A Controlled Clinical Trial on the Effects of Exercise on Lower Urinary Tract Symptoms in Women With Multiple Sclerosis

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Objective: The aim of the study was to investigate the effects of two pelvic floor exercise programs on lower urinary tract symptoms and quality of life in participants with multiple sclerosis.

Design: This is a prospective, single-blind, clinical trial.

Settings: The study used a community rehabilitation program within a large metropolitan health service.

Participants: Thirty women in moderate stage of multiple sclerosis were referred for outpatient rehabilitation.

Interventions: In a period of 6 mos, participants underwent a pelvic floor exercise program, associated or not with vaginal electrotherapy.

Main Outcomes: The main outcomes are overactive bladder, perineal contraction, and quality of life.

Results: The findings showed benefits of both programs on overactive bladder and quality of life. Participants undergoing exercise plus electrotherapy presented greater improvement on contraction of the perineal musculature and quality of life.

Conclusions: Six months of exercise provided benefits on lower urinary tract symptoms and quality of life in women with multiple sclerosis. Electrical stimulation potentiated the improvement on perineal musculature and quality of life. This trial was registered prospectively with the Clinical Trials Register, ID: BR-287q65 (http://www.ensaiosclinicos.gov.br/rg/RBR-287q65/).

Key Words: Multiple Sclerosis, Overactive Bladder, Lower Urinary Tract Symptoms, Physical Therapy Specialty

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Multiple sclerosis (MS) is a chronic, autoimmune, inflammatory, demyelinating disease that causes lesion in the white matter of the central nervous system. The most common form of the disease is the "recurrent remittent," which is characterized by neurological dysfunction episodes followed by remission.[1,2] Depending on the location of lesions, a wide range of neurological symptoms arises, affecting patients' quality of life (QoL).[3]

Many patients with MS develop some form of lower urinary tract dysfunction. Urinary retention is common in MS, and it is associated to disruptions of neurologic signaling.[4] Lesions in brain, for instance, are responsible to detrusor overactivity. Lesions in the sacral area, differently, may cause detrusor underactivity.[5] In both cases, the development of therapies seeking to improve such symptoms and ensuring QoL is noticeable.

Antimuscarinics drugs constitute the first-line pharmacological treatment for neurogenic overactive bladder.[6] However, those medicaments may cause adverse effects, such as dry mouth, constipation, dizziness, and blurred vision, being many times responsible for treatment abandonment.[7]

Electric stimulation is a therapeutic resource that presents rare adverse effects and has been studied for lower urinary tract symptoms (LUTS).[8] It is believed that the stimulation of lower sensory motor nerves potentiates somatic afferent branches that pass through sacral spinal roots, inhibiting the detrusor overactivity.[8,9] However, promising these assumptions may be, Monteiro et al.[10] reinforce the need of more studies on this theme.

Pelvic floor exercises presented noticeable results for overactive bladder treatment in women with MS.[11] It is supposed that pelvic floor muscle contraction is associated with perineal-detrusor reflex activation, promoting relaxation in the detrusor musculature.[12]

Because LUTS in women with MS are responsible for significant impact on QoL, interfering in a negative way in one's emotional state and sexual life,[13] we investigated the effect of two pelvic floor exercise programs (exercise and exercise associated with electrotherapy) on LUTS and QoL in women with MS. The hypothesis delimited by the authors was that exercise plus electrostimulation would engender superior results to patients with MS than exercise alone.

METHODS

To achieve the objectives, we carried out a prospective clinical trial composed by two independent groups: the experimental and the control groups. All participants provided informed consent. The protocol was approved by the Human Research Protection Office and the project was registered in

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the the Brazilian Registry of Clinical Trials (Identifier Code: RBR-287q65). All participants provided written consent before the assessments. This study conforms to all CONSORT guidelines (see Supplemental Checklist, Supplemental Digital Content 1, http://links.lww.com/PHM/A773).

Inclusion criteria involved women older than 18 yrs diagnosed with recurring-remittent MS and presenting symptoms of urinary dysfunctions for at least 6 mos, with at least three of the following symptoms: urgency, urinary urge incontinence, increased micturition frequency, nocturia, and nocturnal enuresis.

Exclusion criteria comprised cases of severe MS (score superior to 6.5 on the Expanded Disability Status Scale in Multiple Sclerosis [EDSS][14]), participants with cognitive decline, genital prolapse, those who were virgin, pregnant, those who had undergone abdominal surgeries, a history of urinary tract infections and treatment with pelvic floor exercises, and those who had already made use of antimuscarinics or another specific medicament for overactive bladder control. If the participant had urinary tract infection during treatment, she could attend the exercise sessions but her data would be excluded from the study.

Settings and Allocation

All subjects underwent an initial evaluation in the Multiple Sclerosis Outpatient Center, during which their clinical conditions were assessed. Physical examination of the participants was conducted by a team of neurologists devoted to treating movement disorders.

The selection of participants was performed based on convenience, because only individuals who could go to the outpatient center were included. An independent researcher was responsible for making a randomized block division and ensuring that the groups were homogeneous for sociodemographic and clinical characteristics. The sample size was estimated assuming a power of 95%, with a 5% type I error and an effect size of 0.349.[15] Figure 1 details the flow of participant selection and monitoring during the study.

Therapeutic Protocols

This study involved two therapeutic protocols applied in women with MS. The experimental group was characterized by sessions undertaken at the Multiple Sclerosis Outpatient Center, and the control group consisted of a set of activities undertaken by the patient herself at home.

Participants of the experimental group performed exercises for LUTS and received intravaginal electrostimulation with the Dualpex 961 Uro device (QUARK, São Paulo, Brazil). The exercise protocol included three sets of 8–10 close-to-maximal contractions, in lying down, sitting up and standing positions. Each contraction should be held according to the endurance of the pelvic floor muscles with the participants aiming to hold the muscles for 10 secs. After the exercise protocol, an intravaginal electrode was introduced into the patient's vaginal introitus, aiming to stimulate S2–S4 dermatomes. Electric parameters used were frequency of 2 Hz, positive pulse duration of 1 millisec, intensity tolerable by the patient, and therapy time of 30 mins. During electric stimulation, participants were requested to perform 20 fast and 20 slow contractions of the pelvic floor musculature. Sessions occurred twice a week for 6 mos.

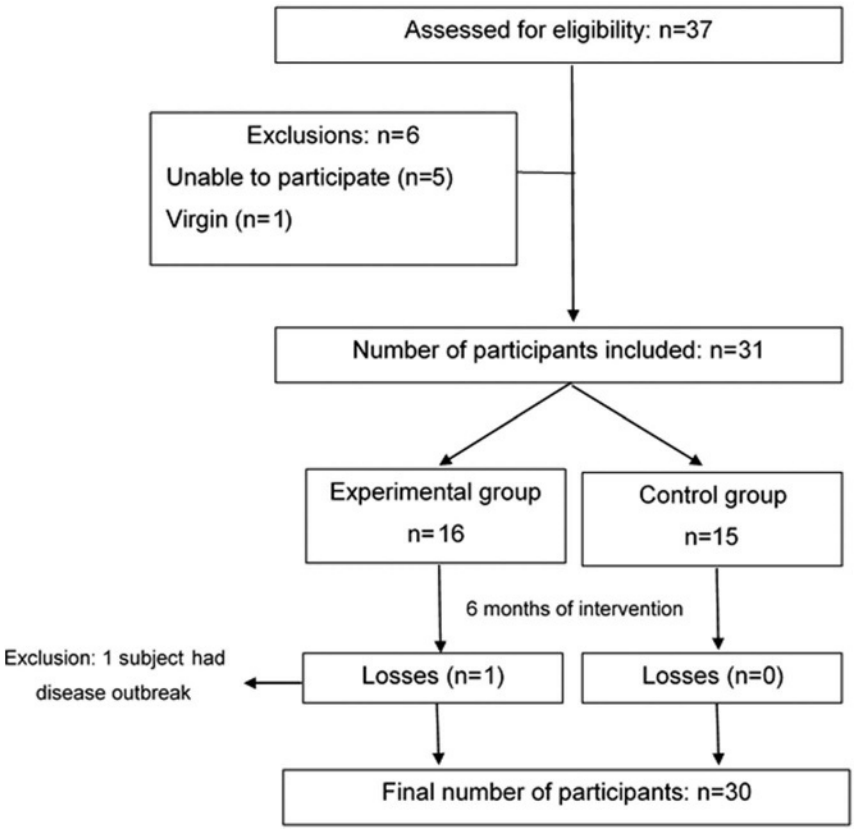

FIGURE 1. Flow diagram of the study.

TABLE 1. Anthropometric and clinical predictors in the experimental and control groups

Variables	Experimental Group	Control Group	*P*
Sample size, *n*	15	15	0.999
Age, yr	38.6 ± 13.5	49.8 ± 16.5	0.052
EDSS scores	3.5 ± 1.0	3.5 ± 0.5	0.907
Sex, male:female	0:15	0:15	0.999
Perineal sensitivity, normal:moderate:severe	14:0:1	13:1:1	0.595
Cutaneous anal reflex, presente:absent	12:3	9:6	0.232
Genital dystopia, yes:no	0:15	0:15	0.999
Voluntary contraction, yes:no	15:0	14:1	0.309
Stress test with loss of urine, yes:no	0:15	0:15	0.999

Age and EDSS are expressed in mean ± standard deviation. *P* values in the Student's independent *t* test. Other variables are arranged by number of cases. *P* values in χ^2 test.

The control group also received a treatment protocol. Participants performed the same training protocol of the experimental group, but without support of electrostimulation, and at home. A physical therapist specialized in urogynecological disorders explained the individuals of the control group about the function and location of pelvic floor muscles and showed the proper technique about how to perform the pelvic floor exercises. To ensure that the activities were undertaken, the researchers kept contact via phone calls every week. Absence of activity performance for 2 wks (whichever group it was) constituted exclusion of the patient from the study.

Evaluation Procedures

As for the evaluative procedures, all participants underwent prior evaluation, where anthropometric and clinical data were collected.

The Qualiveen questionnaire[16] was used for the analysis of QoL. This instrument was chosen because it enables the investigation of the impact of urinary dysfunctions on participants' health. It is divided among the domains "inconvenience," "restrictions," "fears," "impact on daily life," "specific impact of urinary problems," and "general quality of life." Higher scores represent higher impact on the QoL. Although the instrument was originally developed for individuals with spinal cord injury, the Qualiveen questionnaire has proved valid for MS patients.[17]

Overactive bladder, in turn, was assessed by means of the Overactive Bladder Assessment questionnaire.[18] The instrument asks how bothered one is by the following four hallmark symptoms of overactive bladder: urinary frequency, urgency, nocturia, and urge incontinence. In this instrument, higher values are related to worst overactivity of the bladder.

The PERFECT scheme[19] was used in this study, in which it was possible to monitor the progression of the strength of the patients' perineum over the period in which the therapeutic protocols were administered. PERFECT is an acronym with P representing power, E representing endurance, R representing repetitions, F representing fast contractions, and ECT representing every contraction timed. The pelvic floor muscle were examined using the index finger placed approximately 4–6 cm inside the vagina and positioned at 4 and 8 o'clock to monitor muscle activity. Moderate pressure was applied over the muscle bulk to assist in the initiation of the appropriate muscle contraction.[19]

All instruments and tests used in this study present adequate validity and reliability for MS.

Statistical Analysis

Data analysis occurred by means of descriptive and inferential statistics. At first, normality analysis was carried out through the Shapiro-Wilk test. Data that presented parametric patterns were described in mean ± standard deviation and those with nonparametric features were described in median ± interquartile range.

Categorical variables were described in number of events and analyzed according to the χ^2 test. Continuous variables that presented parametric patterns were analyzed by means of the Student's independent *t* test. The variables of the PERFECT scheme, overactive bladder, and QoL remained with nonparametric characteristics even after exclusion of outliers and conversions in logarithmic data. In the face of that, we maintained exclusion of outliers and applied the Mann-Whitney *U* and Wilcoxon tests on raw data. For all analyses, we admitted a level of significance of 5% ($P < 0.05$).

RESULTS

Thirty individuals finished this study. Of them, 15 composed the experimental group and 15 composed the control group. Participants were 44.2 ± 15.9 yrs old at entry and both groups were formed exclusively by women.

Table 1 details anthropometric and clinical values of the subjects at the beginning of the study. As one can observe, groups were similar for all variables. There was a trend of difference for age, pointing out that the control group was relatively older than the experimental group.

The efficacy of the exercise protocols on the participants' perineal musculature is shown in Table 2. At baseline, groups

TABLE 2. Initial and final results of the participants' contraction of the perineal musculature (the PERFECT scheme)

Output	Groups	Assessment		*P*[a]
		Initial	Final	
Power, score	Experimental	2.0 ± 2.0	2.0 ± 1.0	0.999
	Control	2.0 ± 2.0	2.0 ± 1.0	0.317
	P[b]	0.549	0.642	
Endurance, sec	Experimental	5.0 ± 4.0	5.0 ± 8.0	0.109
	Control	3.0 ± 0.7	3.0 ± 1.0	0.317
	P[b]	0.130	0.072	
Repetitions, *n*	Experimental	5.0 ± 1.5	5.0 ± 2.0	0.063
	Control	5.0 ± 0.0	5.0 ± 0.0	0.999
	P[b]	0.213	0.025	
Fast contractions, *n*	Experimental	6.0 ± 3.5	7.5 ± 5.0	0.042
	Control	5.0 ± 1.0	5.0 ± 1.5	0.317
	P[b]	0.156	0.098	

The results are expressed in median ± interquartile range.

[a]*P* values in Wilcoxon test.

[b]*P* values in the Mann-Whitney *U* test.

were homogeneous for all variables. Final intergroups comparisons pointed out a significant difference for "repetitions." Paired analyses pointed out that the control group did not present significant changes on the contraction of the perineal musculature, and the experimental group presented an improvement on "fast contractions."

The effect of the therapeutic protocols on the overactive bladder is found in Table 3. The statistical analysis indicated that both groups improved the score for the overactive bladder in relation to the initial values. However, the absence of difference between groups at baseline and the significant difference between them at the final assessment point out that the improvement of experimental group was more expressive than that of the control group.

Table 4 shows the impact of the exercise protocols on the subjects' QoL. As one can observe, participants of the experimental group showed improvement in all domains of the instrument. Differently, the control group had significant improvement only on the domains "inconvenience" and "specific impact of urinary problems."

DISCUSSION

Urinary dysfunctions are common characteristics in MS and represent a serious problem because of their high prevalence and consequent social repercussion. Urinary urgency, frequency, urge incontinence, and nocturia are symptoms frequently seen.[20] In this scenario, treatments seeking to promote the control of detrusor overactivity, and therefore, control of urination urgency symptoms, pollakiuria, nocturia, and urinary incontinence are noticeable.

The aim of the present study was to analyze the effects of two therapeutic protocols on overactive bladder, perineal contraction, and QoL in women with MS. Results point out benefits in both groups, with the experimental group (that underwent intravaginal electrostimulation and exercise) many times having greater benefit than the control group.

With regard to age, the control group was relatively older than the experimental group. Although this aspect is relevant (because there might be more postmenopausal women in one group than in the other), we believe that it did not interfere in the patients' pelvic characteristics because the groups were homogeneous for all urogenital function (perineal sensitivity, cutaneous anal reflex, genital dystopia, voluntary contraction, and stress test).

The integrity of urogenital functions in both groups reinforces that patients had motor and sensitivity characteristics with no disability. This evidence that urinary symptoms in MS are related to the detrusor hypercontractility, as observed in the overactive bladder assessment. Dermatomes were normal for all patients, demonstrating that the tracts were unobstructed to receive treatment protocol stimuli.

In this study, we used EDSS[14] to access disease severity of the participants. As stated by Meyer-Moock et al.,[21] the instrument is frequently and internationally used in clinical trials, and it is suitable to monitor disease progression. Results of EDSS remained without changes during treatment, indicating that the neurological clinical condition was steady in the 6 mos of intervention. This is an important fact that provides a solid ground for stating that the obtained results stemmed from performed treatments and not from the remission that is characteristic of MS.

The use of perineal electrostimulation in the experimental group was based on the need to inhibit the detrusor muscle involuntary contraction. We used low-frequency stimulation as a way of promoting parasympathetic motor neurons central inhibition, a fact that is known to have generated great results in association with conventional exercise.[15,22]

An interesting finding was associated with the PERFECT scheme assessment, where the experimental group presented improvement in "fast contractions." A previous study showed that pelvic floor muscle contractions lead to a decline of detrusor and increase of urethral pressures.[23] We believe that the association of electrostimulation with exercise is an efficient protocol for strength, with the pelvic floor musculature presenting improvement particularly on fast fibers, responsible for vigorous and reflex contractions.[23,24] Different in the experimental group, the control group did not present any significant improvement in the PERFECT scheme. We associate such result by the inefficiency of performing exercises at home with no direct supervision or by the absence of electrotherapy, which may potentiate the effects of the exercise protocol. Future research should be conducted to address this topic.

In the past, we carried out a study where women with MS used surface electrical stimulation to control LUTS.[15] In the present study, we applied electrical stimulation with an intravaginal electrode. Although both studies showed benefits of electrotherapy on LUTS, surface electrical stimulation might be more interesting because intravaginal electrode is a very invasive treatment in the patient's perception, many times decreasing the acceptance and adherence to use of this treatment. Surface electrical stimulation, differently, have many advantages, such that it is not necessary sterilize the equipment, it is a cheap treatment, and it can be used in women, men, and children, because it is not invasive.[25]

Overactive bladder is a common problem in women with MS.[5] The use of a bladder diary is important to show the patients bladder patter of urination and to help figure out the causes of bladder control trouble. In the present study, no participant had urinary tract infection during evaluation and treatment. The analysis of the Overactive Bladder Assessment questionnaire demonstrated that both groups had an initial involvement and obtained improvement of LUTS through therapeutic protocols. Notwithstanding the more significant results found in patients who carried out electrostimulation associated with exercise, the findings confirm the following: the importance of prescription of exercises to MS patients and the need of associating electrotherapy with exercise in an outpatient clinic environment to potentiate results.

TABLE 3. Initial and final results of the overactive bladder in the experimental and control groups

Output	Groups	Assessment		P^a
		Initial	Final	
Overactive bladder, score	Experimental	24.0 ± 8.5	0.5 ± 5.0	0.001
	Control	22.0 ± 10.0	9.0 ± 18.0	0.008
	P^b	0.429	0.014	

The results are expressed in median ± interquartile range.

[a] P values in Wilcoxon test.

[b] P values in the Mann-Whitney U test.

TABLE 4. Initial and final results of the participants' QoL

Output	Groups	Assessment		P^a
		Initial	Final	
Inconvenience (score)	Experimental	1.1 ± 1.4	0.1 ± 0.3	0.001
	Control	0.7 ± 0.6	0.1 ± 0.5	0.041
	P^b	0.189	0.798	
Restrictions (score)	Experimental	1.4 ± 1.5	0.4 ± 0.7	0.007
	Control	0.7 ± 0.6	0.4 ± 0.5	0.115
	P^b	0.057	0.892	
Fears (score)	Experimental	1.0 ± 1.1	0.3 ± 0.5	0.003
	Control	0.9 ± 0.5	0.5 ± 0.6	0.248
	P^b	0.518	0.085	
Impact on daily life (score)	Experimental	1.2 ± 1.6	0.4 ± 0.2	0.004
	Control	0.7 ± 0.6	0.4 ± 0.5	0.260
	P^b	0.014	0.566	
Specific impact of urinary problems (score)	Experimental	1.1 ± 1.1	0.3 ± 0.3	0.002
	Control	0.7 ± 0.7	0.4 ± 0.4	0.041
	P^b	0.074	0.227	
General QoL (score)	Experimental	−0.6 ± 0.7	0.2 ± 0.9	0.001
	Control	−0.4 ± 0.4	−0.3 ± 0.5	0.243
	P^b	0.292	0.022	

The results are expressed in median ± interquartile range.

[a]*P* values in Wilcoxon test.

[b]*P* values in the Mann-Whitney *U* test.

Although home exercises were not enough to promote perineal strengthening in the control group, they were effective in giving rise to significant results in the control of LUTS. We believe that pelvic floor contraction promotes afferent discharge in the pudendal nerve, leading to sympathetic bladder innervation, and as a reflexive consequence, a disordered detrusor contraction inhibition.

As for QoL, it is much affected in patients with MS.[26,27] Analysis carried out showed that the improvement of urinary symptoms in the experimental group was more expressive than that of the control group, directly impacting on response to QoL. This finding is interesting because it shows that changes in symptoms influence in a positive manner not only specific items of the Qualiveen questionnaire that are related to urinary symptoms but also bringing satisfying results as for the overall QoL.

It is also relevant to say that the protocols presented good acceptance by patients with MS, as evidenced by the low rate of sample loss. As hard as it may be to control exercises performance frequency in the control group (for their activities carried out at home), it is important to highlight that the researchers kept constant contact via phone calls. In addition, beneficial results found in this group would probably not have been achieved in case there was no commitment of participants.

Finally, it should be stressed that by applying two pelvic floor muscle strengthening protocols in patients who did not make use of drug treatment, our objective was not to propose the replacement of a therapy by another. Our intention was to emphasize the effect of the exercise protocol, isolating the effect of medication. We believe that our results meet the American College of Physicians guidelines[28] and such therapy can be applied concomitantly with drug treatment.

Limitations

Although the current study provides important information about the benefits of exercise on LUTS and QoL in women with MS, it has some limitations that need to be considered. Firstly, it is important to underscore that only participants in moderate stage of MS were included. The exclusion of participants in early stage of MS was due to the requirement that subjects possessed urinary dysfunctions symptoms for at least 6 mos, which is infrequent at the beginning of the disease.[29] Furthermore, participants with severe involvement were excluded because their physical incapacity could bring about difficulties in exercises performance and generate bias in results.

Secondly, many may argue on the small size of the sample. In that case, the reader must consider the difficulty of recruiting MS participants with no cognitive impairment. Because cognitive decline affects up to 65% of the patients, many of them early in the course of the disease,[30] we had trouble in getting a more presentative sample.

Finally, there may be a bias caused by the absence of a control group that did not carry out exercise. Although such a fact makes it unviable to affirm the benefits of both protocols on the sedentary patient, the authors have taken into account ethical precepts and opted for not leaving any patient untreated.

CONCLUSIONS

Pelvic floor muscle strengthening exercises have shown to be beneficial for women with MS and promoted improvement in LUTS and QoL. Results demonstrated that electrostimulation associated with pelvic floor strengthening training potentiates the outcomes. New researches are still needed to investigate the exercises effects in the long term and to compare the

benefits of superficial versus intravaginal electrical stimulations in women with MS.

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