Angina, nitrates and erectile dysfunction

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A common vascular pathology means that many patients with coronary artery disease (CAD) also suffer from erectile dysfunction (ED). The use of oral nitrates in these patients excludes them from the help that a PDE5 inhibitor (PDE5I) could offer. Using a case history, Geoffrey Hackett describes how, with some medicines optimisation, this problem can be resolved.

As described in the case history, Derek is referred to the ED clinic because he is taking nitrates and is seeking alternatives to a PDE5I to help with his ED. Derek’s BMI is 32, weight 98kg and waist circumference 98cm. His Sexual Health Inventory for Men score (SHIM) is 9, indicating severe ED. Blood pressure is 120/80, pulse 60, total cholesterol 3.4, HbA1c 6.1 and total testosterone 14.0nmol/l. You explain the links between cardiovascular disease (CVD) and ED, how ED predicts later cardiovascular events and that the smaller arteries of the penis will still be affected by vascular disease, even though his coronary arteries have been improved by his stents.

The treatment options are:
• Suggest that we might be able to stop the oral nitrate and prescribe sildenafil
• Discuss intracavernosal injection or MUSE (alprostadil), explaining that the medication will have to be funded privately at around £20 per dose
• Demonstrate a vacuum device, explaining that this would cost him around £175 as a one-off fee

Derek is concerned about stopping the nitrate, but you tell him that he has excellent exercise tolerance and should be able to manage without them. You offer to contact his cardiologist to confirm that this is appropriate. He has taken a PDE5I in the
past and it worked well. He is attracted by the prospect of not having to pay for the sildenafil. After discussion, Derek decides on this option and you arrange for him to return in four weeks.

FOLLOW-UP AND OUTCOME
The cardiologist confirms that Derek can stop his nitrate, expressing surprise that he was still taking it. He explains that he still has a GTN spray, which he would be able to use as needed. If necessary, he would switch him to ranolazine (Ranexa). In fact, Derek has no difficulties in stopping the nitrate and notices that he has fewer headaches.

Derek returns to the clinic and is prescribed sildenafil 100mg on demand. After eight doses, his SHIM score has increased from 6 to 18, but he is not quite able to reliably maintain his erection. You suggest that he takes sildenafil every day, that his ramipril is changed to valsartan 80mg daily, and that the bisoprolol 5mg is changed to nebivolol 5mg daily. He returns a month later, reporting that these changes have made a significant difference and he can now sustain erections reliably. He also says that he can exercise for longer.

WHAT DOES THE EVIDENCE TELL US?
Studies suggest that approximately 80% of men with stable CAD on nitrates are able to discontinue them and take a PDE5I.1 Calcium-channel blockers and beta-blockers are first-line therapy for stable angina. Nitrates, ivabradine (Procoralan) and ranolazine are second-line alternatives, according to NICE guidelines, suggesting that choice of therapy is dependent on associated comorbidities.2 ED is not considered a comorbidity, despite a prevalence of over 60% in stable angina patients. Unfortunately, sexual function is still rarely discussed during cardiac rehabilitation. Nitrates have not been demonstrated to have any prognostic value in CAD.1

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Several studies have shown that angiotensin-receptor blockers (ARB) improve erection through their enhanced inhibitory effect on angiotensin II at a vascular endothelial level, whereas ramipril has a neutral effect.3 A change from ACE-inhibitor to ARB can have an important impact in men with mild ED or in men with suboptimal response to PDE5Is. Nebivolol acts as a weak nitric oxide donor, producing coronary artery dilatation and improved erectile function.3 As recent studies suggest a reduction in cardiovascular events with PDE5Is in men with type 2 diabetes at high risk of CVD, it is unfortunate if these potential benefits are lost because the patient is taking nitrates.4,5

BOTTOM LINE
Managing ED in the cardiovascular patient is as much about managing risk factors and optimising medications as prescribing effectively for ED. The availability of cheap generic sildenafil compared with expensive second-line options can have a significant impact on the optimal clinical management of the CVD patient with ED.

Declaration of interests
Geoffrey Hackett has been an occasional speaker for Lilly, Besins and Bayer.

REFERENCES
4. Hackett G. Phosphodiesterase type V inhibitors use in type 2 diabetes is associated with reduced all-cause mortality. Poster no. LB-9, presented at American Diabetes Association; 7 June, 2015; Boston, MA.