European Heart Journal (2001) **22,** 201–208
doi:10.1053/euhj.1999.2010, available online at http://www.idealibrary.com on IDEAL®

Review Article

Sex and the heart: what is the role of the cardiologist?

P. Rerkpattanapipat, M. S. Stanek and M. N. Kotler

Division of Cardiology, Department of Medicine, Albert Einstein Medical Center, Philadelphia, Pennsylvania, U.S.A.

Introduction

Sexual activity is a concern both for patients with coronary artery disease and physicians taking care of these patients. Sexual counselling is an important component of treatment for post-myocardial infarction patients. Therefore, it is essential for the cardiologist to understand the physiological and haemodynamic changes that occur during sexual intercourse. It should also be borne in mind that several cardiac medications prescribed by cardiologists are responsible for sexual dysfunction. Finally, sexual dysfunction frequently occurs in cardiac patients and the treatment of sexual dysfunction, especially erectile dysfunction, may be associated with cardiovascular side-effects. The purpose of this review is to familiarize the cardiologist with sexual issues related to the cardiac patient.

Cardiovascular changes during sexual activity

Sexual response can be divided into four phases: excitement, plateau, orgasm, and resolution. The maximal energy expenditure occurs at orgasm and cardiopulmonary changes rapidly return to baseline within 2–3 min[1]. Nemec *et al.*[2] studied the heart rate and blood pressure responses during sexual activity in presumably healthy males in order to compare the cardiovascular response of the 'male-on-top' to the 'male-underneath' position. Ten male patients, ages 24–40 years, monitored themselves during sexual intercourse with their wives in the privacy of their own homes. A Holter monitor was used to continuously measure the heart rate beginning 1 h prior to sexual activity. The blood pressure was measured at rest, intromission, orgasm and 30, 60 and 120 s after orgasm. In the male-on-top position, the investigators found that the resting heart rate was 60 ± 8 beats . min^{-1} and increased to 92 ± 13 beats . min^{-1} at intromission and was 114 ± 14 beats . min^{-1} at orgasm. After orgasm the heart rate fell to 69 ± 12 beats . min^{-1} by 120 s. The heart rate response for the male-underneath was quite similar, with the peak at 117 ± 4 beats . min^{-1} during orgasm. Thus, no significant difference was noted when the two positions were compared. The average blood pressure response for the male-on-top position was 112/66 beats . min^{-1} at rest, 148/79 beats . min^{-1} at intromission, 163/81 beats . min^{-1} during orgasm and 118/69 beats . min^{-1} by 120 s later. The blood pressure for the male-underneath was slightly less during intromission but was similar during the other phases. Therefore there was no significant difference in the heart rate or blood pressure responses of the male during sexual activity in these two positions.

Bohlen *et al.*[3] reported a study to determine whether there were any differences in cardiac and metabolic expenditures in four different sexual activities (man-on-top coitus, woman-on-top coitus, self-stimulation and partner stimulation). Ten healthy married couples were monitored during sexual activity in a laboratory environment. All male subjects were white and 25–43 years old. Heart rate, rate-pressure product, and oxygen consumption were measured and compared among different sexual activities. The peak heart rates at orgasm were 127 ± 23, 110 ± 24, 102 ± 16 and 102 ± 14 beats . min^{-1}, respectively, during the above sexual activities. The metabolic expenditures during stimulation and orgasm were about 3·3 METS (a MET is defined as the energy expenditure at rest, or approximately 3·5 ml O_2 per kg body weight per min) for man-on-top coitus, 2·5 METS for woman-on-top coitus, 1·8 METS for self-stimulation and 1·7 METS for partner stimulation. This study confirmed that heart rate and rate-pressure product during orgasm were not different between man-on-top-coitus and woman-on-top-coitus, however, man-on-top coitus required more metabolic expenditure than woman-on-top coitus.

Key Words: Sex, heart, coital death, drug-induced sexual dysfunction, impotence, sildenafil.

Revision submitted 27 October 1999, and accepted 2 November 1999.

Correspondence: Morris N. Kotler, MD, Albert Einstein Medical Center, Division of Cardiology, Department of Medicine, 5401 Old York Road, Philadelphia, PA19141, U.S.A.

0195-668X/01/220201+08 $35.00/0

Unfortunately, very little information is available with regard to the sexual response in females. Garcia-Barreto *et al.*[4] found no significant differences between male and female post-myocardial infarction patients during coitus for peak heart rate (111 beats . min^{-1} vs 104 beats . min^{-1}), duration of intercourse (17·3 min vs 16·5 min) and time of recovery (3·1 min vs 2·6 min). Skinner suggested that women and men have similar physiological responses except women are multi-orgasmic and can obtain sexual pleasure without an erection[1].

Hellerstein and Friedman[5] studied heart rate during sexual activity by employing Holter monitors. Patients who were then participating in an exercise programme were given instructions to perform their usual activities while wearing the Holter monitors. Fourteen patients did engage in conjugal sexual activity. Heart rate and electrocardiogram changes associated with sexual activity were compared with those occurring during other daily activities. The mean maximum heart rate during orgasm was $117·4 \pm 4·2$ beats . min^{-1} (range 90–144); the average heart rates 2 and 1 min before were $87 \pm 3·95$ and $101·2 \pm 4·89$ beats . min^{-1}; the average heart rates 1 and 2 min after were $96 \pm 5·1$ and $85 \pm 3·9$ beats . min^{-1}. Comparison was made of the maximum heart rate during sexual activity and during work activity. The mean maximum heart rate during occupational or professional activities was 120·1 beats . min^{-1} (range 107–130). This rate is similar to the average heart rate during sexual activity, 117·4 beats . min^{-1}. The work activity producing this rate included walking, climbing stairs and doing paper work. The equivalent oxygen cost of the average maximum heart rate during sexual activity was less than that of climbing two flights of steps or walking briskly. Therefore, it does not appear that conjugal sexual activity is particularly stressful on the cardiovascular system when compared with other everyday physical activities.

Larson *et al.*[6] compared the heart rate and blood pressure responses to both sexual activity and stair-climbing. The stair-climbing test was defined as walking for 10 min on a level surface at a pace of 4·8 km . h^{-1} and climbing 22 steps (height 117 cm) in 10 s. Participants could have sex either in the man-on-top or man-underneath positions. There was no difference in heart rate response in coronary artery disease patients between these two activities (peak heart rate $115 \pm 7·2$ beats . min^{-1} during sex and $118 \pm 5·6$ stair-climbing). However, the average systolic blood pressure was significantly higher in stair climbing compared to that of sexual intercourse ($164 \pm 7·0$ vs $144 \pm 6·0$ beats . min^{-1}). The authors suggested that the stair-climbing test mentioned above might be an adequate challenge, with physiological responses comparable to sexual activity. However, Bohlen *et al.*[3] also reported interesting data that depicted large variations of energy expenditures (2·0–5·4 METS) during orgasm with man-on-top coitus. The authors suggested that the challenge of two flights of stairs might not apply to all patients.

Table 1 The mean peak heart rate during sexual activity

Authors (reference)	Number of patients	Mean peak heart rate (beats . min^{-1})
Nemec *et al.*[2]	10	114
Bohlen *et al.*[3]	10	102, 102, 110, 127*
Garcia-Barreto *et al.*[4]	23	111 (M), 104 (F)
Hellerstein and Friedman[5]	14	117
Larson *et al.*[6]	17	115
Drory *et al.*[7]	88	118
Stein[10]	16	127
Johnston and Fletcher[11]	24	108
Masini *et al.*[12]	10	126 (M), 137 (F)
Jackson[13]	35	122
Range		102–137

*Partner stimulation, self-stimulation, woman-on-top-coitus and man-on-top coitus, respectively.
M = male, F = female.

Drory *et al.*[7] compared the incidence of myocardial ischaemia between sexual activity and near-maximal exercise test in 88 male stable coronary artery disease patients. The mean age was 52 years (range 36 to 66 years). Eighty-seven per cent of patients were classified either as NYHA class I or II. All patients underwent a near maximal ergometric test (85% of predicted maximal heart rate according to age). All patients underwent 24-h Holter monitoring and they were instructed to record precise timing of any symptoms and activities. Peak heart rate during sexual intercourse in patients with ischaemia was significantly lower compared with peak exercise heart rate (117 ± 21 vs 150 ± 13 beats . min^{-1}). The peak heart rate during sexual intercourse was comparable to daily life activity (118 ± 21 beats . min^{-1} range 80–185, vs 113 ± 18 beats . min^{-1}, range 70–155) for all patients. Silent ischaemia occurred more commonly during sexual intercourse than symptomatic ischaemia (24% vs 7%). All patients with ischaemia during sexual intercourse had ischaemia during exercise and none of the patients without ischaemia at exercise had ischaemia during sexual activity. Drory *et al.*[8] also evaluated the presence or absence of ventricular arrhythmias during sexual activity and exercise in coronary artery disease patients. Ventricular ectopic activity occurred in 56% (49 of 88 patients) during sexual activity compared with 43% (38 of 88 patients) during exercise. Complex ventricular ectopic activity (non-sustained ventricular tachycardia, couplets, bigeminy, multiform premature ventricular complexes) were found in 12·5% (11 of 88) of patients during sexual intercourse compared to 9% (eight of 88) of patients during exercise. Most sex-related arrhythmias are simple ventricular ectopic beats, which are similar to the pattern during daily activity. The authors also found that there was no correlation between ischaemia (defined as a horizontal or downsloping ST segment depression of equal or more than 2 mm) and arrhythmia.

Generally, sexual intercourse requires mild-to-moderate effort compared with daily activities. The

Table 2 The frequency of sexual intercourse pre- and post-cardiac event

Author (reference)	Number of patients	Pre-cardiac event (times per month)	Post-cardiac event (times per month)
Hellerstein and Friedman[5]	14	8·4	6·4
Bloch *et al.*[17]	100	5·2	2·7
Papadopoulos *et al.*[18]	130	8·8	5·6
Johnston *et al.*[19]	87	6·4	4·6

mean peak heart rate was within the range 102–137 beats . min^{-1} (Table 1). Systolic blood pressure increases by 40–100 mmHg and diastolic blood pressure increases by 20–55 mmHg[9]. The maximal energy expenditure is about 4–6 METS. Sexual activity can be performed safely if the patient can perform at an activity level of 5–6 METS or is in NYHA functional class I or II[1].

Cardiovascular effects of sexual activity in coronary artery disease patients

Ueno reported that coital deaths accounted for 0·6% (34 of 5559 autopsies) of sudden death. In 34 of those patients who died during coitus, the circumstances of death were determined. Most deaths during coitus occurred in males (28 cases) and were from cardiac causes (18 cases). Most of the deaths (25 cases) occurred in hotels. There was a higher frequency of deaths in men who were older than their female partners by an average of 20 years. A preceding drunken state was noted in 12 cases. Most patients died during intercourse and extramarital relationships[14]. Extramarital sex may be hazardous and stressful because the partner is usually younger than the spouse, and sex occurs more often following excessive drinking and/or eating. In addition the patient may feel guilty, as well as having heightened excitement. Finally the patient may be too embarrassed to complain about chest pain[15].

Although coital death is a concern for cardiac patients, it is rare. Muller *et al.* performed retrospective case-crossover methodology to determine the relative risks of non-fatal myocardial infarction triggered by sexual activity among the general population and in coronary artery disease patients. A total of 1774 patients with myocardial infarction were interviewed: 858 patients reported being sexually active in the year prior to myocardial infarction. Three per cent (27 of 885 patients) of sexually active patients reported sexual activity in the 2 h prior to onset of symptoms of myocardial infarction. The relative risk of myocardial infarction occurring in the 2 h after sexual activity was 2·5 (95% CI, 1·7–3·7). It was noted that the relative risk of triggering the onset of myocardial infarction was not increased among patients with coronary heart disease compared to the general population. Sexual activity was probably a contributor to the onset of myocardial infarction in only 0·9% of cases. The relative risk of myocardial infarction in the 2 h following sexual activity was reduced from 3·0 to 1·9 to 1·2 in patients who were exposed to heavy physical exertion (>6 METS) once or not at all, twice, or three or more times per week, respectively[16].

Counselling cardiac patients

Most physicians do not discuss sexual function in cardiovascular patients and patients themselves are reluctant to bring it up. The frequency of sex has been reported to decrease in post-myocardial infarction patients (Table 2). Sexual dysfunction and decreasing frequency of sexual activity have been previously reported for between 22% and 75% of post-myocardial infarction patients[6,20–22]. There are several reasons for reduced or absent sexual activity in post-myocardial infarction patients (Table 3)[23].

Advising the post-myocardial infarction patient about sexual activity must begin with a careful history of the level of previous sexual activity. Patients who had no sexual activity prior to the myocardial infarction may be perfectly happy and well-adjusted and there is no need to encourage any change. In fact, the resumption of sex after many years of abstinence can be as anxiety-producing as an extramarital relationship. It is also important to evaluate the patient's general health and tolerance for exercise. The extent of the cardiac damage must be considered as well as the frequency and severity

Table 3 Reasons given by coronary artery disease patients for reducing sexual activity

Fear of recurrence of myocardial infarction or coital death
Symptoms of pain
Shortness of breath
Anxiety
Angina
Exhaustion
Change in sexual desire
Depression
Loss of libido
Impotence
Spouse's anxiety and concern
Guilt
Social changes

of symptoms. The spouse should be involved as much as possible in discussions of sexual activity. In general, certain guidelines are helpful for all postmyocardial infarction patients. Sexual activity should be avoided after meals (wait 3 h), after alcohol or in extreme temperatures. At times of fatigue, sex should also be avoided. Ideally the optimum time for coitus is in the morning following a night's rest. Furtive, emotionally stressful situations and time restrictions should be avoided and anginal pain that occurs during or after intercourse should be reported to the physician. Palpitations lasting 15 min or more after intercourse, marked fatigue during the day following intercourse, and sleeplessness caused by sexual exertion should also be reported to the physician[23]. Sexual activity should be resumed as soon as patients desire. The longer the delay in resumption of sexual activity post-myocardial infarction, the lower the frequency of coitus would be expected[19].

The risk of ischaemia during sexual intercourse with a familiar partner in familiar settings is quite low, if the patient can perform equal or more than 5–6 METS on an exercise stress test[24]. Some examples of activities requiring 6–7 METS include: level 2 of the Bruce treadmill, Double Master's step-test, 100–150 watts on a cycle ergometer, cycling 10 miles . h^{-1} on the level, walking 7·2 km . h^{-1} on the level, cross-country hiking, square dancing, cross-country skiing 4 miles . h^{-1} on the level, and carrying 50–60 pounds weight while walking 4·8 km . h^{-1}[1].

Most ischaemic episodes during sexual activity appeared to be related to tachycardic responses, therefore, reduction of the heart rate and improvement of exercise tolerance should be the main goal of the treatment. Nitroglycerin prior to sexual activity can relieve symptoms as well as the fear of anticipating symptoms and is very helpful in patients with coronary artery disease[23]; however, the use of nitrate is contraindicated in patients who use sildenafil citrate for erectile dysfunction. Beta-blocking agents have been used effectively to treat angina pectoris during sexual intercourse. The main action is reduction of the peak heart rate during sexual activity from 122 ± 7·1 to 82 ± 2·8 beats . min^{-1}[13]. Physical fitness programmes have been shown to improve sexual functioning[5,10]. Revascularization procedures should be considered if patients continue to have poor exercise tolerance despite adequate medical regimens and are symptomatic during sexual activity.

Sexual dysfunction related to cardiovascular medications

Drug-induced sexual dysfunction is frequently seen in cardiac patients. Cardiovascular drugs affect sexual function in many ways, inducing impotence, diminished libido, delayed orgasm, inorgasmia, decreased vaginal lubrication, priaprism, retarded ejaculation, retrograde ejaculation, premature ejaculation, gynaecomastia and menstrual irregularity[9,25] (Table 4). Antihypertensive and diuretic medications are the most common causes of drug-induced sexual dysfunction. Hydrochlorothiazide is associated with loss of libido, impotence and inhibition of vaginal lubrication[25,26]. Spironolactone can cause impotence, menstrual irregularities, hirsutism, decreased libido and gynaecomastia[25]. Gynaecomastia and menstrual problems are often seen with the dosage of the drug >200 mg . day^{-1}[9].

Impotence has been reported in a range of 7%–14% in patients taking propanolol[25,26]. Decreased libido has been associated with higher dosage[25]. Erectile dysfunction has been reported with newer beta-adrenergic blocking agents such as pindolol, atenolol, metoprolol, nadolol and labetalol[26,31]. Sexual dysfunction occurs less often in beta-blockers with cardioselectivity and low lipid solubility[32,33]. Peyronie's disease (painful erection and deformity of the penis from plaques of dense fibrous tissue surrounding the corpus carvernosum of the penis) and has been reported to occur following propanolol[25,34,35] and metoprolol therapy[36–38]. Sexual dysfunction has been reported in 14% of patients treated with labetalol[39]. Priaprism, delayed ejaculation, and delayed tumescence have been found in patients using labetalol[9,40,41].

Hydralazine has a low incidence of sexual dysfunction[9]. Priaprism has been reported to be caused by hydralazine[41]. Gynaecomastia, impotence in men and enlargement of the mammary glands in women has been reported in digitalis users[25]. Antiarrhythmic drugs infrequently cause sexual dysfunction. Impotence was found in 1%–3% of patients with disopyramide use[25,42] and it is likely caused by the anticholinergic effect of this drug. Ahmad reported impotence and loss of libido in two patients treated with amiodarone[43]. Impotence has been rarely reported with flecanide use[44]. About four in 1000 patients treated with mexilitine are reported to have impotence[45]. Impotence developed in less than 1% of patients receiving propafenone[46]. Sotalol causes impotence and decreased libido in about 2% of patients[47,48].

ACE inhibitor and angiotensin receptor blocker rarely cause impotence. The incidence of impotence per one million males treated ranges from 7·1 with captopril and 9·8 with enalapril to 15·6 with ramipril and 18·5 with lisinopril[49]. The incidence of impotence from losartan and valsartan is less than 1%[50,51]. Clofibrate and gemfribozil have been reported to cause impotence and loss of libido[25,52,53].

Cardiovascular aspects related to the treatment of erectile dysfunction

Erectile dysfunction is defined as the inability to achieve and/or sustain erection sufficiently to permit satisfactory sexual intercourse[54]. Between 10 and 30 million men in the U.S.A. have erectile dysfunction[55]. The prevalence

Table 4 Sexual dysfunction induced by cardiovascular medication

Medication (reference)	Type of sexual dysfunction
Hydrochlorothiazide[25,26]	Decreased libido
	Impotence
	Inhibition of vaginal lubrication
Spironolactone[25]	Decreased libido
	Gynaecomastia
	Impotence
	Hirsutism
	Menstrual irregularities
Methyldopa[25,26]	Decreased libido
	Ejaculatory difficulty
	Gynaecomastia
	Impotence
	Lactation
Clonidine[26]	Decreased libido
	Gynaecomastia
	Impotence
	Inorgasmia
	Retrograde ejaculation
Reserpine[27,28]	Decreased libido
	Ejaculatory difficulty
	Impotence
Guanethidine[25,26,29,30]	Decreased libido
	Ejaculatory difficulty
	Impotence
Phenoxybenzamine and phentolamine[26]	Ejaculation inhibition
Prazosin[9,25,26]	Impotence
	Priapism
Propranolol[25,26]	Decreased libido
	Impotence
	Peyronie's disease
Metoprolol[26,36–38]	Impotence
	Peyronie's disease
Labetolol[9,26,39–41]	Delayed ejaculation
	Delayed tumescence
	Impotence
	Priapism
Atenolol, nadolol and pindolol[26,31]	Impotence
Hydralazine[9,41]	Priapism
Digitalis[25]	Gynaecomastia
	Impotence
	Enlargement of the mammary glands
Disopyramide, mexilitine, flecanide, propafenone, amiodarone and sotalol[25,43–48]	Impotence (rare)
Captopril, enalapril, ramipril and lisinopril[49]	Impotence (rare)
Losartan, valsartan[50,51]	Impotence (rare)
Clofibrate and gemifibrozil[25,52,53]	Impotence
	Decreased libido

rate of erectile dysfunction of 40–70-year-old men in the Boston area is 52% and the prevalence increases from 39% in 40-year-old to 67% in 70-year-old men[56]. Erectile dysfunction is frequently seen in patients with heart disease, diabetes mellitus, a low high-density lipoprotein level and smokers. The two major causes of erectile dysfunction are organic and psychogenic. Organic causes include vascular diseases, neurogenic disorders, endocrine abnormalities, structural diseases, renal failure and medication effects. The major causes of erectile dysfunction of men more than 45 years of age are vascular and neurogenic[55].

The treatment options for erectile dysfunction include oral phamacotherapy, vacuum constriction devices, self-injection therapy with alprostadil, papaverine or phentolamine, intra-uretral alprostadil suppository, penile prosthesis and vascular surgery[57,58]. Vacuum constriction devices may be difficult to use. Penile prosthetic implantation is invasive, expensive and irreversible and may cause penile deformity. Intracarvernosal injection is effective; however, it is associated with pain, priaprism, penile haematoma and fibrosis. Intra-urethal alprostadil and yohimbine have been used effectively in various causes of erectile dysfunction[59,60]. Since sildenafil citrate was approved by the U.S. Food and Drug Administration (FDA) and marketed in late March 1999, the first-line treatment of erectile dysfunction has changed significantly. Sildenafil

citrate is very effective in the treatment of erectile dysfunction in the male. However, the effect in the treatment of sexual dysfunction in the female is unclear. Kaplan *et al*. prescribed sildenafil citrate to 33 post-menopausal women with sexual dysfunction for 3 months. They concluded that overall sexual function did not improve significantly in women included in this small study[61].

Yohimbine is an alkaloid obtained from the Central African yohimbine tree and acts as an α_2-adrenergic receptor antagonist. As it blocks the presynaptic α_2-adrenergic receptor, it enhances neuronal release of norepinephrine. This drug also works at cholinergic, dopaminergic and vaso-intestinal polypeptidic receptors. Meta-analysis by Ernst and Pittler indicated that yohimbine is better than placebo in the treatment of a variety of causes of erectile dysfunction (odds ratio 3·85, 95% confidence interval 6·67–2·22). The cardiovascular side-effects that were reported included: palpitation, tachycardia, exacerbation of angina and hypertension, which are mild and reversible[59].

Intra-urethral alprostadil (prostaglandin E_1) has been used effectively in erectile dysfunction. Alprostadil increases intracellular cyclic AMP and relaxes smooth muscle directly. Side-effects such as penile pain and urethral trauma, mostly occur locally. Penile haematoma and fibrosis have been reported with intra-carvernosal alprostadil. Cardiovascular side-effects are hypotension (3·3%) and syncope (0·4%)[59,62]. Myocardial infarction has been reported in a patient with spinal cord injury and paraplegia after intra-carvernosal administration of alprostadil[63].

Sildenafil citrate works as a selective inhibitor of cyclic guanosine monophosphate (c-GMP)-specific phosphodiesterase type 5. During sexual stimulation, nitric oxide is released in the corpus carvenosum. This effect produces the initial mechanism of erection of the penis. Later nitric oxide activates enzyme guanylate cyclase which causes increasing levels of c-GMP. c-GMP causes reduction of intracellular calcium, smooth muscle relaxation in the corpus carvenosum and vasodilatation in the penis. By inhibiting the breakdown of c-GMP, sildenafil citrate enhances the effect of and prolongs the action of c-GMP. Nitric oxide is released primarily from stimulation of non-adrenergic, non-cholinergic (nitroxidergic) carvernosal nerves and, therefore, sildenafil citrate cannot work without sexual stimulation[64].

Jackson *et al*.[65] reported that sildenafil citrate reduced systolic (7–9 mmHg) and diastolic (6 mmHg) blood pressure at the end of an intravenous infusion of sildenafil (20 mg, 40 mg and 80 mg). Systemic vascular resistance was reduced by 16% maximally and heart rate was not changed. Cardiac index was not changed significantly during 1–12 h after a single oral dose of sildenafil (100 mg, 150 mg and 200 mg). An 80 mg intravenous dose was comparable to a 200 mg oral dose of sildenafil[65]. Intravenous doses (40 mg) of sildenafil were administered to eight men with stable coronary artery disease. Right atrial pressure, pulmonary arterial pressure, pulmonary capillary wedge pressure, systolic blood pressure, diastolic blood pressure and cardiac output were reduced by 8%, 27%, 20%, 6%, 10% and 7%, respectively, from the baseline level at rest. In addition, the peak plasma concentration of intravenous sildenafil (40 mg) was one to three times higher than a single oral dose of 100 mg of sildenafil (usual therapeutic dosage)[65].

Webb *et al*. reported the interaction of sildenafil and glyceryl trinitrate in healthy men. During sildenafil treatment, systolic blood pressure decreased >25 mmHg after intravenous glyceryl trinitrate was administrated compared with placebo. Systolic blood pressure was reduced more than fourfold after sublingual glyceryl trinitrate was given compared with placebo. There were no synergistic interactions between sildenafil and amlodipine in hypertensive patients[66].

Conti *et al*. reported an incidence of myocardial infarction of 3% and unstable angina of 2% in patients with coronary artery disease treated with sildenafil, similar to those patients taking placebo[67]. From late March to mid-November 1999, 50 million sildenafil citrate tablets were dispensed. In mid-November, the FDA released the reports on 130 U.S. patients who died after using sildenafil: two died from homicide and drowning, 77 had cardiovascular events, three had strokes and the cause of death was unknown in 48 cases. All deaths occurred in men. The average age of death was 64 years (range 29–87 years). In 62 cases in which the dosage taken was known, three had taken 25 mg, 46 had taken 50 mg, nine had taken 100 mg, two had taken 50–100 mg, and two had taken more than 100 mg. Prior nitroglycerin administration had occurred in 16 men and three cases were found with nitroglycerin, but it was unclear whether nitroglycerin was taken. Thirty-four per cent (44 of 128 patients) of deaths occurred within 4–5 h of sildenafil usage (including 27 patients who died during or immediately after sexual intercourse). Six cases died on the same day and eight men died the next day. Seventy per cent (90 of 128 patients) of patients had one or more cardiovascular risk factors[68].

According to epidemiological data, the overall death rate of men in the U.S.A. is 400 deaths per week per million and is 150 deaths per week per million in sildenafil users[69]. Although the death rate from sildenafil is not very impressive, the prevalence of cardiac diseases is significant in erectile dysfunction patients and serious cardiovascular changes may occur from this medication. According to ACC/AHA recommendations, sildenafil is contraindicated with the concurrent use of nitrates because it can potentiate the hypotensive effect of nitrates. Sildenafil may cause significant cardiovascular side-effects in patients with active coronary ischaemia, congestive heart failure with borderline low blood pressure, on a complicated antihypertensive regimen, and taking medications which can prolong the half-life of sildenafil. Cardiovascular drugs that may prolong the clearance of sildenafil include amiodarone, digitoxin, diltiazem, disopyramide, felodipine, isradipine, losartan, mibefradil, nifedipine, quinidine,

verapamil, atorvastatin, cerivastatin, lovastatin and simvastatin. Therefore, the clinician may have to decrease the dosage of sildenafil citrate in patients who take these medications[64]. Nitrates are used to reduce recurrent ischaemic episodes in an acute coronary syndrome; however, nitrates should be avoided in patients taking sildenafil citrate. Patients need to be informed about the dangers of nitrate usage with sildenafil citrate.

Conclusion

The cardiovascular response to sexual intercourse is similar to mild-to-moderate effort encountered in daily activities. The risk of ischaemia during sexual intercourse with a familiar partner, in familiar settings, is quite low, if the patient can perform equal to or more than 5–6 METS on an exercise stress test. Coital death is rare. Myocardial infarction can be triggered by sexual activity within 2 h prior to onset of symptoms of myocardial infarction and the relative risk of triggering the onset of myocardial infarction is not increased among patients with coronary heart disease compared to the general population. Sexual dysfunction in the cardiac patient is common. It is important that cardiologists discuss any sexual problems and concerns that their patients may have. Antihypertensive and diuretic medications are the most frequent drugs to produce sexual dysfunction. Erectile dysfunction is commonly seen in cardiac patients and these are the patients who might take nitroglycerin. Sildenafil citrate is very effective oral phamacotherapy for the treatment of erectile dysfunction. It has a modest effect in altering cardiovascular haemodynamics. However, the concomitant use with nitrates may be hazardous and life threatening and nitrate therapy is contraindicated in patients using sildenafil citrate.

References

[1] Skinner JS. Sexual relation. In: Pollock ML, Schmidt DH, eds. Heart disease and rehabilitation. IL: Human Kinetics, 1995: 367–78.

[2] Nemec ED, Mansfield L, Kennedy JW. Heart rate and blood pressure responses during sexual activity in normal males. Am Heart J 1964; 92: 274–7.

[3] Bohlen JG, Held JP, Sanderson O, Patterson RP. Heart rate, rate-pressure product, and oxygen uptake during four sexual activities. Arch Intern Med 1984; 144: 1745–8.

[4] Garcia-Barreto D, Sin-Chesa C, Rivas-Estany E, Nieto R, Hemdndez-Cafiero A. Sexual intercourse in patients who have had a myocardial infarction. J Cardiopulm Rehabil 1986; 6: 324–8.

[5] Hellerstein HK, Friedman EH. Sexual activity and the postcoronary patient. Arch Intern Med 1970; 125: 987–99.

[6] Larson JL, McNaughton MW, Kennedy JW, Mansfield LW. Heart rate and blood pressure responses to sexual activity and a stair-climbing test. Heart Lung 1980; 9: 1025–30.

[7] Drory Y, Shapira I, Fisman EZ, Pines A. Myocardial ischemia during sexual activity in patients with coronary artery disease. Am J Cardiol 1995; 75: 835–7.

[8] Drory Y, Fisman EZ, Shapira I, Pines A. Ventricular arrhythmias during sexual activity in patients with coronary artery disease. Chest 1996; 109: 922–4.

[9] Seidl A, Bullough B, Haughey B, Scherer Y. Understanding the effects of a myocardial infarction on sexual functioning: a basis for sexual counseling. Rehabil Nurs 1991; 16: 255–64.

[10] Stein RA. The effect of exercise training on heart rate during coitus in the post-myocardial infarction patient. Circulation 1977; 55: 738–40.

[11] Johnston B, Fletcher GF. Dynamic electrographic recording during sexual activity in recent post-myocardial infarction and revascularization patients. Am Heart J 1979; 98: 736–41.

[12] Masini V, Romei E, Fiorella AT. Dynamic electrogram in normal subjects during sexual activity. G Ital Cardiol 1980; 10: 1442–8.

[13] Jackson G. Sexual intercourse and angina pectoris. Int Rehabil Med 1981; 3: 35–7.

[14] Ueno M. The so-called coition death. Jpn J Leg Med 1963; 17: 333–40.

[15] Walbroehl GS. Sexual activity and the postcoronary patient. Am Fam Physician 1984; 29: 175–7.

[16] Muller JE, Mittleman A, Maclure M, Sherwood JB, Tofler Triggering myocardial infarction by sexual activity. Low absolute risk and prevention by regular physical exertion. J Am Med Assoc 1996; 275: 1405–9.

[17] Bloch A, Maeder JP, Haissly JC. Sexual problems after myocardial infarction. Am Heart J 1975; 90: 536–7.

[18] Papadopoulos C, Beaumont C, Shelley SI, Larrimore P. Myocardial infarction and sexual activity of the female patient. Arch Intern Med 1983; 143: 1528–30.

[19] Johnston B, Cantwell J, Watt EW, Fletcher GF. Sexual activity in exercising patients after myocardial infarction and revascularization. Heart Lung 1978; 7: 1026–31.

[20] Singh J, Singh S, Singh S, Singh A, Malhotra RP. Sex life and psychiatric problems after myocardial infarction. J Assoc Physicians India 1970; 18: 503–7.

[21] Abramov L. Sexual life and sexual frigidity among women developing acute myocardial infarction. Psychosom Med 1976; 38: 418–25.

[22] Rahe RH, Ward HW, Hayes V. Brief group therapy in myocardial infarction rehabilitation: three-to-four-year follow-up of a controlled trial. Psychosom Me 1979; 41: 229–42.

[23] Stanek MS. Cardiovascular disease. In: Farber M, ed. Human sexuality psychosexual effects of disease. New York, NY: Macmillan, 1985: 231–9.

[24] Tardif GS. Sexual activity after myocardial infarction. Arch Phys Med Rehabil 1989; 70: 763–6.

[25] Papadopoulos C. Cardiovascular drugs and sexuality. Arch Intern Med 1980; 140: 1341–5.

[26] Wein AJ, Van Arsdalan KN. Drug-induced male sexual dysfunction. Urol Clin North Am 1988; 15: 23–31.

[27] Bulpitt Cl, Dollery CT. Side-effects of hvpotensive agents evaluated by a self-administered questionnaire. Br Med J 1973;3: 485–90.

[28] Laver MC. Sexual behavior patterns in male hypertensives. Aust N Z J Med 1974; 4: 29–31.

[29] Glazer N. Comparison of guanethidine and methyldopa in essential hypertension: a controlled study. Curr Ther Res Clin Exp 1975; 17: 249–56.

[30] Bauer GE, Hull RD, Stokes GS, Raftos J. The reversibility of side effects of guanethidine therapy. Med J Aust 1973; 1: 930–3.

[31] Product Information: Corgard(R), nadolol. Princeton, NJ: Bristol Laboratories, 1996.

[32] Smith PJ, Talbert RL. Sexual dysfunction with antihypertensive and antipsychotic agents. Clin Pharm 1986; 5: 373–84.

[33] Stokes GS, Mennie BA, Gellatly R, Hill A. On the combination of alpha- and beta-adrenoceptor blockade in hypertension. Clin Pharmacol Ther 1983; 34: 576–82.

[34] Osborne DR. Propranolol and Peyronie's disease. Lancet 1977; i: 111.

[35] Wallis AA, Bell R, Sutherland PW. Propranolol and Peyronie's disease. Lancet 1977; 1: 980.

[36] Product Information: Lopressor(R), metoprolol. East Hanover, NJ: Novartis Pharmaceutical, 1998.

[37] Product Information: Toprol XL(R), metoprolol succinate. Westborough, MA: Astra USA, 1998.
[38] Yudkin JS. Peyronie's disease in association with metoprolol. Lancet 1977; ii: 1355.
[39] Michelson EL, Frishman WH, Lewis JE *et al*. Multicenter clinical evaluation of long-term efficacy and safety of labetalol in treatment of hypertension. Am J Med 1983; 75: 68–80.
[40] Abramowicz M (ed.) Drugs that cause sexual dysfunction. Med Lett Drugs Ther 1987; 29: 65–70.
[41] Law MR, Copland RF, Armitstead JG *et al*. Labetalol and priapism. Br Med J 1980; 280: 115.
[42] Product Information: Norpace(R), disopyramide immediate-release and controlled-release capsules. Skokie, IL: GD Searle & Company, 1998.
[43] Ahmad S. Amiodarone and sexual dysfunction. Am Heart J 1995; 130: 1320–1.
[44] Gentzkow GD, Sullivan JY. Extracardiac adverse effects of flecainide. Am J Cardiol 1984; 53: 101B–105B.
[45] Product Information: Mexitil(R), mexiletine. Ridgefield, CT: Boehringer Ingelheim, 1998.
[46] Product Information: Rythmol(R), propafenone. Whippany, NJ: Knoll Pharmaceuticals, 1998.
[47] Product Information: Betapace(R), sotalol HCl. Wayne, NJ: Berlex Laboratories, 1998.
[48] Singh BN, Deedwania P, Nademanee K, Ward A, Sorkin EM. Sotalol: a review of its pharmacodynamic and pharmacokinetic properties, and therapeutic use. Drugs 1987; 34: 311–49.
[49] Carvajal A, Lerida MT, Sanchez A, Martin LH, de Diego IM. ACE inhibitors and impotence; a case series from the Spanish drug monitoring system. Drug Saf 1995; 13: 130–1.
[50] Product Information: Cozaar(R), losartan. West Point, PA: Merck & Co, Inc, 1998.
[51] Product Information: Diovan(R), valsartan. Summit, NJ: Ciba-Geigy, 1998.
[52] Pizarro S, Bargay J, D'Agosto P. Gemfibrozil-induced impotence (letter). Lancet 1990; 336: 1135.
[53] Bain SC, Lemon M, Jones AF. Gemfibrozil-induced impotence (letter). Lancet 1990; 336: 1389.
[54] NIH Concensus Development Panel on Impotence. NIH Concensus Conference: Impotence. J Am Med Assoc 1993; 270: 83–90.
[55] Kloner RA, Jarow JP. Erectile dysfunction and sildenafil citrate and cardiologists. Am J Cardiol 1999; 83: 576–82.
[56] Feldman HA, Goldstein I, Hatzichristou DG, Krane RJ, McKinlay JB. Impotence and its medical and psychological correlates: results of the Massachusetts male aging study. J Urol 1994; 151: 54–61.
[57] Burnett A. Erectile dysfunction: a practical approach for primary care. Geriatrics 1998; 53: 34–48.
[58] Dewire DM. Evaluation and treatment of erectile dysfunction. Am Fam Physician 1996; 53: 2101–6.
[59] Ernst E, Pitteler MH. Yohimbine for erectile dysfunction: a systematic review and meta-analysis of randomized clinical trials. J Urol 1998; 159: 433–6.
[60] Padma-Nathan H, Hellstrom WJG, Kaiser FE *et al*. for the Medicated Urethral System for Erection (MUSE) Study Group. Treatment of men with erectile dysfunction with transurethral alprostadil. N Engl J Med 1997; 336: 1–7.
[61] Kaplan SA, Reis RB, Kohn IJ *et al*. Safety and efficacy of sildenafil in postmenopausal woman with sexual dysfunction. Urology 1999; 53: 481–6.
[62] Linet OI, Ogrinc FG for the Alprostadil Study Group. Efficacy and safety of intracavernosal alprostadil in men with erectile dysfunction. N Engl J Med 1996; 334: 873–7.
[63] Vaidyanathan S, Soni BM, Krishnan KR. Special precautions to be observed while using alprostadil in patients with spinal cord injury. Spinal Cord 1997; 35: 402–3.
[64] Cheitlin MD, Hutter AM Jr, Brindis RG *et al*. ACC/AHA expert consensus document. Use of sildenafil (Viagra) in patients with cardiovascular disease. American College of Cardiology/American Heart Association. J Am Coll Cardiol 1999; 33: 273–82.
[65] Jackson G, Benjamin N, Jackson N, Allen MJ. Effects of sildenafil citrate on human hemodynamics. Am J Cardiol 1999; 83: 13C–20C.
[66] Webb DJ, Freestone S, Allen MJ, Muirhead GJ. Sildenafil citrate and blood-pressure-lowering drugs: results of drug interaction and a calcium antagonist. Am J Cardiol 1999; 83: 21C–28C.
[67] Conti CR, Pepine CJ, Sweeney M. Efficacy and safety of sildenafil citrate in the treatment of erectile dysfunction in patients with ischemic heart disease. Am J Cardiol 1999; 83: 29C–34C.
[68] Food and Drug Administration Web site. Postmarketing safety of sildenafil citrate (viagra). Available at: http://www.fda.gov/cder/consumerinfo/viagra/safety3.htm (accessed November 28, 1998).
[69] Zusman RM, Morales AA, Glasser DB, Osterloh LH. Overall cardiovascular profile of sildenafil citrate. Am J Cardiol 1999; 83: 35C–44C.