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Abstract- Spinal cord injured (SCI) patients have sexual disorders including erectile dysfunction (ED), impotence, priapism, ejaculatory dysfunction and infertility. Treatments for erectile dysfunction include four steps. Step 1 involves smoking cessation, weight loss, and increasing physical activity. Step 2 is phosphodiesterase type 5 inhibitors (PDE5I) such as Sildenafil (Viagra), intracavernous injections of Papaverine or prostaglandins, and vacuum constriction devices. Step 3 is a penile prosthesis, and Step 4 is sacral neuromodulation (SNM). Priapism can be resolved spontaneously if there is no ischemia found on blood gas measurement or by Phenylephrine. For anejaculatory dysfunction, massage, vibrator, electrical stimulation and direct surgical biopsy can be used to obtain sperm which can then be used for intra-uterine or in-vitro fertilization. Infertility treatment in male SCI patients involves a combination of the above treatments for erectile and anejaculatory dysfunctions. The basic approach to and management of sexual dysfunction in female SCI patients are similar as for men but do not require treatment for erectile or ejaculatory problems.

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Introduction

Spinal trauma complicated by spinal cord injury (SCI) is a devastating event on a personal and family level, as well as a great financial burden to society because of its attendant morbidity, expense, and prolonged treatment requirements (1, 2).

The prevalence of SCI has been evaluated in two papers reporting ranges from 110 to 1120 and 223 to 755 per million people (3,4). In a population based study, the point prevalence of SCI in Tehran was 440/million (95% CI: 120-1140) (5). In Tehran, the incidence was 98/million in males and 47/million in females (6). SCI complications were evaluated in 5995 complete motor SCI (ASIA A and B) patients supported by the Welfare Organization in Iran (7). The prevalence of sexual dysfunction in males was 32.4% and in females was 13.9%. Prevalence of infertility was 12.1% and 7.0% in males and females, respectively.

Materials and Methods

A literature review was performed using the terms “spinal cord”, “injury”, “patient”, “treatment”, “management”, “sex”, “sexual”, and “erectile dysfunction” in PubMed from 1966 to 20th July 2011. The reference lists of the identified articles were also reviewed.

Results

There is less known about SCI-related sexual dysfunction in females than in males. However, these studies have shown that when vaginal stimulation is done in SCI females and a normal control group, orgasm will happen in 100% of normal controls but in less than 50% of T12-L1 SCI patients. In females with S2-S5 lesions, only 17% achieved orgasm (8).

In female SCI patients, fertility is possible. However, pregnancy needs careful observation for autonomic dysreflexia. For delivery, Oxytocin induction is contra-indicated but epidural anesthesia is recommended to decrease the risk of autonomic dysreflexia. Careful observation for bed sores, urinary tract infections (UTI), leg edema, thrombophlebitis, transient ischemic attack (TIA) and anemia is important. Meanwhile, sequential breast examination is necessary. In patients with cervical lesions, lactation typically continues for 3 months and then stops because of lack of stimulation.

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Most men with SCI are infertile. Erectile dysfunction (ED), ejaculatory dysfunction and semen abnormalities contribute to the problem. Although sperm count is normal in SCI men, sperm motility is low. There is abnormal sperm viability and morphology, too. Genitourinary infection and endocrine abnormalities can also be present (9-11).

Erectile dysfunction (ED)

ED is defined by the National Institutes of Health (NIH) as the inability to achieve or maintain an erection sufficient for satisfactory sexual performance. ED is the most common sexual problem in men (10). The incidence increases with age and affects up to one third of men throughout their lives. It causes a considerable negative impact on close relationships, quality of life, and confidence (12).

ED pathophysiology

ED may result from variety of psychological and/or organic causes including vascular, neurogenic, hormonal, anatomic and drug-induced conditions. A normal sexual erectile response results from the interaction between neurotransmitters and vascular smooth muscle initiated by parasympathetic and sympathetic neuronal triggers that combine physical stimulation of the penis with sexual perception and desire. Nitric oxide produced from endothelial cells after parasympathetic stimuli triggers a molecular cascade that results in smooth muscle relaxation and arterial influx of blood into the corpus cavernosum. Then, compression of venous return occurs, and an erection arises (13).

History taking and physical examination

In a patient with SCI, history and physical examination are adequate in making an accurate diagnosis of ED in most cases. Sexual history should focus on erection adequacy, altered libido, quality and timing of orgasm, volume and form of ejaculate, presence of sexually-induced genital pain or penile curve and partner sexual function.

The physical examination should evaluate blood pressure and heart rate; body habitus, for central obesity; and cardiovascular, neurologic, and genitourinary systems, including penile, testicular, and digital rectal examinations.

Laboratory tests

Laboratory workup is not initially necessary in SCI patients. However, if the first line of treatment for ED is not successful, laboratory assessment is recommended to include a fasting blood glucose level and lipid panel, thyroid-stimulating hormone, and testosterone level (14).

Conservative management

First-line therapy for ED consists of lifestyle changes, modifying drug therapy that may cause ED, and pharmacotherapy with phosphodiesterase type 5 inhibitors (PDE5I). Obesity, inactive lifestyle, and smoking greatly increase the risk of ED. Grade A treatment recommendations, based on high-quality patient-oriented studies, suggest that PDE5I are the most effective oral drugs for the treatment of ED in SCI patients (15,16). Retail sales of the three most popular PDE5Is Sildenafil (Viagra), Tadalafil (Cialis), and Vardenafil (Levitra) approached $1.48 billion in 2007 (17).

Compared with placebo, Sildenafil has been shown to improve erections (74% versus 21%) (18) and results in more frequent intercourse attempts (57% versus 21%) (19).

Approximately one third of men with ED do not respond to therapy with PDE5 inhibitors. In addition, these agents are not effective for improving libido (20).

The three PDE5I are considered to be somewhat similar in effectiveness, but there are differences in dosing, onset of action, and duration of therapeutic effect (21).

The standard dose for Sildenafil is 50 to 100 mg daily. Recommended time between onset of dosing and intercourse is one hour. Drug action starts in 14 to 60 minutes and drug duration extends for up to four hours. Tadalafil and Vardenafil dose is 10 to 20 mg daily. Although the duration of action in Vardenafil and Sildenafil are similar, the duration of action for Tadalfil is up to 36 hours.

There are no conclusive data to suggest that one PDE5I is better than others. An open-label trial established that patients preferred Tadalafil and Vardenafil over Sildenafil (22). However, nearly all evidence supports equal efficacy between Sildenafil and Vardenafil (23).

Headache is the most frequently reported side effect of PDE5Is, occurring in roughly 10% of patients. PDE5Is should not be taken simultaneously with nitrates because this may lead to a synergistic effect, resulting in a potentially severe, even lethal, decrease in blood pressure.

The most frequent predictor of success for PDE5I is upper motor neuron (UMN) lesion. Most patients

tolerate these medications well, and in a meta-analysis, only 1% of patients discontinued their PDE5I. However, PDE5Is had no positive effect on ejaculation except in one study (24).

Testosterone

There is a limited indication for testosterone in SCI patients. Testosterone supplementation in men with hypogonadism improves ED and libido but requires interval monitoring of hemoglobin, serum transaminase, and prostate-specific antigen levels because of an increased risk of prostate adenocarcinoma (25,26).

Intracavernosal pressure and PDE5 activity are androgen-dependent. The prevalence of hypogonadism in men with ED is estimated to be 5 to 10 percent (27).

In men with hypogonadism, testosterone is superior to placebo in improving erections and sexual function. Response rates are higher in primary versus secondary testicular failure. Testosterone is also associated with improved satisfaction with erectile function and sexual desire (28).

Second line treatment

Intracavernous and intraurethral injection of Papaverine, intraurethral prostaglandins (29), and vacuum constriction devices are alternative therapeutic options when PDE5Is fail. Much lower doses of intracavernous injection is prescribed in SCI patients than those who have vasculopathies (29). Intra-cavernosal Papaverine is more effective, better tolerated, and preferred by men over the intraurethral form. There is a danger for prolonged erection (priapism), which is a medical emergency. Priapism is most frequently treated with aspiration of blood from the corpus cavernosum. If this treatment is inadequate, then intra-cavernosal injections of Phenylephrine should be performed with hemodynamic monitoring. There is similar efficacy for intracavernosal Papaverine and oral PDE5I Sildenafil (30).

Vacuum constriction devices

Some patients refuse vacuum constriction devices treatment due to negative cultural perceptions, minor complications such as ecchymoses or petechiae, and lack of motivation. However, vacuum constriction is a reasonable, safe, and noninvasive alternative, and possibly a better initial treatment for the management of impotence secondary to SCI.

Vacuum constriction is a noninvasive second-line option and has minor side effects. It is contraindicated in men with sickle cell anemia or blood dyscrasias and in those taking anticoagulants. The worst complication of constriction devices in SCI patients with loss of penile sensation would be ischemic gangrene of penis.

Third line: Surgically implanted penile prostheses

When first and second line therapies have failed, surgical implantation of an inflatable penile prosthesis can be considered in consultation with an urologist (31,32). There is a 16.7% complication rate associated with penile prostheses, which include wound infections, penile pain due to excessive prosthesis length, and displeasure due to the partner's abnormal sensation (33).

Fourth line: Sacral neuromodulation (SNM)

The fourth line of treatment can be SNM, which can be performed in patients with complete SCI in detrusor atonic phase 2-3 months after SCI (34). This minimally invasive surgical operation can be performed under local anesthesia. It involves insertion of an electrode in each S3 root, using anal sphincter contraction following stimulation to determine correct placement. Sievert *et al.*, performed the procedure in 10 patients and 6 controls and showed the procedure prevented detrusor overactivity and urinary incontinence, ensured normal bladder capacity, reduced urinary tract infection rates, and improved bowel and erectile functionality without nerve damage (34).

Cognitive behavioral therapy

Cognitive behavioral therapy aimed at improving relationships may help to improve ED (35). Education about medical and psychosocial etiologies of ED in combination with physician assurance may help patients return to normal male sexual function.

Screening for cardiovascular risk factors should be considered in men with ED because symptoms of ED present on average three years earlier than symptoms of coronary artery disease. Men with ED are at increased risk of vascular diseases (36).

Management of anejaculation

Semen retrieval is necessary in the management of anejaculatory patients hoping to conceive and can be performed by penile vibratory stimulation, electroejaculation, prostate massage, and surgical sperm retrieval, Intravaginal insemination, intrauterine insemination (pregnancy rate 28.6% per couple), and *in vitro* fertilization (pregnancy rate of 68.75% per couple) can all be used (37). Intracytoplasmic sperm injection can be required if there is a low total motile sperm count.

Priapism might be seen in SCI males. Corporal blood gas measurement is recommended to confirm non-ischemic priapism. Intracorporeal phenylephrine is used for priapism treatment. Spontaneous resolution might happen within 5 hours (38).

Detrusor-external sphincter dyssynergia (DSD) is seen in SCI patients. DSD is a debilitating problem and even life expectancy can be affected. This can be managed with urethral stents and botulinum toxin injection. First line treatment is the use of antimuscarinic medication and catheterization. External sphincterotomy is the surgical option in refractory cases. However, it can lead to ED (39).

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