 days.
- AndroFeme® [[Lawley Pharmaceuticals] 1% testosterone cream in 50 ml tubes with screw cap) (only available privately): starting dose 0.5 ml/day = 5 mg/day, that is, each tube should last 100 days.

Box 2. Practical points

- Testosterone can be a useful adjunct to HRT care in many women.
- Check the patient is well oestrogenised before starting (no vasomotor symptoms).
- Calculate FAI = total testosterone/SHBG × 100 and if in the lowest quartile (<1%) consider a trial of testosterone.
- Check FAI after starting treatment and aim to keep it <5%.

tests do not provide the accuracy or precision required when testing the low serum concentrations in women. As most testosterone is protein bound to sex hormone-binding globulin (SHBG), there is only a small circulating free fraction, which is difficult to measure reliably. The level of bioavailable testosterone can be estimated using Free Androgen Index (FAI). BMS guidance suggests that in a symptomatic woman with an FAI of <1%, a trial of testosterone supplementation could be considered.[5]

It can sometimes take several weeks or even months for a woman to notice the beneficial effects of testosterone. If they have not noticed an improvement after 6 months, then it is unlikely to be beneficial.

Current BMS guidance suggests that, when monitoring women who are using testosterone, the level of FAI should be maintained at <5% but that clinical improvement in symptoms is more important than aiming for a specific level on treatment (Box 2).[5]

An international task force of experts from leading medical societies, brought together by the International Menopause Society, has recently produced a Global Position Statement to provide clear guidance regarding the prescribing and measurement of testosterone for female testosterone therapy, as well as advice on testosterone prescribing practices that have the potential to be ineffectual or cause harm. They concluded that testosterone can be effective at improving sexual wellbeing for postmenopausal women with hypoactive sexual desire dysfunction (HSDD). Recognised benefits included improved sexual desire, arousal, orgasm, and pleasure, together with reduced concerns and distress about sex.[6] They advise measuring testosterone levels at baseline and at 3–6 weeks after treatment initiation. Patients should be monitored for their clinical response to treatment and assessed for signs of androgen excess, with a serum total testosterone level every 6 months to screen for overuse. There should be cessation after 6 months if there has been no response to treatment.[6]

SAFETY OF TESTOSTERONE

Testosterone appears to be safe when used transdermally and in low doses. There are little long-term safety data on the use of testosterone in menopausal women beyond 2 years. What is available is reassuring in that transdermal testosterone is not associated with an increase in blood pressure and has no adverse effects on lipid profile.[6] Evidence shows that there are also no changes in renal function, liver function, or blood cell indices with transdermal testosterone in women.[7] There is no increased risk of breast cancer in the short term[6] and it does not appear to stimulate the endometrium.[8] It is currently not known how safe it is to prescribe testosterone to women who have breast cancer, and this would be a decision for a secondary care menopause service, on a case-by-case basis and after discussion with an oncologist.

Side effects can occasionally occur including acne and increased hair growth at the site of application, but increase in facial hair, alopoecia, or voice deepening does not occur if testosterone levels are kept within the female physiological range.[4]

There is an urgent need to ensure gender equality in effectively managing women with sexual dysfunction related to hypoandrogenic states. Having a licensed testosterone preparation available for women would certainly be a step in the right direction.

As most menopausal women can be managed in primary care, the new BMS guidance will aid GPs to feel confident to initiate testosterone, if appropriate, or to continue prescriptions that have been started in specialist clinics.

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