Clinical reviews

Our panel of GPs review recent research papers in their specialist areas that may influence the way you practise

Reviewers

Addiction
Dr Jez Thompson
GP Leeds and Clinical Director Lifeline (North) RCGP regional lead substance misuse

Cardiovascular disease
Dr Peter Savill
GP Watercress Medical, Medstead
GPwSI Cardiology, Southampton

Diabetes
Dr Matthew Lockyer
GP with an interest in diabetes, Suffolk

Dr Peter Savill
GP Watercress Medical, Medstead
GPwSI Cardiology, Southampton

Mental health
Dr Phillip Bland
GP with an interest in mental health, Dalton-in-Furness

Obstetrics and gynaecology
Dr Chris Barclay
GP with an interest in O&G, Suffolk

Paediatrics
Dr Chris Barclay
GP with an interest in O&G, Suffolk

Sexual health
Dr Richard Ma
GP with an interest in sexual health and NIHR Research Fellow, Imperial College, London

Smoking cessation
Dr Jez Thompson
GP Leeds and Clinical Director Lifeline (North) RCGP regional lead substance misuse

Urology
Dr Jonathan Rees
GPwSI Urology, Bristol

Urology

What are the benefits of testosterone treatment in older men?

Testosterone therapy in men 65 and over with low testosterone levels produced moderate improvements in sexual function and some improvement in mood but had no effect on vitality or walking, a study published in the *New England Journal of Medicine* has found.

A series of trials was set up in the Unites States to investigate whether testosterone treatment would benefit older men 'who had low testosterone levels for no known reason other than age and who had clinical conditions to which low testosterone might contribute'.

A total of 51,085 men, aged 65 or older, recruited through mass mailings were screened by phone interview and two clinic visits. Of these, 790 men with a serum testosterone < 275 ng/dl (this equates to < 9.5 nmol/L - the more commonly used unit in UK practice) met the inclusion criteria and were enrolled in the study. All the men had symptoms that could be explained by low testosterone. They were randomised to either testosterone gel or a placebo gel for one year.

Depending on their symptoms, patients could be included in one or more of three trials:

- the sexual function trial (men with decreased libido)
- the physical function trial (those with reduced mobility/slow walking speed)
- the vitality trial (men with self-reported 'low vitality' and fatigue)

Testosterone levels were measured at 1, 2, 3, 6 and 9 months. For those on active treatment, the dose of testosterone gel was adjusted to keep the testosterone level within the normal range for men aged 19-40.

The sexual function trial had 230 men in the testosterone arm of the study and 229 in the placebo arm. Men receiving testosterone therapy had significantly increased sexual activity, as assessed by the Psychosexual Daily Questionnaire, (treatment effect 0.62; $P < 0.001$), sexual desire (treatment effect 2.93; $P < 0.001$), and erectile function (treatment effect 2.64; $P < 0.001$). However, while statistically significant, the actual effect size of testosterone treatment was fairly low, and the impact on erectile function less than that seen in trials of phosphodiesterase type 5 (PDE5) inhibitors. Hence, the clinical significance of this change remains uncertain.

The physical function trial had 193 men in the testosterone group and 197 in the placebo group. The percentage of men who had an increase of at least 50 metres in the six-minute walking distance did not differ significantly between men on testosterone and those on placebo. Men on testosterone were more likely than those on placebo to report that their walking ability was better, but the difference was small.

The vitality trial included 236 men receiving testosterone and 238 on placebo. No significant benefit was seen from testosterone therapy, as assessed by the Functional Assessment of Chronic Illness Therapy-Fatigue scale, although there were small but significant benefits with respect to mood and depression, and men on testosterone were more likely to report that their energy levels were better.

It would appear reasonable to conclude that, for older men, the main indication for testing testosterone levels remains bothersome erectile dysfunction, when considering treatment with PDE5 inhibitors. Co-prescription of testosterone replacement in those with low levels may improve libido and sexual function above and beyond treatment with PDE5 inhibitors alone.

However, the benefit of testing testosterone levels for more non-specific symptoms remains questionable. If treatment is trialled for these men, a course of six months' treatment is probably prudent, with reassessment at this stage for clinical benefit, with therapy discontinued for those men who have not noticed any improvement.

DR JONATHAN REES

Snyder PJ, Bhasin S, Cunningham GR et al. Effects of testosterone treatment in older men. *N Engl J Med* 2016;374: 611-24

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