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The impact of Multiple Sclerosis and Lower Urinary Tract Symptoms on Patients' Quality of Life

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Abstract: Background: Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system (CNS). Bladder dysfunction is a common consequence of MS. The prevalence and severity of bladder dysfunction increase depending on the severity of MS. Due to the fact that several components of the CNS are associated with regulating urination, thus MS may lead to a wide range of urinary symptoms and urologic complications. Although lower urinary tract symptoms (LUTS) are not a major cause of mortality, they are highly prevalent chronic conditions which negatively affect health-related quality of life (HRQOL). Due to the chronic and non-fatal nature of LUTS, most patients have to learn to live with their urinary problems. Therefore, improving HRQOL are often the key goals of most LUTS intervention. LUTS are associated with high personal and societal costs, both in direct medical costs and indirect losses in daily functioning. The substantial impact of LUTS on QoL reinforces the need for their treatment, and indicates the potential benefits of effective intervention. In addition, treatment of LUTS has been shown to improve QoL.

Keywords: Multiple Sclerosis, Lower Urinary Tract Symptoms, Quality of Life.

Introduction

Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system (CNS). Most patients (~90%) have relapsing–remitting disease at onset, which typically is followed by a secondary progressive course, while a minority of patients have a primary progressive course from onset (~10%). Relapsing–remitting MS (RRMS) is characterized by frequent formation of inflammatory lesions in the brain and spinal cord. Approved disease-modifying therapies target the inflammatory component of the disease, and strong evidence supports their effectiveness in RRMS (1).

There are 2.8 million people living with MS around the globe. This is our most accurate and up-to-date estimate of the number of people living with MS worldwide. This equates to 1 in 3,000 people in the world living with MS. The estimated number of people with MS globally has increased from 2.3 million people in 2013. Every 5 minutes, someone, somewhere in the world is diagnosed with MS. MS not only affects adults, there are at least 30,000 people living with MS who are under 18 years old (2).

In a previous Egyptian retrospective meta-analysis study in different referral centers, including five centers in Cairo metropolitan, and five other centers in different governorates, one center in each city of Alexandria in north Mediterranean coast, Mansoura, Tanta, and Zagazig in Delta, and Assiut in Upper Egypt, the prevalence

of MS in Egypt was found to be 14.1/100,000 (3). The ratio of women with MS to men with the disease is two to one (4). There are several countries where females with MS outnumber males on a ratio of 3 or even 4 to 1. Examples include: Egypt, Iran, the Palestinian Authority and Sudan (2).

Urinary Symptoms in Multiple Sclerosis Patients

Bladder dysfunction is a common consequence of MS. The prevalence and severity of bladder dysfunction increase depending the severity of MS. Due to the fact that several components of the CNS are associated with regulating urination, thus MS may lead to a wide range of urinary symptoms and urologic complications. The bladder dysfunction symptoms tend to occur more frequently usually around 6 to 8 years after the onset of MS. However, in some patients, it may occur earlier (5).

Pathophysiology of Lower Urinary Tract Symptoms (LUTS) in MS patients

The pontine micturition center (PMC) is regulated by complex brain networks involved in the two processes of bladder storage and voiding. Direct pathways from the PMC project to the sacral segments (S2–S4) of the spinal cord and determine parasympathetic outflow to the detrusor and reciprocal activity of the motor neurons innervating the striated urethral sphincter (6).

Bladder fills as a result of inhibition of parasympathetic innervation of the detrusor, and pressure within the urethra is maintained at a higher level than within the bladder by tonic firing of the motor units of the striated urethral sphincter and pelvic floor (7).

At the initiation of micturition, there is relaxation of the striated urethral sphincter and pelvic floor, followed by a coordinated contraction of the detrusor muscle. This synergistic activity between the sphincter and the detrusor is dependent on connections with the pontine region. The multitude of lesions that characterize MS makes difficult to establish the relative contributions of individual lesions to LUTS (6). In general, lesions that are more caudally placed have a greater effect on LUTS and they occur most often following spinal cord involvement (7).

A condition known as 'detrusor sphincter dyssynergia' (DSD) is the urodynamic description of bladder outlet obstruction from detrusor muscle contraction with concomitant involuntary urethral sphincter activation. The most marked abnormality occurs because of disconnection of sacral segments from the PMC (8).

Evidence from animal experiments and human studies had revealed that any form of spinal cord lesion should activate unmyelinated C fibers that become mechanosensitive and respond to bladder stretch. This process determines detrusor overactivity, the pathophysiology underlying the common complaints of urinary frequency, urgency, and urgency incontinence, referred to collectively as overactive bladder syndrome (9).

Lesions above the PMC produce an overactive bladder with coordinated sphincter, lesions involving the PMC or the spinal pathways to the detrusor and sphincter nuclei in the sacral spinal cord cause an overactive bladder with uncoordinated (dyssynergic) sphincter, and lesions to the peripheral sacral reflex arc cause an underactive bladder with underactive (denervated) sphincter (10).

The neurological condition progresses over time and the bladder dysfunction can become more difficult to treat. This can be attributed to different element such as the worsening paraparesis, recurrent urinary tract infections (UTI), spasticity, reduction in general mobility, and sometimes cognitive impairment (11).

Most common bladder dysfunctions in MS patients

Multiple Sclerosis is a leading cause of lower urinary tract dysfunction which may manifest as storage dysfunction or voiding dysfunction or combined dysfunction (11).

Storage dysfunction defines as the bladder failure to store urine which may be caused by an overactive detrusor muscle also known as overactive bladder (OAB). It means the bladder starts to contract as soon as a small amount of urine has accumulated in the bladder. This causes the person to feel urinary urgency. An intense urinary urgency may also cause urge incontinence. Moreover, it can also be correlated with increased urinary frequency during day and night. Voiding dysfunction includes hesitation to start micturition, slow urine flow, difficulty urinating (feeling of difficulty or incomplete bladder emptying), and urinary retention (when significant postvoiding residues are noted, overflow incontinence may occur) (12).

Diagnosis of lower urinary tract symptoms

A. Bladder diary:

The use of a bladder diary is recommended by the International Continence Society to sign each symptom and define the better therapeutic strategy, independently from the neurological syndrome underlying LUTS (13).

B. Urinalysis and Urine culture:

Urinalysis is a rapid method of screening for UTI. The presence of nitrites in the urine has a sensitivity of 45–60% and specificity of 85–98% for a UTI, leukocyte esterase test positivity a sensitivity of 48–86% and specificity of 17–93% and combined nitrites and leukocyte esterase test positivity a sensitivity of 75–92% and specificity of 65–87% (8).

However, there are some limitations to the use of urine dipsticks because leukocyte esterase activity is not specific for a UTI and may be positive in patients using a urinary catheter in the absence of UTI and nitrites (7). The combination of negative nitrites and leukocyte esterase was useful to exclude UTI in all groups of patients in study, including neurological patients, with a negative predictive value of 95%. However, since the negative predictive value is not as 100%, it is useful perform a urine culture if there is a high clinical suspicion for a UTI, such as malodorous or turbid urine (14).

The gold standard for UTI diagnosis is urine culture. Urine specimens may be collected either as a clean-catch midstream sample, from an indwelling urethral catheter or a suprapubic aspiration from a suprapubic catheter (7).

C. Urodynamics

Urodynamic techniques include uroflowmetry and filling cytometry and enable evaluations of the pressure–volume relationship during non-physiological filling of the bladder and during voiding (15).

Urodynamic is a useful test to understand the mechanisms of the symptoms, and to look for risk factors of upper urinary tract damage such as detrusor overactivity with high pressure, low bladder compliance, or DSD. It also represents a valuable assessment of treatment efficiency, for example, after intradetrusor botulinum toxin injection (16).

Understanding Quality of Life (QoL) in Healthcare

There is a continuing conceptual and methodological debate about the meaning of Quality of life and about what should be measured. There is no uniform definition of the concept; however, The World Health Organization outlines one definition of QoL; “An individual’s perception of their position in the life in the context of the culture in which they live and in relation to their goals, expectations, standards and concerns” (17).

Moreover, the term health-related quality of life (HRQOL) is often described as: “A term referring to the health aspects of quality of life, generally considered to reflect the impact of disease and treatment on disability and daily functioning; it has also been considered to reflect the impact of perceived health on an individual’s ability to live a fulfilling life (18). Quality of life has become established as a significant concept and target for research and practice in the fields of health and medicine (19).

Understanding QoL is important for improving symptom relief, care, and rehabilitation of patients. Problems revealed by patients’ self-reported QoL may lead to modifications and improvement in treatment and care or may show that some therapies offer little benefit. QoL is also used to identify the range of problems that can affect patients (19). Quality of life is also important for medical decision-making because QoL is a predictor of treatment success and is therefore of prognostic importance (18).

Impact of Multiple Sclerosis on Quality of life

Patients with MS have lower QoL in comparison to the general population, as well as compared to patients with other chronic illnesses. The extensive physical disability of, lack of effective treatment for, and unknown causes of MS are indicative of its negative impact on the QoL of patients (20).

Many complications of MS have a negative effect on quality of life-related health factors. MS is a progressive disease of the CNS that causes sensory impairment, weakness, muscle cramps, visual impairment, cognitive impairment, fatigue, limb tremors, urinary incontinence (UI), defecation disorders, sexual dysfunction,

disorders of balance, forgetfulness, hearing loss, numbness, blurred vision, diplopia and speech disorders in the patient. Together, these problems affect most of a person's daily activities such as dressing, bathing, self-care, etc., and reduce personal independence, feelings of inadequacy, and also reduce a person's QoL (21).

One of the factors affecting the QoL of patients was psychological disorders. Psychological disorders are the most effective factor in patients' QoL. The prevalence of psychological disorders in MS patients can be attributed to neurological factors, disease complications (pain and fatigue) and social factors. Fatigue is an inhibitory factor of effective activity that reduces patients' QoL and makes them prone to psychological problems (22).

The neuropsychological perspective attributes the prevalence of psychological symptoms to inflammation and destruction of the nerve sheath in people with MS. The disease is associated with social isolation and eventually psychological symptoms appear in response to a decrease in positive performance in people with MS (23).

Most of the single subjects were concerned about the issue of marriage. These are concerns about being unable to start a family, the ability to have children, transmitting the disease through genetics to children, as well as not predicting the course of the disease and anxiety about the aggravation of symptoms during pregnancy. The issue of fertility and heredity in pregnancy in patients with MS is an issue that severely affects marital relationships in these individuals (24).

Patients who experience stressful relationships and family conflicts, there is a concern that these relationships become severe due to the disease and the conflicts will take a more serious form; even in some cases, there are fears of separation and the breakdown of marital relationships. The disease does not lead to widespread family conflicts, but rather exacerbates existing family disputes and, in particular, existing conflicts between couples. Families with pre-illness cohesion may face challenges and differences due to illness, but this does not mean that these challenges will lead to the widespread conflicts (25).

The disease leads to a decrease in the level of activities of daily living and performing enjoyable activities. The onset of MS often causes an initial or complete reduction in a person's physical, social, and cognitive functions and has a devastating effect on the QoL of the patient, family, and loved ones. It can also have a profound effect on the person's social activities. Functional changes such as limited mobility, premature fatigue, and problems with bowel and bladder control can make it impossible to continue participating in many social and occupational activities and will affect the patient's relationships with others. This causes depression and isolation. These patients need the help of others in personal affairs and home activities (26).

Multiple Sclerosis is a chronic debilitating CNS disease that is associated with high unemployment rates in early adulthood. Many people with MS lose their jobs or have to change jobs due to symptoms such as fatigue, inability to function, and cognitive impairments. Hence, job may be considered as a sign of the patient's overall performance, which has a significant impact on his QoL (27).

Multiple Sclerosis is associated with high direct and indirect costs. Direct costs include medical expenses such as hospitalization, inpatient care, and outpatient and pharmaceutical care. Indirect costs include costs associated with short-term and long-term disabilities, illness-related absences from work, workers' compensation, and early retirement (28).

Improvements can be made in the QoL of MS patients only through understanding effective, behavioral, mental, and social factors. Therefore, studying the QoL of MS patients would help health authorities and policymakers in planning and implementing interventions to increase MS patients' QoL (29)

Impact of Lower Urinary Tract Symptoms on Quality of life

Lower Urinary Tract Symptoms are reported to affect over half of the world's adult population (30). Although LUTS are not a major cause of mortality, they are highly prevalent chronic conditions which negatively affects HRQOL. Due to the chronic and non-fatal nature of LUTS, most patients have to learn to live with their urinary problems. Therefore, improving HRQOL are often the key goals of most LUTS intervention (31).

Storage symptoms are considered by patients to be the most bothersome symptoms. The sensation of urgency to urinate, frequent urination and nocturia limit the daily living activities of an individual with LUTS; these limitations adversely affect the QoL because urgency and frequency of urination cause social isolation, and

nocturia causes daytime fatigue and insomnia. Mental and social concept that urination is a very personal matter that should be kept private. Therefore, leakage of urine in public is one of the most miserable incidents in social life. The mental trauma associated with leakage is severe and it may induce a feeling of embarrassment, alienation, isolation, or depression. Urinary frequency or UI affects a person's relationships both with the surrounding people and society as a whole (32).

Urinary Incontinence is rarely reported by the patient, because it is considered a natural consequence of ageing and, most of all, due to a sense of shame. Often, affected individuals deny and hide UI, which results in physical and psychosocial restrictions to enjoyment in life. LUTS are associated with high personal and societal costs, both in direct medical costs and indirect losses in daily functioning (33).

The substantial impact of LUTS on QoL reinforces the need for their treatment, and indicates the potential benefits of effective intervention. In addition, treatment of LUTS has been shown to improve QoL. However, many patients with LUTS do not seek healthcare and LUTS therapy may not be regarded as a high priority by primary care physicians (34).

Relation between Urinary Symptoms and Quality of Life in Multiple Sclerosis patients

People with MS, one of the most common progressive neurological disorders, frequently experience LUTS. Studies estimate that LUTS affect 50 to 80 percent of MS patients throughout the course of their illness. These symptoms can significantly reduce a patient's QoL and hinder their ability to participate in social activities (35). Neurogenic LUTS in MS can include UI or urinary retention or a combination of both. Over 90% of patients with MS show some LUTS 10 years after the onset of the disease (36). LUTS differ to a large extent from one patient to the other and are accompanied by significant psychological effects and the highest rate of socially debilitating outcomes of MS, which cause severe limitations in activity levels (37).

Patients with MS and bladder dysfunction reported that LUTS constrained their daily activities, and the physical and clinical burden associated with MS and UI negatively affected their QoL, causing feelings of shame, depression, skin fragility, and social isolation. LUTS can also restrict a patient's lifestyle choices. They may require special bathroom facilities to manage urination and potentially become reliant on caregiver assistance. This complication can further limit their participation in health development programs, potentially leading to increased secondary complications of MS and a further decline in their QoL (38).

Lower urinary tract symptoms in MS patients can lead to a significant rise in healthcare costs. This is due to increased needs for nursing care, incontinence treatments, and management of related urinary tract infections. In addition, bladder dysfunction has a negative effect on the sexual performance of the patient and is a threat to the upper urinary tract as it can lead to permanent urinary tract disorder; thus, it has been recognized as a health problem among this population (39).

The results of a study revealed that the mean score of HRQOL among patients with MS with overactive bladder symptoms was significantly lower in comparison to that of the control group (40). In addition, it was reported in another study that the QoL scores of patients with MS with UI were significantly lower compared with patients with MS without UI in physical and mental performance dimensions (41).

Patients with MS have lower QoL in comparison to the general population, as well as compared to patients with other chronic illnesses. The extensive physical disability of, lack of effective treatment for, and unknown causes of MS are indicative of its negative impact on the QoL of patients (20).

A longitudinal study showed that the ratio of patients with MS and at least one symptom of bladder dysfunction significantly increased over time both among men and women and had a significant relationship with high levels of physical disability and HRQOL at any point of follow-up for both men and women with MS (42). Mixed urinary symptoms are highly prevalent among MS patients and affect QoL dimensions. The chance of having a urinary disorder was higher among patients with MS and high age (43).

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