Sexual dysfunction

Additional clinical benefits of PDE-5 inhibitors beyond restoration of erections when taken regularly?

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People with diabetes and nephropathy are at greater risk of developing erectile dysfunction (ED) and it has been suggested that this may be due to accelerated endothelial dysfunction (McCulloch et al, 1980). Even in the earliest stages of renal dysfunction with the presence of microalbuminuria, greater endothelial dysfunction is observed (Dogra et al, 2001). It is of great interest therefore to see two papers (summarised alongside and below) which examine the effects of daily phosphodiesterase type 5 (PDE-5) inhibitors, typically used to treat ED, upon renal function in diabetes.

In an animal study (Lau et al, summarised below), diabetic rabbits were given vardenafil with resultant normalisation of microalbuminuria after 6 months associated with an improvement in creatinine clearance. In the paper by Grover-Páez et al (abstracted alongside) in men with type 2 diabetes and microalbuminuria, administration of 50 mg sildenafil citrate for 30 days was associated with improvement in IIEF scores (a measure of erectile function), a significant reduction in urinary albumin and a 0.59 percentage point decrease in glycated haemoglobin values. The authors speculate that reduction in microalbuminuria may be related to better glycaemic control and enhanced nitric oxide availability that, through improved endothelial function, diminishes transcapillary escape of albumin. Although these are pilot studies (n=8 and n=40 respectively), they provide significant merit to support larger prospective trials.

Intriguingly, in the US, the Food and Drug Administration have licensed the use of tadalafil to be taken on a regular basis for the treatment of erectile dysfunction – this would provide a useful observational database in the population with diabetes to monitor microalbuminuria status. This class of drugs may well yet turn out to positively impact upon the cardiovascular burden associated with diabetes.

McCulloch DK, Campbell IW, Wu FC et al (1980) The prevalence of diabetic impotence. *Diabetologia* **18**: 279–83

Dogra G, Rich L, Stanton K, Watts G (2001) Endothelium-dependent and independent vasodilation studied at normoglycaemia in Type 1 diabetes mellitus with and without microalbuminuria. *Diabetologia* **44**: 593–601

IN VIVO

Vardenafil improves renal function

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

1 In order to investigate the effect of vardenafil, a PDE-5 inhibitor, on renal function in rabbits, blood was taken from control and alloxan-induced diabetic rabbits at 4 and 6 months (n=8 per group).

2 Half of each group were given either vardenafil (3 mg/kg) or vehicle for 4 weeks, after which a further blood sample was taken at 7 months.

3 The group with diabetes had a significant increase in serum creatinine concentration at 6 months. This was reduced significantly by vardenafil.

4 The total protein/creatinine ratio as measured by spot urine tests was higher in the group with diabetes than controls at 6 months, indicating proteinuria. Vardenafil also normalised the TP/C ratio in those with diabetes.

5 These results suggest that vardenafil could be a successful treatment of diabetic nephropathy in humans.

Lau DH, Mikhailidis DP, Thompson CS (2007) The effect of vardenafil (a PDE type 5 inhibitor) on renal function in the diabetic rabbit: a pilot study. *In Vivo* **21**: 851–4

DIABETES RESEARCH AND CLINICAL PRACTICE

Sildenafil improves microalbuminuria, HbA_{1c} and sexual function

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

1 Beneficial cardiovascular effects are known to be displayed by sildenafil citrate. The authors proposed that other systemic effects may involve the endothelium.

2 They aimed to assess whether or not sildenafil citrate improves microalbuminuria and HbA_{1c} in men with type 2 diabetes.

3 In a 30-day double-blind, randomised controlled trial, participants were allocated to one of two groups (n=20 in each) to receive either sildenafil citrate 50 mg daily or placebo.

4 At baseline and throughout the study, hs-CRP, microalbuminuria, homocysteine, HbA_{1c} and erectile function were measured.

5 Microalbuminuria improved significantly in the group receiving sildenafil citrate ($P<0.01$ versus baseline; $P=0.02$ versus placebo), as did HbA_{1c} ($P<0.01$ versus baseline; $P=0.01$ versus placebo).

6 Treatment with the drug for 30 days increased the international index of erectile function (IIEF) score significantly versus baseline and placebo ($P<0.01$ for both).

7 The authors concluded that sildenafil citrate treatment for 30 days hints at the improvement of microalbuminuria, HbA_{1c} and sexual function.

Grover-Páez F, Villegas Rivera G, Guillén Ortíz R (2007) Sildenafil citrate diminishes microalbuminuria and the percentage of A1c in male patients with type 2 diabetes. *Diabetes Research and Clinical Practice* **78**: 136–40

'ED is affected by BMI and physical activity independently.'

INTERNATIONAL JOURNAL OF OBESITY

BMI and physical activity affect erectile dysfunction independently

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

1 This was a population representative, cross-sectional analytical study of 1506 men in Hong Kong aged 26–70 years and diagnosed with diabetes.

2 The aim was to investigate the relationship between BMI, physical activity and erectile function using face-to-face interviews.

3 Erectile dysfunction (ED) was predicted independently by age (OR: 1.30; 95% CI: 1.20–1.40), physical activity (OR: 0.91; 95% CI: 0.84–0.98) and psychological distress (OR: 1.03; 95% CI: 1.00–1.06).

4 In men who did not exercise, BMI and ED exhibited a U-shaped relationship. For BMIs of <18.5kg/m^2, 18.5–19.9kg/m^2, 20.0–20.9kg/m^2, 22.0–22.9kg/m^2, 23.0–24.9kg/m^2 and >25.0kg/m^2, the odds ratios for ED using BMI 21.0–21.9kg/m^2 as a reference were 2.99, 2.66, 1.37, 1.36, 1.66 and 2.47, respectively.

5 Physical activity (burning 1000kcal/week) reduced the risk of ED only in men who were obese (OR: 0.40; 95% CI: 0.16–0.95), adjusting for other variables.

6 In conclusion, ED is affected by BMI and physical activity independently. BMI has a greater effect when there is little exercise and physical activity has a more pronounced benefit in those with a high BMI. Underweight may also be a risk factor for ED.

Cheng JY, Ng EM (2007) Body mass index, physical activity and erectile dysfunction: an U-shaped relationship from population-based study. *International Journal of Obesity* **31**: 1571–8

INTERNATIONAL JOURNAL OF CLINICAL PRACTICE

Alternative therapy needed for ED

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

1 This multinational study investigated the prevalence of erectile dysfunction (ED) in men with diabetes and their attitudes compared to men with ED without diabetes (n=27 839) by questioning them about ED, diabetes and cardiovascular conditions.

2 In Phase II of the study, 2912 men aged 20–75 years with reported ED completed questionnaires about the condition, seeking treatment and influences that affected their treatment-seeking behaviour.

3 ED was clearly associated with diabetes, hypertension, angina and high cholesterol.

4 Men with diabetes generally considered their ED more severe and permanent and were more likely to seek treatment.

5 Sildenafil was used by men with or without diabetes, although those with diabetes were more likely to discontinue use owing to lack of efficacy.

6 These results highlight a need for alternative treatment for ED, especially in those with diabetes.

Eardley I, Fisher W, Rosen RC (2007) The multinational Men's Attitudes to Life Events and Sexuality study: the influence of diabetes on self-reported erectile function, attitudes and treatment-seeking patterns in men with erectile dysfunction. *International Journal of Clinical Practice* **61**: 1446-53

BJU INTERNATIONAL

ED reduces sexual life quality

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

1 A 35-item questionnaire was sent to 10 000 men to assess the prevalence of erectile dysfunction (ED) and the population's knowledge and general attitudes towards its treatment.

2 Included were the IIEF and sociodemographic questions on lifestyle, comorbidities, sexual life quality and therapy knowledge.

3 Of the 3124 responses, 2499 were included since they were in well-established heterosexual partnerships.

4 In this population, 40.1 % had ED, although only a minority used treatment.

5 Age, peripheral arterial occlusive disease, hypertension, ischaemic heart disease, diabetes and liver disease were all independent risk factors for ED.

6 ED significantly reduced sexual life quality (P<0.01). While 96% of the population knew a PDE-5 inhibitor by name, only 53 % considered taking one and 9 % had experience of them.

May M, Gralla O, Knoll N et al (2007) Erectile dysfunction, discrepancy between high prevalence and low utilization of treatment options: results from the 'Cottbus Survey' with 10000 men. *BJU International* **100**: 1110-5

ATHEROSCLEROSIS

ED may precede CVD

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

1 Men with erectile dysfunction (ED) but no known cardiovascular risk factors or disease (n=49) were compared with 50 age-matched controls to investigate the association between idiopathic ED and vascular or autonomic dysfunction.

2 The two groups had similar BMI, testosterone, fasting lipids and glucose. However, in the ED group, standing pulse pressure was higher (50±1 versus 43±2 mmHg; P<0.004) and the 30:15 RR ratio (the ratio of the cardiac cycle at the 30th and 15th beat) was lower (0.97±0.01 versus 1.01±0.01; P<0.02).

3 During forearm reactive hyperaemia, flow debt repayment was lower in the group with ED than controls (7.2±0.7 versus 9.5±0.8 ml per 100 ml; P<0.02).

4 These results support the concept that ED predicts CV dysfunction and may precede clinical CVD.

Stuckey BG, Walsh JP, Ching HL et al (2007) Erectile dysfunction predicts generalised cardiovascular disease: evidence from a case-control study. *Atherosclerosis* **194**: 458-64

'ED predicts CV dysfunction and may precede clinical CVD.'