Prevalence of sexual disorders in relapsing-remitting multiple sclerosis patients depending on various risk factors

By Tetiana Odintsova

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T. Odintsova, O. Kopchak

Private Higher Education Institution "Kyiv Medical University", Kyiv, Ukraine

Corresponding author:
Tetiana Odintsova
E-mail: t.odintsova@kmu.edu.ua

ABSTRACT

Objective. Multiple sclerosis is a perilous, disabling, physically as well as mentally, demyelinating disease of the central nervous system. This work aims to evaluate prevalence of sexual dysfunctions and their correspondence with non- and disease related risk factors, as well as with MRI findings in patients with relapsing-remitting multiple sclerosis.

Results. Based on conducted multifactorial analysis, the most prominent risk factor associated with presence of sexual dysfunctions in in patients with relapsing-remitting multiple sclerosis was depression. Sexual dysfunctions are tied to cognitive deficit, in general and in separate domains, particularly in memory, executive functions and language. Considering disease-related agents, sensory and motor deficits are linked to the development of sexual dysfunctions in case of relapsing-remitting multiple sclerosis. Among non-disease-related factors, unemployment, marital status, level of education and tobacco smoking affecting sexual dysfunctions ` severity. According to the MRI, frontal lobe and corpus callosum and periventricular area were affected more often comparing to other brain regions in case of sexual dysfunctions.

Conclusions. Patients suffering from relapsing-remitting multiple sclerosis encounter secondary and tertiary sexual dysfunctions. Knowing all struggles of MS patients can offer a more nuanced management options that will improve their quality of life on a deeper level.

Key words: multiple sclerosis, sexual disorders, depression, demyelination plaques, cognitive impairment

INTRODUCTION

Multiple sclerosis (MS) is a chronic inflammatory autoimmune neurodegenerative disease of the central nervous system (CNS), which relatively rapidly causes a severe long-term disability of a significant number of young working-age population due to the impact of the complex heterogeneous clinical picture [1;2].

Among the clinical manifestations of MS, sexual dysfunctions (SD) are one of the crucial though underdiagnosed and often unreported symptoms of various etiology [3]. Reportedly 40-80% of MS patients, both men and women, have SD, although SD are more prevalent in female patients (70.3% among women) [4]. SD in case of MS can be primary, secondary and tertiary. Primary SD occur due to demyelination of the sensitive pathways [5]. Secondary SD are indirectly caused by fatigue or spasticity [6]. Tertiary SD are a result of psycho-emotional disorders of MS patients [7]. The most frequent complaints of women suffering from MS are reduced libido, difficulty in achieving orgasm, reduction in the tactile sensations originating from the thigh and genital regions and vaginal dryness with consequent dyspareunia (pain during intercourse). The common complaints of SD in men with MS include erectile dysfunction (50%–75%), ejaculatory dysfunction and/or orgasmic dysfunction (50%), reduced libido (39%) and anorgasmia (37%) [8]. In spite of SDs' great influence on the patient's quality of life, in majority of cases patients do not report such issues to their treating neurologist for various reasons, nor do clinicians emphasize their attention on the particular symptoms [9]. Yet not many studies focus on SD and their development particularly in relapsing-remitting course of MS, nor on their potential appearance in the later stages of the disease.

OBJECTIVE

The aim of this study was to evaluate prevalence of SD among RRMS patients as well as clinical characteristics and social factors affecting their appearance.

MATERIALS AND METHODS

This study included one hundred and six patients with RRMS (81 female and 25 male) aged from 22 to 67 years (mean age: 41.8±10.7, disease duration (DD): 10.3±8.5 years). The study subjects were diagnosed RRMS in accordance with McDonald's

Criteria 2017 [10]. A medical history was collected from each patient. The examination consisted of a standard clinical evaluation, neurological examination, the application of neuropsychological questionnaires and laboratory tests (complete blood count, biochemical parameters, TSH). Kurtzke's Expanded Disability Status Scale (EDSS) was applied to establish the level of disability in MS patients. Mild disability was within the range of 1-3.5 points, moderate – 4-6 points and severe within 6.5-8 [11]. Screening and evaluation of the severity of depression was assessed by means of Beck Depression Inventory (BDI). The questionnaire consists of 21 items that tackle major signs of depression according to the Diagnostic and Statistical Manual for Mental Disorders criteria. Each answer is scored from 0 to 3 points. Mean score of 0–9 points indicates absence of depression, 10–18 – mild depression, 19–29 – moderate depression and 30–63 – severe depression [12]. The instrument applied for the screening of the presence and the severity of anxiety was Hamilton Anxiety Rating Scale (HAM-A). The scale is composed of 14 items, each defined by a number of symptoms, and measures both psychic (mental agitation and psychological distress) and somatic symptoms of anxiety (physical complaints caused by anxiety). Each question is scored from 0 (not present) to 4 (severely bothering), with a total score range from 0 to 56, where 0-13 stands for absence of anxiety, 14-17 – mild severity, 18–24 – moderate and ≥25 indicates severe level of anxiety [13]. The Pittsburgh Sleep Quality Index (PSQI) was the scale applied to check for presence of sleep disorders and assess the quality of sleep. The PSQI scale consists of 19 items and covers 7 components: subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbance, use of sleep medication, daytime dysfunction. The score 0-15 points indicates absence of sleep disorders, 16-25 points – presence of mild sleep disorders, 26-35 points – moderate and 36-45 points – severe sleep disorders [14]. Each participant was screened for the level of education.

The patients were excluded from the study if they had one or more of the following: age younger than 18, progressive types of MS, stage of exacerbation of MS or severe disability (EDSS score: 6.5 – 8 points), severe level of depression, pelvic disorders (urine incontinence, imperative urges to urinate and urine retention), pregnancy, cerebrovascular pathology or risk factors (stroke of any origin, arterial hypertension,

obesity, dyslipidemia, diabetes mellitus), treatment with corticosteroids or INF-β at the time of the study (it could alter the study's parameters).

All participants provided written informed consent and the study was approved by the Institutional Ethics Committee.

The statistical data was processed by means of Graph Pad Prism version 9. Student's t-test (t) was applied for evaluating credibility between mean quantitative positions of two samples. Proportions were compared using χ2. Relationships between different indicators were assessed using the Pearson's correlation coefficient (r) according to statistical distribution. A $p<0.05$ value was considered statistically significant.

RESULTS

Among 46.2% (n=49) patients, who reported SD, the majority – 79.5% (n=39) were female, although no significant difference between incidence of SD in men and women (p=0,4750) was discovered. It is worth noting that presence of SD did not correlate with age among all study subjects (p=0,0579).

In order to determine factors affecting appearance of SD the multifactorial analysis was conducted. It included the following elements: MoCA score, BDI score, HAM-A score, PSQI score, age, disease duration, EDSS score, sex, marital status, presence of higher education, tobacco smoking, number of relapses and presence of a developing hobby. According to the results, among all participants only depression had a significant impact on presence of SD (p=0,0005). SD were present significantly more frequent on the background of depression (p=0,0004) in comparison to the depression-free patients among all study subjects.

Appearance of SD was tied to the presence of cognitive deficit (p=0,0191) in patients with RRMS, hence we also analyzed the impact of separate cognitive domains impairment on SD prevalence in the study subjects. Therefore, positive influence was uncovered in relation with memory decline (p=0,0009), executive dysfunctions (p=0,0005) and language disorders (p=0,0240). Attention (p=0,0685) and abstract thinking impairment (p=0,6342) did not affect presence of SD.

According to HAM-A score, presence of anxiety influenced SD appearance (p=0,0009) among the study participants. Unemployment was tied to the SD in the RRMS

patients both directly (p=0,0389) and indirectly, via aggravating depression's level of severity. Single patients suffered from SD more frequently in comparison to their married peers (p=0,0025). Level of education also contributed to the SD development among the study subjects, therefore patients lacking higher education were more prone to SD occurrence (p=0,0277). Tobacco smoking also had a direct impact on SD presence (p=0,0010) in the study subjects. Among all participants, a connection between sex (p=0,4750), sleep disorders (p=0,2663) and presence of SD was not detected. Additionally, we did not find any dependence between SD and age (p=0,0579) or disease duration (p=0,7563).

A positive correlation was found between presence of SD and EDSS score (p=0,0287). The study participants had diverse neurological deficit, including motor deficit (mild mono-, para- or tetraparesis; moderate mono- and paraparesis; severe monoparesis, pathological reflexes, increased muscle tone), pelvic (urination urge, urinary and/or fecal incontinence), sensory disorders (decreased deep and superficial sensitivity, paresthesia). During our research we established that sensory (p<0,0001) and motor deficits (p=0,0025) were tightly linked to the presence of SD. Whereas, presence of pelvic disorders was not connected to the SD development (p=0,3314).

In this research we also studied the relations between presence of SD with the location of demyelination plaques in the brain and cervical part of the spinal cord. Presence of SD was associated with lesions in frontal lobe (p=0,0014) and corpus callosum (p=0,0005). Demyelination of temporal lobe (p=0,4920), parietal lobe (p=0,4920), brainstem (p=0,4889), cerebellum (p=0,2163) and brain atrophy (p=0,0685) were not tied to the SD development in the study subjects.

DISCUSSION

Numerous researchers claim that women suffering from MS experience higher prevalence of SD comparing to men [15;16]. Although some studies reported that among RRMS patients, men were the ones to suffer from SD more frequently [17], whereas the given study did not reveal a significant difference depending on sex. Our research did not demonstrate a relationship between presence of SD and patents' age, which coincides with the results of other studies [18;19]. Nonetheless, several studies revealed a positive

correlation between age and SD [20;21]. Kołtuniuk A. et al. discovered that insomnia in MS patients is associated with SD [22], however our research did not find the connection between presence of SD and sleep disorders. According to several researchers, anxiety and depression can indirectly impact SDs' appearance and level of severity [23;24], especially depression [25;26], which is in line with our results. Among all assessed risk factors, depression has the most prominent impact on SD prevalence in our RRMS patients. Wu J. et al. demonstrated that SD are more frequently observed in MS patients who are also suffering from cognitive deficit, furthermore that men with cognitive deficit are more prone to development of SD compare to women [27]. The data found in our study confirm the relationships between SD and cognitive deficit, but not the differences depending on patients' sex. Several researchers studied the relations between separate cognitive domains and SD. For instance, Petracca M. et al. declare that disorders of executive functions, measured through neuropsychological tests like D-KEFS ST and the Stroop Test, demonstrate a relationship with SD [28;29], which is in line with our results. Marinetto S. et al. state that there is no dependence of SD presence from memory decline [29], nonetheless, our study demonstrates this connection.

SD are considered more common with increasing EDSS score [30;31], similarly our study showcases a positive correlation between EDSS score and SD presence among the participants as well. Among the neurological deficit, motor [32], sensory [33] disorders are linked to SD prevalence. These results are confirmed by our findings. Bladder dysfunction is repeatedly reported to be correlated with SD in MS patients [34], nonetheless the current study does not demonstrate such connection in our patients. Some studies showcase a direct correlation between presence of SD and disease duration in MS patients [28].

Ramezani M. et al. state that SD are associated with location of plaques in the brainstem, specifically in pons, also in occipital and hippocampal areas [35], whereas our study demonstrates connection between SD and lesions located in frontal lobe and corpus callosum.

There is no evidence of tobacco smoking instigating or effecting presence of SD in MS patients, only indirectly through deteriorating cognitive deficit and depression [36;37], though our research demonstrates a connection between tobacco smoking and

SD intensity. Correspondingly, marital status also has mediated influence on SD via depression and anxiety caused by solitude [38;39], which is in line with our results. According to Kołtuniuk A. et al. unemployment negatively impacts presence of SD on the background of MS [40], which furthermore is confirmed by the current study as well.

The aforementioned data can suggest that RRMS patients are experiencing secondary and tertiary SD.

Limitations

The given study has several limitations. First, self-report survey tools were applied, which inherently carry the risk of self-report bias. Second, the control group was not included to the research.

CONCLUSIONS

Multiple sclerosis is a complex progressive disease involving apart from severe neurological deficit and psycho-emotional disorders, also sexual disfunction. Patients suffering from relapsing-remitting multiple sclerosis encounter secondary and tertiary sexual disorders. Knowing all struggles of MS patients can offer a more nuanced management options that will improve their quality of life on a deeper level. The fundamental message arising from this study will be useful in future designs of therapeutic interventions, and of more appropriate working and leisure adjustments, that will ultimately help lifting the burden posed on MS patient's quality of life.