Caspian Journal of Neurological Sciences
"Caspian J Neurol Sci"
Journal Homepage: http://cjns.gums.ac.ir

Research Paper: Comparison of Bladder Dysfunction and Urinary Symptoms Between Multiple Sclerosis and Neuromyelitis Optica Spectrum Disorder

Farid Nasr Esfahani[1,2], Navid Manouchehri[1,2], Nasim Nehzat[1], Omid Mirmosayyeb[1,2], Mahdi Barzegar[1,2], Vahid Shaygannejad [1,3*]

1. Isfahan Neurosciences Research Center, Alzahra Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran
2. Student Research Committee, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran
3. Department of Neurology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran

Use your device to scan and read the article online

Citation Nasr Esfahani F, Manouchehri N, Nehzat N, Mirmosayyeb O, Barzegar M, Shaygannejad V. Comparison of Bladder Dysfunction and Urinary Symptoms Between Multiple Sclerosis and Neuromyelitis Optica Spectrum Disorder. Caspian J Neurol Sci. 2019; 5(3):105-110. https://doi.org/10.32598/CJNS.5.18.105

Running Title Bladder Dysfunction in NMO and MS Patients

https://doi.org/10.32598/CJNS.5.18.105

Article info:
Received: 24 May 2019
First Revision: 15 Jun 2019
Accepted: 20 Jun 2019
Published: 01 Jul 2019

ABSTRACT

Background: Neuromyelitis optica (NMO) and multiple sclerosis (MS) are auto immune demyelinating disorders. Both MS and NMO patients suffer from urinary dysfunction.

Objectives: Investigation of frequency and severity of urinary symptoms in two groups of MS and NMO patients.

Materials & Methods: 56 MS patients and 20 NMO patients were enrolled in this cross sectional study conducted in Isfahan Kashani hospital from March 2018 to September 2018. Frequency and severity of urinary symptoms were assessed using the urogenital distress inventory (UDI-6) and international prostate symptom score (IPSS) questionnaire. Data were analyzed using independent t-test, Mann Whitney U test and Pearson correlation coefficient with the SPSS V. 18.

Results: The Mean±SD of age was 40.2±11.45 and 34.1±9.09 in NMO and MS group respectively. There was a significant difference between MS and NMO patients regarding their overall IPSS score (9.8±7.9 and 14.6±11.3 respectively). The frequency of mild, moderate and severe urinary symptoms was 25%, 50 % and 25% among NMO patients and 48.2%, 35.7% and 16.1% among MS patients respectively. Based on UDI-6 questionnaire the most frequent symptoms in MS and NMO patients were frequency and urgency respectively and they are more frequent among NMO patients rather than MS patients.

Conclusion: Our results showed a significant difference in frequency and severity of urinary symptoms between NMO and MS patients and NMO patients tend to experience more severe urinary symptoms.

Keywords: Multiple Sclerosis; Neuromyelitis Optica; Urinary Bladder, Neurogenic

*** Corresponding Author:**
Vahid Shaygannejad
Address: *Isfahan Neurosciences Research center, Alzahra Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran*
Tel: *+98 (913) 3133550*
E-mail: *shaygannejad@med.mui.ac.ir*

Caspian Journal of Neurological Sciences

Highlights

- NMO patients experience more severe bladder dysfunction in compare to patients with MS.
- Voiding frequency and urgency are more prevalent among NMO patients rather than MS patients.

Introduction

Neuromyelitis optica (NMO) and multiple sclerosis (MS) are auto immune demyelinating disorders of the Central Nervous system (CNS). While NMO is known for involving the optic nerve and spinal cord during its clinical course, MS presents with a variety of symptoms depending on the location and severity of the demyelinated neurons including sensory, motor or cognitive impairments [1-3].

Although there have been reports of spinal lesions in MS patients, the affected areas are limited to one spinal segment, where in NMO patients the spinal lesions damage three or more spinal segments during the attacks [4]. Spinal lesions in NMO patients are in the form of Transverse Myelitis, accompanied by clinical manifestations such as paraplegia, sensory deficit levels and bladder dysfunction [5]. MS patients suffer from bladder dysfunction as well with urgency being the most common symptoms early in the course of the disease. These symptoms later develop towards urinary incontinence as the disease progresses [6].

Dyssynergia between the detrusor muscle and the external urethral sphincter and detrusor over activity are suggested to be responsible for urinary dysfunction in NMO and MS patients [7, 8]. Because NMO and MS are distinctive diseases with overlapping clinical manifestations, we decided to compare the distribution and severity of urinary dysfunction symptoms between two groups of NMO and MS patients.

Materials and Methods

Study design

A cross sectional study was conducted from March to September 2015. Samples were selected from the neurology clinic of Kashani hospital, Isfahan, Iran. We consecutively enrolled 56 MS patients (based on the McDonald criteria 2017) [9] and 20 NMO patients (based on the Wingerchuk criteria) [10]. Exclusion criteria was defined as positive history for hormonal disease, previous pelvic surgery or radiation and use of medication for urinary bladder dysfunction. Patients with confirmed symptomatic non-neurogenic bladder problems were also excluded from the study. Informed consents were taken from all patients upon enrollment.

Data collection

Demographic and baseline data including age, BMI, duration of disease, duration of urinary symptoms, smoking, alcohol consumption, history of diabetes mellitus and kidney and bladder disease were obtained from all patients. Female participants were also asked about previous history of uterine cysts or infections, menstrual problems and gestational history while male participants were asked about previous history of prostate problems. The level of clinical disability was determined using the expanded disability status scale (EDSS).

All participants were evaluated regarding urinary symptoms. Each patient was individually interviewed and asked about the severity of different urinary symptoms using a urinary distress inventory 6 (UDI-6) questionnaire. Since UDI-6 has not been validated in Persian language, patients also filled out the Persian version of international prostate symptom score (IPSS) questionnaire (previously validated by Panahi et al.) [11]. The overall IPSS score was calculated for each patient. Mild, moderate and severe urinary symptoms were defined as IPSS overall score of 0 to 7, 8 to 19 and 20 to 35 respectively.

Data analysis

Data was analyzed using the SPSS software (version 18.0, Chicago, IL, USA). Frequency reporting measures was used for categorical data. Quantitative values were compared using independent t-test or Mann Whitney U test where data was not normally distributed. A two tailed P-value of less than 0.05 was considered as statistically significant. Pearson correlation coefficient was used for investigation of correlations between groups. We assumed $0.2<r<0.4$ as low correlation, $0.4<r<0.5$ as moderate correlation and $r>0.5$ as a high correlation.

Results

A total of 76 patients were enrolled in the study including 56 MS patients and 20 NMO patients. The Mean±SD of age was 40.2±11.45 and 34.1±9.09 in NMO and MS group respectively (P=0.41). The Mean±SD of BMI was 27.15±4.01 and 23.98±3.17 in NMO and MS patients, respectively (P= 0.001). The Mean±SD of disease duration was 8.07±9.2 and 6.6±5.2 years in NMO and MS patients respectively. Regarding the duration of urinary symptoms the Mean±SD was 1.5±2.7 and 0.9±2.3 among NMO and MS patients respectively. Neither the disease duration (P=0.41) nor the duration of the urinary symptoms (P=0.38) were significantly different between patient groups. EDSS score of NMO and MS group was 2.9±2.2 and 2.3±1.9 and the difference was not statistically significant (P>0.05).

All patients were asked about different urinary symptoms based on the UDI-6 questionnaire. Table 1 presents the distribution and severity of urinary symptoms among patients in each group. The IPSS score for MS and NMO patients was 9.8±7.9 and 14.6±11.3 respectively; the difference was statistically significant (P=0.04). There was also a significant difference regarding voiding frequency (P=0.009) and urgency (P=0.03) between NMO and MS patients. The frequency of mild, moderate and severe urinary symptoms was 25%, 50% and 25% among NMO patients and 48.2%, 35.7% and

Table 1. Prevalence and severity of Urinary symptoms in MS and NMO patients (based on UDI-6 questionnaire)

Variable		No. (%)	
		MS	NMO
UDI*-6 Q1 (frequency)	Never	24(42.8)	3(15.0)
	Slight	18(32.1)	6(30.0)
	Moderate	7(12.5)	5(20.0)
	Severe	7(12.5)	6(30.8)
UDI-6 Q2 (urgency)	Never	29(51.7)	7(35.0)
	Slight	14(25.0)	3(15.0)
	Moderate	8(14.2)	1(5.0)
	Severe	5(12.5)	9(45.0)
UDI-6 Q3 (stress incontinence)	Never	31(55.3)	10(50.0)
	Slight	15(26.7)	4(20.0)
	Moderate	4(7.1)	3(15.0)
	Severe	6(10)	3(15.0)
UDI-6 Q4 (small leakage)	Never	29(51.3)	10(50.0)
	Slight	23(41)	7(35.0)
	Moderate	3(7.7)	2(10.0)
	Severe	0	1(5.0)
UDI-6 Q5 (straining)	Never	6(10.7)	0
	Slight	40(71.4)	15(75.0)
	Moderate	10(17.8)	1(5.0)
	Severe	0	4(20.0)
UDI-6 Q6 (pain)	Never	31(55.3)	7(35.0)
	Slight	21(37.5)	12(60.0)
	Moderate	4(7.1)	1(5.0)
	Severe	0	0

*UDI: Urinary distress inventory

Table 2. Severity of urinary symptoms in MS and NMO patients (based on IPSS questionnaire)

Urinary Symptoms	Mean±SD		P
	NMO	MS	
Incomplete emptying	2.2±1.6	2.3±1.5	0.56
Frequency	2.7±1.9	1.4±1.7	0.009*
Intermittency	1.8±2.1	1.2±1.7	0.27
Urgency	2.6±2.3	1.2±1.7	0.03*
Weak stream	1.3±1.9	0.6±1.1	0.15
Straining	1.3±2.03	0.8±1.6	0.58
Nocturia	2.5±2.2	1.9±1.8	0.34
Overall score	14.6±11.3	9.8±7.9	0.04*
Quality of life	2.3±1.6	2.5±1.6	0.61

P<0/05

16.1% among MS patients respectively. Table 2 shows the distribution of urinary symptoms in each group.

There was a significant correlation between IPSS overall score and EDSS score in NMO (r=0.57, P=0.008) and MS patients (r=0.41, P=0.002). IPSS overall score also had a significant correlation with duration of urinary symptoms, (r=0.40, P=0.002) in MS patients; however the correlation between IPSS overall score and duration of urinary symptoms in NMO patients was not significant (r=0.19, P=0.4). There was no significant correlations between IPSS overall score and age, BMI or duration of disease in either of the group.

Discussion

Bladder dysfunction is a frequent symptom in the course of both NMO and MS. Detrusor hyper activity and detrusor-external sphincter dyssynergia are the most frequently reported disorders in this regard [7, 8].

We have shown in our study that NMO patients had significantly higher IPSS scores (i.e. worse bladder function) compared to MS patients. Based on the overall IPSS scores, the NMO group had a higher percentage of severely and moderately symptomatic patients compared to patients in the MS group.Similarly in a study by Chanson et al. they found that when compared for health related quality of life, while MS patients scored lower on cognitive abilities, the NMO patients had significantly lower scores regarding sphincter dysfunction [12].

Regarding each individual symptom, frequency and urgency had the highest scores among NMO patients; however in MS patients, frequency was rated as the second most irritating symptom of the disease, with sensation of "incomplete emptying of bladder" as the worst symptom based on IPSS scores. Investigation of symptoms prevalence using the UDI-6 questionnaire revealed "frequency" and "urgency" as the most frequent severe complaint among MS and NMO patients respectively. Huppke et al. mentioned in their study that pre pubertal MS patients have a multi symptomatic first attack that includes sphincter dysfunction and that post pubertal patients mostly had optic neuritis and sensory dysfunctions [13]. Nakipoglu reported in his study that urgency was the most common urinary symptom among MS patients [6]. Urgency was also reported as the most frequent urinary symptom amon MS patients in a study by Ukkonen et al [14]. Regarding NMO patients, Urgency was also reported as the most frequent urinary symptom [7].

Both frequency and urgency point to detrusor muscle hyper activity, with a reflexive bladder causing discomfort for the patients, while sensation of incomplete emptying of bladder is more suggestive of a hyper activity of the external sphincter muscle or detrusor-sphincter dyssynergia. The observed differences between various studies regarding the prevalence of urinary symptoms can be addressed by variable prevalence of detrusor-external sphincter dysfunction in their samples. A major determinant of bladder-urethral dysfunction type in MS and NMO patients is the location of CNS lesions. In their

study, Araki et al. have stated that a there was an association between pontine and cervical cord lesions with detrusor hyporeflexia and detrusor-sphincter dyssynergia [15].

Although the overall IPSS score had no significant correlation with the disease duration in our patients; it was directly correlated to the EDSS score of each group. There was no significant difference in EDSS scores or disease duration between the two groups. In a study by Cobo et al. presence of urinary sphincter dysfunction and longitudinally extended transverse myelitis was reported to be related to worse outcomes. This is also indicated in a study by Cabre et al. that sphincter symptoms was associated with a relatively shorter time to death in NMO patients [16]. Other studies have also shown that there was a direct correlation between severity of urinary symptom and neurological impairment among NMO patients. Presence of urinary symptoms and bladder dysfunction have also been reported to be related to poor outcomes in MS patients [17-19].

The observed significant difference in overall IPSS scores suggests that in a similar conditions regarding the severity of disease induced disability or disease longevity, NMO patients are more affected by the urinary symptoms compared to the MS patients. This could be due to higher rates of spinal cord involvement in NMO patients compared to MS patients. While brain lesions can increase clinical disability of MS patients due to various motor, sensory and cognitive deterioration, NMO patients mostly suffer from direct effects of spinal cord lesions including urinary dysfunction [12].

Although in our study the duration of urinary symptoms since its onset was not significantly different between the two groups, yet the NMO patients had these symptoms for relatively twice as long as the MS patients. On the other hand there was no direct correlation between overall IPSS score and duration of urinary symptoms among NMO patients while such correlation was established among MS patients. The observed difference could be due to the lower number of patients in the NMO group in our study, but it can also suggest that development of urinary symptoms in MS patients has progressive and additive attributes compared to NMO patients regardless of the severity of the disease.Direct association of urinary dysfunction and increasing brain and spinal abnormalities has been previously reported by Ukkonen et al [14].

There was a significant difference between our groups regarding their BMI with NMO patients being relatively older and heavier; however we found no direct correlations between overall IPSS score and age or BMI of patients. One of the most important limitation of our study is small sample of patients. Due to our small sample groups and following limited male NMOSD patients, gender based comparison was not possible. All MS patients who was enrolled in the study had not spine lesion. Further investigation on MS patients with spine lesion is required to reveal difference of bladder dysfunction among NMOSD and MS patients. In this study, we didn't assess bladder dysfunction in healthy controls. However, the aim of the study was comparison bladder dysfunction between NMOSD and MS patients, evaluation of healthy controls in future investigation is necessary.

Conclusion

In conclusion we found that there is a significant difference in prevalence and severity of urinary symptoms between NMO et al. and MS patients and NMO patients tend to experience more severe urinary symptoms. The most frequent symptoms in MS and NMO patients and they are more frequent among NMO patients rather than MS patients.

It is also suggested that urodynamic studies be considered for MS and NMO patients with urinary dysfunction since the underlying detrusor/external sphincter problems can vary between patients and require tailored treatment strategies.

Ethical Considerations

Compliance with ethical guidelines

The study protocol was approved by the Ethics Committee of Isfahan University of Medical Sciences (No. 293008). All the study procedures were in compliance with the ethical guidelines of the Declaration of Helsinki 2013.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors contributions

Conceptualization: Farid Nasr; Methodology: all authors; Investigation: Farid Nasr, Mahdi Barzegar, Omid Mirmosayyeb, and Navid Manouchehri; Writing-original draft: Navid Manouchehri, Mahdi, Omid Mirmosayyeb; Writing-review & editing: Vahid Shaygannejad, Farid Nasr; Supervision: Vahid Shaygannejad.

Conflict of interest

The authors declared no conflict of interest.

References

[1] Jacob A, McKeon A, Nakashima I, et al. Current concept of neuromyelitis optica (NMO) and NMO spectrum disorders. J Neurol Neurosurg Psychiatry. 2013; 84(8):922-30. [DOI:10.1136/jnnp-2012-302310] [PMID]

[2] Sellner J, Boggild M, Clanet M, et al. EFNS guidelines on diagnosis and management of neuromyelitis optica. Eur J Neurol 2010; 17(8):1019-32. [DOI:10.1111/j.1468-1331.2010.03066.x] [PMID]

[3] Coles AJ, Cox A, Le Page E, et al. The window of therapeutic opportunity in multiple sclerosis. J Neurol. 2006; 253(1):98-108. [DOI:10.1007/s00415-005-0934-5] [PMID]

[4] Weier K, Eshaghi A, Magon S, et al. The role of cerebellar abnormalities in neuromyelitis optica-a comparison with multiple sclerosis and healthy controls. Mult Scler. 2015; 21(6):757-66. [DOI:10.1177/1352458514554051] [PMID]

[5] Wingerchuk DM, Lennon VA, Lucchinetti CF, et al. The spectrum of neuromyelitis optica. Lancet Neurol. 2007; 6(9):805-15. [DOI:10.1016/S1474-4422(07)70216-8]

[6] Nakipoglu G, Kaya A, Orhan G, et al. Urinary dysfunction in multiple sclerosis. J Clin Neurosci. 2009; 16(10):1321-4. [DOI:10.1016/j.jocn.2008.12.012] [PMID]

[7] de Carvalho FL, Gomes CM, Apostolos-Pereira SL, et al. Voiding dysfunction in patients with neuromyelitis optica spectrum disorders. Neurourol Urodyn. 2016; 35(1):39-43. [DOI:10.1002/nau.22667] [PMID]

[8] Puccini F, Bhide A, Elneil S, et al. Sacral neuromodulation: an effective treatment for lower urinary tract symptoms in multiple sclerosis. Int Urogynecol J. 2016; 27(3):347-54. [DOI:10.1007/s00192-015-2771-0] [PMID]

[9] Thompson AJ, Banwell BL, Barkhof F, et al. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. Lancet Neurol. 2018; 17(2):162-73. [DOI:10.1016/S1474-4422(17)30470-2]

[10] Wingerchuk DM, Banwell B, Bennett JL, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. Neurology. 2015; 85(2):177-89. [DOI:10.1212/WNL.0000000000001729] [PMID] [PMCID]

[11] Panahi A, Bidaki R, Mehraban D, et al. Validity and reliability of Persian version of international prostate symptom score. Galen Medical Journal. 2013; 2(1):18-21.

[12] Chanson JB, Zéphir H, Collongues N, et al. Evaluation of health-related quality of life, fatigue and depression in neuromyelitis optica. Eur J Neurol. 2011; 18(6):836-41. [DOI:10.1111/j.1468-1331.2010.03252.x] [PMID]

[13] Huppke B, Ellenberger D, Rosewich H, et al. Clinical presentation of pediatric multiple sclerosis before puberty. Eur J Neurol 2014; 21(3):441-6. [DOI:10.1111/ene.12327] [PMID]

[14] Ukkonen M, Elovaara I, Dastidar P, et al. Urodynamic findings in primary progressive multiple sclerosis are associated with increased volumes of plaques and atrophy in the central nervous system. Acta Neurologica Scandinavica. 2004; 109(2):100-5. [DOI:10.1034/j.1600-0404.2003.00184.x] [PMID]

[15] Araki I, Matsui M, Ozawa K, et al. Relationship of bladder dysfunction to lesion site in multiple sclerosis. J Urol . 2003; 169(4):1384-7. [DOI:10.1097/01.ju.0000049644.27713.c8] [PMID]

[16] Cabre P, González-Quevedo A, Bonnan M, et al. Relapsing neuromyelitis optica: long term history and clinical predictors of death. J Neurol Neurosurg Psychiatry. 2009; 80(10):1162-4. [DOI:10.1136/jnnp.2007.143529] [PMID]

[17] Hasan ZN. Disability and prognosis of relapsing remitting multiple sclerosis, is it different in Iraqi patients. Neurosciences (Riyadh). 2011; 16(3):233-6.

[18] Bergamaschi R. Prognostic factors in multiple sclerosis. Int Rev Neurobiol. 2007; 79:423-47. [DOI:10.1016/S0074-7742(07)79019-0]

[19] Langer-Gould A, Popat RA, Huang SM, et al. Clinical and demographic predictors of long-term disability in patients with relapsing-remitting multiple sclerosis: A systematic review. Arch Neurol. 2006; 63(12):1686-91. [DOI:10.1001/archneur.63.12.1686] [PMID]