Short-term reproducibility of cystometry in multiple sclerosis patients

Reproductibilité à court terme de la cystomanométrie chez des patients atteints de sclérose en plaques

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Summary
Objective. — To assess the reproducibility of detrusor activity cystometric pattern in multiple sclerosis (MS) patients, which is poorly documented in the medical literature, by means of successive filling.
Methods. — We conducted a prospective study in MS patients; cystometry was repeated twice at 5 minutes of interval if a detrusor overactivity before 300 mL of filling was observed. Thus, 3 successive cystometries were analysed. The following characteristics were recorded: detrusor maximum pressure (Pmax), volume at the first involuntary detrusor contraction (IDC), maximum cystometric capacity (MCC), pressure at the first IDC, the existence of an overactive detrusor classified as phasic or terminal.
Results. — We included 31 patients (19 women and 12 men); only 6 patients were naïve treatment, the mean EDSS was: 5.3 (±1.6) and the mean age was 48.4 (±12.5) years. All the patients had an overactive detrusor for each cystometry. The reproducibility was good for all the parameters (range ICC between 0.7 and 0.83).
Conclusion. — Quantitative and qualitative cystometric data have a good reproducibility in MS patients with detrusor overactivity before 300 mL of filling.
Level of proof. — 3.
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Introduction

Lower urinary tract symptoms (LUTS) are often observed in multiple sclerosis (MS) and affect nearly 90% of patients [1]. Overactive bladder (OAB), combined with urgency, increased daytime urinary frequency, nocturia and urge urinary incontinence, is the most common syndrome, which is sometimes also associated with voiding dysfunction and urinary retention. The most common urodynamic pattern is the association of overactive detrusor with detrusor—sphincter dyssynergia [2,3]. Urodynamic studies are considered the "gold standard" to identify involuntary detrusor contractions (IDCs) during filling cystometry characterising a urodynamic detrusor overactivity [4]. The presence (or persistence) of detrusor overactivity in MS patients can lead to introduce specific treatments such as anticholinergic drugs or botulinum toxin injections. Urodynamic evaluation attempts to reproduce symptoms under non-physiological circumstances and can be complex to analyse. Moreover, urodynamic evaluations are associated with a risk to develop urinary tract infection [5,6]. This raises the question to repeat in a same session, successive cystometries to confirm the presence or not of a detrusor overactivity and quantify the global risk of this overactivity in terms of intravesical pressure. Moreover, the patients with a neurogenic bladder in evolving pathology, (like multiple sclerosis), need to be evaluated with reproducible measurements in order to allow the clinician a good follow-up of the patient and a good evaluation of the treatment. Some studies have evaluated the reproducibility of urodynamics in women with stress incontinence, and demonstrated a poor reproducibility of urodynamic parameters for a part of the studies [7,8] and a good reproducibility for the others [9]. Only three studies have investigated the reproducibility of repeated cystometries in patients with overactive detrusor and neurogenic lower tract dysfunction [10–12]. The most common aetiology in these studies was spinal cord injury. Only one study included MS patients with lower urinary tract symptoms (22 patients among 226 with other aetiologies) [12]. To our knowledge, our study is the first one to evaluate the short-term reproducibility of urodynamic studies in the MS population exclusively. The aim of this study was to assess the short-term reproducibility in multiple sclerosis patients (with detrusor overactivity observed before 300 mL of filling) of qualitative and quantitative urodynamic data.

Materials and methods

Study design

This study was conducted prospectively in a neuro-urology department of a university hospital between May 2017 and November 2017. All patients with multiple sclerosis consulting for a urodynamic evaluation with detrusor overactivity, which appeared before 300 mL of filling during the first cystometry, were included. The main exclusion criteria were: a significant difference (50 mL or more) between the filling volume during the study and the volume collected after catheterisation, the presence of a urinary tract infection, or another acute disease. None of the patient treatments were suspended.
For each patient, symptoms scores were collected: urinary symptom profile overactive bladder (USP OAB), urinary symptom profile voiding dysfunction (USP voiding dysfunction), urinary symptom profile stress incontinence (USP SI); and quality of life score (Qualiveen). Moreover, all treatments for urinary disorders were reported and classified in: anticholinergic drug, catheterisation, alpha blocking drug, botulinum toxin, and beta 3 adrenergic drug.

The urodynamic studies were performed according to “the good urodynamic practice” recommended by the International Continence Society (ICS) [13]. All definitions were used in accordance with the International Continence Society report [14].

We used a Laborie Aquarius TT® equipment (LABORIE Medical Technologies) to perform the urodynamic studies with water-filled pressure lines and 8 F double-lumen catheters to fill and measure bladder pressure. Rectal balloon catheters were used to measure abdominal pressure. The bladder was totally emptied by catheterisation before filling at a filling rate of 50 mL/min using saline at room temperature. The catheters were attached to the body surface, using tape to assure correct placement during the entire study. The vesical catheter was attached close to the urethral meatus to avoid expelling during the study. The tracing from each study was manually inspected and artefacts corrected. The maximum cystometric capacity (MCC) was the bladder volume where urine leakage was observed, or the volume at the end of filling at 400 mL. An involuntary detrusor contraction was defined as a sudden rise in detrusor pressure of any magnitude, whether spontaneous or provoked without rise in abdominal pressure.

During the first cystometry, if an involuntary detrusor contraction for a filling of 300 mL or less appeared, we realised two other cystometries (filling rate of 50 mL/min) at 5-minute intervals. The volume and pressure, at first, and the maximal involuntary detrusor contraction, and the MCC were documented for each cystometry. We also noted the typology of the overactive bladder; phasic overactive bladder with involuntary detrusor contraction during the bladder filling which may or may not lead to urinary incontinence and the terminal, which is a single involuntary detrusor contraction that results in complete bladder emptying [4].

Statistical analysis

Statistical analysis was carried out using R 3.2.3 software (R Development Core Team, http://www.R-project.org) and R studio version 1.0.136.

The descriptive statistics were expressed as the mean ± SD. The Shapiro–Wilks test was used to evaluate each quantitative variable and establish the type of statistical model to be used (ANOVA test or Kruskall–Wallis test). The differences between groups were assessed with the ANOVA test for quantitative variables with normal distribution and the Kruskall–Wallis test for quantitative variables with non-normal distribution. Chi-squared or Fisher tests were used for categorical variables. Agreements between the urodynamic parameters during the three cystometries were evaluated using an intra-class correlation coefficient (ICC) (with a 95% confidence interval calculated using the bootstrap method). A P < 0.05 level was considered statistically significant.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Demographic data.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Female</td>
<td>19, (61.3)</td>
</tr>
<tr>
<td>Evolution years</td>
<td>16.5 (9.7)</td>
</tr>
<tr>
<td>Age</td>
<td>48.4 (12.5)</td>
</tr>
<tr>
<td>EDSS</td>
<td>5.3 (1.6)</td>
</tr>
<tr>
<td>BMI</td>
<td>22.9 (4.5)</td>
</tr>
<tr>
<td>USP OAB</td>
<td>9.9 (3.4)</td>
</tr>
<tr>
<td>USP SI</td>
<td>2.4 (3.1)</td>
</tr>
<tr>
<td>USP voiding dysfunction</td>
<td>4.4 (3.2)</td>
</tr>
<tr>
<td>Qualiveen total</td>
<td>8.1 (4.1)</td>
</tr>
<tr>
<td>Overactive bladder syndrome</td>
<td>28, (90.3)</td>
</tr>
<tr>
<td>Voiding dysfunction</td>
<td>28, (90.3)</td>
</tr>
<tr>
<td>Urinary retention</td>
<td>9, (45.0)</td>
</tr>
<tr>
<td>Treatment</td>
<td>25, (80.6)</td>
</tr>
<tr>
<td>Catheterisation</td>
<td>11, (35.5)</td>
</tr>
<tr>
<td>Anticholinergic</td>
<td>22, (71.0)</td>
</tr>
<tr>
<td>Alpha -</td>
<td>10, (32.3)</td>
</tr>
<tr>
<td>Botulinum toxin</td>
<td>11, (35.5)</td>
</tr>
<tr>
<td>Mirabegron</td>
<td>0, (0)</td>
</tr>
</tbody>
</table>

EDSS: expanded disability status scale; USP: urinary symptom profile; BMI: body mass index; OAB: overactive bladder; SI: stress incontinence.

Ethics

This study was approved by the local ethics committee (CPP Ile de France II, EudraCT/ID-RCB: 2015-A00125-44), performed according to the guidelines of Good Clinical Practice, and registered at ClinicalTrials.gov (NCT03451175). All study participants provided informed consent before enrolment.

Results

Demographic characteristics

Thirty-one patients (19 women, and 12 men) were included (Table 1). The mean age was 48.4 years (± 12.5), the mean delay from the onset of MS was: 16.5 (± 9.7) and the mean EDSS was: 5.3 (± 1.6), 64.51% of the patients had a relapsing remitting form (n = 28), 90.32% of the patients had a voiding dysfunction (n = 28), and 90.32% had an overactive bladder (n = 28). Among these patients, 35.48% (n = 11) had a treatment with botulinum toxin injections and, as a consequence, 35.48% (n = 11) used intermittent catheterisation as voiding mode. The other treatments were: 71% (22 patients) anticholinergic, 32.3% (10 patients) used an alpha-adrenergic blocking drug. Among the patients, 64.51% had a detrusor sphincter dyssynergia (n = 20).

Qualitative and quantitative comparison and reproducibility

For all the patients, the detrusor overactivity was present during the three cystometries (Table 2). Only one patient shifted from terminal detrusor overactivity to a phasic detrusor overactivity during the three cystometries. During
Table 2  Urodynamic parameters in the three cystometries.

<table>
<thead>
<tr>
<th></th>
<th>Cystometry 1 mean (SD)</th>
<th>Cystometry 2 mean (SD)</th>
<th>Cystometry 3 mean (SD)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCC (mL)</td>
<td>205.7 (119.6)</td>
<td>215.1 (134.9)</td>
<td>219.4 (137.8)</td>
<td>0.79</td>
</tr>
<tr>
<td>Volume of the first IDC (mL)</td>
<td>126.8 (79.5)</td>
<td>159.0 (107.2)</td>
<td>159.1 (105.2)</td>
<td>0.18</td>
</tr>
<tr>
<td>Pmax (cm H₂O)</td>
<td>58.5 (24.1)</td>
<td>56.9 (25.3)</td>
<td>51.8 (23.5)</td>
<td>0.98</td>
</tr>
<tr>
<td>Pressure of the first IDC (cmH₂O)</td>
<td>38.8 (22.6)</td>
<td>38.7 (25.2)</td>
<td>35.2 (21.8)</td>
<td>0.77</td>
</tr>
<tr>
<td>n (%)</td>
<td>31 (100)</td>
<td>31 (100)</td>
<td>31 (100)</td>
<td></td>
</tr>
<tr>
<td>Detrusor overactivity</td>
<td>12 (38.7)</td>
<td>12 (38.7)</td>
<td>11 (35.5)</td>
<td></td>
</tr>
<tr>
<td>Phasic overactivity detrusor</td>
<td>19 (61.3)</td>
<td>19 (61.3)</td>
<td>20 (64.5)</td>
<td></td>
</tr>
</tbody>
</table>

MCC: maximum cystometric capacity; IDC: involuntary detrusor contraction; Pmax: maximum pressure.

Figure 1. Evolution of urodynamic parameters. MCC: maximum cystometric capacity; IDC: involuntary detrusor contraction; Pmax: maximum pressure.

the three cystometries, there were no changes of the urodynamic parameters. The reproducibility of the urodynamic parameters was good; concerning the MCC (ICC: 0.84 with a confidence interval from 0.67 to 0.93), the Pmax (ICC: 0.79 with a confidence interval from 0.66 to 0.88), the volume of the first IDC (ICC: 0.70 with a confidence interval from 0.50 to 0.89), the pressure of the first IDC (ICC: 0.80 with a confidence interval from 0.70 to 0.87) (Fig. 1).

Discussion

To our knowledge, this work is the first to study the reproducibility of cystometry in multiple sclerosis patients with detrusor overactivity observed before 300 mL of filling. Our results demonstrated a good reproducibility of the qualitative parameters. Indeed, in all cystometries, detrusor overactivity was present. Moreover, the typology of overactive detrusor was similar. The reproducibility of the quantitative data was also good with an ICC range between 0.7 and 0.8, concerning all urodynamic data.

A review of multiple studies was realised, focusing on botulinum toxin in overactive detrusor treatment [15–20]. The mean differences concerning the urodynamic parameters (MCC and maximum pressure) were calculated in the placebo group and the treatment group (300 U, botox injected) for each study. The total number of patients was 1915 (including a majority of spinal cord injury patients), the interval of time for the measures (before and after the treatment) was 6 weeks; the mean difference concerning MCC was respectively +12.7 mL for the placebo group and +162.5 mL for the treatment group. The mean difference concerning the maximum pressure was respectively +0.36 cmH₂O for the placebo group and −31.8 cmH₂O for the treatment group. Compared with our results, our differences were very inferior to the treatment group and closer to the placebo group. The stability of the urodynamic parameters (MCC and maximum pressure) and the global reproducibility were also confirmed.
Reproducibility of cystometry in multiple sclerosis

The reproducibility of cystometry was studied in many articles; however, only a few of them were focused on detrusor activity and the results remain unclear. Moreover, most of the studies have included non-neurologic patients. Ho et al. evaluated the short-term reproducibility (two trials with 5 minutes interval) of urodynamic studies in neurogenic bladders in subjects with spinal cord injuries. The parameters collected were: bladder volume at first sensation to void, maximum cystometric capacity, presence of uninhibited contraction, opening pressure, maximum detrusor pressure, duration of contraction, volume voided, and post-void residual volume. Statistical analysis showed significant levels of agreement between the two trials for all parameters [10]. Ockrim et al., in 2004, realised a study evaluating the variability of detrusor overactivity in 60 men with lower tract urinary symptoms, and comparing results between neurologic (spinal cord injury) and non-neurologic patients. Three sequential filling studies were performed. Number and pressure of involuntary detrusor were significantly lower among non-neurologic patients throughout the three studies. In men with spinal cord injury, detrusor overactivity remained consistent over sequential studies [11]. More recently, Bellucci et al. studied short-term reproducibility (two urodynamic investigations immediately repeated) in patients with neurogenic lower urinary tract dysfunction (226 patients with 70% spinal cord injuries, and 10% multiple sclerosis). The parameters assessed were maximum cystometric capacity, bladder compliance, maximum detrusor pressure during storage, the presence or absence of detrusor overactivity, maximum flow rate, detrusor pressure at maximum flow rate, voided volume and post-void residual urine. Detrusor overactivity repeatability was excellent between the 2 urodynamic investigations; however, all other urodynamic parameters had poor repeatability. All of these data are in agreement with our results: the reproducibility of the overactive detrusor in the neurologic population is good; the urodynamic parameters concerning detrusor activity are close for each trial.

This study had several limits; the included patients were consulting in a neuro-urology department, leading to a selection bias. The voiding phase parameters have not been considered because of the high number of the patients using catheterisation as voiding mode (n = 11, 35.5%). As a result, there was no possibility to study the maximum flow rates, the voiding time and the post-void residual volume. Also, the desire to void (first, normal or strong) during the filling wasn’t noted because this parameter has been studied, and remains complex to evaluate. The studies in the non-neurologic patients had various results; some articles finding a good reproducibility between the evaluations [7,21], and others a poor repeatability of these parameters [8,22]. In the same way, the reproducibility of the desire was good [10] or poor [11] in the neurologic population, depending on the studies.

Conclusion

The reproducibility of same session repeated cystometries among multiple sclerosis patients with detrusor overactivity was good, concerning the qualitative and the quantitative urodynamic parameters.

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The study did not receive any funding.

Disclosure of interest

The authors declare that they have no competing interest.

References


