The use of sildenafil in heart disease

Erectile dysfunction (ED) is common, affecting 30% of men between the ages of 40–70 years to some degree (National Institutes of Health Consensus Development Panel on Impotence, 1993). It increases in incidence with age as does coronary heart disease (CHD), and with an ageing population treating ED co-existing with CHD has become an increasing management challenge. As vascular diseases and diabetes are the major causes of ED, an asymptomatic male presenting with ED should be screened for evidence of occult vascular pathology (Jackson et al, 1999a), with one study identifying a 50% incidence of silent CHD (Pritzer, 1999).

SEXUAL ACTIVITY AND RISK OF MYOCARDIAL INFARCTION

Sexual activity does slightly increase the risk of myocardial infarction but the absolute annual risk increase is small for a typical 50-year-old healthy male (from 1.00 to 1.01%), increasing to 1.10% for a man with a previous myocardial infarct (Muller et al, 1996).

Expressed as the metabolic equivalent of energy expenditure in the resting state the standard clinical measure of physical exertion is the MET. For most people sex is equivalent to an exercise workload of 2–3 METS pre-orgasm and 3–4 METS during orgasm, although more vigorous sexual activity may equate to 5–6 METS (Jackson et al, 1999a). Comparison can be made to walking 1 mile in 20 minutes on the level (3–4 METS), or 3 minutes of the standard Bruce treadmill exercise electrocardiography protocol (4.5 METS). The latter can offer reassurance about physical ability, presence or absence of ischaemia or arrhythmias and also reassure the partner who can be invited to be present (ED affects couples, not individuals).

VIAGRA

Viagra (sildenafil citrate, Pfizer, Sandwich, Kent) is a phosphodiesterase V inhibitor which prevents the breakdown of cyclic guanine monophosphate (cGMP), thereby promoting vascular smooth muscle relaxation and vasodilatation as a result of enhanced nitric

TABLE 1.
Management recommendations based on graded cardiovascular risk assessment

Grade of risk	Categories of cardiovascular disease	Management recommendations
Low risk	Asymptomatic, < 3 major risk factors for coronary artery disease	Primary care management
	Controlled hypertension	Consider all first-line therapies
	Mild, stable angina	Reassess at regular intervals (6–12 months)
	Post-successful coronary revascularization	
	Uncomplicated past myocardial infarction (>6–8 weeks) with negative stress test	
	Mild valvular disease	
	Congestive heart failure (NYHA Class I)	
Intermediate or indeterminate risk	>3 major risk factors for coronary artery disease, excluding gender	Specialized cardiovascular testing (e.g. exercise tolerance testing, echo)
	Moderate, stable angina	
	Recent myocardial infarction or cerebrovascular accident (< 6 weeks)	Re-stratification into high risk or low risk based on the results of cardiovascular assessment
	Left ventricular disease/congestive heart failure (NYHA Class II)	
	Non-cardiac sequelae of atherosclerotic disease (e.g. cerebrovascular accident, peripheral vascular disease)	
High risk	Unstable or refractory angina	Priority referral for specialized cardiovascular management
	Uncontrolled hypertension	Treatment for sexual dysfunction to be deferred until cardiac condition stabilized and dependent on specialist recommendations
	Congestive heart failure (NYHA Class III, IV)	
	Recent myocardial infarction (<2 weeks), cerebrovascular accident	
	High risk arrhythmias	
	Hypertrophic and other cardiomyopathies	
	Moderate/severe valvular disease	

NYHA = New York Heart Association

oxide (NO) donation (Lantry and Markham, 1999). Nitrates act at a different point in the NO-cGMP pathway, but lead to similar haemodynamic effects and the combination can lead to a profound fall in blood pressure.

Currently oral nitrates are not advised in the week before or after Viagra use and sublingual nitrates not for 24 hours before or after Viagra use. If a person develops anginal pain during sex after taking Viagra, intercourse should cease and the male should stand up — a means of reducing preload. Stopping intercourse may not be as easy as it appears on the written page, but this is an essential part of counselling.

If a nitrate is taken with Viagra and the blood pressure falls, immediate management includes laying the patient flat, raising the legs and replacing volume before hospital transfer. Currently it is recommended that other NO donors should also be avoided, e.g. nicorandil, although this is not evidence-based. No other significant drug interactions have been reported, probably because of the infrequent and intermittent use of Viagra.

CLINICAL TRIALS OF VIAGRA

Viagra has been studied in double blind and open label studies. It is effective in 80% of cases overall but in only 60% of diabetics. Its efficacy does not decrease with time (87% still benefit at 1 year) (Goldstein et al, 1998). Small transient falls in blood pressure can occur (mean 8/7 mmHg) but are not dose-dependent or usually clinically significant. The only haemodynamic effect documented in men with stable coronary artery disease is a slight fall in pulmonary artery pressure (similar to a nitrate), there being no effect on heart rate or cardiac output (Jackson et al, 1999b).

A meta-analysis of 53 studies involving over 11 000 patients receiving Viagra showed no excess risk of myocardial infarction or death. Importantly, however, high risk cardiac cases were not included. Thus while overall there is no evidence of excess cardiovascular risk, it is important to stratify risk before advising on the individual use of Viagra. A consensus panel has produced practical guidelines with regard to assessing risk (Jackson et al, 1999a) (*Table 1*).

CONCLUSIONS

Viagra is a safe and very effective treatment for ED with no evidence of increased cardiovascular risk secondary to its medically supervised use. This statement assumes stratification of cardiovascular risk (*Table 1*) and appropriate advice as a consequence. Random use of Viagra may undermine a highly effective treatment for ED and its casual use is a concern. ED is a common and emotionally traumatic problem which frequently affects patients with cardiovascular disease (and their partners). None of the currently available treatments have been shown to increase cardiovascular risk and all are effective (Jackson et al, 1999a).

Sexual advice should be routinely offered as part of cardiac rehabilitation programmes and doctors and nurses should ask their at-risk patients in a sensitive but matter of fact way if they are experiencing sexual difficulties. Safe use of Viagra in cardiac patients is feasible and will lead to significant improvement in their quality of life. HM

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Goldstein I, Lue TF, Padma-Nathan H et al (1998) Oral sildenafil in the treatment of erectile dysfunction. *N Engl J Med* **338:** 1397–404
Jackson G, Betteridge J, Dean J et al (1999a) A systematic approach to erectile dysfunction in the cardiovascular patient: A consensus statement. *Int J Clin Pract* **53:** 445–51
Jackson G, Benjamin N, Jackson N, Allen MJ (1999b) Effects of sildenafil citrate on human haemodynamics. *Am J Cardiol* **83:** 13C–20C
Lantry HD, Markham A (1999) Sildenafil – a review of its use in erectile dysfunction. *Drugs* **57:** 967–89
Muller JE, Mittleman MA, Maclure M et al (1996) Triggering myocardial infarction by sexual activity. *JAMA* **275:** 1405–9
National Institute of Health Consensus Development Panel on Impotence (1993) Impotence. *JAMA* **270:** 83–90
Pritzer MR (1999) The Penile Stress Test: A window to the hearts of man? *Circulation* **100:** I–711

Further reading

DeBush R, Drory Y, Goldstein I et al (2000) Management of sexual dysfunction in patients with cardiovascular disease: recommendations of the Princeton Consensus Panel. *Am J Cardiol* **86**: 175–81

KEY POINTS

- Viagra is effective in up to 80% of men with erectile dysfunction (ED).
- Nitrate use is an absolute contraindication.
- ED and cardiovascular disease (CVD) often co-exist.
- ED is an independent risk factor for CVD.
- ED increases with age and with an ageing population its prevalence will increase.
- Risk stratification will reduce adverse events.
- In appropriately selected patients Viagra is a safe and effective therapy for patients with ED and CVD.