# Sexual dysfunction

## Is erectile dysfunction in diabetes really non-reversible?

*Mike Cummings, Consultant Physician and Honorary Professor, Queen Alexandra Hospital, Portsmouth*

Traditionally, both microvascular and macrovascular complications of diabetes have been considered non-reversible, and medical treatment has focused on retardation of progression or alleviation of symptoms associated with complications. Erectile dysfunction has not been regarded as an exception to this rule, and previous studies have shown the relentless, progressive nature of this complication (McCulloch et al, 1980; 1984). However, the two studies summarised on this page call into question this long-standing belief.

Khatana et al sought to improve traditional cardiovascular risk factors in men with type 2 diabetes through aggressive management with an initial weekly review. The investigators focused on improvements in $HbA_{1c}$, blood pressure and total cholesterol. Overall, however, reductions in $HbA_{1c}$ and both systolic and diastolic blood pressure (but not total cholesterol) were associated with improvement in erectile performance.

In support of this paradoxical association between lowering blood pressure and improved erectile performance, Baumhäkel et al examined the impact of irbesartan upon the presence of erectile dysfunction over 6 months. In hypertensive individuals with the metabolic syndrome, the use of irbesartan was associated with significant improvement in not only erections but also orgasmic function.

Although we are aware that "classically" antihypertensive drugs may be associated with a fairly abrupt onset of erectile dysfunction in a subgroup of people with (and without) diabetes, these studies suggest that if this initial side-effect is avoided, reducing blood pressure may actually retard or even reverse erectile dysfunction progression. The evidence is by no means conclusive, but merits further investigation.

McCulloch DK, Campbell IW, Wu FC, Prescott RJ, Clarke BF (1980) The prevalence of diabetic impotence. *Diabetologia* **18**: 279–83

McCulloch DK, Young RJ, Prescott RJ Campbell IW, Clarke BF (1984) The natural history of impotence in diabetic men. *Diabetologia* **26**: 437–40

INTERNATIONAL JOURNAL OF IMPOTENCE RESEARCH

## Irbesartan improves erectile function

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

1 Endothelial dysfunction is closely associated with impaired erectile function, and there is a strong link between cardiovascular risk factors and the extent of erectile dysfunction (ED).

2 This study examined the influence of the angiotensin-receptor antagonist, irbesartan, on improving endothelial and erectile function in men with hypertension and the metabolic syndrome.

3 In total, 1069 men with hypertension and the metabolic syndrome were treated with irbesartan, alone or in combination with hydrochlorothiazide, for 6 months; erectile function was assessed at baseline and at 6 months.

4 Erectile function significantly increased ($P<0.0001$) after 6 months of irbesartan, irrespective of dosage or combination, with a corresponding decline in the prevalence of ED (reduced from 78.5% at baseline to 63.7% at 6 months).

5 Irbesartan improved sexual desire and frequency of contacts, as well as improving erectile function in hypertensive men with the metabolic syndrome.

Baumhäkel M, N Schlimmer, M Böhm et al (2008) Effect of irbesartan on erectile function in patients with hypertension and metabolic syndrome. *Int J Impot Res* **20**: 493–500

INTERNATIONAL JOURNAL OF IMPOTENCE RESEARCH

## CVD risk reduction alleviates ED in men with diabetes

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

1 Erectile dysfunction (ED) and cardiovascular disease (CVD) are highly prevalent in men with diabetes, and risk factors include elevated $HbA_{1c}$, raised blood pressure, and hyperlipidaemia, dyslipidaemia or both.

2 This study assessed the effect of multifactorial CVD risk reduction on ED in 41 men with type 2 diabetes.

3 Participants enrolled in an intensive behavioural and pharmacological intervention targeting hyperglycaemia, hypertension and hyperlipidaemia for 4 weeks, and were followed for 4 months.

4 ED was measured using the self-reported 5-item International Index of Erectile Function (IIEF-5) at baseline and at follow-up. All measured CVD risk factors and medication use were compared at baseline and follow-up; changes in IIEF-5 scores were analysed.

5 At 4-month follow-up there were significant improvements in participants' $HbA_{1c}$ levels, total cholesterol and diastolic blood pressure.

6 Change in systolic and diastolic blood pressure and a reduction in $HbA_{1c}$ or maintenance of $HbA_{1c}<7.0\%$ were significantly associated with change in IIEF-5 score from baseline to the 4-month follow-up, with an additive effect.

7 Results show that improved blood pressure and glycaemic control in men with type 2 diabetes may lead to an improvement in their ED.

Khatana SAM, Taveira TH, Miner MM, et al (2008) Does cardiovascular risk reduction alleviate erectile dysfunction in men with type II diabetes mellitus? *Int J Impot Res* **20**: 501–6

JOURNAL OF SEXUAL MEDICINE

## Increased TGF-β1 expression may have a role in ED

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

1 It has been postulated that changes in growth factors, such as transforming growth factor-β1 (TGF-β1), have a key role in the pathogenesis of erectile dysfunction (ED) in men with diabetes.

2 This study investigated the expression and activity of the TGF-β1-Smad signalling pathway in the penis of rats with streptozotocin-induced diabetes and ED.

3 Rats were allocated into control ($n$=26) and diabetic ($n$=26) groups; erectile function was determined at 8 weeks by cavernous nerve electrical stimulation.

4 Penis specimens were taken for immunoassay testing for TGF-β1, P-Smad 2 and P-Smad 3 protein, Western blot and histological examination.

5 All erectile function measures were significantly lower in the diabetic rats than in the controls.

6 The diabetic rats had higher expression of TGF-β1, P-Smad 2 and P-Smad 3 protein than the control animals.

7 Increased P-Smad 2 expression may play a key part in diabetes-induced structural changes in the penis, such as loss of smooth muscle cell content.

8 In this rat model, upregulation of TGF-β1 and activation of the Smad signalling pathway in the penis of rats with induced diabetes may play an important part in diabetes-induced structural changes and deterioration of erectile function.

Zhang LW, Piao S, Choi MJ et al (2008) Role of increased penile expression of transforming growth factor-β1 and activation of the Smad signalling pathway in erectile dysfunction in streptozotocin-induced diabetic rats. *J Sex Med* **5**: 2318–29

JOURNAL OF DIABETES AND ITS COMPLICATIONS

## Elevated Hcys levels may be a risk factor for ED in diabetes

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

1 This study examined the relationship between erectile dysfunction (ED) and high levels of homocysteine (Hcys) in 62 men with type 2 diabetes.

2 Diagnostic evaluation included erectile function, $HbA_{1c}$, plasma Hcys levels, fasting and postprandial plasma glucose.

3 $HbA_{1c}$, and fasting and postprandial plasma glucose levels were significantly higher in the 32 men with diabetes and ED; plasma Hcys levels were also higher in this group.

4 High levels of Hcys are a risk factor for ED in men with diabetes, in addition to smoking and poor glycaemic control.

Demir T, Cömlekci A, Demir O et al (2008) A possible new risk factor in diabetic patients with erectile dysfunction: homocysteinemia. *J Diabetes Complications* **22**: 395–9

JOURNAL OF SEXUAL MEDICINE

## ED linked with PE and reduced libido

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

1 The study objective was to determine the prevalence of premature ejaculation (PE) and reduced libido, and their links with erectile dysfunction (ED), in 253 men with type 2 diabetes.

2 Interviewer- and self-administered questionnaires determined the presence of PE and reduced libido, clinical data were obtained and erectile function assessed.

3 The overall prevalence of ED was 73.1%, with 33.2% of men having severe or complete ED.

4 After excluding men with complete ED, the prevalence of PE was 40.2%. The overall prevalence of reduced libido was 25%.

5 ED was strongly associated with PE (odds ratio [OR]=4.41, 95% confidence interval [CI]=2.08–9.39) and reduced libido (OR=4.38, 95% CI=1.39–13.82).

6 When treating ED in men with diabetes, clinicians should determine the presence of PE and reduced libido, as these conditions are closely linked.

Malavige LS, Jayaratne SD, Kathriarachchi ST et al (2008) Erectile dysfunction among men with diabetes is strongly associated with premature ejaculation and reduced libido. *J Sex Med* **5**: 2125–34

JOURNAL OF ANDROLOGY

## Caffeine improves erectile function

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

1 Phosphodiesterase-5 (PDE-5) inhibitors degrade cyclic guanosine monophosphate (cGMP) and are used to treat erectile dysfunction (ED) in men with diabetes. However, caffeine is a non-selective inhibitor of PDE-5, and its effect on ED is uncertain.

2 The study aim was to determine the effect of caffeine on erectile function using a diabetic rat model.

3 Four groups of rats (healthy; diabetic/saline; diabetic/caffeine 10 mg/kg/day; and diabetic/caffeine 20 mg/kg/day) were treated for 8 weeks; intracavernous pressure (ICP) and cavernous cGMP were measured to determine erectile function.

4 The diabetic rats treated with caffeine had increased ICP and cavernous cGMP, with improved erectile function.

Yang R, Wang J, Chen Y et al (2008) Effect of caffeine on erectile function via up-regulating cavernous cGMP in diabetic rats. *J Andro* **29**: 586–91

***"When treating erectile dysfunction in men with diabetes clinicians should determine the presence of premature ejaculation and reduced libido, as these conditions are closely linked."***