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Lower Urinary Tract Dysfunction in Multiple Sclerosis Patients

Multipl Skleroz Hastalarında Alt Üriner Sistem Disfonksiyonu

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Abstract

Objective Lower urinary tract dysfunction (LUTD) are quite commonly seen in Multiple Sclerosis (MS). In this study we aimed to show the relationship between the LUTD symptoms and disease related parameters including the severity, duration, subtypes and the lesion localization of MS.

Material and Method In a prospective study, we recorded demographic information, MS subtypes, disease duration, disease severity, neurological examinations, scores of Expanded Disability Status Scale (EDSS), lower urinary tract symptoms (LUTS), duration of the symptoms, urinary tract examination, urinary function tests (Overactive Bladder Symptom Score (OABSS), International Prostate Symptom Score (IPSS)), urodynamic evaluation results of 42 MS patients whom admitted to our neurology department during the last 3 months. Statistical analysis was performed by using ANOVA, Mann Whitney-U test and non-parametric Pearson test. $p<0.05$ was considered statistically significant.

Results 42 patients (13 male, 29 female) who were diagnosed with MS according to the 2010 revised McDonald criteria included in our study while patients with history of diabetes mellitus, urinary tract infections, and urological surgery were excluded. There was no significant relationship between the presence of LUTS, and age, gender, EDSS, MS subtypes, duration of illness ($p>0,05$). A statistically significant difference was found between the genders, EDSS and irritative symptoms ($p<0,05$) while no significance was found between obstructive symptoms ($p>0,05$). There was no statistically significant difference between the localization of the lesion and presence of the irritative and obstructive symptoms ($p>0,05$).

Conclusion Our study indicates that, disease severity is an important determinant factor of irritative urinary symptoms in MS patients.
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Keywords Multiple Sclerosis, urinary system, questionnaire

Öz

Amaç *Multipl Sklerozda (MS), alt üriner sistem fonksiyon bozuklukları oldukça sık görülmektedir. Çalışmamızda, MS hastalarında alt üriner sistem disfonksiyon semptomları ile hastalığın şiddeti, süresi, alt tipi ve lezyon lokalizasyonu arasındaki ilişkiyi göstermeyi amaçladık.*

Materyal ve Metod *Son 3 ay içinde nöroloji polikliniğimize başvuran, MS tanılı 42 hastanın demografik özellikleri, MS alt tipi, hastalık süresi, hastalık şiddeti, nörolojik muayeneleri, genişletilmiş özürlülük durum ölçeği (EDSS) puanları, üriner sisteme ait yakınmaları, semptomların süreleri, üriner sistem muayeneleri, fonksiyon testleri (aşırı aktif mesane semptom skoru (OABSS), uluslararası prostat semptom skoru (IPSS)), ürodinamik değerlendirme sonuçları prospektif olarak kaydedildi. İstatistiksel analiz ANOVA, Mann-Whitney U ve non-parametrik Pearson testleri kullanılarak yapıldı. $P<0.05$ anlamlı olarak kabul edildi.*

Bulgular *Çalışmaya 2010 revize Mc Donald kriterlerine göre MS tanısı almış 42 hasta (13 erkek, 29 kadın) dahil edildi. Diyabet, üriner sistem enfeksiyonu ve ürolojik girişim öyküsü olan hastalar çalışmadan dışlandı. Alt üriner sistem semptomlarının varlığı ile yaş, cins, EDSS, MS alt tipi, hastalık süresi arasında anlamlı bir ilişki bulunmadı ($p>0,05$). İrritatif semptomlar ile cins ve EDSS arasında istatistiksel olarak anlamlı bir farklılık bulunurken ($p<0,05$), obstrüktif semptomlar konusunda benzer ilişki saptanmadı ($p>0,05$). İrritatif ve obstrüktif semptomların varlığı ile lezyon lokalizasyonu arasında da istatistiksel olarak anlamlı bir farklılık saptanmadı ($p>0,05$).*

Sonuç *Çalışmamız MS' te hastalık şiddetinin irritatif üriner semptomlar üzerinde önemli bir belirleyici faktör olduğunu göstermektedir.*
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Anahtar Kelimeler *Multipl Skleroz, üriner sistem, sorgulama formu*

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INTRODUCTION

Multiple Sclerosis (MS) is an autoimmune neurodegenerative disease, characterized by inflammation, gliosis, and demyelinationof the central nervous system (CNS). Attacks, remissions and progressive neurological symptoms could be observed[1]. The exact pathogenesis and pathophysiology of MS are still unknown.MS is usually diagnosed between the ages of 25-40 and seen twice as often in women.In young adults of the developed societies, MS is the most common cause of non-traumatic neurological disability.[2,3]

Clinical signs and symptoms of MS may vary according to the lesion localization in the CNS.[4] Neurological control of bladder function is provided with a complex mechanism consisting of cortex, thalamus, midbrain, brainstem (pontine micturition center), posterior and lateral spinal cord, sympathetic and parasympathetic system.[5,6,7,8] MS plaques frequently affect pyramidal and reticulospinal tractsthat provide innervation to bladder detrusor muscle and external urethral sphincter. Therefore, lower urinary tract symptoms (LUTS)which are observed in 75% of the patients areconsidered as the most common symptoms of MS.[9,10] The importance of early diagnosis and treatment is to prevent irreversible damage of the lower and upper urinary systems.[11,12]

In this study, we aimed to investigate the relationship between the frequency and severity of the LUTSand the severity of the MS.

METHODS

Forty-tworegistered MS patients of our clinicwho were diagnosed according to the 2010 revised Mc Donald criteriawere participated in our study. Accompanying diabetes, prior history of urological surgery or urinary tract infection were excluded from the study. The demographic data, detailed medical history, neurological evaluation, expanded disability status scale scores (EDSS) of the patients were recorded.EDSSrepresents the level of neurological disability and the severity ofMS, thatranges from 0 to 10 in 0.5 unit increments.[13]

Each patient's urinary tract symptoms, duration of symptoms, findings of urinary tract examinations and urodynamic evaluation results were recorded by an urologist.OABSS and IPSS forms were usedto evaluate the LUTS in patients with face to face interviews.

OABSSevaluates the presence and severity of the irritative symptoms[14]. Patients with OABSS8 and above has 'overactive bladder' and 16 and above were considered as 'severe symptomatic patients'[15]. The severity of urinary tract symptoms, irritative and obstructive symptoms could be assessed individually by using IPSS[16]. IPSS form consists of 7 questions. 1, 3, 5 and 6. questions were calculated for evaluating voiding, 2, 4 and 7. questions were calculated for evaluating storage function.[17] Symptoms of bladder storage phase (frequency, urgency, and nocturia)refer to IPSS storage (IPSSs) and symptoms of bladder emptying phase (incomplete emptying, intermittency, weak stream and straining) refers to IPSS voiding (IPSSv). The threshold values for IPSSs and IPSSv were determined 7 and 9 respectively. The severity of LUTS was further stratified according to the total IPSS on the questionnaire: mild: lower than 7; moderate: 8-19; severe: 20-35.[17]

Uroflowmetry test was performed for patients with severe obstructive symptoms. PVR measurements were made during uroflowmetry and PVR 50-100 ml were considered as normal[19]. Abdominal Ultrasonography was performed in patients with elevated PVR levels in order to investigate the upper urinary tract status. Patients with abnormal (low or elevated) PVR levels were directed to urodynamic evaluation to detect detrusor sphincter dyssynergia.

The study was conducted in accordance with the revised Declaration of Helsinki (1998) and approved by the Sakarya University Ethics Committee. Written informed consent was obtained from all participants.

Statistical Evaluation

Statistical analysis of our study was performed by using statistical package for social sciences program for Windows 18.0' (SPSS 18.0 İnc). ANOVA test was used for the comparison of two independent groups with normally distributeddataand Mann-Whitney U was used to test for the abnormally distributed data. Non-parametric Pearson test was used for the correlation analysis. $p<0.05$ was accepted as the level of significance.

RESULTS

Out of 42 MS patients, 13 (30.9%) were male, 29 (69.1%) were female. Demographic and clinical characteristics of the patients are outlined in Table 1.

Table 1:Demographic and clinical characteristics of the patients

Number of patients:	42	P values
Male (%): Female (%):	13 (30.9%) 29 (69.1%)	p>0.05
Age (Mean±SD) total: Male: Female:	36±10.16 38.30±12.33 36.37±9.22	p>0.05
Disease Duration (Years):	8.76±7.03	p>0.05
EDSS (Mean±SD) total: Male: Female:	3.40±2.39 4.03±2.60 36.37±9.22	p>0.05
MS subtype no (%): PPMS: RRMS: SPMS: RPMS:	 5 (11.9%) 27 (64.3%) 9 (21.4%) 1 (2.4%)	p>0.05
Lesion Localization (Mean±SD): Cortical: Brainstem: Spinal:	(n:41) 8.29±6.97 (n:9) 6.33±3.87 (n:26) 6.84±4.58	p>0.05

Table 2 shows LUTS, including obstructive and irritative symptoms of the patients. There was no statistically significant difference detected between the localization of lesions and the presence of irritative and obstructive symptoms (p>0.05).

Table 2: LUTS of the patients

LUTS	n: (%)
Dysuria	13 (%31)
Urgency	20(%47.6)
Pollakuria	26(%61.9)
İncontinence	16(%38)
Nocturia	20(%47.6)
İncomplete emptying	13(%28.5)
Straining	20(%50)

According to the IPSS, 19 (45.2%) patients had mild, 18 (42.9%) patients had moderate, 5 (11.9%) patients had severe LUTS. When the LUTS were examined in subgroups of storage and discharge symptoms, 9 (21.4%) (male:3, female:6) out of 42 patients had obstructive symptoms. There was no statistically significant relationship between the obstructive symptoms and gender, age, EDSS, disease duration, MS subtype(p>0.05). No statistically significant difference was detected between IPSS severity subgroups (mild, moderate, severe), EDSS and MS subtypes (p>0.05). On the other hand, 13 patients (30.9%) (male:1, female:12) out of 42 MS patients had irritative symptoms. The presence of irritative symptoms revealed no correlation with age, disease duration, MS subtypes (p>0.05) while there was a positive correlation with gender and EDSS (ANOVA p=0.03). High points of IPSS was related to the symptom of dysuria (p=0.03). (Table 3)

Table 3:IPSS of the patients

IPSS	Mild	Moderate	Severe	P values
Gender (m/f)	7/11	4/15	2/3	p>0.05[2]
Age (Mean±SD)	38.66±11.94	7.94±6.48	30.80±8.34	p>0.05[1]
Disease duration (Years)	7.94±6.48	9.47±7.70	6.40±6.38	p>0.05[1]
EDSS	2.55±1.74	2.55±1.74	8.45±6.97	p>0.05[1]
MS subtype: PPMS: RRMS: SPMS: RPMS:	 0 13 5 0	 3 12 3 1	 2 2 1 0	p>0.05[2]
1)ANOVA 2)Fisher (p=0.50/0.31/0.63/0.06/0.14 respectively)				

According to the OABSS, 20 (male:5, female:15) patients (47%) had overactive bladder. Out of 20 patients, 13 (30.9%) of them were in 'severe symptomatic' group. No significant relationship was found between the presence of overactive bladder and the gender, age, EDSS, disease duration, MS subtype (p>0.05). (Table 4)

Table 4:OABSS of the patients

OABSS	OABS positive	OABS negative	P values
Gender (m/f)	5/15	8/14	p>0.05[4]
Age (Mean±SD)	35.60±6.70	38.22±12.55	p>0.05[2]
Disease duration	7.40±4.41	9.40±8.67	p>0.05[2]
EDSS	3.65±2.20	3.18±2.58	p>0.05[1]
MS subtype: PPMS: RRMS: SPMS: RPMS:	 1 12 6 1	 4 15 3 0	p>0.05[3]
1) ANOVA 2)Mann-Whitney U 3)Fisher 4)Chi-Square (p=0.51/0.79/0.36/0.53/0.26 respectively)			

PVR values could not be measured for all of the patients because of thepatientincompliance. Out of 26 patients in whom PVR could be measured, irritative symptoms were detected in 4 patients according to the IPSS and 11 patients according to the OABSS. There was no significant difference between the PVR measurements of the patients with and without irritative symptoms (ANOVA: p=0.64, p=0.63 respectively).

DISCUSSION

A broad clinical spectrum of LUTShavepreviously been defined in MS, ranging from incontinence to incomplete emptying.[5] The most frequent complaints are urgency, pollakiuria and urge incontinence.[10,20] LUTS have a negative effect on health-related quality of lifeand observed in more than 80% of MS patients. If the duration of MS is over a decade, the incidence of LUTS could be up to 96%.[10,20] In our study, 66% of the patients had LUTS. Theprevalence of LUTS in MS patients have been reported with the ratios of urgency 60-86%, pollakiuria 50-83%, incontinence 19-83%, intermittency 28-58% and 2-20% incomplete emptying.[30,31] In our study we found the ratios of 47.6%,61.9%,38%, 30.9%, 47.6%, 28.5% and 50% for the symptoms of urgency, pollakiuria, incontinence, intermittency, nocturia, incomplete emptyingandstraining respectively.

In various studies including ours, no correlation was detected between the urinary symptoms and the duration of MS.[14,20,21,24] A positive correlation was reportedbetween the duration of MS and irritative symptoms whereas no correlation was found with obstructive symptoms.[18,22] Our data showed no significant relationship between the duration of disease with both obstructive and irritative symptoms.

LUTS and MS-related disability are shown to be related. While there were studies indicating a correlation between the prevalence of overactive bladder symptoms with thephysical disabling situation and decreased thequality of life[23], hypercontractility of bladder and EDSS[14]; there are studies indicating a negative relationship between LUTS and disability[24]. In a study the patients with pyramidal lesions were excluded and a positive correlation was found between thelevel of disability and detrusor dysfunction.[21] A statistically significant relationship was reported between the urodynamic abnormalities, disease duration and disability status.[20,24] In two studies ofMS patients questioned by the IPSS, the results revealed a positive relationship between EDSS and irritative symptoms whileno relationship was detected between EDSS and obstructive symptoms, which were consistent with our results.[18,22]

Besides several studiesindicatingthat the LUTS was17 times frequent in RRMS than in SPMS[25]; some studies reported urinary tract symptoms very often in CIS.[26] Voiding dysfunction is observed with higher frequency-possibly due to remain higher EDSS scores-in PPMS patients[27,28]. In terms of the urinary tract dysfunction in MS subtypes, our study revealed no significant difference. The majority of our patients being in RRMS subtype, having a small number of PPMS patients and no patients in SPMS subtype group might be the cause of this result.

Localization of the CNS lesions affects the nature and the severity of LUTS.[10,22] Cortical lesions could be observed in approximately 60-90% of MS patients and these may cause the detrusor overactivity by blocking the conduction of the sensory afferents or disrupting the function of pontine micturition center which providesa supraspinal suppression of bladder contractility. Spinal lesions between the pontine and sacral centers may cause detrusor sphincter dyssynergiaand could be observed in 80% of MS patients.[10,29] Sacral involvementmay be relevant with insufficient detrusor contraction.[10] LUTSin MS patients were often associated with spinal lesions[9]. In our study, 41 (97%) patients had cortical, 26 (0.61%) patients had spinal and 9 (0.21%) patients had brainstem lesions. There was no statistically significant difference between the presence of irritative-obstructive symptoms and the localization of lesions (p>0.05). The incompatibility with former studiesmay be due toa limited number of patients having isolated spinal lesions and almost all patients having cortical lesions in our study.

Type and the severity of LUTSwere frequentlyevaluated by using the IPSS and OABSS. In our study, we used these two questionnairesand found similar results consistent with the literature.[18,22,32,33] According to the IPSS; 19 (45.2%) patients had mild, 18 (42.9%) patients had moderate, 5 (11.9%) patients had severe LUTS.9 (21.4%) (male:3, female:6) patients had obstructive, 13 patients (30,9%) (male:1, female:12) had

female:15) patients (47%) had overactive bladder and 13 (30.9%) of them were in 'severe symptomatic' group.

Urodynamic studies demonstrated that theMS patients may show detrusor overactivity, detrusor sphincter dyssynergia and detrusor hypocontractility.[27,28] Detrusor overactivity and detrusor sphincter dyssynergia (DSD) are the most common urodynamic findings.[10,20,33] The urodynamic studies are highly reccomended to all MS patients with voiding symptoms.[34]

Early diagnosis and proper treatment provides an improvemenet in thequality of life and reduces the disability of the patients. This evidence reveals the importance of investigating the LUTS in the early asymptomatic stages of MS. In our study, we found clinical benefits of the LUTS even in asymptomatic MS patients.

There were two main limitations of our study. First, the small sample sizeand the secondis the urodynamic evaluation could not be applied to all patients. Our observation suggests that further studies are needed tobe done with a larger sample size and more advanced technique.

In conclusion,our study revealed no significant correlation between urinary symptoms and gender, MS type, duration of the disease and lesion localization.However, a positive significant correlation found between EDSS and irritative symptoms.

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