

Management and treatment of diabetes, erectile dysfunction and hypogonadism

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Article points

1. Penile erection is a complex neurovascular phenomenon that takes place under androgenic hormonal control.
2. There are three drugs that are well known and are in common use for the treatment of erectile dysfunction (ED), all of which are phosphodiesterase type 5 (PDE5) inhibitors. The three selective PDE5 inhibitors in use are sildenafil, tadalafil and vardenafil.
3. ED is a common condition in men with diabetes, having a significant impact on wellbeing as well as being a marker for cardiovascular disease.

Key words

- Erectile dysfunction
- Phosphodiesterase type 5 inhibitor
- Testosterone deficiency

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Erectile dysfunction is an important but often ignored and poorly managed condition that should occupy a more prominent position when consulting with people with diabetes. Evidence is now emerging of the link between type 2 diabetes and testosterone deficiency and this article explores this in a little more detail as well as providing a revision of the assessment, investigation and treatment of erectile dysfunction in people with diabetes.

The British Society for Sexual Medicine (BSSM) guidelines, produced in 2007, reflect that erectile dysfunction (ED) is a persisting inability to attain and or maintain an erection sufficient for sexual performance (Hackett et al, 2008).

The physiology of penile erection is an intricate neurological and vascular process underpinned by androgenic hormonal control (Hackett et al, 2008). Androgens function both within the central and peripheral nervous system as well as having an important role to play within the tissues of the penis itself. Animal studies reveal testosterone to be critical in maintaining a normal penile architecture (Jones, 2008). Testosterone regulates the expression and activity of the phosphodiesterase type 5 (PDE5) inhibitor within the penis and, therefore, testosterone deficiency can adversely affect the response to PDE5 inhibitors.

Diabetes and erectile dysfunction

ED is recognised as a frequent complication of diabetes. In the Massachusetts male aging

study the age-adjusted probability of complete ED was three times greater in men with type 2 diabetes (De Berardis et al, 2002).

Although ED itself is not a life-threatening condition, its importance comes from the significant psychological burden it must surely place on the individual and his partner. Moreover, it can be a strong clue to the presence of underlying atheromatous disease elsewhere, and ED should not be ignored but be regarded as a cardiovascular risk factor in its own right. The penile arteries are significantly smaller than the main coronary arteries and ED can and often does precede coronary artery disease.

Assessment and management of ED

In the author's experience, the management of ED frequently seems to fall short of what should be expected. There are a number of reasons to consider to help explain this.

First, there are a number of competing interests to address in a consultation – diet and lifestyle concerns, glycaemic control,

hypertension, hyperlipidaemia, retinopathy and foot care to name just a few. Often it seems that time constraints simply prevent a thorough assessment and management of people with ED.

Second, the management of ED does not form part of the Quality and Outcomes Framework (QOF) indicators, and in the author's opinion this represents a short-coming in the QOF parameters for diabetes. The reasons for suggesting this are that the condition has a negative effect on people's quality of life and can be an important clue to more serious disease elsewhere.

Third, information regarding ED is infrequently volunteered by people with diabetes. It is useful for us as healthcare professionals to help individuals with diabetes to overcome any anxieties by being open in making an enquiry about ED. To this end, although not forming part of QOF, a prompt for ED should certainly be included in the computer-based diabetes template used within the practice.

On a positive note of course, most people with diabetes are managed solely within the sphere of primary care. In the author's opinion, it is even more unlikely that an assessment of ED will be made by our secondary care colleagues. Primary care practitioners are excellently placed to gather sensitive information on sexual function aided by the long, well trusted and privileged relationships they share with patients and their families. A huge concern must be that if those of us working on the front-line do not offer an enquiry relating to ED then many people will seek advice from other potentially damaging sources (namely the internet) and will not receive appropriate evaluation or treatment.

History and examination

As with everything else in medicine, a detailed history for a person with ED is important. The following points to review are detailed below (Hackett et al, 2008):

- The duration of symptoms.
- Precipitating or predisposing factors.

- Any prior investigation and treatment, along with response.
- An expression of tumescence and assessment of quality of morning awakening erections.
- Sexual desire, ejaculatory and orgasmic dysfunction.
- Partner-related issues (such as menopause).
- Issues regarding sexual orientation and gender identity.
- Alcohol and smoking history.

Questionnaires are available to aid the assessment of ED. However, with pressing time constraints in primary care a full and clear history is of more importance. ED is a recognised side-effect both of thiazides and non-selective beta-blockers (Grimm et al, 1997). Angiotensin-converting enzyme (ACE) inhibitors and calcium channel blockers are unlikely to be a major contributory factor in the development of ED. Guidelines from the BSSM endorse the fact that prescribing cheaper drugs is unlikely to be cost-effective if more expensive therapy is required to reverse adverse sexual performance (Hackett et al, 2008).

In addition to gathering information on blood pressure, heart rate, waist circumference and weight there should be a focused physical examination. This should include a genital examination. A digital rectal examination of the prostate is not mandatory but should be conducted in the presence of urinary or ejaculatory symptoms.

Treatment

Along with other aspects of diabetes care, treatment of ED should begin with advice on lifestyle modification. There are three drugs that are well known and are in common use for the treatment of ED, all of which are PDE5 inhibitors. Drugs that inhibit PDE5 increase arterial blood flow leading to smooth muscle relaxation, vasodilation and penile erection.

Contraindications to using nitrates include the concomitant prescribing of organic nitrates to treat ischaemic heart disease, and this includes nicorandil. Care should also be taken when a person is also taking an alpha

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2. Primary care practitioners, are excellently placed to gather sensitive information on sexual function aided by the long, well trusted and privileged relationships they share with patients and their families.
3. In addition to gathering information on blood pressure, heart rate, waist circumference and weight there should be a focused physical examination. This should include a genital examination.
4. Treatment of ED should begin with advice on lifestyle modification.

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1. The three selective phosphodiesterase type 5 inhibitors in use are sildenafil (Viagra; Pfizer, Surrey), tadalafil (Cialis; Lilly, Basingstoke) and vardenafil (Levitra; Bayer, Newbury).
2. There is a high prevalence of symptomatic hypogonadism in men with type 2 diabetes.
3. Testosterone administration in men with diabetes has been shown to have beneficial effects on glycaemic control, insulin resistance and visceral adiposity.

blocker. Similarly to the interaction with nitrates, this combination of therapy can lead to hypotension.

The three selective PDE5 inhibitors in use are sildenafil (Viagra; Pfizer, Surrey), tadalafil (Cialis; Lilly, Basingstoke) and vardenafil (Levitra; Bayer, Newbury). The major difference in these drugs is that sildenafil and vardenafil are relatively short-acting drugs, with a half-life of approximately 4 hours. The half-life of tadalafil is significantly longer and, as such, potentially more flexible for some people to use. Individuals should undergo thorough counselling and instruction on the use of these medications prior to their prescription. PDE5 inhibitors are not initiators of erection but should be used within the sexual environment to be effective.

Individuals should ideally be followed-up within 6 weeks of starting a PDE5 inhibitor and should receive eight doses, with sexual stimulation, at maximum dosage before being classified as a non-responder (Hackett et al, 2008). Treatment failure is often as a result of suboptimal counselling at the initial consultation. If people are not responding to primary care management despite all these factors being met, they may well need secondary care referral.

Other options for management may include the use of a medicated urethral system for erection (MUSE) – a preparation of alprostadil inserted into the urethra – intracavernosal injection therapy, vacuum devices or the use of a penile prosthesis.

Testosterone deficiency syndrome

There is now a large body of evidence that establishes the link between type 2 diabetes and low testosterone with ED and cardiovascular disease. There is a high prevalence of symptomatic hypogonadism in men with type 2 diabetes. A UK study found that 20% of men with type 2 diabetes had a total testosterone less than 8 nmol/L and 31% had total testosterone between 8 and 12 nmol/L. Put another way, 51% of men with type 2 diabetes have low testosterone (Kapoor et al, 2007). Another study

conducted in Barnsley found 42% of men with diabetes had a free testosterone level below 2.5 nmo/L (Jones, 2006).

Testosterone administration in men with diabetes has been shown to have beneficial effects on glycaemic control, insulin resistance and visceral adiposity (Kapoor et al, 2006), which importantly leads to a reduction in cardiovascular risk. There is also evidence to show that, in men with testosterone deficiency (who have previously failed to respond to a PDE5 inhibitor), combining such a therapy with testosterone significantly improves erectile function (Shamloul et al, 2005).

One way of identifying people with testosterone deficiency is with the use of the Androgen Deficiency in the Aging Male (ADAM) questionnaire (Morley et al, 2000). It is a validated questionnaire used to assess the likelihood of androgen deficiency and can be used in males aged over 40. Testosterone has important influences not only on sexual desire but it also has effects on musculature, mood and energy. *Table 1* shows some common symptoms and signs associated with male hypogonadism. The 10-point ADAM questionnaire is also shown in *Table 2*. A positive ADAM questionnaire is revealed by an affirmative response to a decrease in libido,

Table 1. Signs, symptoms and long-term risk of testosterone deficiency.
<p>Signs:</p> <ul style="list-style-type: none"> ● Small, firm testes. ● Loss of body or facial hair. ● Gynaecomastia. ● Fine, wrinkled skin, especially on the face. <p>Symptoms:</p> <ul style="list-style-type: none"> ● Erectile dysfunction. ● Loss of libido. ● Fatigue/lethargy. ● Depression. ● Muscular weakness. <p>Long-term risks:</p> <ul style="list-style-type: none"> ● Osteoporosis.

Table 2. The 10-point androgen deficiency in the aging male questionnaire.	
Do you have a decrease in libido?	Yes/No
Do you have a lack of energy?	Yes/No
Do you have a decrease in strength and/or endurance?	Yes/No
Have you lost height?	Yes/No
Have you noticed a decreased “enjoyment of life”?	Yes/No
Are you sad or grumpy?	Yes/No
Are your erections less strong?	Yes/No
Have you noticed a deterioration in your ability to play sports?	Yes/No
Are you falling asleep after dinner?	Yes/No
Has there been a recent deterioration in your work performance?	Yes/No

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or strength of erections or a positive response to three non-specific questions regarding fatigability, strength and mood.

It is clear that by receiving a positive response to a single enquiry about ED would merit assessment of an individual’s testosterone level. In practical terms, therefore, this could obviate the need to go through the whole questionnaire, which in busy clinics is an important consideration. However, the author’s research reveals that only asking about ED will miss nearly 50% of men who would otherwise respond positively to the ADAM questionnaire and identifies some of the problems of undertaking such screening in primary care (Downie and Ulahannan, 2009).

There is a lot more to consider regarding the assessment investigation and management of hypogonadism. The purpose of this article is to provide some insight into this exciting area. The take-home message is to consider testosterone deficiency in men with ED who have not had treatment success with a PDE5 inhibitor.

Conclusion

ED is a common condition in men with diabetes, having a significant impact on wellbeing as well as being a marker for cardiovascular disease. An assessment of ED should be made on at least an annual basis. In those who fail to respond to medication, consideration should be given to investigating for hypogonadism. ■

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