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Research Article

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Sexual Dysfunction Related to Multiple Sclerosis: Literature Review

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ABSTRACT

Multiple sclerosis is a common autoimmune disorder that affects young individuals. Sexual dysfunction among those populations has recently gained the researcher's attention since the finding of the higher prevalence of sexual dysfunction than general populations. Several articles have addressed the causality, but the exact etiology remains unclear. We aimed in this article to review the causality, prevalence, impact, and management of sexual dysfunction in multiple sclerosis. We used the PubMed database and searched for relevant articles on the topic. We used the following MeSh words: Multiple sclerosis, Sexual dysfunction, Erectile dysfunction. Sexual dysfunction is significantly prevalent among multiple sclerosis patients compared to the general population. It leads to impaired self-esteem and affects the sexual quality and overall quality of life. Therefore, due to being underdiagnosed and undertreated condition, the clinician must address this issue with the patient encounter soon after the diagnosis and continue on follow-up visits. Several therapeutic approaches have been proposed, including counseling, pharmacotherapy, and implantable devices.

Key words: *Multiple sclerosis, Sexual dysfunction, Erectile dysfunction, Quality of life, Sexual desire*

INTRODUCTION

Multiple sclerosis (MS) is a chronic inflammatory demyelinating disorder affecting the central nervous system (CNS) by a combination of genetic and environmental factors [1-3]. MS is one of the most frequent chronic autoimmune diseases and represents a significant burden on the affected young individuals [4]. Although the precise pathophysiology of MS is not entirely understood, it is thought that the primary pathogenesis is secondary to neuroinflammation and subsequent neurodegeneration [2]. Several studies have shown that axonal and neuronal damage starts at the earlier phases of the disease process, which leads to cognitive disability and other early disabilities [2].

Furthermore, MS patients with clinically progressive phenotypes have shown evidence of continuous inflammatory process proved by clinical relapses or new MRI lesions [2]. Diagnosing MS is mainly by patient's clinical manifestations with classical symptoms and demyelination-related signs, which are compatible with MS,

distributed in both space and time, after excluding another inflammatory, structural, and hereditary disorder [1, 2]. MS is classified into three types; relapsing-remitting MS, characterized by episodic neurological deficit interspersed with a period of stability; primary-progressive MS, characterized by outset progressive neurological deficit; and secondary-progressive MS, which developed following the primary disease course [1].

There is ongoing evidence on the increasing prevalence of sexual dysfunction (SD) in MS-affected individuals. SD directly affects the mental and health-related quality of life and is more significant than the effect of physical disability [5, 6]. MS can affect sexual pleasure and activities that are frequently underreported and under-diagnosed. Moreover, MS patients may suffer from SD, sexual dissatisfaction, and impaired relationships with their spouses, given that the disease's high prevalence among the young population [7]. Several factors were suggested to be involved in the progression of SD in MS individuals, including brain and spinal cord lesions, in addition to peripheral fibers that regulate sexual arousal. Additionally, demyelination and neural atrophy affecting various body areas may lead to other symptoms (spasticity, tremor, tiredness, muscle weakness, incontinence), which indirectly influence SD [5].

In men, erectile dysfunction (ED) and ejaculatory dysfunction are the most common unpleasant symptoms. ED might present with premature ejaculation (up to 60%) and ejaculation difficulty (up to 33%). In women, poor vaginal lubrication, impaired clitoral erection, and pain during intercourse are the most frequent symptoms, while in both sexes, reduced libido is highly reported [7].

The prevalence of SD in MS patients

The prevalence of SD among MS patients are broadly high, with an estimation of 40 to 80% in women and 50 to 90% in men. A recent study that included a large sample of women (1663) across 54 countries revealed that the majority of patients, approximately 55.6% experienced one or more sexual problems, and decreased sexual interest in 41.8%, which subsequently influenced the women's reproductive health and quality of life [7]. Moreover, it has been found that the association between SD and MS is higher than other neurological disorders and around five-fold higher compared to the overall population [8]. Besides, various factors keep clinicians away from addressing SD in MS patients, such as patients accompanied by a family or friend, waiting for the clinician to initiate discussion about their sexual life, and limited time during the clinical encounter. Nonetheless, a recent growing concern on SD among women with MS, particularly among the youth population [7]. Therefore, it remains an underdiagnosed and undertreated condition [8].

RESULTS AND DISCUSSION

Normal sexual cycle and the influence of MS in sexual Response

The normal male physiologic sexual cycle is classified into libido (sexual passion), erection, ejaculation, orgasm, and detumescence; while in females, the sexual cycle starts as follows: libido, arousal, orgasm, and satisfaction. The integrity among the sexual cycle components is crucial to maintaining the human sexual response and functioning, and any disturbance can lead to SD [9]. Sexual arousal starts in the CNS, while the brain transmits signals to the sexual organs through the spinal cord (descending pathway) and obtains signals from the genital organs (ascending pathway) [9]. Although SD can result when MS directly damage one or more of these sexual pathways, such as sexual desire (31.4-63.6%), arousal (33-51.1%), and orgasm (37-38.3%), indirect pathways influencing sexual response might emerge, including chronic pain, malaise, spasticity, or dysfunction of the urinary system (frequency, urgency, incontinence, and obstruction symptoms) [5, 9, 10].

It is worth mentioning that a single pathologic CNS lesion does not necessarily indicate a certain SD [10]. Furthermore, SD can result from psychosocial impairment due to poor self-esteem and mood changes as a result from decrease quality of life, social and emotional function [9]. Depression was the most common comorbidities with SD among MS patients in several studies, of which the neuropsychological complications of MS, such as depression, are strongly associated with SD [7, 9]. Several authors had reported that the duration of the disease (time since diagnosing MS) was not a predictor of sexual functioning, and some had found a negative association [5, 10]. Some studies had correlated the severity of SD to the course of MS disorder, where severe SD was correlated to primary progressive and secondary progressive disease, and less SD was correlated to the relapsing-remitting type [5].

In male MS patients, the prevalence was estimated in one study about 64-91% patients, and the most frequently reported was ED (52.9%). Other common SD manifestations include lack of sexual desire (26.8%) and sexual stimulation sensation, ejaculatory (17.9%), and orgasm dysfunction (23.1%) [10]. Based on a cross-sectional

observational study evaluating 41 men, 29 patients (74.4%) have SD. Also, voiding and sexual dysfunction increased with the neurological impairment degree, in addition to lower urinary tract symptoms that were significantly correlated with SD [11]. In a cohort study evaluating the prevalence of SD among MS women compared to healthy subjects, several factors have found a strong correlation with SD in women with MS, such as increased age and disability and depressive symptoms coexistence [12].

Type of sexual dysfunction in multiple sclerosis

MS-related SD may be categorized into: **1) Primary**, which directly resulted from neurological damage that influences the sexual response; **2) Secondary**, which is attributed to symptoms and physical disturbances that indirectly alter the sexual response, including spasticity and contracture, fatigue, bladder dysfunction, and cognitive symptoms OR iatrogenic SD, which resulted from medications adverse effects, such as antidepressants, antiepileptics, and benzodiazepines; **3) Tertiary**, which resulted from psychosocial (depression) and cultural impairment of having a chronic neurological disorder that depleted sexuality [13, 14]. Patients with MS are predominantly reported primary SD, followed by secondary and tertiary. On the other hand, Tudor *et al*. had reported primary SD followed by tertiary being more common than secondary SD [15].

Clinical impact of MS on sexual function

MS causes a significant sexual function impairment in men's lives. Men with MS are commonly had once weekly to once monthly intercourse. Moreover, SD induced by MS was found to be higher in men in comparison with patients affected by other chronic diseases, such as rheumatoid arthritis, systemic lupus erythematosus, psoriatic arthritis, and ankylosing spondylitis. More notably, SD-related conditions that seriously impair sexual function, such as diabetes mellitus, chronic kidney disease, and obstructive sleep apnea, have a similar impact and prevalence compared to patients with MS. Hence, MS should be considered as serious as other diseases that affect men's sexual life.

Interestingly, patients who developed MS for ten years or less have greater satisfaction with their sexual life [14]. Although ED is the most frequently reported symptom of SD in men with MS, sustained prolonged adequate erection was also an issue. Besides, several depressive symptoms that coexist with SD have been reported, including muscle cramps in arms and legs or body, hands or body tremor or jerking, poor self-attractiveness feeling, fear of being sexually rejected, decreased sexual appeal, decreased intense or satisfying orgasms or climaxes. Patients who experienced one or more of the aforementioned symptoms also reported symptoms of depression. Thus, those patients need a comprehensive approach in managing their MS-associated symptoms of SD and confirming that all aspects are taken into consideration [15].

Dastoorpoor *et al*. has reported in their systematic review that sexual dysfunction among male MS patients is not associated with age. Also, several previous studies showed no significant correlation between worsening ED and age. Winder *et al*. and Balsamo *et al*. reported no significant correlation between worsening ED and the time of MS diagnosis (duration of the disease). Regarding the severity of MS disease, there was no significant association between MS severity and SD [16].

On the contrary, the relation between MS disease duration and SD in women was statistically significant in some studies. The reason is thought to be related to the disease's progressive nature, leading to psycho-mental and physical/neurological disorders that might decline along with the disease progression. Moreover, MS patients with a prolonged period of disease are often under certain medications for a long term, of which some of these medications cause sexual dysfunction. Expanded Disability Status Scale (EDSS) is a modality for evaluating the degree of neurological damage or rating the physical disability among MS individuals. A positive relationship has been found between the degree of EDSS and SD by Merghati-Khoei *et al*. In addition, Mohammadi *et al*. documented that the frequency of SD was noted in MS women with severe disabilities [17].

On the other hand, SD affects women with MS even in earlier phases without disabilities. Regarding the association between SD and age, it was inversely correlated among women with MS, reported by Nazari *et al*. Depression was inversely correlated with female sexual function, except for sexual desire, lubrication, and pain [18].

Management of sexual dysfunction in MS

Investigations for SD are commonly unnecessary in many cases when a neurogenic cause is strongly presumed. However, laboratory tests must tailor risk factors to rule out other possible comorbidities that cause SD, including HbA1c, fasting glucose, lipid profile in patients with high cardiovascular risk as ED can be an early presentation

of atherosclerotic disease. Although the National Institute of Health and Care Excellence (NICE) guidelines recommend testing plasma testosterone in every patient with ED, this may not be indicated in the case of non-neurogenic SD. If hypogonadism is highly suspected or fails to respond to the first-line ED therapy, the total serum testosterone level should be checked in the morning (8-10 am) [19].

Different healthcare providers' specialties can address SD in MS patients, including clinicians (urologist, gynecologist, neurologist, psychiatrist, and primary care physician), nurses, psychologists, social workers, physical therapists, occupational therapists, and marriage counselors. Cooperation among healthcare providers may enhance the feasibility of managing SD in MS patients and the population in general. Evaluation and treatment of SD must start soon after MS diagnosis and upon follow-ups. Questionnaires may also be a helpful tool in assessing and encouraging discussion about sexual life during the clinic visit [20].

Pharmacological therapy can be used in men with ED, such as phosphodiesterase type-5 inhibitors (sildenafil), significantly improving 95% of 217 participants [21, 22]. Sildenafil use resulted in enhanced sexual activity and orgasm [21]. Tadalafil was proven to be effective as well in treating ED among MS patients [21]. Vacuum constriction devices (VCDs) are another option for treating ED, which showed an excellent efficacy for patients with spinal injuries [21]. Prostaglandin E1 intracavernous injection (papaverine and phentolamine) are highly effective in treating ED [21, 22]. These agents are vasoactive, injected inside the penile corpus cavernosal, inducing an erection by smooth muscle relaxation regardless of the sexual arousal [21]. The adverse outcome, particularly priapism, is considered a potentially dangerous complication of intracavernous (1%) or intraurethral (<1%) administration of these vasoactive agents. Dose titration in the early phases can be used to avoid priapism [22].

Due to abnormal sex steroids levels among men and women with MS, hormonal sex therapy may benefit as a possible therapeutic option for SD. Foster *et al*. used testosterone therapy for four male MS patients with SD, which improved SD, particularly erectile function [22]. Alprostadil injected intraurethral in the form of a jellied pellet is another option that successfully induces erection within 15 minutes. Success rates have been shown in 65-69% of cases, but adverse events such as urethral burning or irritation are also reported. Invasive options, such as penile prosthesis implantation, can be used in case of failure to oral or locally administered pharmacological therapy [21]. In patients who suffer from neurogenic ED, vibratory stimulation might be useful to achieve an erection. Moreover, psychotherapy is an essential treatment modality, which requires a multidisciplinary team and cooperation with specialists, partners, and society. Foley *et al*. counseled nine partners using a quasi-experimental research design, resulting in significant progress in problem-solving communication, marital and sexual satisfaction [22].

CONCLUSION

Multiple sclerosis is a complex autoimmune demyelinating disease that commonly affects the young population. The prevalence of sexual dysfunction is higher than the general population, which can be attributed to multiple factors, including pathological neuronal damage, the psychosocial impact of the disease, and multiple sclerosis medications' side effects. Sexual dysfunction leads to impaired self-esteem and affects the sexual quality and overall quality of life. Therefore, due to being underdiagnosed and undertreated, the clinician must address this issue with the patient encounter soon after the diagnosis and continue on follow-up visits.

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