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Effectiveness of interventions aimed at improving the sexuality of women with multiple sclerosis: a systematic review

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Abstract

Objective: To evaluate the effectiveness of interventions aimed at improving the sexuality of women with multiple sclerosis.

Data sources: MEDLINE, CINAHL, PsycINFO, Web of Science, Scopus, Embase and the Cochrane Library, as well as doctoral thesis databases Teseo and ProQuest Dissertations & Theses Global and the grey literature database Opengrey were searched, last on 15 October 2019. Journals related to the topic were also consulted. The bibliographic references of the articles included were reviewed.

Method: Studies were selected if they included women with multiple sclerosis in whom interventions aimed at reducing sexual dysfunction were applied. Data extraction was carried out by two independent reviewers. The Jadad scale was used to evaluate the methodological quality of the studies included.

Results: In total, 12 clinical trials were selected, and 611 patients were examined. Studies were classified into six interventions: sexual therapy (4), pharmaceutical drugs (3), pelvic floor exercises (2), yoga (1), mindfulness (1) and vaginal devices (1). Most of them improved some primary outcomes of sexual dysfunction such as lubrication, arousal, desire or orgasm. Pain was the most common secondary outcome evaluated and it became better in two studies including sexual therapy and in one intervention with pelvic floor exercises. Tertiary outcomes such as anxiety or depression were rarely examined, and they improved with sexual therapy and with OnabotulinumtoxinA.

Conclusion: Sexual therapy, administration of OnabotulinumtoxinA, pelvic floor muscles exercises alone or combined with electrostimulation and the use of clitoral devices could be the most recommended interventions to improve the sexuality in women with multiple sclerosis.

Keywords

Multiple sclerosis, women, sexuality, intervention

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Introduction

Multiple sclerosis is a chronic neurodegenerative disease that affects sexual function.[1,2] The way in which the disease affects women's sexuality has previously been described by Foley and Iverson, who established that sexual dysfunction can be a

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result of primary causes (resulting from lesions in the nervous system), secondary causes (referring to further physical issues as well as the side effects of treatments) and/or tertiary causes (described as sociocultural, emotional and psychological factors).[2–5]

Sexual issues in women with multiple sclerosis are common (40%–74%)[6] and more prevalent than in the population at large.[3] There are interventions that can be used to address sexuality in women with multiple sclerosis. These interventions are pharmacological (such as treatment modification, PDE-5 inhibitors and oestrogen) and non-pharmacological (such as education, support from partners and aerobic exercise).[6,7] A combination of both kinds of intervention could be a reasonable way to approach sexual problems in women with multiple sclerosis,[6] considering that sexual rehabilitation requires comprehensive attention.[7]

Therefore, it is important to determine the effectiveness of these interventions in improving sexual dysfunction and patients' quality of life,[8] as it would make available to clinicians a set of effective interventions to address these health outcomes. As far as we know, there are no studies synthesizing information about interventions aimed at improving sexual function in women with multiple sclerosis, which could be of great help to the different healthcare professionals working with people with multiple sclerosis. The aim of the present systematic review is to evaluate the effectiveness of interventions described in the available literature, with a goal of improving the sexuality of women with multiple sclerosis.

Methods

A systematic review to evaluate interventions aimed at reducing sexual dysfunction in women with multiple sclerosis was performed.

To obtain the original documents, an electronic search was conducted in the following databases: international databases MEDLINE, CINAHL, PsycINFO, Web of Science, Scopus, Embase and the Cochrane Central Register of Controlled Trials; doctoral thesis databases Teseo and ProQuest Dissertations & Theses Global; and the grey literature database Opengrey (from inception to 15 October 2019–15 November 2019).

The search strategy was performed as described in Appendix 1.

This strategy was complemented with manual searches in international journals addressing the topic of interest (from 2010 to 2019): *Multiple Sclerosis Journal, Journal of Sex and Marital Therapy, The Journal of Sexual Medicine and Multiple Sclerosis and Related Disorders*. Furthermore, the bibliographic references of the articles included in this study were also scrutinized.

Studies were included if they evaluated an intervention aimed at improving the sexuality of women with multiple sclerosis. Only randomized controlled trials and quasi-randomized trials in English and Spanish were selected. Studies were excluded if they performed an analysis of both sexes.

To select articles, titles and abstracts were reviewed with respect to the inclusion and exclusion criteria by two independent researchers. A full-text review was made of the articles selected to verify that they met the criteria. If consensus was not reached, a third researcher was consulted.

Data extraction was performed by two independent researchers previously trained in the critical analysis of scientific articles and data extraction for systematic reviews. Any lack of consensus was discussed with a third researcher.

To facilitate data extraction, an evidence table was created in which the most relevant data were summarized. The table contained information regarding the characteristics of the studies selected (author(s), year, country, research design, inclusion criteria, exclusion criteria, sample size, ages and methodological quality measured via the Jadad scale)[9] as well as information relevant to the intervention (author(s), year, intervention, professionals, sessions and their duration, variables and results).

Results

The search provided 8680 results, 6 of which were identified through manual searches. No studies were obtained via grey literature and doctoral thesis databases. The review of the references of the studies selected provided one further addition to

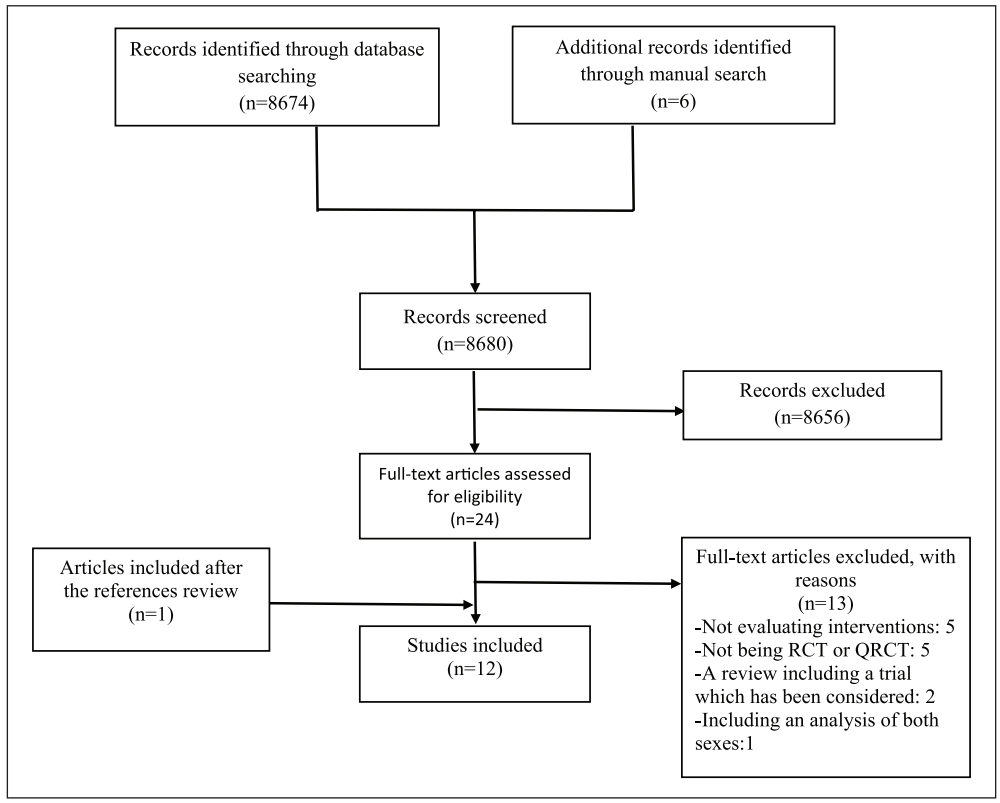

Figure 1. Flow diagram.

the sample. The final sample comprised 12 articles (Figure 1).

The topics of the articles analysed included sexual therapy (four studies),[10–13] the use of pharmaceutical drugs (three studies),[14–16] pelvic floor muscle exercises in combination with other therapies (two studies),[17,18] practising yoga (one study),[19] applying mindfulness (one study)[20] and the use of vaginal stimulation devices (one study).[21] The main characteristics of the articles included and the evaluated interventions are summarized in Table 1. The Jadad scale was used to assess the methodological quality of the studies selected.[9] Nine of these studies obtained a score of less than 3 on the Jadad scale (low methodological quality), and three studies scored 3 or higher (good methodological quality).

The main results were analysed as follows: with respect to their effects on primary (directly related to sexual function), secondary (referring to further physical issues as well as the side effects of treatments) and tertiary (psychological aspects) outcomes of sexual dysfunction.

Primary outcomes of sexual dysfunction

All the included studies evaluated the effectiveness of interventions with respect to some primary causes of sexual dysfunction except for studies pertaining to yoga.[19] Lubrication, arousal, orgasm and desire were the main evaluated outcomes.

Lubrication significantly improved in all of the interventions except for the use of vibrating devices.[21] Arousal also improved in all studies except for those pertaining to vibrating devices[21] and the use of sildenafil,[14] which did not include this variable. Orgasm improved in all interventions but not significantly in the strategies that included mindfulness[18,20] and in

Table 1. Description of interventions.

Author(s) (year, country)	Design (Jadad scale)	Sample size (ages)	Inclusion criteria	Exclusion criteria	Intervention	Variables	Results
Sexual therapy							
Khakbazan Z et al. (2016, Iran)[10]	RCT (<3)	*N* = 88 EG = 43 (34.77 ± 5.541) CG = 45 (35.64 ± 7.05)	Women married for one year, had a multiple sclerosis diagnosis, were 18–55 and did not have a history of alcohol/ drug abuse or other chronic diseases, FSFI score ⩽28, an EDSS score <7 and a BDI score ⩾31	EDSS score >7, pregnancy, taking any sexual treatment and a multiple sclerosis relapse in the last month	One 90–120 minutes session per week for four weeks of sexual therapy based on the PLISSIT model conducted by a midwife previously trained	Assessment before the intervention and two and three months after the intervention with the FSFI.	FSFI total score between groups: improvement at two and three months in the experimental group ($P < 0.001$) FSFI total score before and after in the experimental group Significant difference at two and three months ($P < 0.001$) No differences when comparing two months against three months ($P > 0.999$)
Christopherson JM et al. (2006, Canada)[11]	RCT (<3)	*N* = 62 (44 (24–57)) EG = 31 CG = 31	Sexually active women aged 18 or older registered in one multiple sclerosis clinic	Women with cognitive limitations or unable to provide informed consent	GI: received written materials and additional resources GII: received written materials, additional resources and three counselling sessions. A multiple sclerosis clinic nurse did one 20–30 minutes session in person. The second and the third were done by telephone at two and four months and lasted between 10 and 15 minutes	Assessment before the intervention and six months after the intervention with the MSISQ-19	Primary causes of sexual dysfunction: significant differences in both groups when compared to onset ($P < 0.001$) Secondary causes: not differences when compared to onset Tertiary causes: improvements in both groups but not significant
Zamani M et al. (2017, Iran)[12]	Q (<3)	*N* = 30 EG = 15 (37 ± 5.87) CG = 15 (34 ± 8.08)	Women aged 17–45 years who were seeking treatment for multiple sclerosis and willing to participate in the trial	Patients with cognitive problems, too ill to participate, those who had sexual problems due to marital dissatisfaction and those with diagnoses of bipolar disorder, psychotic disorders or drug dependence	12-weekly sessions conducted by a clinical psychologist expert in sexual dysfunctions of sexual therapy which included information about sexual anatomy and physiology, instructions about the initiation of sexual activities and preferences and skills about the self and interpersonal pleasuring	Assessment before and after the intervention with the FSFI and the MSQoL-54	Significant improvements in the experimental group when comparing against the control group in domains of desire ($P < 0.0001$), arousal ($P < 0.022$), lubrication ($P < 0.001$), orgasm ($P < 0.001$), satisfaction ($P < 0.0001$) and pain ($P < 0.026$). Significant differences between groups in satisfaction with sexual function ($P < 0.001$), improved sexual function ($P < 0.001$), overall quality of life ($P = 0.001$) and variables related to emotional factors
Daneshfar F et al. (2017, Iran)[13]	RCT (<3)	*N* = 60 EG = 30 (541/5 ± 77/34) CG = 30 (075 ± 842/37)	Married women with multiple sclerosis aged 20–50 years. No history of alcohol or drugs abuse and no history of other chronic disease	EDSS score >7, having a relapse in the last month, pregnancy and receiving treatment for sexual dysfunction	Four-weekly 60 to 100 minutes sessions based on the Extended version of PLISSIT model	Assessment before intervention, 8 and 12 weeks after with MSISQ-19, FSS and BDI	Primary causes of sexual dysfunction: improvements at 8 and 12 weeks: $P < 0.001$ Secondary causes of sexual dysfunction: improvements at eight weeks, $P < 0.001$, and 12 weeks, $P = 0.001$ Tertiary causes of sexual dysfunction: Improvements at 8 and 12 weeks, $P < 0.001$

(Continued)

Table 1. (Continued)

Use of pharmaceutical drugs							
DasGupta R et al. (2004, UK)[14]	RCT (<3)	*N* = 38 EG = 19 (unidentified) CG = 19 (unidentified)	Premenopausal women in a stable heterosexual relationship, development of sexual dysfunction after the onset of multiple sclerosis and no history of cardiovascular, renal or hepatic problems	Patients were excluded if they were on serotonin selective reuptake inhibitors or nitrates and if they were pregnant	Oral treatment with 50 mg of sildenafil. After two weeks, the dose could be modified to 25 mg if there were side effects or 100 mg if there was no benefit. The treatment lasted for 12 weeks. After that, groups were crossed over for a further 12 weeks. There was an optional extension phase until week 36	Assessment after 12 and 36 weeks with the SFQ.	Significant improvements in the domains of lubrication ($P < 0.01$ versus baseline; $P < 0.03$ versus placebo) and sensation ($P < 0.001$ versus baseline; $P < 0.059$ versus placebo). There was no improvement in orgasm capacity ($P > 0.441$ versus placebo) nor in desire for intercourse ($P > 0.196$ versus placebo). In the optional extension phase, there was a significant difference for the orgasm domain ($P < 0.024$).
Giannantoni A. et al. (2015, Italy)[15]	Q (<3)	*N* = 31 (44.5 ± 13.7)	Women with multiple sclerosis who displayed periventricular, juxtacortical, infratentorial and spinal lesions and symptoms of overactive bladder and detrusor overactivity that did not respond to conventional therapy	Overactive bladder due to obstruction, high-grade urogenital prolapse, recurrent urinary tract infections, cognitive impairment pregnancy, anticoagulant therapy, psychoactive agents, drugs that interfere with bladder function and a relapse in the last six months	A single administration 100 U of OnabotulinumtoxinA diluted in 10 mL NaCl injected into the detrusor muscle at 20 sites, avoiding the trigone, under cystoscopic control	Assessment before the intervention and three months after with the FSFI, HAM-D, HAM-A, I-QoL	Significant improvements in the domains of desire ($P < 0.005$), arousal ($P < 0.0005$), lubrication ($P < 0.005$), orgasm ($P < 0.005$) and satisfaction ($P < 0.004$) in those women who managed to maintain urinary continence. There were also improvements in anxiety ($P = 0.001$), depression ($P = 0.0003$) and in quality of life ($P = 0.001$)
Giannantoni A. et al. (2017, Italy)[16]	Q (<3)	*N* = 62 EG = 41(44.5 ± 13) CG = 21(43.2 ± 10.6)	The same criteria used than in the study before	The same criteria used than in the study before	The same intervention used than in the study before	Assessment before the intervention and six months after with the FSFI, HAM-D, HAM-A and I-QoL	Significant improvements in the domains of desire ($P < 0.005$), arousal ($P < 0.0005$), lubrication ($P < 0.005$), orgasm ($P < 0.005$) and satisfaction ($P < 0.004$) in those women who managed to maintain urinary continence. Improvements in anxiety ($P = 0.001$) depression ($P = 0.0002$) and in quality of life
Pelvic floor muscle exercises in combination with other therapies							
Lúcio AC et al. (2014, Brazil)[17]	RCT (<3)	*N* = 20 GI = 6 (44.5 (36–51)) GII = 7 (47 (27–54)) GIII = 7 (47 (27–52))	Women ⩾ 18 with multiple sclerosis who had been stable over the previous four months, an EDSS <6.5 and have an adequate cognitive capacity. They were in a sexual relationship and were sexually active for at least four weeks	Pregnancy, women with a gynecologic surgery, a caesarean or a vaginal delivery within the previous six months. Organ prolapse greater than stage I, urinary tract infection or were perimenopause or menopause	GI: pelvic floor muscle exercises with simulated electrostimulation. GII: with intravaginal electrostimulation. GIII: with transcutaneous stimulation of the tibial nerve. The intervention was done by a physiotherapist previously trained and lasted for 12 weeks with 30 minutes sessions twice per week	Assessment before and after the intervention with the FSFI	Before and after the intervention: GI: improved in all domains except for desire orgasm and pain. GII: improved in all domains. GIII: improved in all domains except for pain. Between groups: significant difference between GII and GIII for the pain domain ($P < 0.01$)
Pelvic floor muscle exercises in combination with other therapies							
Mosalanejad F et al. (2018, Iran)[18]	RCT (>3)	*N* = 70 (35.7 ± 6.5) GA = 23 (36 ± 7.2) GB = 23 (35.7 ± 6.8) GC = 24 (35.5 ± 5.7)	Women with multiple sclerosis for at least six months, in remission period, having husband, FSFI <28, not included in a similar study and not having any other disease	Unwillingness to participate, disease relapse during the study, absence of the participant for more than one session, separating from husband and being pregnant	GA: pelvic floor exercises two times per day over eight weeks. GB: mindfulness sessions once a week over eight weeks. Each session lasted 90 minutes. GC: both mindfulness and pelvic floor exercises for eight weeks	Assessment before the intervention and eight and 12 weeks after the intervention with the FSFI	Significant differences between all three groups for the domain arousal ($P = 0.004$) at eight weeks and for lubrication ($P = 0.002$) at 12 weeks

(Continued)

Table 1. (Continued)

Practicing yoga							
Najafidoulatabad S et al. (2014, Iran)[19]	RCT (<3)	*N* = 60 (31.6 ± 8.0 (18–45)) EG = 30 CG = 30	Women 18 years or older with multiple sclerosis for the past two years, no other disabling diseases and physically able to participate in the study	Patients at the acute phase of the disease, under simultaneous therapeutic interventions or suffering from metabolic and psychical disorders and cardiovascular diseases	Eight 60–90 minutes session per month for three months performing exercises based on the principles of Hatayoga (slow movements), Pranayama (breathing exercises and Rajayoga (mental concentration)	Assessment before and after the intervention with the MSQoL-54 Questionnaire	Statistically significant differences were found in the intervention group ($P = 0.001$) for the subscale sexual satisfaction when compared to onset
Applying mindfulness							
Hocaloski S et al. (2016, Canada)[20]	Q (<3)	*N* = 7(47.9 ± 11.2 (25–61)) MS = 6 SCI = 1	Women aged 19–65 with MS or SCI for at least one year, fluent in English and who met the criteria for female sexual arousal disorder or hypoactive sexual desire disorder according to the *DSM*	Participants were excluded if they had a score >19 in BDI	Five 90 minutes sessions of mindfulness spaced two weeks apart for 10 weeks conducted by a registered nurse specializing in sexual health rehabilitation	Assessment before and two weeks and six months after intervention with FSDS, FSFI, DASA y PBSDE	Significant differences in the FSFI domains of desire ($P < 0.038$), arousal ($P < 0.006$) and sexual function ($P = 0.25$), albeit none was found for FSDS ($P > 0.05$). The DASA results showed significant differences for the subscale genital wetness ($P < 0.03$) alone. No significant differences were found for PBSDE dimensions
Vaginal stimulation devices							
Alexander M et al. (2017, USA)[21]	RCT (<3)	*N* = 23 (43.3 ± 10.2) MS = 18 (46.7 ± 8.7) SCI = 5 (37.1 ± 10.3)	Women with SCI or MS.	Genital malformation, previous neurosurgery affecting genital responsiveness, premorbid sexual dysfunction, pregnancy, pressure ulcers, psychiatric disturbance, narcotic dependency, serious medical illness, use of serotonin reuptake inhibitors, antipsychotic or other drugs	Use of clitorial vacuum suction device and vibratory stimulation. Women could use them any time either alone or during sexual activity	Assessment before the intervention and 12 and 16 weeks after with FSFI and FSDS. Orgasm characteristics were assessed in women with MS via the MSISQ-19 and ORS at 16 weeks	Clitoral suction devices: significant improvements at week 12 in total FSFI score ($P = 0.009$) and in desire ($P = 0.009$), arousal ($P = 0.009$), lubrication ($P = 0.008$), orgasm ($P = 0.012$) and satisfaction ($P = 0.049$). Sexual distress decreased ($P = 0.020$). At week 16 improvements in orgasm ($P = 0.028$), lubrication ($P = 0.043$), FSFI total score ($P = 0.028$) and sexual distress ($P = 0.027$) Vibrating devices: improvements in orgasm domain at week 12 versus baseline ($P = 0.028$). There were not significant differences at week 16. Not differences in orgasm characteristics

BDI: Beck Depression Inventory; CG: control group; EDSS: Expanded Disability Status Scale; EG: experimental group; FSS: Fatigue Severity Scale; FSFI: Female Sexual Function Index; MSISQ-19: Multiple Sclerosis Intimacy and Sexuality-19; MSQoL-54: Multiple Sclerosis Quality of Life-54; PLISSIT: Permission, Limited Information, Specific Suggestions, Intensive Therapy; Q: quasi-experimental.; RCT: randomized controlled trial; HAM-A: Hamilton Anxiety Rating Scale; HAM-D: Hamilton Depression Rating Scale; I-QoL: Incontinence Quality of Life; SFC: Sexual Function Questionnaire. DASA: Detailed Assessment of real-life Sexual Arousal; FSDS: Female Sexual Distress Scale; MS: multiple sclerosis; MSISQ-19: Multiple Sclerosis Intimacy and Sexuality-19; MSQoL-54: Multiple Sclerosis Quality of Life-54; ORS: Orgasm Rating Scale; PBSDE: Physical Disability Sexual and Body Esteem Scale; SCI: spinal cord injury; FSDS: Female Sexual Distress Scale; *DSM: Diagnostic and Statistical Manual of Mental Disorders.*

women who practised pelvic floor muscle exercises with electromyographic biofeedback and sham neuromuscular electrostimulation.[17] The use of sildenafil demonstrated improvements in orgasm in an extension phase.[14] The studies indicated that desire improves with sexual therapy,[10–13] the administration of Onabotulinumtoxin A,[15,16] an intervention combining pelvic floor exercises with tibial and intravaginal stimulation,[17] mindfulness[20] and the use of clitoral suction devices.[21]

Secondary outcomes of sexual dysfunction

Pain was the main secondary outcome of sexual dysfunction evaluated in most of the studies included. It was reduced significantly in two of the studies that evaluated sexual therapy[12,13] and only in one group of women who practised pelvic floor muscle exercises in combination with electromyographic biofeedback and intravaginal neuromuscular electrostimulation.[17] The remaining interventions identified did not show a significant improvement in pain.

Another secondary outcome evaluated was urinary incontinence, which improved in the two studies that applied Onabotulinumtoxin A.[15,16]

Tertiary outcomes of sexual dysfunction

The main outcomes evaluated were anxiety and depression, distress, self-esteem, satisfaction and quality of life.

Anxiety and depression were measured in the two studies that used Onabotulinumtoxin A.[15,16] In both cases, they decreased significantly. Distress was evaluated in the study including vaginal devices.[21] The use of clitoral suction devices reduced it significantly.[21] In contrast, the use of vibrator devices[21] did not improve these outcomes. There were also aspects related to self-esteem that were evaluated in two studies that used the extended version of the model of sex therapy, consisting of four different levels of intervention (Permission, Limited Information, Specific Suggestion and Intensive Therapy (PLISSIT))[13] and mindfulness.[20] In the first case, the outcomes improved significantly, but mindfulness did not demonstrate effectiveness in this aspect. Satisfaction improved in studies including sexual therapy,[10,12] the administration of Onabotulinumtoxin A,[15,16] pelvic floor muscles in combination with electrostimulation,[17] yoga[19] and the use of clitoral devices.[21] Trials in which mindfulness was used did not reach a significant improvement in satisfaction.[18,20] Quality of life was examined via sexual therapy,[12] the administration of Onabotulinumtoxin A,[15,16] yoga[19] and the use of sildenafil.[14] It improved significantly in all of the studies except for those including sildenafil.

Discussion

The present systematic review found that sexual therapy, the use of Onabotulinumtoxin A, pelvic floor exercises and the use of vaginal devices could improve some aspects of the sexuality of women with multiple sclerosis. The use of sildenafil, yoga and mindfulness could also lead to improvements, but the evidence is more limited.

Although sexuality is a holistic dimension that can be modified by physiological, psychological and sociocultural factors in women with multiple sclerosis, it seems that it is more common to evaluate the physiological factors.

Outcomes related to the primary causes of sexual dysfunction in women with multiple sclerosis, such as lubrication, arousal, orgasm or desire, have also been improved in female oncology patients using the PLISSIT model.[22] Therefore, the use of a standardized plan of sexual therapy could improve sexual function in women independently of the illness. Among sexual therapies that have also improved these outcomes in other groups of women are yoga[23] and mindfulness.[24] Nonetheless, although they also seem to improve sexual function in women with multiple sclerosis, the evidence is limited. In addition, these interventions may not be effective in women in whom multiple sclerosis has affected their physical and cognitive function to the point of preventing them from performing these interventions.[19,20]

A comprehensive approach to sexual dysfunction should also include a combination of these psychoeducational interventions and pharmacological

treatments. Sildenafil is the most widely known drug used in sexual dysfunction, and it has proven to be beneficial in primary outcomes such as erectile dysfunction in men with multiple sclerosis.[25] Nevertheless, there are limitations in terms of the safety and effectiveness of this drug.[25] In fact, the study of Alexander et al.[26] did not find significant improvements in women with spinal cord injury. Therefore, the benefit of sildenafil in women with multiple sclerosis may be minimal, and there is no evidence that it improves any aspect that other less-invasive interventions cannot achieve.

To complete any type of intervention, the involvement of partners in therapy is necessary to achieve positive results.[12] Nevertheless, it is important to consider that sexual satisfaction is derived not only from intercourse but also from other actions, such as tenderness, caresses and affection,[11] and a relationship is not always needed to improve sexual satisfaction. The option of utilizing devices, either with one's partner or on one's own, has shown significant improvements among women with sexual dysfunction.[21] Some of these device-based approaches, such as vaginal vibration, could improve some aspects, such as orgasm, not only in women with multiple sclerosis but also in women with spinal cord injury.[27] Specifically, devices that include clitoral stimulation provide more benefit than others. This could be related to the fact that physiologically, the clitoris is a very sensitive zone.[21]

Related to the secondary outcomes of sexual dysfunction, pain is the most frequently evaluated outcome in women with multiple sclerosis, and sexual therapy and pelvic floor exercises seem to be effective in reducing it. Related to sexual therapy, the PLISSIT model seems to reduce levels of pain not only among women with multiple sclerosis but also in other populations, such as female oncology patients.[22]

The administration of OnabotulinumtoxinA seems to improve urinary incontinence in women with multiple sclerosis,[15,16] but there is no evidence of a significant reduction in pain in these women. Nevertheless, Morrissey et al.[28] found evidence of the positive effects of the administration of OnabotulinumtoxinA in women with dyspareunia with hypertonic pelvic floor muscles.

Another strategy to improve urinary incontinence could be the use of pelvic floor muscle exercises.[29] These exercises alone or in combination with electrostimulation could improve urinary problems and, therefore, sexual function.[17] Nevertheless, it has not been directly measured in any of the studies that include women with multiple sclerosis, although this relationship is well known.[30] On the other hand, vaginal electrostimulation could also be effective in addressing sexual function in women without urinary incontinence,[30] so this intervention could be considered for women with multiple sclerosis and could improve other areas of functioning, such as bowel function.[31]

Tertiary outcomes are the least frequently evaluated outcomes, with quality of life being the most commonly evaluated. It has been demonstrated that sexual dysfunction affects quality of life in people with multiple sclerosis even more than physical disability does.[32] In this review, this variable improved with sexual therapy,[12] the administration of OnabotulinumtoxinA[15,16] and yoga.[19] These findings have also been noted in other populations, such as oncology female patients[22] and in women with hypertonic pelvic floor muscles,[28] for whom sexual therapy[22] and the administration of OnabotulinumtoxinA[28] have improved sexual function and quality of life. However, sildenafil did not improve quality of life variable in women with multiple sclerosis.[14] This finding has also been observed in women with spinal cord injury, for whom sildenafil did not demonstrate an improvement in quality of life.[26]

Finally, it is important to emphasize the fact that most of the studies regarding sexual dysfunction in women with chronic illness involve the illnesses that are most prevalent in society (e.g. cancer, cardiopathy), whereas multiple sclerosis, as well as its effects on sexuality, is less widely known. Furthermore, due to factors such as religion or the patriarchal culture of many countries, women may find it difficult to express sexual problems, and healthcare professionals could avoid treating them.[5]

The main limitation revealed by this review is the poor methodological quality of 8 of the 11 studies included. This may be related to the use of the

Jadad scale, which considers a limited number of variables.[33] Moreover, it is important to emphasize the difficulty of finding studies that include women with multiple sclerosis because most of the studies regarding sexual dysfunction in women with chronic illness mainly involve women affected by the most prevalent chronic diseases in society, such as cancer and cardiopathy. Due to the lack of research on this topic, highly sensitive searches were used as a compensatory measure.

This review has identified effective interventions for improving sexual function in women with multiple sclerosis. Although the available studies and their quality are thus far insufficient, most of the interventions described, or a combination of them, could be taken into account as clinical resources for the improvement of the sexuality of women with multiple sclerosis. Since all the interventions examined in this study included women who were physically and cognitive capable of performing them, further research should be conducted in patients with more advanced stages of the illness.

Clinical Messages

The following findings were observed in women with multiple sclerosis:

- The PLISSIT model could be used to improve sexual function.
- The administration of OnabotulinumtoxinA can improve urinary incontinence and therefore sexual function.
- Pelvic floor muscle exercises alone or in combination with electrostimulation can improve functioning and, consequently, sexual function.
- Vaginal devices may be recommended, but those that apply clitoral stimulation could be more effective than others.

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References

1. Porth CM and Curtis RL. Trastornos de la función motora. In: Porth CM (ed.) *Fisiopatología. Salud-enfermedad: Un Enfoque Conceptual*. 7th ed. Madrid: Médica Panamericana, 2006, pp.1215–1217.
2. Gumus H, Akpinar Z and Yilmaz H. Effects of multiple sclerosis on female sexuality: a controlled study. *J Sex Med* 2014; 11(2): 481–486.
3. Lew-Starowicz M and Rola R. Prevalence of sexual dysfunctions among women with multiple sclerosis. *Sex Disabil* 2013; 31: 141–153.
4. Merghati-Khoei E, Qaderi K, Amini L, et al. Sexual problems among women with multiple sclerosis. *J Neurol Sci* 2013; 331(1–2): 81–85.
5. Ashtari F, Rezvani R and Afshar H. Sexual dysfunction in women with multiple sclerosis: dimensions and contributory factors. *J Res Med Sci* 2014; 19(3): 228–233.
6. Bronner G, Elran E, Golomb J, et al. Female sexuality in multiple sclerosis: the multidimensional nature of the problem and the intervention. *Acta Neurol Scand* 2010; 121(5): 289–301.
7. Lew-Starowicz M and Gianotten WL. Sexual dysfunction in patients with multiple sclerosis. *Handb Clin Neurol* 2015; 130: 357–370.
8. Nortvedt MW, Riise T, Myhr KM, et al. Reduced quality of life among multiple sclerosis patients with sexual disturbance and bladder dysfunction. *Mult Scler* 2001; 7(4): 231–235.
9. Jadad AR, Moore RA, Carroll D, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary. *Control Clin Trials* 1996; 17(1): 1–12.
10. Khakbazan Z, Daneshfar F, Behboodi-Moghadam Z, et al. The effectiveness of the Permission, Limited Information, Specific Suggestions, Intensive Therapy (PLISSIT) model based sexual counselling on the sexual function of women with multiple sclerosis who are sexually active. *Mult Scler Relat Disord* 2016; 8: 113–119.
11. Christopherson JM, Moore K, Foley FW, et al. A comparison of written materials vs materials and counselling for women with sexual dysfunction and multiple sclerosis. *J Clin Nurs* 2006; 15(6): 742–750.
12. Zamani M, Tavoli A, Yazd Khasti B, et al. Sexual therapy for women with multiple sclerosis and its impact on quality of life. *Iran J Psychiatry* 2017; 12(1): 58–65.

13. Daneshfar F, Behboodi-Moghadam Z, Khakbazan Z, et al. The influence of Ex-PLISSIT (Extended Permission, Limited Information, Specific Suggestions, Intensive Therapy) model of intimacy and sexuality of married women with multiple sclerosis. *Sex* 2017; 35: 399–414.
14. Dasgupta R, Wiseman OJ, Kanabar G, et al. Efficacy of sildenafil in the treatment of female sexual dysfunction due to multiple sclerosis. *J Urol* 2004; 171(3): 1189–1193; discussion 1193.
15. Giannantoni A, Proietti S, Giusti G, et al. OnabotulinumtoxinA intradetrusorial injections improve sexual function in female patients affected by multiple sclerosis: preliminary results. *World J Urol* 2015; 33(12): 2095–2101.
16. Giannantoni A, Gubbiotti M, Rossi de Vermandois JA, et al. Effects of onabotulinum toxin A intradetrusor injections on urinary symptoms and sexual life in women affected by multiple sclerosis: a prospective controlled study. *J Neurol Neurophysiol* 2017; 8: 427.
17. Lucio AC, D'Ancona CA, Lopes MH, et al. The effect of pelvic floor muscle training alone or in combination with electrostimulation in the treatment of sexual dysfunction in women with multiple sclerosis. *Mult Scler* 2014; 20(13): 1761–1768.
18. Mosalanejad F, Afrasiabifar A and Zoladl M. Investigating the combined effect of pelvic floor muscle exercise and mindfulness on sexual function in women with multiple sclerosis: a randomized controlled trial. *Clin Rehabil* 2018; 32(10): 1340–1347.
19. Najafidoulatabad S, Mohebbi Z and Nooryan K. Yoga effects on physical activity and sexual satisfaction among the Iranian women with multiple sclerosis: a randomized controlled trial. *Afr J Tradit Complement Altern Med* 2014; 11(5): 78–82.
20. Hocaloski S, Elliott S, Brotto LA, et al. A mindfulness psychoeducational group intervention targeting sexual adjustment for women with multiple sclerosis and spinal cord injury: a pilot study. *Sex Disabil* 2016; 34: 183–198.
21. Alexander M, Bashir K, Marson L, et al. Randomized trial of clitoral vacuum suction versus vibratory stimulation in neurogenic female orgasmic dysfunction. *Arch Phys Med Rehabil* 2018; 99: 299–305.
22. Faghani S and Ghaffari F. Effects of sexual rehabilitation using the PLISSIT model on quality of sexual life and sexual functioning in post-mastectomy breast cancer survivors. *Asian Pac J Cancer Prev* 2016; 17(11): 4845–4851.
23. Dhikav V, Karmarkar G, Gupta R, et al. Yoga in female sexual functions. *J Sex Med* 2010; 7(2 Pt. 2): 964–970.
24. Stephenson KR and Kerth J. Effects of mindfulness-based therapies for female sexual dysfunction: a meta-analytic review. *J Sex Res* 2017; 54(7): 832–849.
25. Xiao Y, Wang J and Luo H. Sildenafil citrate for erectile dysfunction in patients with multiple sclerosis. *Cochrane Database Syst Rev* 2012; 18: CD009427.
26. Alexander MS, Rosen RC, Steinberg S, et al. Sildenafil in women with sexual arousal disorder following spinal cord injury. *Spinal Cord* 2011; 49(2): 273–279.
27. Sipski ML, Alexander CJ, Gomez-Marin O, et al. Effects of vibratory stimulation on sexual response in women with spinal cord injury. *J Rehabil Res Dev* 2005; 42(5): 609–616.
28. Morrissey D, El-Khawand D, Ginzburg N, et al. Botulinum toxin A injections into pelvic floor muscles under electromyographic guidance for women with refractory high-tone pelvic floor dysfunction: a 6-month prospective pilot study. *Female Pelvic Med Reconstr Surg* 2015; 21(5): 277–282.
29. Ferreira CH, Dwyer PL, Davidson M, et al. Does pelvic floor muscle training improve female sexual function? A systematic review. *Int Urogynecol J* 2015; 26(12): 1735–1750.
30. Aydin S, Arioglu Aydin C, Batmaz G, et al. Effect of vaginal electrical stimulation on female sexual functions: a randomized study. *J Sex Med* 2015; 12(2): 463–469.
31. Sipski ML. Sexual response in women with spinal cord injury: neurologic pathways and recommendations for the use of electrical stimulation. *J Spinal Cord Med* 2001; 24(3): 155–158.
32. Schairer LC, Foley FW, Zemon V, et al. The impact of sexual dysfunction on health-related quality of life in people with multiple sclerosis. *Mult Scler* 2014; 20(5): 610–616.
33. Berger VW and Alperson SY. A general framework for the evaluation of clinical trial quality. *Rev Recent Clin Trials* 2009; 4(2): 79–88.

Appendix 1

Search strategy: examples

Medline.

Search	Query	Items found
1	Multiple sclerosis [Mesh]	56,450
2	Multiple sclerosis [Title/Abstract]	71,729
3	1 OR 2	79,130
4	Women [Mesh]	35,270
5	Women [Title/Abstract]	925,320
6	4 OR 5	939,526
7	Sexuality [Mesh]	102,732
8	Sexuality [Title/Abstract]	15,278
9	7 OR 8	109,570
10	3 AND 6 AND 9	56
11	Female [Title/Abstract]	671,990
12	4 OR 5 OR 11	1,514,290
13	Sexual dysfunction [Title/Abstract]	9910
14	Sex*[Title/Abstract]	707,835
15	7 OR 8 OR 13 OR 14	741,080
16	3 AND 12 AND 15	970

CINAHL.

Search	Query	Items found
1	(MH 'multiple sclerosis')	16,893
2	TI multiple sclerosis	10,528
3	AB multiple sclerosis	9897
4	1 OR 2 OR 3	19,841
5	(MH 'women')	17,270
6	TI women	107,083
7	AB women	296,382
8	5 OR 6 OR 7	343,966
9	(MH 'sexuality')	27,172
10	TI sexuality	3521
11	AB sexuality	5986
12	9 OR 10 OR 11	30,584
13	4 AND 8 AND 12	25
14	TI female	19,288
15	AB female	157,713
16	5 OR 6 OR 7 OR 14 OR 15	479,457
17	TI sexual dysfunction	1273
18	AB sexual dysfunction	2409
19	TI sex*	58,531
20	AB sex*	150,473
21	9 OR 10 OR 11 OR 17 OR 18 OR 19 OR 20	181,151
22	4 AND 16 AND 21	228

PsycINFO.

Search	Query	Items found
1	MA (multiple sclerosis)	7617
2	ti (multiple sclerosis)	9543
3	ab (multiple sclerosis)	14,308
4	1 OR 2 OR 3	15,340
5	MA (women)	12,417
6	ti (women)	90,526
7	ab (women)	282,919
8	5 OR 6 OR 7	297,198
9	MA (sexuality)	1851
10	ti (sexuality)	7633
11	ab (sexuality)	24,963
12	9 OR 10 OR 11	27,643
13	4 AND 8 AND 12	22
14	ti (female)	37,658
15	ab (female)	301,721
16	5 OR 6 OR 7 OR 14 OR 15	548,862
17	ti (sexual dysfunction)	1972
18	ab (sexual dysfunction)	5797
19	ti (sex*)	114,093
20	ab (sex*)	291,825
21	9 OR 10 OR 11 OR 17 OR 18 OR 19 OR 20	306,012
22	4 AND 16 AND 21	318