

Sexual dysfunction

Concomitant drug therapy and the risks of erectile dysfunction in diabetes: Common sense should prevail



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

Traditionally, we have been led to believe that a number of drugs commonly prescribed for people with diabetes may lead to erectile dysfunction (ED). Broadly speaking, they may fall into three main groups.

First, cardiovascular drugs, including the majority of anti-hypertensive agents. Second, drugs used to treat painful neuropathy such as the anti-depressant and anti-convulsant classes of agents. Third, with the least frequently seen effects, are lipid-lowering agents such as statins and fibrates. However, previous work has identified that macrovascular disease and risk of symptomatic neuropathy are also risk markers for the development of ED in diabetes (McCulloch et al, 1980). This leaves us with the chicken and egg scenario – which comes first?

This question is, in part, addressed by Francis et al (2007) whose elegant study, summarised below, teases out how men with hypertension who used selected anti-hypertensive agents (in particular thiazide diuretics, β blockers, spironolactone, clonidine and methyl dopa) were almost two and a half times more likely to develop ED compared with men with hypertension who did not take blood pressure medication (and three times higher than

normotensive individuals).

This contrasts with a further article reviewed in this issue, which suggests that ED is associated with the presence of diabetes and cardiovascular disease but not hypertension or current treatment with β blockers, diuretics, ACE inhibitors, ARBs or calcium channel blockers (Böhm et al, 2007).

This makes everything very confusing. How am I going to manage my patient with diabetes and ED when he is taking a drug associated with ED development? The answer is simple: I shall continue with the pragmatic clinical approach we have always been taught. If a man presents with ED within a short time frame (usually 2 weeks) of starting a new drug known to cause the problem, I will try switching to an alternative class of agent wherever possible. However, if the individual has been on the drug for several years and then presents with ED, it would be my view that removal of that drug is extremely unlikely to help.

Böhm M, Baumhäkel M, Probstfield JL et al (2007) Sexual function, satisfaction, and association of erectile dysfunction with cardiovascular disease and risk factors in cardiovascular high-risk patients: substudy of the Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial/Telmisartan Randomized Assessment Study in ACE-Intolerant Subjects with Cardiovascular Disease (ONTARGET/TRANSCEND). *American Heart Journal* **154**: 94–101

Francis ME, Kusek JW, Nyberg LM, Eggers PW (2007) The contribution of common medical conditions and drug exposures to erectile dysfunction in adult males. *Journal of Urology* **178**: 591–6

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

JOURNAL OF UROLOGY

Common medical conditions elevate ED risk

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

1 This study involved US men over 40 years of age who had taken part in the 2001–2002 National Health and Nutrition Examination Survey and aimed to examine the association between existing medical conditions and treatment and the occurrence of ED.

2 The results showed that 8% of men had complete ED (defined as never

able to achieve an erection sufficient for intercourse).

3 Following a multivariate analysis of the collected data, the following were identified as factors that increased the odds of complete ED: obstructive urinary symptoms (OR: 2.0; 95% CI: 1.2–3.4), diabetes (OR: 2.6; 95% CI: 1.3–5.2), hypertension with selected antihypertension therapy (OR: 3.0; 95% CI: 1.6–5.9) and selected antidepressant therapy (OR: 5.2; 95% CI: 1.7–15.9).

4 CVD, urinary incontinence and hypertension without drug therapy were found to have no impact on the risk of complete ED.

Francis ME, Kusek JW, Nyberg LM, Eggers PW (2007) The contribution of common medical conditions and drug exposures to erectile dysfunction in adult males. *Journal of Urology* **178**: 591–6

AMERICAN HEART JOURNAL

CVD significantly influences erectile dysfunction

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

1 This is a substudy of the ONTARGET/TRANSCEND trials aiming to characterise the relationship between baseline characteristics, current treatment and the level of erectile function in men.

2 In total, 1357 men classified as CVD high risk were evaluated at baseline, 2 years and 4 years for erectile dysfunction using the Cologne Male Survey and the 5-item International Index of Erectile Function.

3 Of the participants, 34.2% had been diagnosed with diabetes, the mean BMI was $27.8 \pm 4.3 \text{ kg/m}^2$, mean age was 64.9 ± 6.4 years and 82.5% were permanently living with a partner.

4 The Cologne Male survey found that 50.7% of participants had ED, compared with 54.3% diagnosed via the 5-item International Index of ED.

5 Diabetes was found to significantly correlate with the severity of ED ($P < 0.00001$). Also associated with the level of ED reported were stroke ($P = 0.0026$), pelvic surgery ($P = 0.025$) and age > 65 years ($P < 0.00001$).

6 Current use of ACE inhibitors, angiotensin 1 antagonists, diuretics, β -blockers and calcium-channel blockers were not found to have any significant association with ED.

7 ED was also found to be independent of cholesterol status, hypertension and smoking status.

8 In conclusion, CVD was cited as a key influence on erectile function in men at high risk of CVD.

Böhm M, Baumhäkel M, Probstfield JL et al (2007) Sexual function, satisfaction, and association of erectile dysfunction with cardiovascular disease and risk factors in cardiovascular high-risk patients: substudy of the Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial/Telmisartan Randomized Assessment Study in ACE-Intolerant Subjects with Cardiovascular Disease (ONTARGET/TRANSCEND). *American Heart Journal* **154**: 94–101

‘Men who were given group therapy plus sildenafil citrate were significantly more likely to report a reduction in persistent ED than those receiving sildenafil alone.’

AMERICAN JOURNAL OF CARDIOLOGY

BP benefits with PDE5i treatment

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

- 1 A retrospective cohort study design was used to investigate the effect of newly treating ED on the management of hypertension (systolic BP>140 mmHg).
- 2 Inclusion criteria were the diagnosis and treatment of hypertension and a prescription for a PDE5i. Medical records from 6768 men (mean age: 61.6±9.9 years) were included in the study, 50% of which documented systolic BP ≥140 mmHg before taking a PDE5i for the treatment of ED.
- 3 The records showed a mean decrease in systolic BP of 1.43 mmHg after initiation of PDE5i therapy (95% CI: -1.69 to -1.18).
- 4 Individuals who had a baseline systolic BP ≥160 mmHg were most likely to see the greatest decline in systolic BP (mean: -17.8; 95% CI: -18.8 to -16.8).
- 5 Participants were also more likely to have started antihypertensive medication than to cease any existing therapy (17.3% incidence versus 2.3%, respectively) or add additional agents to their antihypertension regimen rather than decrease the number taken (42.2% incidence versus 17.3%).
- 6 The frequency of BP measurements increased by 42% as part of monitoring the ED treatment.
- 7 The authors highlighted that there is a known link between ED and risk of a CV event. This study has shown that treatment of ED by a PDE5i can also improve the management of CV risk factors pharmacologically and via associated aggressive monitoring and treatment with antihypertensive medications.

Scranton RE, Lawler E, Botteman M et al (2007) Effect of treating erectile dysfunction on management of systolic hypertension. *American Journal of Cardiology* **100**: 459–63

JOURNAL OF SEXUAL MEDICINE

Hypogonadism and lower testosterone linked to IR

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

- 1 The aim of this study was to examine any association between hypogonadism and metabolic syndrome (MetS) and/or insulin resistance (IR) in men with ED.

- 2 Over 6 months, data from 154 consecutive ED consultations were recorded, with ED defined as a Sex Health Inventory for Men score of ≤21/25.
- 3 IR was associated with a low level of testosterone and hypogonadism (P=0.02 for both).
- 4 These results suggest that men presenting with ED should be evaluated for CVD risk and be screened for hypogonadism, the treatment of which may improve insulin sensitivity.

Guay A, Jacobson J (2007) The relationship between testosterone levels, the metabolic syndrome (by two criteria), and insulin resistance in a population of men with organic erectile dysfunction. *Journal of Sexual Medicine* **4**: 1046–55

COCHRANE DATABASE OF SYSTEMATIC REVIEWS

Evidence supports group psychotherapy as ED treatment

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

- 1 In order to systematically evaluate the effectiveness of psychosocial interventions for the treatment of ED compared with other interventions, data from nine randomised and two quasi-randomised trials were examined (data from 398 men in total).
- 2 Evidence collected from five randomised trials showed that group psychotherapy was more likely to reduce

- the proportion of men with persistent ED (NNT: 1.61). This effect was sustained at 6 months post treatment.
- 3 No significant difference in efficacy was found between psychosocial interventions and local injection or vacuum devices.
 - 4 Men who were given group therapy plus sildenafil citrate were significantly more likely to report a reduction in persistent ED than those receiving sildenafil alone (RR: 0.46; NNT: 3.57). Additionally, they were less likely to drop out of the study (RR: 0.29).
 - 5 One small study (n=20) suggested that group therapy was more efficacious than sildenafil citrate (WMD: -12.40; 95% CI: -20.81 to -3.99).

Melnik T, Soares BG, Nasselo AG (2007) Psychosocial interventions for erectile dysfunction. *Cochrane Database of Systematic Reviews* **3**: CD004825

BJU INTERNATIONAL

Sildenafil citrate effective and safe in elderly men

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

- 1 With increasing life expectancy, the prevalence of ED is also on the rise. Thus, the aim of this study was to investigate the efficacy and tolerability of the PDE5i sildenafil citrate in men over 60 years of age.
- 2 Data from a US sexual medicine practice were taken for all sildenafil

- users over 60 years of age (n=167). Participants were divided into the following age groups: 60–69 years, 70–79 years and >80 years of age.
- 3 Overall, 54% of men responded to sildenafil treatment (mean increase in International Index of Erectile Function score was 5.7).
 - 4 There was a significant age-related decrease in response rate; normal erection function scores were reported in 36% of the ≥80s, 42% in the 70–79 age group, and 46% in the 60–69 age group (P<0.05).
 - 5 Age was not associated with a change in the frequency of AEs.

Müller A, Smith L, Parker M, Mulhall JP (2007) Analysis of the efficacy and safety of sildenafil citrate in the geriatric population. *BJU International* **100**: 117–21