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An Undisclosed Affair: Sexual Dysfunction in Diabetes

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Editor's Note

Sex is not just a physical act: It results from a combination of physiologic, affective and cognitive factors. Because of the complexity of sexual functioning—with both organic and psychological factors—it tends to be poorly understood. This issue of *Canadian Diabetes* provides us with 2 excellent papers on this sensitive subject (pages 2 and 5).

One of the more common complications of diabetes is sexual dysfunction, which affects approximately one-third of women and more than one-half of men with diabetes (1). The literature on prevalence is inconsistent, with estimates ranging from 11 to 80%; however, those of us in practice know that it is a common and sensitive indicator of poor glycemic control. Enzlin (1) showed that the prevalence of sexual dysfunction in a group of patients with type 1 diabetes was 27% for women and 22% for men. The Massachusetts Male Aging Study (3) showed the prevalence of erectile dysfunction (ED) to be 52%. While one can have sexual dysfunction without ED, it is unlikely that one would see ED without sexual dysfunction; once again the only consistency is inconsistency.

Women with diabetes and sexual dysfunction have different concerns and needs than men. In women with diabetes, sexual dysfunction is most closely related to psychosocial problems and depression (1). In the literature, there is little association between sexual dysfunction and glycemic control. Deterioration of glycemic control, however, is frequently associated with depression, which in turn is associated with sexual dysfunction. Therefore, in women, the predominance of psychosocial and depressive etiologies should not blind us to the possible role of blood glucose (BG) levels or the consequent vascular disease as the root cause or a contributory factor in sexual dysfunction.

Although commonly used synonymously, we should not confuse sexual dysfunction in men with ED, as they are 2 separate conditions. By concentrating on erectile function alone, we may do a disservice to the patient by failing to recognize other factors. There is a strong possibility that psychosocial and depressive factors affect men as much as they do women.

One common factor between men and women with diabetes is that sexual dysfunction is underdiagnosed and undertreated. We rarely diagnose sexual dysfunction unless we ask the right questions; thus, a complete sexual history must be part of our assessment of the patient with diabetes. Generally speaking, healthy or responsive sexual functioning involves the participation of a partner; therefore, diagnosis and treatment should involve both partners.

Patients are reluctant to discuss their sexual function, but once they do open up, they often describe a long and complex history that might have been dealt with years previously. The combined use of such tools as the Sexual Health Inventory for Men and the Hamilton Depression Scale will provide the clinician with objective information to assist diagnosis and treatment. The use of these tools is a good, non-judgemental trigger to elicit disclosure of extremely sensitive patient concerns.

ED is primarily a vascular and neuropathic disease; as with other microvascular complications of diabetes, the best treatment is prevention. It should be noted that our diagnosis of diabetes is based on the threshold at which microvascular complications (particularly retinopathy) start, and that the incidence of those complications is directly related to BG levels. The best way to avoid or control microvascular complications is to treat according to the Canadian Diabetes Association's Clinical Practice Guidelines (5). The vascular changes that lead to ED may be virtually eliminated by keeping preprandial BG <7.0 mmol/L, blood pressure ≤130/80 mm Hg, LDL-C ≤2.5 mmol/L, and by appropriate use of ACE inhibitors and ASA. ED in men is often the result of failure to adequately control glycemia and other comorbidities. Any symptoms of neuropathy, such as burning pain or dysthesia of the feet, decrease in fine touch, vibration or temperature sense should presume ED unless proven otherwise. Similarly, if vascular disease is present, we should always ask about adequacy of

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In This Issue

Sexual Dysfunction in Men With Diabetes

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INTRODUCTION

Erectile dysfunction (ED) is one of the most neglected complications of diabetes mellitus, mainly due to the psychosocial issues associated with it. Previously, both physicians and patients believed that sexual dysfunction was an inevitable consequence of aging. This misconception, coupled with the natural reluctance to discuss sexual problems and many physicians' discomfort with raising sexual issues, has resulted in this problem not being addressed properly.

EPIDEMIOLOGY AND PATHOPHYSIOLOGY

The Massachusetts Male Aging Study (MMAS), a longitudinal, epidemiological study of 1290 men age 40 to 70 years, found the mean probability of some degree of ED was 52%. For men with diabetes, the age-adjusted prevalence of complete ED was 28% vs. 9.6% among the general population (1). Other studies have shown that the prevalence of impotence among men with diabetes ranges from 35 to 75%, depending on age, duration of diabetes, glycemic control, body mass index (BMI) and other risk factors (presence of retinopathy, peripheral neuropathy, hypertension and dyslipidemia) (2,3).

ED is found among 50% of patients within 10 years of diagnosis of diabetes; in as many as 12%, ED is the presenting symptom. ED onset occurs 10 to 15 years earlier in men with diabetes compared with the general population (4).

Among populations with diabetes, a wide range of potential causes of ED exist. In men with diabetes, the prevalence of moderate to severe depressive symptoms ranges from 22% to 60% and is more pronounced in patients with diabetes-related complications (5). Despite this, physiologic factors are still the most prominent in the cause of ED in males with diabetes. The primary organic, pathophysiological factors causing diabetes-associated ED can be categorized as vascular, neurological and endocrinological.

Vasculopathy

Diabetes is associated with intimal, medial and luminal changes within the artery, leading to atherosclerosis. Atherosclerosis can affect the penile and pudendal arteries, limiting blood flow to the corpus cavernosum. Hypoxia in the corpus cavernosum leads to increased connective tissue synthesis and atrophy of smooth muscle. These structural changes correlate with an increased incidence of veno-occlusive dysfunction and erectile failure (6). An observational study by Wang examined males with diabetes with ED using sensitive ultrasound examinations after intracorporeal injection of PGE1 (7), and revealed an 87.2% incidence of moderate/severe cavernous arterial insufficiency. This increased to 100% when hypertension or alcohol abuse were added risk factors to diabetes.

In other studies, increased incidence of endothelial dysfunction was found as evidenced by reduced fibrinolysis, enhanced expression of endothelin-1, decreased prostacyclin release, increased adhesion molecule expression and increased platelet adhesion (8). A major consequence of endothelial dysfunction is decreased production and/or action of nitric oxide (NO). It has been documented that diabetic rats exhibit marked decrease in penile NO synthase (NOS) activity and a reduced neuronal NOS (nNOS) content in penile tissue (9).

Hyperglycemia in diabetes causes other metabolic changes that can affect penile physiology. Sobrevia and colleagues noted that elevated blood glucose (BG) causes regional hemodynamic changes and endothelial-dependent relaxation is also impaired. Protein kinase C is activated and oxygen free radicals are generated which inactivate NO and may cause further endothelial damage (10).

Neuropathy

Neural dysfunction that occurs early in diabetes involves the small unmyelinated nerve fibres that innervate the corpora cavernosum. Later, larger myelinated nerve fibres are involved, giving rise to peripheral neuropathy. This microangiopathy can damage the vasa nervorum and account for the early neural dysfunction. Bemelmans studied 27 impotent and 30 potent men with type 1 diabetes, and 102 impotent men without diabetes and determined that 85% of the impotent men with diabetes had some form of neuropathy vs. 40% of the potent men with diabetes and 44% of impotent men without diabetes (11).

Endocrinopathy/Hypogonadism

Diabetes lowers testosterone levels; thus, hypogonadism can be another factor contributing to ED in this population. Results from MMAS found that testosterone and sex hormone binding globulin (SHBG) levels were predictive of new cases of diabetes (12).

MANAGEMENT OF ED

Many men with diabetes (and their partners) experience sexual dysfunction but do not seek any form of treatment because they are not bothered by it or are embarrassed by it. Use of self-administered questionnaires such as the Sexual Health Inventory for Men have facilitated the evaluation of sexual concerns (13).

History should focus on the type of sexual problem (ED, premature ejaculation, loss of libido). Since diabetes and vascular disease often coexist, ED may be a marker of silent occlusive arterial disease; physicians should screen for hypertension, ischemic heart disease, peripheral vascular disease, retinopathy and renal impairment (14).

Perineal or pelvic trauma, previous pelvic surgery or radiation and especially lower-urinary-tract symptoms may affect erectile function. Neurologic manifestations of ED include constipation, diarrhea, orthostasis and postprandial fullness. Peripheral vascular disease as a cause of ED may manifest as buttock or thigh claudication.

Physical examination should include BMI, blood pressure, cardiac examination, identification of peripheral vasculopathy and examination of genitalia.

Autonomic neuropathy is frequently accompanied by loss of ankle jerks and absence or reduction of vibration sense over the large toes. More direct evidence on impairment of autonomic function can be demonstrated by a normal perianal sensation, assessing the tone of the anal sphincter during a rectal examination, and ascertaining the presence of an anal wink when the area of the skin adjacent to the anus is stroked or contraction of the anus when the glans penis is squeezed.

The 3 main treatment options for diabetes-associated ED are lifestyle changes, medical treatment or surgery.

Counselling on smoking cessation, alcohol use, nutrition and physical activity should be done, with the aim of improving general health and in turn improving sexual health.

It is widely believed that drugs cause ED; however, unless there is a strong temporal relationship (incidence of ED within 2 to 4 weeks of commencing a medication), there is no need to switch treatment. Antihypertensives likely to cause ED are thiazides and beta blockers (Table 1) (15,16).

MEDICAL TREATMENTS FOR ED

PDE5 inhibitors: Sildenafil, tadalafil and vardenafil are selective and competitive inhibitors of PDE5, shown to be effective and well-tolerated oral agents for treating ED of broad-spectrum etiology (17).

The normal pathway for penile erection is initiated by sexual arousal, which stimulates release of NO from nerve endings in the penis and vascular endothelial tissue. The NO in turn stimulates the guanylyl cyclase that increases production of cGMP (18). This leads to activation of cGMP-dependent protein kinase and lowering of intracellular calcium, resulting in smooth muscle relaxation and accumulation of blood in the corpus cavernosum (19). Therefore, cGMP is vital in the process of penile erection, which is constantly being degraded by the enzyme PDE5 (20). The PDE5 inhibitor reduces the degradation of cGMP and maintains a higher intracellular level of cGMP in both corpus cavernosum and the vessels supplying it. This increases relaxation of the smooth muscle which dilates the corporal sinusoids, resulting in increased blood flow and allowing an erection to occur.

The most commonly experienced adverse events were headache, flushing and dyspepsia (10 to 15% of patients, mild to moderate in nature). Visual disturbances (transient and mild colour tinge in vision, blurred vision) were experienced by 4% of patients receiving sildenafil.

Intraurethral therapy: The medicated urethral system for erection (MUSE®) contains alprostadil, which relaxes corpus cavernosal smooth muscle. Its action is discussed below.

Intracavernosal injection therapy: Use of alprostadil is a reliable option for treating ED. Its effect is often superior to that of PDE5 inhibitors (21).

Table 1. Medications that could cause ED commonly used in patients with diabetes

Antihypertensive agents	ACE inhibitors Angiotensin II receptor blockers Beta blockers Methyldopa Thiazide diuretics Spironolactone Calcium channel blockers
Agents acting on the central nervous system	Phenothiazines Tricyclic antidepressants Antipsychotics Selective serotonin reuptake inhibitors*
Agents acting on the endocrine system	Alcohol Antiandrogens Cimetidine Estrogens GnRH agonists and antagonists Marijuana Metoclopramide Spironolactone

*Usually ejaculatory delay, but anorgasmia may lead to ED

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PGE1: Alprostadil, or PGE1, mediates relaxation of corpus cavernosum smooth muscle by increasing the intracellular concentration of cAMP in corpus cavernosum smooth muscle (22). PGE1 may also act by inhibiting the release of noradrenaline from sympathetic nerves (23) and suppressing angiotensin II secretion in the cavernosal tissues (24).

Papaverine: In vitro, papaverine induces relaxation of corpus cavernosum smooth muscle, cavernous sinusoids, penile arteries and penile veins and attenuates contractions caused by stimulation of adrenergic nerves and exogenous noradrenaline (25,26).

Phentolamine: Phentolamine is a non-selective alpha-adrenoceptor antagonist with similar affinity for alpha1- and alpha2-adrenoceptors. It induces the relaxation of corpus cavernosum erectile tissue by antagonism of the alpha1 and alpha2-adrenoceptors (27).

Combination therapy: Phentolamine, papaverine and PGE1 are the agents most commonly used in combination therapy; combination therapy is not only more efficacious, it is also associated with a reduction in side effects.

Vacuum constriction device (VCD): These cause rigidity by creating negative pressure suction and trapping the blood in the penis with an elastic band, disc or O ring around the base of the penile shaft. Constriction can be maintained without risk for 30 minutes (28).

The VCD causes penile rigidity sufficient for vaginal penetration in ~80% of men, however, the dropout rate may as high as 50% (29). Complications are usually minor (e.g. petechiae due to rupture of capillaries after use).

Penile implants: These are usually considered for patients who do not respond to less-invasive forms of therapy. Several types of implants—including inflatable and non-inflatable—malleable devices, are available. Patient satisfaction with this procedure is ~90%. Recent reports on the 5-year mechanical survival rate are 90 to 95% (30,31).

Hormone Replacement: Testosterone replacement for the treatment of hypogonadism may correct sexual dysfunction. This can be achieved with oral agents, topical gels and creams or intramuscular injection (32). Daily use of these preparations raises serum testosterone concentration to within the normal range in >90% of men (33-34).

FUTURE TREATMENTS

Combinations of existing oral agents have the potential benefit of similar efficacy at lower doses than monotherapy and, thus, reduced adverse effects. Usually drugs acting on different pathways are combined, such as combining a PDE5 inhibitor with tamsulosin, an alpha-adrenoceptor antagonist (35). There is no data available to prove whether any combination is more effective than single agent.

Another option is non-invasive direct administration of the active agent into the penile corpora cavernosa that could ensure retention of the active compound in the corpora with little systemic dissemination (36).

If a compound has both a PDE5 inhibitor as well as an NO donor, it would provide a sustained production of NO combined with the inhibition of cGMP breakdown. Preliminary results on this combination are encouraging (37). In animal studies, potassium channel openers have been found to relax penile resistance arteries, and can induce vasodilation with PGE1 and other drugs used in ED treatment (38).

Other drugs in development include calcitonin gene-related peptide (CGRP), a neurotransmitter localized in the corpora cavernosa that declines with age (39). An intracavernosal injection of PGE1 and CGRP was effective in a series of patients in whom other ED treatments had been unsuccessful (40).

CONCLUSION

ED is an oft-neglected complication of diabetes that is under-recognized and undertreated. However, knowledge on ED is rapidly expanding. Many pharmacological, mechanical and surgical treatment options are available to manage diabetes-associated ED. Healthcare professionals involved in the care of people with diabetes should be aware of this issue and its management.

REFERENCES

1. Feldman HA, Goldstein I, Hatzichristou D, et al. Impotence and its medical and psychosocial correlates: Results of the Massachusetts Male Aging Study. *J Urol*. 1994;151:54-61.
2. Romeo JH, Seftel AD, Madhun ZT, et al. Sexual function in men with diabetes type 2: Association with glycemic control. *J Urol*. 2000;163:788-891.
3. Klein R, Klein BE, Lee KE, et al. Prevalence of self reported erectile dysfunction in people with long term IDDM. *Diabetes Care*. 1996;19:135-141.
4. Lewis RW. Epidemiology of erectile dysfunction. *Urol Clin North Am*. 2001;28:209-215.
5. Musselman DL, Betan E, Larsen H, et al. Relationship of depression to diabetes types 1 and 2: Epidemiology, biology and treatment. *Biol Psychiatry*. 2003;54:317-329.
6. Azadzoi KM, Siroky MB, Goldstein I. Study of etiologic relationship of arterial atherosclerosis to corporeal veno-occlusive dysfunction in the rabbit. *J Urol*. 1996;155:1795-1800.
7. Wang CJ, Shen SY, Wu CC, et al. Penile blood flow study in diabetic impotence. *Urol Int*. 1993;50:209-212.
8. De Angelis L, Marfella MA, Siniscalchi M, et al. Erectile and endothelial dysfunction in type II diabetes: A possible link. *Diabetologia*. 2001;44:1155-1160.
9. Vernet D, Cai L, Garban H, et al. Reduction of penile nitric oxide synthase in diabetic BB/WORdp (type I) and BBZ/WORdp (type II) rats with erectile dysfunction. *Endocrinology*. 1995;136:5709-5717.
10. Sobrevia L, Mann GE. Dysfunction of the endothelial nitric oxide signaling pathway in diabetes and hyperglycemia. *Exp Physiol*. 1997;82:423-452.
11. Bemelmans BL, Meuleman EJ, Doesburg WH, et al. Erectile dysfunction in diabetic men: The neurological factor revisited. *J Urol*. 1994;151:884-889.
12. Stellato RK, Feldman HA, Hamdy O, et al. Testosterone, sex hormone-binding globulin and the development of type II diabetes in middle aged men: Prospective results from the Massachusetts male aging study. *Diabetes Care*. 2000;23:490-494.
13. Rosen RC, Riley A, Wagner G, et al. The international index of erectile function (IIEF): A multidimensional scale for assessment of erectile dysfunction. *Urology*. 1997;49:822-830.
14. Williams SB, Goldfine AB, Timimi FK, et al. Acute hyperglycemia attenuates endothelium dependent vasodilation in humans in vivo. *Circulation*. 1998;97:1695-1701.
15. Chang SW, Fine R, Siegel D, et al. The impact of diuretic therapy on reported sexual function. *Arch Intern Med*. 1991;151:2402-2408.
16. Mitchell JE, Popkin MK. Antipsychotic drug therapy and sexual dysfunction in men. *Am J Psychiatry*. 1982;139:633-637.
17. Montorsi F, McDermott TE, Morgan R. Efficacy and safety of fixed dose oral Sildenafil in the treatment of erectile dysfunction of various etiologies. *Urology*. 1999;53:1011-1018.
18. Burnett AL, Lowenstein CJ, Bredt DS, et al. Nitric oxide: A physiologic mediator of penile erection. *Science*. 1992;257:401-403.
19. Carvajal JA, Germain AM, Huidobro-Toro JP, et al. Molecular mechanism of cGMP mediated smooth muscle relaxation. *J Cell Physiol*. 2000;184:409-420.
20. Kuthe A, Montorsi F, Andersson KE, et al. Phosphodiesterase inhibitors for the treatment of erectile dysfunction. *Curr Opin Investig Drugs*. 2002;3:1489-1495.
21. Shabsigh R, Padma-Nathan H, Gittleman M, et al. Intracavernous alprostadil alphadex (Edex/Viridal) is effective and safe in patients with erectile dysfunction after failing sildenafil (Viagra). *Urology*. 2000;55:477-480.
22. Lin JS, Lin YM, Jou YC, et al. Role of cyclic adenosine monophosphate in prostaglandin E1 induced penile erection in rabbits. *Eur Urol*. 1995;28:259-265.
23. Molderings GJ, van Ahlen H, Gothert M. Modulation of noradrenaline release in human corpus cavernosum by presynaptic prostaglandin receptors. *Int J Impot Res*. 1992;4:19-25.
24. Kifor I, Williams GH, Vickers MA, et al. Tissue angiotensin II as a modulator of erectile function, I. Angiotensin peptide content, secretion and effects in the corpus cavernosum. *J Urol*. 1997;157:1920-1925.
25. Kirkeby HJ, Forman A, Andersson KE. Comparison of the papaverine effects on isolated human penile circumflex veins and corpus cavernosum. *Int J Impot Res*. 1990;2:49-54.
26. Iguchi M, Nakajima T, Hisada T, et al. On the mechanism of papaverine inhibition of the voltage

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Sexual Dysfunction in Women With Diabetes

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INTRODUCTION

Both women and men with diabetes can experience urologic complications, including bladder dysfunction, urinary tract infections and sexual dysfunction. In men with diabetes, physical factors such as vascular disease and autonomic neuropathy have been identified as predominant causes of sexual dysfunction (1). However, there is currently little research and limited understanding of female sexual dysfunction associated with diabetes (2).

Female sexual dysfunction has been classified as sexual desire disorders, sexual arousal disorders, orgasmic disorders and sexual pain disorders (3). It is a highly complex problem that can be affected by multiple factors including psychogenic, neurogenic and hormonal influences (4). In particular, physical issues such as weight gain, disfigurement from lipoatrophy and psychological issues such as depression, anxiety, worry or altered body image can significantly affect women's sexual function (5).

PREVALENCE OF SEXUAL DYSFUNCTION IN WOMEN WITH DIABETES

Prevalence estimates are difficult to determine and reports vary widely. This is likely due to the fact that most studies are small and use retrospective self-reported questionnaires. Enzlin and colleagues surveyed 240 patients with type 1 diabetes and found that sexual dysfunction was reported by 27% of women and 22% of men. In women, sexual dysfunction was related to depression while in men it was related to age, body mass index (BMI), duration of diabetes and diabetes complications (6).

Interestingly, Jensen (7) reported no significant difference in the prevalence of sexual dysfunction in a group of type 1 women with diabetes (27.5%) and an age-matched healthy control group (25%). However, when men with diabetes were compared with a control group, 44% reported sexual dysfunction compared with 12.5% control in the control group (8).

In a recent study, Doruk and colleagues (9) compared sexual dysfunction between women with type 1 and type 2 diabetes. The prevalence of sexual dysfunction was 71% in type 1 diabetes, which is much greater than previous studies have reported (6,7). In type 2 women with diabetes, the prevalence of sexual dysfunction was 42% and the control group was 37%. No significant risk factors were identified that were predictive of sexual dysfunction in the women with diabetes. However, the women with type 1 diabetes had a longer duration of diabetes (9).

Sexual function in women with diabetes may be affected by such complications as neuropathy or vascular disease.

SYMPTOMS OF SEXUAL DYSFUNCTION

In a study of 48 women with diabetes (10), one-half reported ≥1 of the following symptoms: decreased libido, slow arousal, inadequate lubrication, anorgasmia or dyspareunia. No significant relationship was seen between glycemic control, duration of diabetes or the presence of complications of diabetes. When comparing women with type 2 diabetes and age-matched healthy controls, Erol and colleagues (11) found that lack of libido, diminished clitoral sensation, vaginal dryness, vaginal discomfort and orgasmic dysfunction were all significantly higher in the women with type 2 diabetes. Lower quality of marital relations and increased depressive symptoms have also been described in women with type 1 diabetes with sexual dysfunction (12).

A qualitative study by LeMone (13) to assess sexuality in women with diabetes identified consistent themes, including: fatigue, decreasing sexual desire, changes in perimenstrual blood glucose (BG) control, vaginitis, decreased vaginal lubrication and increased time to reach orgasm. In addition, one woman described her hesitation to ask her physician about changes in her sexual function and a frustration with the lack of information available.

PATHOPHYSIOLOGY

Sexual function in women with diabetes may be affected by such complications as neuropathy or vascular disease. However, in contrast to male sexual dysfunction, it appears that the major contributing factor in women is psychological distress and depression.

Erol and colleagues (14) assessed the function of the somatic sensory system in genital and non-genital sites for a small group of women with diabetes and controls using biothesiometry and threshold sensory values. Somatic sensory sensation was found to be decreased in women with diabetes; however, this did not correlate with sexual function as measured by a self-administered questionnaire.

Women with diabetes with neuropathy have also been found to have more symptoms of depression and sexual dysfunction than those without neuropathy. A significant positive correlation between the degree of depression and sexual dysfunction has been noted, which suggests a psychological component in addition to neuropathy (15). This study did not examine for an independent relationship between neuropathy and sexual dysfunction (i.e. controlling for depression); therefore, it is possible that the sexual dysfunction noted in those with neuropathy is really a result of depression and not neuropathy per se. Indeed, depression has been

reported as a significant predictor for sexual dysfunction in women with type 1 diabetes independent of neuropathy (12,16). Sexual dysfunction has not been found to be associated with age, BMI, glycemic control, duration of diabetes, menopausal status, use of medications, or complications (12,16). Other psychological factors, such as psychological distress and degree of acceptance of chronic disease, have also been reported as predictors of sexual dysfunction in women with diabetes (17).

LIMITATIONS

The literature on sexual dysfunction in women is limited. While it has been recognized for several years that diabetes can negatively affect a woman's sexual function, it has only been in recent years that we have seen studies examining the epidemiology, pathophysiology and impact of sexual dysfunction in women with diabetes. It should be noted, however, that the studies reviewed presently are all small and principally community-based, and likely do not provide an accurate estimate of the scope of the issue. The literature is largely descriptive, highlighting the fact that there appears to be a higher incidence of sexual dysfunction in women with diabetes compared to those without. However, the literature is lacking analytic or explanatory studies that would increase our understanding of how various physiologic and psychosocial correlates are associated with sexual dysfunction in women with diabetes.

CONCLUSIONS

Despite the well-known problems with male sexual dysfunction associated with diabetes, it is important to remember that women with diabetes are also at risk. Most importantly, women with diabetes with sexual dysfunction are more likely to have associated depression, poor relationship satisfaction and poor adjustment to their chronic disease. There is increasing recognition that psychosocial factors such as depression increase not only one's risk for diabetes (18), but also increase the risk of adverse outcomes such as cardiovascular disease (19), and sexual dysfunction. Given this, regular assessment of psychosocial functioning and depression screening would appear prudent.

Treatment should focus on the underlying problems, such as depression, and the alleviation of aggravating factors, e.g. using vaginal lubricants. Whenever possible, a multidisciplinary team approach should be utilized, including psychology, marriage counsellors and therapists. However it should be noted that there are very limited therapeutic options for women with diabetes and sexual dysfunction, and that few trials have examined the efficacy of available interventions on improving sexual function in women with diabetes. Sexual dysfunction in women with diabetes should be assessed during routine clinical visits to ensure that a good quality of life is maintained and that underlying depression or distress can be addressed.

REFERENCES

1. Brown JS, Wessells H, Chancellor MB, et al. Urologic complications of diabetes. *Diabetes Care*. 2005;28:177-185.
2. Rutherford D, Collier A. Sexual dysfunction in women with diabetes mellitus. *Gynecol Endocrinol*. 2005;21:189-192.
3. Basson R, Berman J, Burnett A, et al. Report of the international consensus development conference on female sexual dysfunction: Definitions and classifications. *J Urol*. 2000;163:888-893.
4. Muniyappa R, Norton M, Dunn ME, et al. Diabetes and female sexual dysfunction: moving beyond "benign neglect." *Curr Diab Rep*. 2005;5:230-236.
5. Meeking D, Fosbury J, Cradock S. Assessing the impact of diabetes on female sexuality. *Community Nurse*. 1997;3:50-52.
6. Enzlin P, Mathieu C, Van Den BA, et al. Prevalence and predictors of sexual dysfunction in patients with type 1 diabetes. *Diabetes Care*. 2003;26:409-414.
7. Jensen SB. Sexual dysfunction in younger insulin-treated diabetic females. A comparative study. *Diabete Metab*. 1985;11:278-282.
8. Jensen SB. Diabetic sexual dysfunction: A comparative study of 160 insulin treated diabetic men and women and an age-matched control group. *Arch Sex Behav*. 1981;10:493-504.
9. Doruk H, Akbay E, Cayan S, et al. Effect of diabetes mellitus on female sexual function and risk factors. *Arch Androl*. 2005;51:1-6.
10. Campbell LV, Redelman MJ, Borkman M, et al. Factors in sexual dysfunction in diabetic female volunteer subjects. *Med J Aust*. 1989;151:550-552.
11. Erol B, Tefekli A, Ozbey I, et al. Sexual dysfunction in type II diabetic females: A comparative study. *J Sex Marital Ther*. 2002;28(suppl 1):55-62.
12. Enzlin P, Mathieu C, Van Den BA, et al. Sexual dysfunction in women with type 1 diabetes: A controlled study. *Diabetes Care*. 2002;25:672-677.
13. LeMone P. The physical effects of diabetes on sexuality in women. *Diabetes Educ*. 1996; 22:361-366.
14. Erol B, Tefekli A, Sanli O, et al. Does sexual dysfunction correlate with deterioration of somatic sensory system in diabetic women? *Int J Impot Res*. 2003; 15:198-202.
15. Leedom L, Feldman M, Procci W, et al. Symptoms of sexual dysfunction and depression in diabetic women. *J Diabet Complications*. 1991;5:38-41.
16. Newman AS, Bertelson AD. Sexual dysfunction in diabetic women. *J Behav Med*. 1986; 9:261-270.
17. Jensen SB. The natural history of sexual dysfunction in diabetic women. A 6-year follow-up study. *Acta Med Scand*. 1986; 219:73-78.
18. Brown LC, Majumdar SR, Newman SC, et al. History of depression increases risk of type 2 diabetes in younger adults. *Diabetes Care*. 2005;28:1063-1067.
19. Rosengren A, Hawken S, Ounpuu S, et al. Association of psychosocial risk factors with risk of acute myocardial infarction in 11119 cases and 13648 controls from 52 countries (the INTERHEART study): Case-control study. *Lancet*. 2004;364:953-962.

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dependent calcium current in isolated smooth muscle cells from the guinea pig trachea. *J Pharmacol Exp Ther*. 1992;263:194-200.
27. Traish A, Gupta S, Gallant C, et al. Phentolamine mesylate relaxes penile corpus cavernosum tissue by adrenergic and non adrenergic mechanisms. *Int J Impot Res*. 1998;10:215-223.
28. Oakley N, Moore KT. Vacuum devices in erectile dysfunction: Indications and efficacy. *Brit J Urol*. 1998;82:673-681.
29. Dutta TC, Eid JF. Vacuum constriction devices for erectile dysfunction: A long-term prospective study of patients with mild, moderate and severe dysfunction. *Urology*. 1999;54:891-893.
30. Deuk Choi Y, Jin Choi Y Hwan Kim J, et al. Mechanical reliability of the AMS 700 CMX inflatable penile prosthesis for the treatment of male erectile dysfunction. *J Urol* 2001;165:822-4.
31. Debocq F, Tefilli MV, Gheilder EL, et al. Long-term mechanical reliability of multicomponent inflatable penile prosthesis: Comparison of device survival. *Urology*. 1998;52:277-281.
32. Morales A, Johnston B, Heaton JW, et al. Oral androgens in the treatment of hypogonadal impotent men. *J Urol*. 1994;152:1115-1118.
33. Meikle AW, Mazer NA, Moellmer JF, et al. Enhanced transdermal delivery across nonscrotal skin produces physiological concentrations of testosterone and its metabolites in hypogonadal men. *J Clin Endocrinol Metab*. 1992;74:623-628.
34. Wang C, Berman N, Longstreth JA, et al. Pharmacokinetics of transdermal testosterone gel in hypogonadal men: Application of gel at one site versus four sites. A general clinical research centre study. *J Clin Endocrinol Metab*. 2000;85:964-969.
35. Anderson KE, Hedlund P. New directions for erectile dysfunction therapies. *Int J Impot Res*. 2002; 14(Suppl 1):S82-S92.
36. Hellstrom WJ, Amar E. 2nd International Consultation on Erectile and Sexual Dysfunction. Paris, France; 2003.
37. Seidler M, Uckert S, Waldkirch E, et al. In vitro effects of a novel class of nitric oxide (NO) donating compounds on isolated human erectile tissue. *Eur Urol*. 2002;42:523-528.
38. Ruiz Rubio JL, Hernandez M, Rivera de los Arcos L, et al. Role of ATP-sensitive K+ channels in relaxation of penile resistance arteries. *Urology*. 2004;63:800-805.
39. Bivalacqua TJ, Champion HC, Abdel-Mageed AB, et al. Gene transfer of prepro-CGRP restores erectile function in the aged rat. *Biol Reprod*. 2001; 65:1371-1377.
40. Truss MC, Becker AJ, Thon WF, et al. Intracavernous calcitonin gene-related peptide plus prostaglandin E1: Possible alternative to penile implants in selected patients. *Eur Urol*. 1994;26:40-45.

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confondre dysfonction sexuelle chez l'homme et dysfonction érectile, car il s'agit de deux problèmes différents. En se concentrant sur la dysfonction érectile, on pourrait rendre un mauvais service aux patients puisqu'on négligerait d'autres facteurs. Il est fort possible que des facteurs psychologiques et dépressifs entrent en jeu chez l'homme autant que chez la femme.

Un facteur que les hommes et les femmes atteints de diabète ont en commun est que la dysfonction sexuelle est sous-diagnostiquée et insuffisamment traitée. Il est difficile de diagnostiquer la dysfonction sexuelle sans poser les bonnes questions; la détermination de tous les antécédents sexuels doit donc faire partie de l'évaluation des patients atteints de diabète. En général, un fonctionnement sexuel sain, soit réceptif, comporte la participation d'un partenaire. Par conséquent, le diagnostic et le traitement doivent intéresser les deux partenaires.

Les patients hésitent à discuter de fonction sexuelle, mais une fois qu'ils le font, ils décrivent souvent des problèmes complexes et de longue date qui auraient pu être réglés depuis de nombreuses années. Ensemble, des outils tels que le questionnaire SHIM (*Sexual Health Inventory for Men*) et l'échelle de dépression de Hamilton procurent au clinicien les renseignements objectifs qui faciliteront le diagnostic et le traitement. Ces outils constituent un bon moyen d'obtenir qu'un patient exprime ses préoccupations les plus intimes sans craindre d'être jugé.

La dysfonction érectile est principalement une maladie vasculaire et neuropathique. Comme pour les autres complications microvasculaires du diabète, le meilleur traitement est la prévention. Il ne faut pas oublier que le diagnostic de diabète est basé sur le seuil auquel les complications microvasculaires (surtout la rétinopathie) se manifestent et que l'incidence de ces complications est directement liée à la glycémie. La meilleure façon de prévenir ou de maîtriser les complications microvasculaires est de traiter les patients selon les Lignes directrices de pratique clinique de l'Association canadienne du diabète (5). Les modifications vasculaires qui aboutissent à la dysfonction érectile peuvent être pratiquement éliminées si on garde la glycémie préprandiale à $< 7,0$ mmol/L, la pression sanguine à $\leq 130/80$ mm Hg et le cholestérol LDL à $\leq 2,5$ mmol/L, et si on utilise convenablement un inhibiteur de l'ECA et l'AAS. La dysfonction érectile est souvent le résultat d'un mauvais contrôle de la glycémie et de troubles concomitants. Tout symptôme de neuropathie, tel que douleur à type de brûlure ou dysthésie des pieds, baisse du seuil de sensibilité du toucher fin et baisse de la perception de la vibration ou de la température, doit être évocateur d'une dysfonction érectile, à moins d'indication contraire. Dans le même ordre d'idées, en présence d'une affection vasculaire, il faut toujours demander au patient si ses érections sont suffisantes, compte tenu de l'impuissance iatrogénique attribuable aux médicaments et/ou à l'andropause. Heureusement, les inhibiteurs de la PDE5 permettent maintenant un traitement simple et souvent efficace de la dysfonction érectile. Nous pouvons offrir un soulagement de ce symptôme, mais nous devons nous rappeler que les troubles érectiles sont la plupart du temps attribuables à l'échec du traitement de la maladie initiale et il faut en tenir compte dans le plan de traitement.

La dysfonction sexuelle est une complication courante du diabète qui est sous-diagnostiquée et insuffisamment traitée, aboutissant à un important fardeau morbide non seulement chez les personnes atteintes de diabète, mais aussi chez leur partenaire et leur famille. La prévention, le diagnostic et le traitement de la dysfonction sexuelle doivent faire partie de notre plan de traitement. Nous disposons maintenant de traitements efficaces pour de nombreuses personnes atteintes de dysfonction érectile, mais il ne faut pas oublier que la fonction sexuelle est multifactorielle et que, pour donner des soins de santé intégrés aux patients, nous devons envisager tous les facteurs possibles.

RÉFÉRENCES

1. Enzlin P, Mathieu C, Van Den BA, et al. Prevalence and predictors of sexual dysfunction in patients with type 1 diabetes. *Diabetes Care*. 2003;26:409-414.
2. Klein R, Klein BE, Lee KE, et al. Prevalence of self reported erectile dysfunction in people with long term IDDM. *Diabetes Care*. 1996;19:135-141.
3. Feldman HA, Goldstein I, Hatzichristou DG, et al. Impotence and its medical and psychosocial correlates: results of the Massachusetts male aging study. *J Urol*. 1994;151:54-61.
4. Wang CJ, Shen SY, Wu CC, et al. Penile blood flow study in diabetic impotence. *Urol Int*. 1993;50:209-212.
5. Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2003 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes*. 2003;27(suppl 2):S1-S152.

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erections, taking into account iatrogenic impotence due to medications and/or male andropause. Fortunately, PDE5 inhibitors now offer a simple and frequently effective treatment for ED; but while we can offer relief of this symptom, we must be mindful that erectile difficulties are most commonly due to a failure to control the primary disease and this should be addressed in the treatment plan.

Sexual dysfunction is a common complication of diabetes that is underdiagnosed and undertreated, resulting in a significant burden of disease not only to people with diabetes but also their partners and families. Prevention, recognition and treatment of sexual dysfunction need to be part of our management plan. We now have effective treatments for many people with ED but we need to remember that sexual function is multifactorial and, in order to give comprehensive care to the patient, we need to consider all possible factors.

REFERENCES

1. Enzlin P, Mathieu C, Van Den BA, et al. Prevalence and predictors of sexual dysfunction in patients with type 1 diabetes. *Diabetes Care*. 2003;26:409-414.
2. Klein R, Klein BE, Lee KE, et al. Prevalence of self reported erectile dysfunction in people with long term IDDM. *Diabetes Care*. 1996;19:135-141.
3. Feldman HA, Goldstein I, Hatzichristou DG, et al. Impotence and its medical and psychosocial correlates: results of the Massachusetts male aging study. *J Urol*. 1994;151:54-61.
4. Wang CJ, Shen SY, Wu CC, et al. Penile blood flow study in diabetic impotence. *Urol Int*. 1993;50:209-212.
5. Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2003 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes*. 2003;27(suppl 2):S1-S152.

Message à nos lecteurs

Dans la dernière édition de notre journal, le titre en français de l'article des Dr Pacaud et Meltzer a été incorrectement traduit. Le titre aurait du se lire ainsi: "Mieux vaut prévenir que guérir". Nos excuses à nos fidèles lecteurs.

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La dysfonction sexuelle et le diabète : un secret bien gardé

J. Robin Conway, M.D. et Danièle Pacaud, M.D., FRCPC

Note de la rédaction

Un rapport sexuel n'est pas un simple acte physique : c'est le résultat d'une combinaison de facteurs physiologiques, affectifs et cognitifs. Le fonctionnement sexuel étant complexe, c'est-à-dire qu'il comporte des facteurs organiques et psychologiques, il est plutôt mal compris. Ce numéro de *Le diabète au Canada* contient deux excellents articles sur ce sujet délicat (pages 2 et 5).

Une des complications les plus courantes du diabète est la dysfonction sexuelle, qui touche environ le tiers des femmes et plus de la moitié des hommes (1). Dans la littérature médicale, les chiffres varient, les estimations de la prévalence allant de 11 à 80 %. Toutefois, nous, comme médecins en exercice, savons que la dysfonction sexuelle est un indicateur courant et sensible d'un piètre contrôle de la glycémie. Enzlin (1) a démontré que la prévalence de la dysfonction sexuelle dans un groupe de patients atteints de diabète de type 1 était de 27 % chez les femmes et de 22 % chez les hommes. L'étude *Massachusetts Male Aging Study* (3) a révélé que la prévalence de la dysfonction érectile était de 52 %. Il peut y avoir dysfonction sexuelle sans dysfonction érectile, mais il est peu probable qu'il y ait dysfonction érectile sans dysfonction sexuelle. Encore là, tout ce qui est constant est l'irrégularité.

Les femmes atteintes de diabète et de dysfonction sexuelle ont des préoccupations et des besoins différents de ceux des hommes. Chez les femmes atteintes de diabète, la dysfonction sexuelle est plus étroitement liée à des problèmes psychosociaux et à la dépression (1). Dans la littérature médicale, on fait peu de lien entre la dysfonction sexuelle et le contrôle de la glycémie. Une dégradation du contrôle de la glycémie est toutefois fréquemment associée à une dépression, laquelle est associée à une dysfonction sexuelle. Ainsi, chez les femmes, la prédominance des étiologies psychosociale et dépressive ne doit pas nous faire oublier le rôle possible de la glycémie ni de la maladie vasculaire qui en résulte comme cause profonde de la dysfonction sexuelle ou comme facteur y contribuant.

Même si les deux termes sont souvent employés comme synonymes, il ne faut pas

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