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Testing of urodynamic dysfunctions in patients with multiple sclerosis

Ispitivanja urodinamskih disfunkcija kod bolesnika sa multiplom sklerozom

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Abstract

Background/Aim. Multiple sclerosis (MS) is a chronic autoimmune inflammatory disorder of the unknown origin leading to multifocal demyelization, axonal damage and the loss of the nervous tissue in various parts of the central nervous system. Most MS patients have decreased functionality of the bladder leading to various dysuria disorders during the course of the illness. However, in 2% of the cases dysuric problems are the first symptoms of the disease. Urodynamic testing could help to diagnose functional disorders of the lower urinary tract, which might not be otherwise possible by performing the standard invasive procedures or noninvasive scans, such us ultrasound, computed tomography or functional magnetic resonance imaging (fMRI). **Methods.** Urodynamic testing – cystometry with electromyographic (EMG) potentials from the external anal sphincter (EAS), was performed in 34 patients (25 female and 9 male patients). Those patients fulfilled Mc Donald's multiple sclerosis criteria. The urodynamic values were compared to neurological signs and the present disease symptoms. **Results.** The MS patients with (27) and without (7) miction problems were tested. Detrusor hyperreflexia is the most common finding, present in 58.8% of the cases. More than a half of the patients have detrusor sphincter dissynergia. **Conclusions.** Urodynamic testing helps us to determine neurological disorders characteristics and to prepare an appropriate treatment plan. During the course of the disease different urodynamic disfunctions may occur as well as changes in the urinating functionality. The rationale for urodynamic testing in patients suffering from MS before any other treatment procedure is to confirm the diagnosis of dysuric disorders and to secure appropriate treatment.

Key words:
multiple sclerosis; urination disorders; urodynamics; electromyography.

Apstrakt

Uvod/Cilj. Multipla skleroza (MS) je hronično zapaljensko autoimuno oboljenje nepoznate etiologije koje dovodi do multifokalne demijelinizacije, oštećenja aksona i gubitka nervnog tkiva u različitim delovima centralnog nervnog sistema. Većina bolesnika sa multiplom sklerozom ima i poremećenu funkciju mokraćne bešike koja dovodi do različitih dizuričnih smetnji tokom trajanja bolesti. Samo kod 2% bolesnika ove smetnje su prvi simptom bolesti. Urodinamsko ispitivanje omogućava nam da postavimo dijagnozu funkcionalnih poremećaja donjeg urinarnog trakta, što uobičajenim invazivnim procedurama ili neinvazivnim snimanjima (ultrazvuk, kompjuterizovana tomografija ili funkcionalna magnetna rezonanca) često nije moguće ustanoviti. **Metode.** Urodinamsko ispitivanje – cistometrija i registrovanje elektromiografskih (EMG) potencijala sa spoljašnjeg analnog sfinktera (SAS) urađeno je kod 34 bolesnika (25 žena i 9 muškaraca), koji ispunjavaju Mc Donaldove dijagnostičke kriterijume za multiplu sklerozu. Dobijene vrednosti su upoređivane sa neurološkom simptomatologijom i znacima bolesti. **Rezultati.** Ispitivani su bolesnici sa (n = 27) i bez (n = 7) mikcionih tegoba. Hiperrefleksija detrusor bila je najčešći nalaz, prisutan čak kod 58,8% bolesnika. Više od polovine ovih bolesnika imalo je detrusor-sfinkter disinergiju. **Zaključak.** Urodinamsko ispitivanje može pomoći da se utvrde postojeći neurourološki poremećaji i na osnovu njih planira sprovođenje odgovarajućeg terapijskog plana. Tokom trajanja bolesti mogu se ustanoviti različiti oblici urodinamskih nalaza disfunkcije, kao i promena funkcije mokrenja. Razlog za sprovođenje urodinamskog ispitivanja kod bolesnika sa MS pre svake terapije bio bi postavljanje jasne dijagnoze dizuričnih poremećaja koja bliže određuje pravilnu i adekvatnu terapiju.

Ključne reči:
multipla skleroza; mokrenje, poremećaji; urodinamika; elektromiografija.

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Introduction

Multiple sclerosis (MS) is a chronic disease of the central nervous system (CNS) characterized by the widespread multifocal lesions in the brain and spinal cord, leading to visual, sensory, motor and urogenital impairments. The first attack of the disease usually occurs between the second and third decade of life, affecting working and living activity of the patients, depending on the severity and the diversity in the clinical course of the disease [1, 2].

MS is the disease with extremely varying clinical expression, with remissions and exacerbations of different symptoms, usually starting with visual impairments, weakness of extremities, diplopia, sensory disturbances and gait difficulties and disturbances, and urinary and anal sphincter dysfunctions [3]. Those dysfunctions comprise of frequent urinating, urgency, incontinency, retention or hesitance. According to several studies, the incidence of dysuric disorders in MS is 50–97% [3–5]. The form of the present dysuric disorder depends on the size and the position of demyelinated plaques. Therefore, any type and combination of neurogenic bladder and sphincter dysfunctions is possible during the course of the disease [6].

Urodynamic testing is a useful tool in lesion localization, determination of neurogenic bladder type and might help to apply the appropriate therapy protocol, based on findings during the disease progression.

Urinary disturbances are caused by the lesion of the neural systems controlling the act of miction, and the consequences of these disturbances have to be monitored during rehabilitation of the disease [4]. Therefore, the aim of this study was to choose adequate functional diagnostic tests which could enable us to distinguish the causes of disturbed urodinamics. Performing rehabilitation of MS patients with neurogenic dysfunctions of urination enables preservation of the anatomic integrity and functionality of the structures involved in the act of urination. Depending on the phase of the illness, and the type of dysuric disfunctions, proper therapies and procedures should been applied.

Methods

At the Urodynamic Department, Clinic for Rehabilitation "Dr Miroslav Zotović", Belgrade, Serbia, patients with urinary disturbances were tested. The testing protocol comprises of reviewing patients medical documentation, as well as urodynamic testing. A total of 34 patients, 25 female and 9 male patients, previously diagnosed with MS were examined.

Medical data were obtained from anamnesis data, the history of the disease, the order of the symptoms and signs of the disease appearance, so the phases of exacerbation and remission of the symptoms were noted. Obtaining data on urination function is important, as well as the problem onset and the type of dysuric disorders and the duration of the previous predicaments.

Prior to start of the urodynamic testing, post mictional residual urine was determined. Also, laboratory analysis of urine, urinoculture, blood analysis, sedimentation, and the serum urea, creatinine, uric acid, bilirubin and glucose levels were determined.

In order to choose adequate functional tests which could enable distinguishing disturbances in urodynamics, cystometry was used, combined with description of neurogenic dysfunction of urination. Measurement gives important data concerning the act of urination – function of the bladder and preserved sphincter mechanisms [7].

Urodynamic studies were performed using a Dantec Logic (Dantec Inc, Copenhagen, Denmark). A double lumen 6–8 F urethral catheter was introduced and normal saline solution (0.9% sodium chloride) was used at the rate of 10–20 mL/min to fill the bladder. Bladder volume, maximum bladder capacity, bladder compliance, vesical (Pves), abdominal (Pabd) and detrusor pressures (Pdet) were monitored simultaneously during the filling and voiding phases [8–10]. Surface electromyography of the external sphincter activity was performed.

On the basis of urodynamic studies according to International Continence Society standards [7], bladder dysfunction was classified into 3 groups: detrusor areflexia (*DA*), defined as acontractility caused by abnormality of nervous control, and detrusor hyporeflexia, defined as detrusor contraction of inadequate magnitude and/or duration to effect bladder emptying in a normal time span. The patients with detrusor areflexia and detrusor hyporeflexia were grouped together for analyses due to the small sample size in our study and similar procedure management; detrusor external sphincter dyssynergia (*DSD*), defined as detrusor contraction concurrent with an involuntary contraction of the urethral and/or periurethral striated muscle; detrusor hyperreflexia (*DH*), defined as involuntary detrusor contraction during the filling phase which may be spontaneous or provoked, and cannot be completely suppressed due to disturbances of nervous control mechanisms.

The presence of urinary infection changes the severity of the disease symptoms. Therefore, infection must be treated early with the appropriate therapy before urodynamic investigation takes place. At the time of urodynamic investigation, patients were without urinary tract infection and no drugs that influence detrusor and striated sphincter behavior.

The numerical data are described by mean and their standard deviations ($\bar{x} \pm$ SD), and the categorical data are expressed as counts and percentages. The numerical data were compared with the *t*-test, and χ^2-square or Fisher's exact test were used to compare the categorical data. Two-sided tests are used, and p-value < 0.05 was considered to indicate statistical significance. All the data in the present study were analyzed with the commercial statistical software (SPSS version 13.0 for Windows; SPSS Inc, Chicago, Il, USA).

Results

The study included 34 MS patients – 25 (73.5%) females and 9 (26.5%) males with urinary symptoms and disturbances (Table 1).

Table 1

Demographic and clinical characteristics of the patients with urodynamic dysfunction (n = 34)

Demographic and clinical characteristics	Female	Male	*p*
Number (%)	25 (73.5)	9 (26.5)	< 0.01
Age of the moment of testing (years), $\bar{x} \pm SD$	32.6 ± 9.7	35.5 ± 10.4	n.s.
Age at the disease onset (years), $\bar{x} \pm SD$	30.1 ± 10.2	27.6 ± 9.1	n.s.
Years elapsed from the disease onset. $\bar{x} \pm SD$	5.3 ± 3.9	4.9 ± 3.4	n.s.
Years elapsed from the urodynamic dysfunction onset, $\bar{x} \pm SD$	4.3 ± 2.1	4.1 ± 1.9	n.s.

n.s. – no significant difference

Comparing the mean age of the patients at the moment of testing, no statistically significant difference between the male and female patients was found. The youngest participant was a male, aged 15, and the oldest was a female patient, aged 57. The average age at the onset of the disease was 30.1 years for the female and 27.6 years for the male patients, and no statistically significant difference between the male and female patients was found concerning this parameter. Also, no significant difference between the patients with or without bladder symptoms was found ($t = 0.62$, $p > 0.05$) (Table 1).

The duration of the disease varies from 1 to 15 years; however, most patients had urinary dysfunctions in the range from 1 to 6 years. There was no statistically significant difference in the duration of the disease between the females and males also (Table 1). Most patients developed bladder dysfunction several years after the first neurological symptoms but in 4 of the patients only urinary symptoms were present at the time of the disease onset. However, urinary dysfunction was not the sole presenting symptom of MS in any of our patients.

A total of 27 (79.4%) patients suffered from dysuric disturbances and in 7 (20.6%) patients no irritation or obstruction was found. However, there was a statistically significant difference in the duration of the disease between the patients with and without the symptoms concerning urinary system (Table 2).

The symptoms of irritation (urgency, frequency, urge incontinency) were present in 59% of the symptomatic patients, contrary to obstructive symptoms (hesitancy, retention, interrupted stream, sensation of incomplete bladder emptying) present in 41% of the symptomatic patients (Table 3). The most common urinary symptoms were irritative. Difficulty in initiating voluntary voiding was a concurrent symptom in approximately half of the patients. The patients with more severe bladder dysfunction became unable to void voluntarily and could empty the bladder only when they had spontaneous hyperreflexic detrusor contractions.

The relation between dysuric disturbances and the neurological findings did not meet the criteria for applying proper statistical tests, but the tendencies pointed to the occurrence of irritative disturbances combined with pyramidal symptomatology. The majority of patients with MS and lower limbs pyramidal signs (13 patients) had dysuric disturbances of both types (Figure 1).

Table 3

Distribution of urinary symptoms in the multiple sclerosis (MS) patients

Symptoms	Patients, n (%)
Irritative	
urgency	10 (29)
frequency	2 (6)
urge incontinency	4 (12)
Obstructive	
hesitancy	7 (21)
retention	4 (12)
Without simptoms	7 (21)

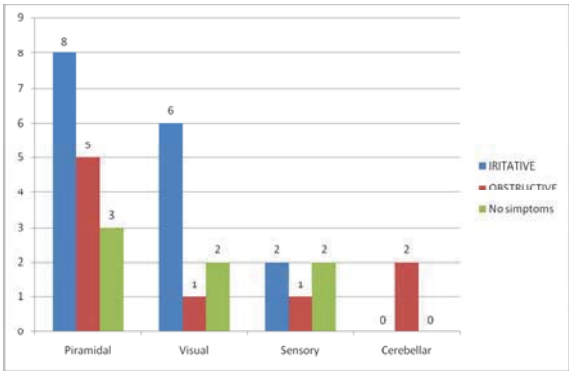

Fig. 1 – Number of the patients with (irritative and obstructive) and without urinary symptoms related to various nervous system dysfunctions.

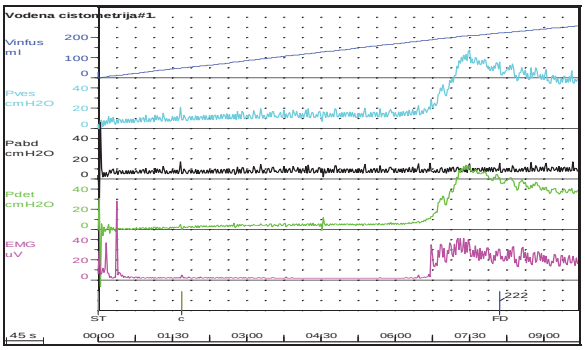

Fig. 2 – An example of cystometry with electromyography (EMG) of external anal sphincter in a patient with multiple sclerosis (MS) (findings: small capacity, high detrusor pressure, detrusor sfincter dyssinergia).

Vinfus = infusion fluid volume; Pves = vessical pressure; Pabd = abdominal pressure, Pdet = detrusor pressure; FD = first desire to void.

Table 2

Correlation between the duration of the disease and the patients with and without urinary simptoms

Parameters	Symptomatic	Asymptomatic	*p*
Number (%) of patients	27 (79.4)	7 (20.6)	< 0.01
Disease duration (years), $\bar{x} \pm SD$	6.1 ± 3.7	1.7 ± 1.3	< 0.01

Cystometry showed detrusor hyperreflexia in 20 (59%) of the patients, detrusor areflexia in 10 (29%), normal detrusor activity in 4 (12%) of the patients, implying 3 more MS patients (comparing to subjective report) with subclinical urinary dysfunction who did not recognize symptoms.

Comparative analysis of EMG potential from the external urethral sphincter (EUS) registered indirectly with cystometrography *via* the external anal sphincter (EAS) (Figure 3), demonstrated a high occurrence of detrusor-sphincter dissynergia in more than 40% of the patients (Figure 3).

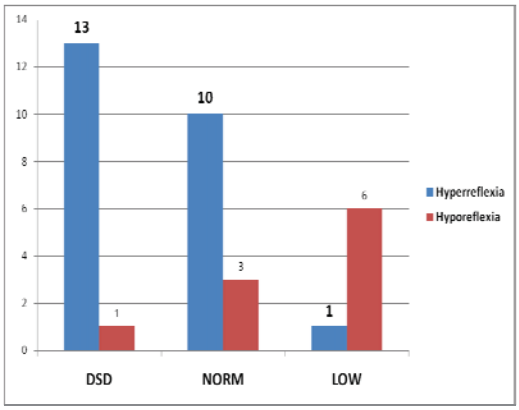

Fig. 3 – Number of the patients with detrusor hyper- and hyporeflexia related to external anal sphincter (EAS) electromyographic (EMG) activity
(DSD = detrusor sphincter dyssynergia; NORM = normal EMG activity; LOW = decreased EMG activity).

Discussion

The bladder, sphincter mechanisms and urethra forming the terminal parts of the urinary tract can be seen as a functional unit. Their basic function, filling the bladder, continence and miction make a group of very complex mechanisms and activities of antagonistic groups of smooth and skeletal muscles combined with complex innervations. The interruption of the nervous pathways with occurrence of demyelinating plaques in multiple sclerosis causes different forms of neurogenous bladder, with different disturbances and outcomes during the disease progress.

Our study included 34 MS patients – 25 (73.5%) females and 9 (26.5%) males with urinary symptoms and disturbances. It was in accordance with earlier studies, confirming predomination of female MS patients [3, 6, 11]. Symptom severity ranged from mild to very severe.

The most common urinary symptom of patients with MS is urgency. Series of urodynamic studies have shown that this is due to underlying detrusor hyperreflexia [3, 6, 12]. Urge incontinence is likely to be a problem if the patient also had impaired mobility and difficulty to access a toilet [10, 13]. The symptoms of impaired voiding are usually less prominent in testing and may be disclosed only during anamnesis or self reports.

The most common urodynamic finding was detrusor hyperreflexia suggesting that MS patients with irritative bladder symptoms and with lower limb pyramidal involvement are highly likely to have detrusor hyperreflexia. However, the explanation for detrusor areflexia in MS remains uncertain. Several investigators have reported that in some patients with MS initial urodynamic tests showed detrusor areflexia but subsequent studies demonstrated also hyperreflexia [5, 6, 12]. The neurological basis for this complete change in detrusor activity remains unclear [11].

Similar findings related to DSD in our study were also reported in previous studies [14, 15], although with significant differences in DSD appearance between patients with hiperreflexic and hyporeflexic bladder. The urodynamic finding of hyperreflexia correlated well with the symptoms of urgency, frequency and urge incontinence [16].

A modern concept of neural control of the bladder is based on long loop reflexes *via* the pontine tegmentum [3, 10, 16]. Pathways interruption between the sacral cord and pons may result in detrusor hyperreflexia and the loss of a coordinated action of a detrusor and the external striated urethral sphincter during voiding, the condition known as DSD. The reported incidence of DSD in MS patients varies from 18% to 66% [16]. DSD is important in the treatment of MS patients due to the tendency for incomplete bladder emptying, accompanied by poorly sustained detrusor contractions [10, 17]. Hesitancy of micturition, interrupted urinary stream and the finding of a high postmicturition residual volume in a patient with spinal cord disease therefore suggest DSD.

Applying classical urological diagnostic procedures could help to describe changes in parts of the lower urinary tract. Functional diagnostics provides monitoring and registering parameters of urination during filling and emptying of the bladder at approximately physiological conditions. Collected data could describe the degree of damage of bladder function as a consequence of the present CNS lesions [11, 18]. It is evident that in MS patients urodynamic findings can be changed through the disease duration, as well as the neurological signs and symptoms [10]. Different forms of dysfunctions are the result of the form of the disease, and the character and localization of demyelinating plaques in MS. Some of those signs and symptoms may develop before neurological changes, therefore urodynamic testing should be a part of routine testing of the disease, especially in patients developing changes during the course of the disease.

Appropriate therapeutic planning should be based on urodynamic findings. Some authors state that there is a poor correlation between subjective discomfort and objective neurological parameters [1, 2, 11, 19]. Therefore, neurological testing has important role not only in patients with dysuric disturbances, but also in patients without urinary discomfort, which was shown in this study.

By combining cystometry and EMG of EAS it is possible to register the occurrence of detrusor sphincter dissinergy which is an important urodynamic indicator of the progression of the disease disturbances (Figure 2). Those findings combined with hyperreflexia of m. detrusor appear to be most important urodynamic finding in patients during progressing MS. The data described here as neurogenous dysfunction of the bladder are in agreement with the criteria according to meta-analyses of urodynamic findings of 22 studies with 1882 patients diagnosed with MS [4].

Analysis of the urodynamic findings of this study emphasizes significant changes in the function of the bladder in MS patients, which further deteriorate their clinical picture and symptoms during the course and progression of the disease. During the progression of the disease, bladder dysfunction may become more and more difficult to treat. Main reasons could be described as worsening detrusor hyperreflexia, decreased efficiency in emptying due to worsening of the paraparesis neurological condition, appearance of recurrent urinary infections, spasticity and worsening of patients general immobility, and possibly their cognitive impairment [10, 20].

Conclusion

Based on the findings of this study we can conclude that: urodynamic tests of dysuric disturbances enable us to properly describe and monitor changes in factors of urination; the results of testing show the severity of urinary tract disturbances in patients with MS; the results of urodynamic test allow as to make appropriate urinary bladder training in patients with MS; an early therapeutic approach to preservation of physiological features of the bladder (elasticity and contractility) is very important due to the fact that satisfactory effect of the newly reorganized nervous control can be valid only in case of preserved physiological functions and structures. However, higher number of patients and broader variety of applied tests might give clearer perspective of urinary dysfunctions treatment in MS patients with different MS subtypes and forms.

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