Sexual dysfunction

Testosterone treatment for men with diabetes and ED

Mike Cummings, Consultant Physician and Honorary Reader, Queen Alexandra Hospital, Portsmouth

Previous studies of erectile dysfunction (ED) in men with diabetes have suggested that hypogonadism (best defined as a 9 am serum testosterone or measure of free testosterone activity below the normal range) is no greater in men with diabetes compared with men without diabetes. The conclusion has been that hypogonadism is not a significant aetiological factor in the development of ED in men with diabetes.

This concept could be challenged given the observations of Kaplan et al (summarised on right), who have demonstrated that ageing men with obesity and the metabolic syndrome appear to have a significant decrease in total serum testosterone levels compared with healthy men without the metabolic syndrome. This accelerated decline in testosterone levels within a man with diabetes, associated with age or body mass index increase, may contribute to the development of ED despite the testosterone value still being within the normal quoted range. This would support the measurement of a testosterone value at the time of diagnosis with diabetes for future comparison, and merits a trial looking at testosterone replacement in men with diabetes presenting with ED who have subsequent impressively declining testosterone levels.

Shabsigh et al (summarised below) also provide a timely review of the role of testosterone in the treatment of ED. The mechanisms by which testosterone affect the nitric oxide pathway (essential for normal penile erectile activity) and maintains the normal penile structural and functional integrity are discussed.

Moreover, Shabsigh et al review outlines the difficulties in defining and treating hypogonadism, largely based upon the paucity of carefully conducted studies aimed at clarifying the role of androgen replacement. This is particularly important because they review data showing that oral phosphodiesterase type 5 (PDE5) inhibitors may be more effective in men with declining testosterone levels when combined with testosterone replacement.

INTERNATIONAL JOURNAL OF CLINICAL PRACTICE

Combined treatment effective for ED

Readability	✓✓✓✓✓
Applicability to practice	✓✓✓✓✓
WOW! factor	✓✓✓

1 The authors used a scientific literature search to investigate the role of testosterone replacement therapy in the treatment of erectile dysfunction (ED), both alone and in combination with phosphodiesterase type 5 (PDE5) inhibitors.

2 It was found that testosterone replacement monotherapy is effective in men with hypogonadism.

3 However, monotherapy for ED is of limited effectiveness and may be restricted to young men with hypogonadism and without vascular risk factors for ED.

4 PDE5 inhibitors are the first-line therapy in men who do not have potentially reversible causes of ED such as hypogonadism, although 23–50% of men do not respond to PDE5 inhibitors alone.

5 Combining testosterone with PDE5 inhibitors is valuable in men with ED and hypogonadism, and should be considered when monotherapy treatment has failed. Combination therapy may be useful in men with type 2 diabetes or the metabolic syndrome.

Shabsigh R, Rajfer J, Aversa A et al (2006) The evolving role of testosterone in the treatment of erectile dysfunction. *International Journal of Clinical Practice* **60**: 1087–92

JOURNAL OF UROLOGY

Age, obesity and the MetS decrease serum T levels

Readability	✓✓✓✓✓
Applicability to practice	✓✓✓✓✓
WOW! factor	✓✓✓✓

1 As testosterone (T) has an important role in maintaining normal male sexual function, the authors examined data to establish the relationship between total serum T levels, obesity and the metabolic syndrome (MetS) in ageing men.

2 Baseline total serum T levels, lipid, glycaemic control and anthropometric data were examined from 864 men participating in two lipid treatment studies; inclusion criteria for these studies were LDL cholesterol levels of 130–160 mg/dl and triglyceride levels ≤350 mg/dl.

3 Mean total serum T levels were compared in men with and without the MetS across different subgroups of body mass index (BMI).

4 For all participants, total serum T levels decreased with increasing BMI. This decrease was significantly greater for men with the MetS versus men without; the mean total serum T level in the ageing, severely obese men with the MetS was approximately 300 mg/dl less than that of ageing, lean men who did not have the MetS.

5 In terms of the relative contributions of individual components of the MetS to low serum T in ageing men, the presence of obesity (BMI ≥30 kg/m^2), diabetes (or fasting serum glucose >110 mg/dl) and hypertriglyceridaemia (triglycerides ≥150 mg/dl) appear to have a clinically relevant association.

Kaplan SA, Meehan AG, Shah A (2006) The age-related decrease in testosterone is significantly exacerbated in obese men with the metabolic syndrome. What are the implications for the relatively high incidence of erectile dysfunction observed in these men? *Journal of Urology* **176**: 1524–8

'Nitric oxide-mediated vasodilation was similar in men with and without ED, suggesting that ED itself may not be linked with enhanced endothelial dysfunction.'

AMERICAN JOURNAL OF HYPERTENSION

Sildenafil efficacy determined by CV risk factors

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1 Erectile dysfunction (ED) is related to endothelial cell dysfunction caused by cardiovascular (CV) risk factors, such as diabetes and smoking.

2 The phosphodiesterase type 5 inhibitor sildenafil is effective in the treatment of ED, but with variable results.

3 The authors looked at whether CV risk factors can influence the erectile and acute vascular responses to sildenafil.

4 All 45 men recruited showed evidence of ED, with an international index of erectile function (IIEF) score of 5 points at baseline.

5 CV risk profiles and acute and chronic pulse wave responses to a single 50 mg dose of sildenafil were assessed at baseline and after 70 days of chronic treatment with sildenafil.

6 After 70 days, IIEF scores had increased by a median of 13 points; 24 men achieved an IIEF score of >21 points, indicating a normalisation of sexual function. Overall improvement was dependent on initial erectile function and baseline apolipoprotein B.

7 Pulse wave analysis showed that acute changes in stiffness index induced by sildenafil were related to apolipoprotein A-1, B and lipoprotein(a) concentrations, whereas reflection index was related to pulse pressure, albumin:creatinine ratio and lipoprotein(a).

8 The effect of sildenafil on erectile function and pulse wave profiles is determined by metabolic CV risk factors. Improved CV risk factor control is likely to increase the efficacy of sildenafil in the treatment of ED.

Solomon H, Wierzbicki AS, Lumb PJ, Lambert-Hammill M, Jackson G (2006) Cardiovascular risk factors determine erectile and arterial function response to sildenafil. *American Journal of Hypertension* **19**: 915–19

INTERNATIONAL JOURNAL OF CLINICAL PRACTICE

ED not linked with further endothelial dysfunction

Readability	✓✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓✓

1 The aim of the study was to determine whether erectile dysfunction (ED) is an indicator of generalised endothelial dysfunction in men with type 2 diabetes.

2 The study comprised 22 men with type 2 diabetes but with no established cardiovascular (CV) risk factors; 11 men had ED.

3 Characteristics between the men with and without ED were similar. The exception was HbA_{1c}, which was higher in the men with ED.

4 Nitric oxide-mediated vasodilation was similar in men with and without ED, suggesting that ED itself may not be linked with enhanced endothelial dysfunction.

Browne DL, Meeking DR, Allard S et al (2006) Diabetic erectile dysfunction — an indicator of generalised endothelial function *per se*? *International Journal of Clinical Practice* **60**: 1323–6

INTERNATIONAL JOURNAL OF IMPOTENCE RESEARCH

Biochemical markers predict ED

Readability	✓✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓✓

1 The study aim was to determine the diagnostic value of peripheral and cavernous blood markers (nitric oxide [NO], lipoprotein (a) [LP(a)] and malondialdehyde [MDA]) as predictors of penile arterial insufficiency in 26 men with diabetes and erectile dysfunction (ED), 15 men with psychogenic ED and 10 healthy men were comparisons.

2 Men with diabetes and ED had significantly lower erectile responses to the intracavernosal injection of a trimix, lower peak systolic velocity and smaller increase in cavernosal artery diameter than the psychogenic ED group.

3 LP(a) and venous MDA levels were significantly higher, and peripheral NO levels significantly lower, in the men with diabetes and ED compared with the other two groups; these levels of biochemical markers correlate with the severity of ED.

4 This study provides a rationale for studies of biochemical markers in the diagnosis of penile arterial insufficiency.

El-Latif MA, Makhlouf AA, Moustafa YM et al (2006) Diagnostic value of nitric oxide, lipoprotein(a) and malondialdehyde levels in the peripheral venous and cavernous blood of diabetics with erectile dysfunction. *International Journal of Impotence Research* **18**: 544–9

BRITISH JOURNAL OF UROLOGY INTERNATIONAL

Tadalafil appears to be preferred over sildenafil

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓

1 Sildenafil and tadalafil are effective therapies for the treatment of erectile dysfunction (ED), although preferences between these treatments might be determined by many factors.

2 Data were collected from men with ED, at baseline and after switching treatment 4-12 weeks later, from tadalafil to sildenafil (695 men) or from sildenafil to tadalafil (1681 men), and from partners and physicians regarding treatment preference.

3 Physicians, partners and the study group had a similar pattern of preference for tadalafil over sildenafil.

4 Both treatments improved erectile function in these men.

Lee J, Pommerville P, Brock G et al (2006) Physician-rated patient preference and patient- and partner-rated preference for tadalafil or sildenafil citrate. *British Journal of Urology International* **98**: 623–9