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Cardiovascular Disease: The Effect of Erectile Dysfunction on adherence to cardiovascular disease medication

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Abstract

Due to their similar aetiologies, cardiovascular disease and erectile dysfunction are closely linked, with the prevalence of erectile dysfunction being approximately 75% for individuals at high risk of cardiovascular disease. Erectile dysfunction can have a detrimental effect on quality of life not only for the individual but also his sexual partner which in turn impacts upon their intimate relationship. Some cardiovascular disease medications have been found to have a negative effect on erectile function and therefore act as an influential factor for the cessation of important cardiovascular disease medication. Low adherence to cardiovascular disease medication has been linked to increased health costs, hospitalizations and importantly, a higher risk of mortality. Research has shown that men find it difficult to seek medical help in relation to ED which is also compounded by the notion that health care providers do not address sexual issues adequately. Patients' beliefs about cardiovascular disease medication are modifiable and therefore an opportunity exists not only for health care providers to facilitate discussions in relation to erectile dysfunction and medication adherence but also encompass an opportunity to increase adherence to cardiovascular disease medication through intervention.

Introduction

Erectile Dysfunction (ED) is the persistent inability to attain and maintain a penile erection adequate for sexual performance (Kloner, 1993). A recent review that collated results from 59 studies from across the globe suggests that the prevalence of ED increases with age. Estimations range from 20 – 40% for men 60 – 69 years and 50 – 100% for men in their 70's and 80's (Lewis et al, 2010). Estimations of prevalence vary widely however, due to: the definition of ED that is used; the population studied; and the method by which ED is measured (Rosen et al, 1999; Lewis et al, 2010).

Cardiovascular disease (CVD) and ED share a similar disease profile in relation to their aetiology and risk factors. Vascular diseases have been documented as the most common cause of ED (Hodges et al, 2007) and both share risk factors such as obesity, diabetes mellitus, physical inactivity, hypertension, dyslipidaemia and tobacco usage (Ponholzer et al, 2005). Exposure to such risk factors can result in the build-up of plaque around arteries or atherosclerosis, which can in turn lead to CVD. Arteries in the penis are small (around 1 – 2 mm) in comparison to e.g. coronary arteries (around 3 – 4 mm) (Jackson, 2013) and as a result, arteries in the penis suffer obstruction caused by atheromatous plaque earlier than coronary arteries or indeed other arteries. Therefore ED is typically experienced before the onset of a cardiac event and is regarded as an indication of the presence of CVD (Montorsi et al, 2003). Solomon et al (2003) found that 40% of men experience ED before they are diagnosed as suffering from coronary artery disease (CAD). Further, a retrospective cohort study of 26,000 participants found a two-fold increase in risk of myocardial infarction at 1 year follow-up for 13,000 men who reported ED at baseline (Blumentals et al, 2004). Baumhäkel et al (2006) suggest that the prevalence of ED equates to 75% for individuals at

high-risk of CVD. Studies such as these indicate not only a relationship between ED and CVD but also that ED is an important indicator of increased CVD risk.

The aim of this paper is twofold. Firstly, the paper will consider both CVD, ED and the contemporary understanding of the link that exists between the two conditions. Further, the similarities between their disease profiles such as their risk factors and aetiologies will be considered. Secondly, adherence to CVD medication regimes and the mediating role of ED will be considered. The impact of suffering with CVD and ED will be approached from the individual level and will consider both help-seeking behaviour and quality of life. Finally, suggestions are offered in relation to the role future research could take in exploring the link between ED and adherence to CVD medication.

Cardiovascular Disease

Cardiovascular disease (CVD) includes all diseases of the heart and circulatory system, including coronary heart disease (angina and myocardial infarction), heart failure, congenital heart disease and stroke (BHF, 2013). CVD is the number one cause of mortality, responsible for 17.3 million (30%) of total deaths worldwide in 2008 (WHO, 2013).

The Relationship between CVD and ED

From the onset of ED, the mean time to a cardiac event such as coronary artery disease (CAD), myocardial infarction or stroke, is approximately three years (Jackson, 2013). This highlights the importance of diagnosing ED as early as possible and provides an important

window of opportunity in which preventative action can be taken to avoid a potential cardiac event. For health care professionals, this provides an important opportunity to identify any underlying CVD in patients. Therefore it is essential to discuss ED with the patient at the earliest possible opportunity (refer to Box 1).

Insert box 1

Studies have shown that ED, after controlling for age, body mass index (BMI), blood pressure, diabetes, cholesterol and smoking, is likely to be an independent risk factor for CVD. In a meta-analysis of 12 prospective cohort studies, Dong et al (2011) found that ED was shown to significantly increase the risk of CVD, stroke, CAD and all-cause mortality. The severity of CVD has also been shown to correlate with the severity of ED. For example, men with single vessel CAD have been found to experience firmer erections than men with two or three vessel CAD (Johannes et al, 2000). The severity of ED can be indicated by using the 5-item International Index of Erectile Function (IIEF-5) (Rosen et al, 1997; 1999, refer to box 2). The severity of ED is classified with these breakpoints: score of 1-7 = severe ED; score of 8-11 = moderate ED; score of 12-16 = mild to moderate ED; score of 17-21 = mild ED. Scores >21 indicate 'normal' erectile function (Cappelleri and Rosen, 2005). Using an instrument such as the IIEF-5 can help to identify both the presence of ED and also be used as an entry point into discussing adherence with CVD medication. Baumhäkel et al (2011) suggest that in the last four decades both the medical press and lay media have reported an association between drugs used for treating CVD and their negative effect on erectile function. Baumhäkel et al (2011) contend that this has had an impact on patient adherence to important cardiovascular medical regimes.

Insert box 2

Adherence

Unwanted or unused medication is estimated to cost the National Health Service (NHS) in excess of £100 million annually (Nunes et al, 2009). The cost of CVD medication to the NHS is approximately £2.8 billion per annum which constitutes 20% of the health care costs associated with CVD (Knapton, 2012). This figure becomes salient in light of research such as that of Naderi et al (2012) who carried out a meta-analysis of 376,162 patients with CVD and found that approximately 50% of individuals do not take CVD medication as prescribed.

Adherence to CVD medications can involve a complex interplay of patient and treatment characteristics (Munger et al, 2007). Factors that have been suggested to influence non-adherence to CVD medication include being of a younger age (Hassan et al, 2005), suffering with depression (Aggarwal and Mosca, 2010), complexity of the prescription regimen (Grégoire et al, 2006), beliefs about necessity (Ruppar et al, 2012), beliefs about medication (Benson and Britten, 2002; Ogedegbe et al, 2004; Fergus, 2009) and beliefs about the severity of CVD (Stafford et al, 2008).

Voils et al (2008) carried out a qualitative study of 38 male hypertensive patients and 13 spouses. Sexual dysfunction emerged as a factor preventing people from taking their antihypertensive medication as prescribed. Participants reported ceasing their medication or missing doses to preserve erectile function, however, Voils et al (2008) did not report

which antihypertensive medications participants were taking. In a randomised placebo-controlled trial of the thiazide diuretic, bendrofluazide, and the beta-blocker, propranolol, ED as a reason for withdrawal from treatment was significantly higher in both treatment groups than in the placebo (MRC, 1985). Baumhäkel et al (2011) examined the evidence for the effect of ACE-inhibitors, angiotensin-receptor-blockers, beta blockers, calcium channel-blockers, and diuretics on erectile function. They concluded that thiazide diuretics and beta-blockers (excluding nebivolol) may have an adverse effect on erectile function; however they report that ACE-inhibitors, angiotensin-receptor-blockers and calcium channel-blockers have no effect and in fact potentially have a positive effect. It has also been suggested that the effect of beta-blockers on ED may be partly related to patient expectations about side effects.

The notion that patient beliefs about CVD medications and erectile function can potentially impact upon response to medication has been explored by studies such as Silvestri et al (2003). In a cohort of 96 men prescribed atenolol for CVD, one third were not advised which drug they had been given, one third were advised of the drug but not told about ED as a potential side effect and the remaining third were informed about the drug and the side effect. ED was reported in 3.1%, 15.6% and 31.2% of the groups respectively. At the end of the 90-day treatment period, those reporting ED were randomised to receive sildenafil citrate or a placebo, which were reported to be equally effective, although it must be borne in mind that the sample size was very small.

The type of medication prescribed and patients' perceptions in relation to side effects are therefore important factors to consider in non-adherence to CVD medication (Vlachopoulos

et al, 2013). If patients believe that CVD medications impair their sexual function they may be less likely to adhere to treatment; non adherence has serious consequences, in relation to increased health costs, hospitalisation, as well as increased morbidity and mortality (Baroletti et al, 2010). It is important therefore that healthcare professionals discuss ED with patients so that they can identify concerns, clarify any misconceptions and choose the most suitable treatments. Scranton et al (2013) suggests that such discussions are important because they have the potential to lead to improved adherence to CVD medication. An observational study by McLaughlin et al (2005) examined men's prescription claims for antihypertensive, oral hypoglycaemic, lipid lowering or antidepressant medication in the 12 months before and 12 months after they were first prescribed sildenafil citrate. Patients classified as non-adherent (a medication possession ratio of <0.8, which means that less than 80% of doses were collected from the pharmacy) before being prescribed sildenafil citrate were more likely to have been prescribed antihypertensive and antidepressant medications. McLaughlin et al (2005) found that in the period after sildenafil citrate was prescribed, adherence to all the comorbid medications increased significantly.

Help-seeking

Research from Kirby et al (2001) found that out of 980 men consulting a clinician for help in relation to ED, 60% had lipid abnormalities, 18% were suffering with undiagnosed hypertension and 5% had ischemic heart disease. One possible reason for such diseases going undiagnosed can be found in studies such as that of Laumann et al (2009), who found that less than 25% of men actively seek treatment for ED. Avoiding medical help has been attributed to embarrassment, difficulties accepting ED as a consequence of ageing or

disease, as well as the expectation that healthcare professionals should be responsible for broaching the subject (Steggall et al, 2006). Further, Steggall (2012) suggests that the terminology used to describe ED may not be understood by all patients, they may not know which words are appropriate to use when describing the problem and therefore will not approach the issue with their health professional. A further barrier to effective communication includes language. The term ED does not easily translate into languages such as Bengali and therefore an alternative term may be needed for patients whose first language is not English (Steggall, 2009).

Byrne et al (2013) carried out research into both male and female patients' and their cardiac healthcare providers' experiences of communication in relation to sexual issues. They found that sexual issues were more likely to be addressed in hospital cardiac rehabilitation settings rather than in general practice. The majority of cardiac rehabilitation staff as well as patients reported that they believed sexual issues were poorly addressed within their service. Patients felt that it would be easy to discuss such issues and reported a desire for more opportunities during consultations to discuss sex with their healthcare provider. It is interesting to note that patients identified embarrassment as their greatest barrier when discussing sexual health issues, while simultaneously health providers reported that they feared causing patients discomfort and anxiety. Therefore, this simultaneous desire to avoid upsetting or embarrassing one another needs to be addressed as it has important implications for not only for diagnosing and managing both ED and CVD, but also in relation to the consequences that CVD and ED can have on an individual's quality of life.

Psychosocial well-being

CVD has been found to impact significantly on a person's psychological well-being including their quality of life and mood (Ôunpuu et al, 2001). A key component of quality of life is an individual's sexuality and for men, an important aspect of sexuality is the ability to have and maintain an erection in order to carry out sexual intercourse. Kushiro et al (2005) investigated the impact of ED on health-related quality of life in a group of patients with hypertension and compared them to a matched normotensive control group. Whereas men with hypertension only had lower scores on general health compared to those without hypertension, men with ED had significantly lower scores in physical, mental health, emotional, vitality, and general health-related quality of life compared to those without ED. This suggests that ED has a more serious impact on quality of life than hypertension; interestingly men living with both hypertension and ED scored the lowest in relation to quality of life compared to all other groups.

Depression is recognised as a particularly important factor in understanding the relationship between ED and CVD. Men, post myocardial infarction, are likely to experience a significant amount of distress and are also more likely to have ED despite age, current medication, smoking, weight and other co-morbidities (Vacanti and Caramelli, 2005). Research suggests that almost 40% of men with CVD experience co-morbid ED and depression (Lemogne et al, 2010). However, the impact of this co-morbid triad is complicated; not only are men with depression more likely to develop chronic heart disease (CHD) and ED, older men with CHD and ED are more likely to suffer from depression (Tan and Pu, 2003). Epidemiological

research suggests that these three conditions overlap (Feldman et al, 1994) and therefore presentation of one should trigger further investigations of one or both other conditions.

To understand the overlap between CVD, ED and depression, Goldstein (2000) proposed an integrated model (See figure 1) in order to understand that depressive illness, CVD and ED share many of the same risk factors and etiological associations. The model highlights the potential impact of psychosocial well-being, treatment, overall health status, personal characteristics and lifestyle behaviours in aetiology and the cyclical relationship between these co-morbid conditions. Goldstein (2000) suggests that a practical implication of the model is that patients presenting with symptoms of ED should be routinely screened for symptoms of depression and CVD. Equally those that present with depressive symptoms should be screened for ED and CVD. Clinicians involved in the management of sexual dysfunction are encouraged to be particularly sensitive to the potential comorbidity of CVD and depression as well as the potential increased risk of cardiac morbidity and mortality in patients with such conditions (Goldstein, 2000).

Insert Figure 1.

Research has been conducted that supports the theory that ED in CVD is independently associated with depressive symptoms (Lemogne et al, 2010). Further work has also linked this relationship to overall quality of life. In order to estimate the prevalence of sexual disorders and depressive symptoms in patients attending cardiac rehabilitation and examine the association between sexual disorders, depressive symptoms and quality of life, Kriston et al (2010) carried out a survey involving 395 male participants. It was found that 20% had

moderate to severe ED and 14% of the sample had moderate or severe depression. It was found that impaired sexual functioning was moderately associated with decreased quality of life and this relationship was mediated by depression.

In addition to depression, anxiety and specifically performance anxiety can have a significant impact on the ability of men to resume sexual activity and function after a cardiac event. This may be further amplified if a couple had interpersonal or sexual difficulties prior to the cardiac event. Friedman (2000) suggests that cardiac rehabilitation should integrate sexual activity in discussions around regaining and maintaining quality of life and this should include a patient's sexual partner (Friedman, 2000). Partner involvement in the rehabilitation process is particularly important given the impact ED can have on intimate relationships. Fisher et al (2005) carried out a study of a general sample of men with ED and their partners. Self-reported severity of ED by both males and their respective partners were found to be highly correlated. Both partners reported dramatic reductions in sexual activity after the onset of ED, compared to retrospective reports prior to onset. Research carried out by Günzler et al (2009), used self-report methods to investigate sexual problems in a sample of men attending cardiac rehabilitation. Sexual problems were associated with greater engagement in quarrelling, significantly less tenderness and communication as well as poorer quality of partnership in comparison to men without sexual problems. In addition, orgasmic function, sexual desire, intercourse satisfaction, overall sexual satisfaction and ED were significantly correlated with aspects of partnership quality indicating that as sexual functioning improved so did partnership quality.

Implications for practice

There are potential opportunities to improve the care of individuals living with CVD and ED. One such opportunity is how healthcare providers discuss ED (refer to Box 1 and 2). The terminology used by healthcare professionals to describe ED may not be understood by all patients. For example 'Erectile dysfunction' does not translate directly into other languages, such as Bengali. Therefore an alternative term may be needed (Steggall, 2012). Difficulties such as language barriers as well as cultural differences can therefore create difficulties for clinical practitioners to identify ED. Byrne et al (2013) suggest that patients not only report that they would find it easy to discuss sexual issues with their healthcare provider but also report a desire for more opportunity during consultations to discuss sexual issues. This indicates that healthcare professionals could create an environment in which issues around sexuality can easily be raised and discussed. This may mean that specific training should be offered in order for healthcare professionals to possess the awareness and skills to facilitate this in clinic. Clinicians unused to assessing sexual dysfunction may find the assessment guide helpful to identify the severity and nature of the problem (refer to Box 2).

Research also highlights the importance of involving the patient's partners, where possible, in the rehabilitation process. This not only provides an opportunity for the clinician to have an understanding of how ED may be impacting on a patients' quality of life and that of their partner; it also permits a discourse to emerge in which ED and the couple's intimate relationship can be discussed.

Implications for research

Research and anecdotal evidence suggests an association between ED and adherence to CVD medication. However, the strength and direction of that relationship has not been confirmed. Further research needs to be carried out in order to investigate the prevalence of non-adherence to cardiac medication in those with ED as well as how treatment for ED and beliefs about these co-morbid conditions influence adherence behaviour. By identifying the demographic, clinical and psychosocial factors which predict adherence to CVD treatment only then can research begin to look at the possibility of designing a behaviour change intervention aimed at improving adherence.

Conclusion

There is a growing body of literature indicating that men with CVD either cease taking their prescribed medications, or miss doses; this may be related to the common side effect of reduced erectile strength. Non-adherence poses significant risk to these men, in terms of morbidity and mortality, but also in terms of their sexual relationship. Opportunities have to be created to facilitate discussions of adherence and ED, and these can be facilitated by using the IIEF-5 either at the point of prescribing CVD medication or during the annual medication review. Where ED has been identified, patients will need to be assessed for the severity of their ED and appropriate treatment instigated.

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Box 1. Creating the opportunities for discussing ED

Ask: 'Some men who are taking medication for cardiovascular disease may have trouble with erections. If you have any questions or would like to discuss that, I can arrange an appointment for you'

Awareness: Posters informing men of the prevalence of ED can be used to create the environment where questions can be asked

Inform: ED is common. There are several treatment options that can be considered. If you want to discuss these options, speak with your clinician, GP, pharmacist, or visit websites such as www.menshealthanswers.co.uk

Box 2. 5-item International Index of Erectile Function (IIEF-5) Adapted from Rosen, et al. (1999)

How do you rate your <u>confidence</u> that you could get and keep an erection?				
Very low 1	Low 2	Moderate 3	High 4	Very high 5
When you had erections with sexual stimulation, <u>how often</u> were your erections hard enough for penetration?				
Almost never/Never 1	A few times (much less than half the time) 2	Sometimes (about half the time) 3	Most times (much more than half the time) 4	Almost always/always 5
During sexual intercourse, <u>how often</u> were you able to maintain your erection after you had penetrated (entered) your partner?				
Almost never/Never 1	A few times (much less than half the time) 2	Sometimes (about half the time) 3	Most times (much more than half the time) 4	Almost always/always 5
During sexual intercourse, <u>how difficult</u> was it to maintain your erection to completion of sexual intercourse?				
Extremely difficult 1	Very difficult 2	Difficult 3	Slightly difficult 4	Not difficult 5
When you attempted sexual intercourse, <u>how often</u> was it satisfactory for you?				
Almost never/Never 1	A few times (much less than half the time) 2	Sometimes (about half the time) 3	Most times (much more than half the time) 4	Almost always/always 5
Score _____				
The IIEF-5 score is the sum of questions 1 to 5. The lowest score is 5 and the highest score 25. If the score is 21 or less you may be showing signs of erectile dysfunction (ED). Please speak with the person who gave you this form, or ask your GP for advice.				

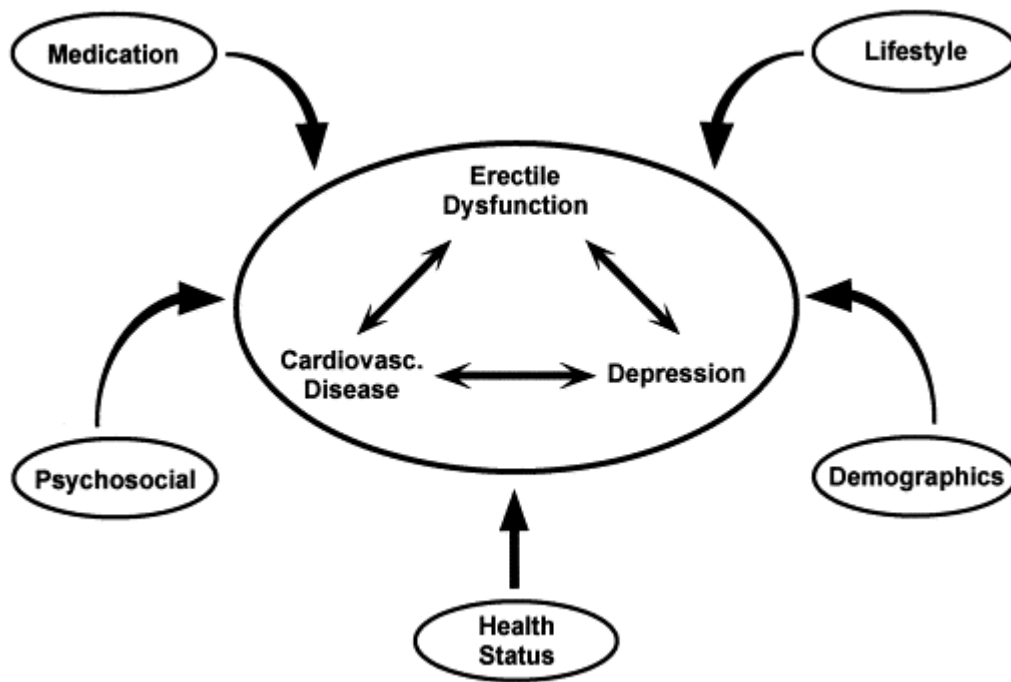


Figure 1 Integrated model of depression, erectile dysfunction and cardiovascular disease
Adapted from (Goldstein, 2000)