Research article

Overactive bladder symptoms in patients with multiple sclerosis: Frequency, severity, diagnosis and treatment

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Objective: To determine the frequency and severity as well as the diagnosis and treatment of overactive bladder problems in patients with multiple sclerosis (MS) followed up at five centers in Turkey.
Design: Survey study.
Setting: Outpatient tertiary clinics of physical medicine and rehabilitation and neurology.
Participants: Consecutive MS patients scheduled for outpatient follow-up ($n = 309$).
Intervention: MS patients were asked to complete a questionnaire regarding the frequency and severity, as well as the diagnosis and treatment of their overactive bladder problems.
Results: The mean age ± SD was 39.3 ± 10.6 years. Urinary urgency was the most common urinary symptom (62%), followed by frequency (50.4%), urge incontinence (44.7%) and nocturia (33%). Residual urine volume was measured using a portable ultrasound instrument in 13.3% of the patients and by catheterization in 16.2% of them. Urodynamic investigations and urinary tract ultrasound were performed on 26.5% and 35.3% of the patients, respectively. Anticholinergic medications were prescribed for 27.5% of the patients. Intermittent catheterization and indwelling catheterization were used on 8.1% and 1.9% of the patients, respectively. The overactive bladder symptom score (OABSS) was significantly higher in patients who had had residual urine measurement ($P < 0.001$), upper urinary tract assessment by ultrasound ($P < 0.001$), urodynamic assessment ($P < 0.001$), admitted to a doctor for urinary symptoms ($P < 0.001$), and current or past catheter use ($P = 0.002$).
Conclusion: Urgency was the most common urinary symptom followed by frequency, urge incontinence and nocturia in MS patients. The patients with lower OABSS had detailed urological assessments less frequently than the patients with higher OABSS.

Keywords: Multiple sclerosis, Neurogenic bladder, Urinary symptom, Intermittent catheterization, Indwelling catheterization

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Introduction

Multiple sclerosis (MS) is a progressive, demyelinating disease of the central nervous system.[1] MS patients frequently suffer from urinary complaints.[2–4] De Seze and colleagues[5] report a prevalence of 37–99% for overactive bladder syndromes, characterized by irritative bladder symptoms, a prevalence of 34–79% for obstructive symptoms and 25% for chronic urinary retention. Quarto *et al.*[6] showed that over active bladder (OAB) symptoms had a major impact on the quality of life (QoL) of patients with MS Mahajan *et al.*[7] investigated the prevalence of overactive bladder symptoms as well as the rates of evaluation and treatment of urinary complaints in patients with MS in a large-scale study. They found that urological evaluation and treatment were significantly underused in the care of patients with MS[7] Our aim was to investigate the frequency and severity of OAB symptoms as well as to document the modalities used to diagnose and treat the patients who were followed up at five centers in Turkey. The results obtained in this manner, might help in increasing the awareness of neurologists, physiatrists and urologists interested in this subject and displaying the deficiencies in the diagnosis and treatment of urinary symptoms in MS patients.

Materials and methods

The five centers including physical and rehabilitation medicine (PRM) and neurology clinics participated in this joint study. After approval by the Institutional Ethics and Review Board, MS patients scheduled for outpatient follow-up appointments were asked to complete a questionnaire regarding the frequency and severity, as well as diagnosis and treatment of their overactive bladder complaints.

The demographic data of the patients were recorded. Presence of the OAB symptoms including frequency, urgency, urge incontinence and nocturia were asked. Severity of the OAB symptoms was determined according to the overactive bladder symptom scores (OABSS). The OAB symptom score ranging from 0 to 12 was calculated according to the degree of discomfort experienced by the patients regarding frequency, urgency, urge incontinence and nocturia, as follows, 0: not at all, 1: slightly, 2: moderately, 3: greatly.[7]

The patients were questioned whether they had sought any medical advice for their urinary complaints, or whether they had been questioned by a physician regarding bladder problems The specialty of the physicians was also questioned.

Additionally, history of diagnostic testing including residual urine measurement, urinary tract ultrasound (US) and urodynamic assessment was recorded. They were asked whether they had been prescribed anticholinerjic medications (ACM), clean intermittent or continuous catheterization, intradetrusor injections of botulinum neurotoxin type A (BoNT-A), pretibial nerve stimulation and pelvic floor muscle exercise (PFME) training.

Multiple sclerosis related physical disability was assessed by using the Patient Determined Disease Steps scale (PDDS). The PDDS is a validated measure of disability based on self-reporting. The PDDS scale scores corresponds to 0 = Normal; 1 = Mild disability, mild symptoms or signs; 2 = Moderate disability, visible abnormality of gait; 3 = Early cane, intermittent use of cane; 4 = Late cane, cane-dependent; 5 = Bilateral support; 6 = Confined to wheelchair; and U = Unclassifiable.[8]

Statistical analysis

Data were summarized as percentages, mean ± standard deviation, median (minimum-maximum). Non-parametric tests were used for hypothesis testing due to violation of normal distribution. The χ^2 test, Mann-Whitney *U* test and the Spearman Correlation test were used. A P value less than 0.05 was considered as statistically significant.

Results

There were 309 MS patients (200 women, 109 men) with a mean age of 39.3 ± 10.6 (range: 19–69) years. The mean age at disease onset was 32.89 ± 10.11 (19–64) years and the mean illness duration was 6.9 ± 5.9 (1–30) years. Urgency was the most common urinary symptom (62%), followed by frequency (50.4%), urge incontinence (44.7%), and nocturia (33%). Urgency was more common in men ($P < 0.05$), however, there was no sex difference in other urinary symptoms The OABSS was similar in men and women (3.21 ± 3.67 and 2.90 ± 3.50, respectively; $P = 0.514$) (Tables 1 and 2).

Overall, 81.9% of the patients had been questioned about their urinary complaints by a neurologist and/or a physiatrist. 47.6% of the patients sought medical advice concerning their urinary complaints. The OABSS was 4.37 ± 3.78 in patients and it was higher compared to those who had not sought any medical advice (1.76 ± 2.85) ($P < 0.001$).

Residual urine volume was measured using a portable ultrasound instrument in 13.3% of the patients and using an urinary catheter in 16.2% of them. The OABSS was higher in the patients who had residual

Table 1 Demographic and clinical characteristics of the patients

Age (years)(Mean ± SD)(Range)	39.3 ± 10.6 (19–69)
Disease duration (years)((Mean ± SD)(Range)	6.9 ± 5.9 (1–30)
Urgency (%)	62
Frequency (%)	50.4
Urge incontinence (%)	44.7
Nocturia (%)	33
Patients questioned about urinary complaints (%)	81
Patients seeking medical advice for urinary complaints (%)	47.6
Residual urine measurement by ultrasound (%)	13.3
Residual urine measurement by catheter (%)	16.2
Upper urinary tract assessment by ultrasound (%)	35.3
Urodynamic Investigations (%)	26.5
Anticholinergic medication prescribed (%)	27.5
Tolterodine (%)	8.4
Oxybutinin (%)	6.8
Trospium (%)	5.8
Current or past urinary catheter use (%)	10
Intra-detrusor BoNT-A injection (%)	0.97
Pelvic floor exercises (%)	4.8
Electrical stimulation (%)	0.64

urine measurement compared to those who had not (4.91 ± 3.83 vs. 2.21 ± 3.12) ($P < 0.001$).

Urinary tract scanning by US was performed in 35.3% of the patients. The OABSS was higher in patients who had had urinary tract US compared to those who had not (4.33 ± 3.72 vs. 2.28 ± 3.26; $P < 0.001$).

Urodynamic investigations were performed on 26.5% of the patients. The OABSS of those who had urodynamic investigations were also significantly higher compared to those who had not (5.01 ± 3.68 vs. 2.28 ± 3.23; $P < 0.001$).

Anticholinergic medications were prescribed for the 27.5% of the patients. Tolterodine, oxybutynin and trospium were prescribed for 8.4%, 6.8% and 5.8% of the patients, respectively. Of the respondents, 10% reported current or past urinary catheter use including clean intermittent catheter (8.1%) and indwelling catheter (1.9%). Anticholinergic medication use was significantly higher in those using a catheter ($P < 0.001$). Furthermore, the OABSS was significantly higher in the respondents using catheters compared to those who were not (5.22 ± 4.39 vs. 2.75 ± 3.37; $P = 0.002$) (Tables 1 and 2).

Table 2 Comparison of the overactive bladder symptom scores (OABSS)

	OABSS	P value
Seeking medical advice for urinary complaints		
Yes	4.37 ± 3.78	<0.001
No	1.76 ± 2.85	
Residual urine measurement		
Yes	4.91 ± 3.83	<0.001
No	2.21 ± 3.12	
Assessment of upper urinary tract by ultrasound		
Yes	4.33 ± 3.72	<0.001
No	2.28 ± 3.26	
Urodynamic assessment		
Yes	5.01 ± 3.68	<0.001
No	2.28 ± 3.23	
Current or past urinary catheter use		
Yes	5.22 ± 4.39	0.002
No	2.75 ± 3.37	

The respondents with longer disease duration more commonly received ACM ($P < 0.001$) and urinary catheterization ($P = 0.018$). The ACM use ($P < 0.001$) and urinary catheterization were significantly more common in MS patients with an OABSS of 5 or greater ($P = 0.01$).

Correlation analysis revealed a positive correlation between the disease duration ($P < 0.001$), difficulty in walking (PDDS) and the OABSS ($P < 0.05$). There was also a positive correlation between the ACM use and urinary catheterization ($P < 0.001$) and between the ACM use, urinary catheterization and difficulty in walking ($P < 0.01$). Intradetrusor injections of BoNT-A were applied only to 3 patients. Pelvic floor muscle exercises and electrical stimulation therapy were used on 15 and 2 patients, respectively.

Discussion

In the cross-sectional survey performed on 9702 MS patients registered in the North American Research Committee on MS (NARCOMS), Registry, Mahajan ST *et al.* reported that 65% of the patients had at least one moderate to severe urinary symptom.[7] Complaints of nocturia and urinary leakage were more common in women, and compatible with our study urgency was more common in men. Similar to the results of the NARCOMS survey,[7] we found a positive correlation between disease duration, difficulty in walking (PDDS) and OABSS.

Our findings showed the need of questioning MS patients about urinary symptoms In our sample many patients with urinary complaints had simply tolerated the symptoms and had not sought for medical help. As expected the OABSS was significantly higher in patients who had visited a physician with urinary complaints. A large-scale study performed by Mahajan *et al.*[7] also confirmed that patients with more OAB complaints were more likely to be evaluated by an urologist than those with fewer urinary complaints. Long-term outcomes of the patients with less urinary symptoms needs to be clarified by the future studies to determine the necessity of further assessment among these patients.

According to the UK consensus on the management of the bladder in multiple sclerosis, the post micturition residual urine volume has to be measured as part of the initial assessment, and preferably before an antimuscarinic treatment is started. Measurement of the post micturition residual volume by abdominal ultrasound has to be made in all patients with bladder symptoms prior to treatment or if there is reason to suspect that they have incomplete emptying of bladder.[9] In our study, the number of patients who had been prescribed AC medications was similar to that of patients who had had post micturition residual volume measurements. Despite the high rates of patients with urological symptoms, the limited number of patients undergoing post micturition residual volume measurement may be explained by the low rate of patients seeking medical advice for their urinary complaints or the absence of a portable ultrasound device in many of the centers.

The results of the systematic review performed by Cetinel *et al.*[10] showed that available data does not support the use of invasive urodynamics in the initial evaluation of patients with MS urodynamic investigations including filling cystometry and pressure/flow studies of voiding should be carried out only in those who are refractory to conservative treatment or bothered by their symptoms and wish to undergo further interventions.[9] In contrary to this, French health authorities recommended urodynamic studies in all MS patients with symptomatic lower urinary tract disease (LUTD).[5] In our study, about a quarter of the patients had been evaluated by urodynamic investigations. We did not question the time interval between the first urinary symptoms and the urodynamic investigation.

In our study, 35.3% of the patients had undergone US scans. This rate was less than both the rate of the symptoms, and the rate of seeking medical advice for urological complains. Results of a systematic review showed that 10 studies with 1460 patients showed upper urinary tract (UUT) deterioration in the range of 0.9–5%; and 4 studies reported higher deterioration rates in the UUT (15.5–21% in 367 patients).[10] In studies reporting higher UUT deterioration rates, the reason for deterioration was renal stones and calcifications or minimal caliceal dilatations in most of them.[10] The low frequency of UUT pathology in MS has led to the opinion that clinically stable patients with a normal baseline renal US study do not require annual-follow-up UUT studies.[11] De Seze *et al.*[5] identified the duration of MS, the presence of an indwelling catheter, high-amplitude neurogenic detrusor contractions and permanent high detrusor pressure as risk factors for UUT damage. Fletcher *et al.*[12] found that clinically stable MS patients were at a low risk for having UUT pathology. It is not entirely clear whether patients with adverse urodynamic findings require ongoing UUT evaluation.

According to our results, the patients with higher OABSS had had further urological assessments (residual urine measurement, urinary tract US or urodynamic assessment) while the patients with lower OABSS had not undergone detailed assessment including residual urine measurement, urinary tract US or urodynamic assessment. As we mentioned previously the consensus report[9] and the guidelines[5] also support the adequate assessment of MS patients. Thus we think that residual urine measurement and urinary tract US investigation should be carried out invariably in all MS patients.

Anticholinergic medications were prescribed for the 27.5% of the patients. Although several newer ACMs with fewer adverse effects have become available, they had been used by a few of the study participants (2%). In our health system, there are limitations for the prescription of these medications, except oxybutynin. If a patient experiences a side effect with the use of oxybutynin, then another ACM can be prescribed. The other explanation of the limited use of the newer ACMs might be the low familiarity level of the doctors with advances in OAB treatment.

The major issue in assessing ACM use in MS is the lack of data.[13] There is a need to assess the absolute and comparative efficacy, tolerability and safety of anticholinergic agents. Measurement of post-void residual volume and the necessity of intermittent catheterization (IC) during ACM use are important issues in MS patients. A recently published systematic review stated that there was no evidence-based cut off post-void residual value for the recommendation to start IC in MS patients.[10] Current guidelines for the evaluation and treatment of OAB in MS do not state which ACMs should be used in this condition nor do they provide guidance as to which agents should be used as first line or second line treatment.

Injection of BoNT-A into the detrusor muscle is an effective treatment modality for intractable neurogenic detrusor overactivity (NDO) in patients with MS A recommendation with an evidence level of 1 was stated by the UK consensus for intravesical BoNT-A treatment in patients with MS and NDO.[9] However, the European Association of Urology (EAU) guidelines for neurogenic LUTD do not contain a separate MS-related LUTD section.[15] Khan *et al.*[16] showed that the efficacy of repeated injections was well sustained in terms of improving OAB symptoms and QOL; however, 95% of

their patients needed IC after BoNT-A treatment. It is an important point to explain the patients the need for IC after BoNT-A treatment during counseling before treatment. Our study showed that BoNT-A intradetrusor injections were applied only to 3 MS patients. BoNT-A injections are easily accepted by the patients with spinal cord lesions as almost all of them already have had IC. In our opinion, the obligation that drug costs are paid by the patient in our health care system and the need for IC after this treatment might explain the limited number of MS patients that had received BoNT-A injections in the present study. Most of the patients with MS do not accept IC.

The results of our study show that PFME and electrical stimulation therapy were used on 15 and 2 patients, respectively. The UK consensus recommended that physical interventions such as PFME should be offered to MS patients with mild disability (recommendation grade B).[9] The EAU guidelines do not have a recommendation grade for PFME, they emphasized that this treatment could have some benefit in selected patients.[15] The results of a systematic review on the management of LUT dysfunction in MS, recommended pelvic floor rehabilitation together with neuromuscular electrical stimulation as it increased the success of symptomatic treatment.[10] The limited use of these treatment modalities in our patient group might be attributed to the limited number of centers using these modalities and noncompliance of MS patients to this treatment modality.

Each MS patient with LUT complaints should be assessed by a well-trained health care prof.essional, knowledgeable about MS and its effects on LUT function. Patients should be periodically examined for new or changing LUT symptoms[9] Neurologists, physiatrists and urologists need to work more closely in the diagnosis and treatment of LUT symptoms in MS patients.

Conclusion

This multicenter survey study presents the frequencies of the urological symptoms, the practice of assessment and treatment methods in patients with MS. Urgency was the most common urinary symptom followed by frequency, urge incontinence and nocturia in MS patients. Patients with higher OABSS have further urological assessments while patients with lower OABSS do not undergo detailed assessment. Compatible with the previous consensus reports we think that residual urine measurement and urinary tract US investigations should be carried out invariably in all MS patients.

Disclaimer statements

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