Infectious Diseases

Effects of Physiotherapy in the Treatment of Neurogenic Bladder in Patients Infected With Human T-Lymphotropic Virus 1

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OBJECTIVE To evaluate the efficacy of physiotherapy for urinary manifestations in patients with human T-lymphotropic virus 1–associated lower urinary tract dysfunction.

METHODS Open clinical trial was conducted with 21 patients attending the physiotherapy clinic of the Hospital Universitário, Bahia, Brazil. Combinations of behavioral therapy, perineal exercises, and intravaginal or intra-anal electrical stimulation were used.

RESULTS The mean age was 54 ± 12 years and 67% were female. After treatment, there was an improvement in symptoms of urinary urgency, frequency, incontinence, nocturia, and in the sensation of incomplete emptying ($P < .001$). There was also a reduction in the overactive bladder symptom score from $10 ± 4$ to $6 ± 3$ ($P < .001$) and an increase in the perineal muscle strength ($P < .001$). The urodynamic parameters improved, with reduction in the frequency of patients with detrusor hyperactivity from 57.9% to 42.1%, detrusor-sphincter dyssynergia from 31.6% to 5.3%, detrusor hypocontractility from 15.8% to 0%, and detrusor areflexia from 10.5% to 0%, with positive repercussions in the quality of life in all patients.

CONCLUSION Physiotherapy was effective in cases of human T-lymphotropic virus 1–associated neurogenic bladder, reducing symptoms, increasing perineal muscle strength, and improving urodynamic parameters and quality of life. UROLOGY 89: 33–39, 2016. © 2016 Elsevier Inc.

Human T-lymphotropic virus (HTLV-1) is the etiological agent of HTLV-1–associated myelopathy or tropical spastic paraparesis (HAM or TSP). Although it only occurs in 2% of the infected individuals,1,2 other isolated or assorted syndromes may occur in a large percentage of HTLV-1–infected subjects.3,4 Urinary complaints are present in virtually all patients with HAM or TSP and occurs in around 30% of HTLV-1–infected individuals.5

The most common urodynamic finding in HTLV-1–infected patients is detrusor overactivity (DO). Later, detrusor-sphincter dyssynergia (DSD) or detrusor areflexia (DA) may develop,6 with the two dysfunctions possibly coexisting in HTLV-1–infected patients.7 These dysfunctions may cause severe and irreversible consequences to the lower urinary tract.8 Moreover, neurogenic bladder (NB) is the principal cause of the urinary symptoms in HTLV-1–infected individuals.9 Nocturia was reported as the most common complaint, occurring in 84.6% of cases, followed by urgency, increased frequency, urinary incontinence, and urge incontinence.10 The high frequency of these symptoms have been documented in several series of HTLV-1–infected subjects previously considered as carriers, as they do not fulfill the criteria for HAM or TSP.11,12 Moreover, urinary dysfunction in HTLV-1–infected individuals has a great impact in quality of life (QoL).10

The most common drugs used for DO are the anticholinergic agents. However, due to the high incidence of side effects, compliance with these drugs tends to be poor.13 In cases of areflexia, catheterization has been the most common approach. Botulinum toxin type A is indicated when patients are refractory to conventional treatment. However,
complications such as urinary retention and urinary tract infection limit their use.\textsuperscript{14} In this respect, physiotherapy for overactive bladder (OAB) and urinary incontinence has been confirmed as a good option, rendering satisfactory results in patients with urinary symptoms of idiopathic or neurogenic origin through the use of behavioral therapy,\textsuperscript{15} electrical therapy, and kinesiotherapy.\textsuperscript{16,18} The aim of all these therapeutic resources is to improve urinary symptoms and QoL.\textsuperscript{19}

The objective of the present study was to evaluate the efficacy of physiotherapy in the treatment of urinary symptoms secondary to NB in HTLV-1–infected individuals.

METHODS

Study Design

This was an open, uncontrolled clinical trial developed in the physiotherapy outpatient clinic for perineal dysfunction at the Professor Edgard Santos University Hospital, between March 2012 and December 2013. The Institutional review board approved the study protocol and all the participants signed an informed consent form.

Patients

Participants of the study were 21 HTLV-1–infected patients diagnosed by a serologic test (Cambridge Biotech, Worcester, MA) and confirmed by Western Blot (HTLV Blot 2.4, Genelabs, Science Park Drive, Singapore). The sample consisted of patients with NB, with or without associated myelopathy (HAM or TSP). All were over 18 years of age, had lower urinary tract dysfunction diagnosed by urodynamic study, and, in all cases, the condition had proven refractory to anticholinergic drugs. Patients with diabetes mellitus, had cerebrovascular accident, with multiple sclerosis, with Parkinson’s disease, wearing a pacemaker, and with a genitourinary infection were excluded from the study.

The sample consisted of patients with probable or definite HAM or TSP according to De Castro Costa 2006 criteria.\textsuperscript{20} Patients were selected at random by a simple draw. The draw was made in order to allow everyone who fulfill the inclusion criteria (N = 70) have a chance to participate. All the participants were included in a single treatment group. Results following intervention were compared with baseline values.

Definition of Variables and Evaluation’s Instruments

The symptoms of OAB were evaluated using the score of the Symptoms of OAB (OABSS), which has a score ranging from 0 to 14 points, with the sum of individual issues 0–5.\textsuperscript{10} The perineal muscle strength was evaluated using the Oxford score or PERFECT assessment scheme.\textsuperscript{21} The King’s Health Questionnaire was used to evaluate QoL.\textsuperscript{22} These instruments were used prior to and following urological physiotherapy.

Treatment

The intervention consisted of combined therapy including the following: behavioral therapy, with guidance being provided on the need to modify dietary habits and lifestyle; kinesiotherapy, which consisted of specific exercises for the pelvic floor with the objective of improving contractility and the endurance of the muscle fibers and electrical stimulation, with intravaginal or intranal probe. This procedure is based on neuromodulation principles to reduce DO or improve urinary voiding symptoms associated with perineal exercises to be performed at home. In cases of DO, low-frequency biphasic current of 12 Hz, with a pulse duration of 0.2 milliseconds, was applied continuously for 30 minutes. In the case of detrusor hypocontractility and DA, a medium-frequency current was used (50 Hz, 250 \textmu s), with an intermittent 3-second stimulus followed by 1 second of rest over a total period of 30 minutes. In cases of DSD, the frequency of the current was 100 Hz, 40/70 \textmu s, and the stimulus was applied continuously for 30 minutes. The treatment was carried out twice weekly for a total of 60 minutes, over at least 10 sessions and for a maximum of 40 sessions. Patients were reevaluated to monitor progress every 10 sessions until the end of treatment and periodically every 3 months thereafter for 1 year. They were oriented to keep the behavioral guidelines and home perineal exercise.

Evaluation Criteria and Outcome

The clinical improvement was defined as a reduction of at least 50% in urinary complaints at the end of therapy compared with the urinary complaints made at baseline. The clinical failure was defined as a reduction of less than 50% in the urinary complaints recorded at baseline, or therapy discontinuation due to adverse reactions to electrical stimulation.

Statistical Analysis

The statistical program R.Version 3.1.3 (R Foundation for Statistical Computing, Vienna, Austria) was used. Data were described by mean ± standard deviation or median and interquartile range (IQ). The McNemar test and Wilcoxon paired t-test were used for paired samples and Mann-Whitney test for independent samples. The Kaplan-Meier survival curve was used to assess the probability of the event over time and compare between the clinical form and gender with log rank test. The level of significance adopted for this work was 5%.

RESULTS

Of the 25 patients chosen to be included in the study, 21 accepted to participate in the clinical trial. The mean age was 54 ± 12 years, most were female (14 [67%]), were non-white (18 [86%]), had only elementary school education (10 [48%]), and had a family income of 2 to 3 minimum salaries (8 [48%]).

Regarding the clinical presentation of HTLV-1, 16 patients (71.4%) had probable HAM or TSP and 5 (28.6%) had definite HAM or TSP. The medians of the number of physiotherapy sessions attended by patients with these 2 clinical forms were 11.5 (IQ = 11) and 28 (IQ = 16), respectively (\textit{P} = .006). A reduction in the frequency of the symptoms was recorded in all cases (\textbf{Table 1}), being more important regarding urgency (\textit{P} < .001), urge incontinence (\textit{P} = .001), and frequency and sensation of incomplete emptying and straining to void (\textit{P} = .004).

The treatment impact on OABSS is shown in \textbf{Figure 1}. The mean overall OABSS decreased (\textit{P} < .001) from 10 ± 4 at baseline to 6 ± 3 following the intervention. A contractile gain and an improvement in the quality of the endurance of the muscle fibers of the perineum were found. \textbf{Figure 2} shows a muscle strength increasing from a median of 2.0 (IQ = 3.0) at baseline to 3 (IQ = 2.5) at the end of the treatment (\textit{P} < .001).
Urodynamic studies were performed in 17 patients after therapy. Some patients had two types of dysfunction before therapy. Changes in urodynamic parameters were found both in the storage phase and in the voiding phase, with a numerical improvement although without statistical significance. Prior to treatment, the most common finding was DO (11 [57.9%]), followed by DSD (6 [31.6%]), hypocontractility (3 [15.8%]) defined as low voiding pressure and low flow, and areflexia (2 [10.5%]). After intervention, there were no cases of stress urinary or incontinency, detrusor hypocontractility, areflexia, or hyposensitivity defined as the first voiding desire above 150 mg or maximum bladder capacity up to 500 ml in urodynamic study. Moreover, there was a decrease of the DO in 8 cases (42.1%).

There was a reduction in the negative impact of the urinary symptoms on the QoL of all the patients (Table 2). Statistical significance (P < .05) were detected in 6 of the 9 domains measured (impact of incontinence, limitations in daily life, physical limitations, social limitations, emotions, and sleep and energy).

During the follow-up, 90% of patients remained without failure at day 90, 60% for at least 210 days, and 40% of the patients have remained without failure until the end of follow-up. The median for the occurrence of the event was 270 days (95% [180-365 days]). Moreover only 5 patients (23, 8%) need to perform new urologic physiotherapy. There was no association between therapeutic failure with age, gender, and HAM or TSP.

**DISCUSSION**

In the present study, we documented that physiotherapy for NB in HTLV-1–infected patients improved clinical and urinary complaints, increased the strength of the perineal muscles, and improved the QoL of the patients. Some urinary symptoms reduced or disappeared as there was also difference between the number of sessions among patients with the 2 clinical forms presented, probably due to the degree of neurological impairment and severity of voiding dysfunction in patients with myelopathy installed.

The treatment of OAB includes behavioral therapy, consisting of dietary counseling, water control consumption, and adopting a micturitional schedule. Behavioral interventions have proven to represent an important and effective tool for controlling micturition.

Kinesiotherapy is used as a form of pelvic floor training for the treatment of urinary incontinence. The exercises and manual techniques improve perineal perception in voiding dysfunctions, reducing the incidence of urgency, frequency, nocturia, and urinary incontinence.

In this study, an increase in muscle strength was found in the majority of the patients, with a consequent reduction in urinary loss corroborating with other.

Although electrical stimulation is a traditional practice, up to the present moment, there is no consensus on the ideal electrical parameters that should be used. In the present study, we used electrical stimulation with a low-frequency current and high pulse width, with a greater time of stimulation for patients with DO. Pannek et al used lower parameters and obtained a decrease in urinary symptoms in 18 of 52 patients (32.7%) with neurogenic DO. The medium-frequency currents were used for patients with acontractile bladder, hypocontractile bladder, and DSD. Primus et al used intraurethral electrical stimulation for acontractile and hypocontractile bladder and found detrusor contraction in 39% of the patients, with a 75% improvement in bladder sensation and a reduction in the mean post-miccional residual volume. Despite the fact that studies differ with respect to the electrical parameters used, improvement in symptoms is usually achieved. Our data suggest that electrical stimulation represents a good alternative for bladder dysfunction associated with HTLV-1 infection. It is simple to perform, safe, cost-effective, and with little or no associated complications.

The changes found in the urodynamic studies were limited, but changes in bladder function were significant. An improvement in urgency, frequency, urge incontinence, and feeling of incomplete emptying was documented, resulting in a decrease in the OABSS. The treatment also resulted in the improvement of the perineal muscle strength. The results were similar to the one found in patients with multiple sclerosis with refractory NB to drug treatment.

The efficacy of the therapy lasted long in most patients. Eight patients remained without urinary complaints in the course of a year. However, the time interval for the reappearance of any symptom was approximately 6 months and the clinical form did not interfere with the decrease in survival. In a previous study in patients with OAB of other causes, the improvement in urinary symptoms and QoL persisted for 3 years.

Urinary symptoms compromise QoL and in patients with HTLV-1, and the negative impact on QoL may be as much

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**Table 1.** Distribution of frequency of urinary symptoms before and after urological physical therapy in 21 HTLV-1 infected subjects.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Before Therapy</th>
<th>After Therapy</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>Urgency Present</td>
<td>21</td>
<td>100</td>
<td>9</td>
</tr>
<tr>
<td>Frequency</td>
<td>12</td>
<td>57.1</td>
<td>3</td>
</tr>
<tr>
<td>Urge-incontinence Present</td>
<td>15</td>
<td>71.4</td>
<td>4</td>
</tr>
<tr>
<td>Nocturia†</td>
<td>16</td>
<td>76.2</td>
<td>10</td>
</tr>
<tr>
<td>Feeling of incomplete emptying Present</td>
<td>15</td>
<td>71.4</td>
<td>6</td>
</tr>
</tbody>
</table>

McNemar test.

* Values before and after therapy were considered statistically significant if P value was lower than .05.
† Nocturia: the act of waking up one or more times during the night to urinate.
as 4 times greater\textsuperscript{10} Physiotherapy positively affected the QoL of these patients, principally with respect to the effect of incontinence on their lives, limitations in their daily life, physical and social limitations, emotions, and sleep and energy. Although no significant differences were found for the domains of general health, personal relationships, or degrees of severity, there was a reduction in the impact of the symptoms in these domains. Personal relationships may be an aspect associated with the progressive worsening of the disease. It deals with the family context, the sexual life of an individual, hygiene, and the patient’s way of confronting the issue. Moreover, it tends to contribute toward isolation and depression, and affects self-perception of their state of health, their disease, and their life.\textsuperscript{10} Therefore,
therapeutic measures for urinary symptoms may reduce the impact of these symptoms on QoL of the patients.

In assessing the follow-up, 8 of the patients (40%) remained asymptomatic for a period of 1 year. The return of some urinary symptoms occurred in 13 of the patients (60%) in the period of 7 months and 5 of them (23.85%) had to return the physical therapy treatment. However, the return of these symptoms did not impact negatively on the QoL thereof. Treatment was able to improve and maintain the QoL of patients after urological physiotherapy for a relevant time.

The results observed here may be promising in the treatment of NB associated with HTLV-1. Moreover, the absence of complications or adverse events is a potential benefit for the electrophysiotherapy.

The limitations of the present study refer to its sample size and to the lack of a control group. Nevertheless, since in all cases, the condition had proven refractory to other types of interventions, delaying treatment could have had undesirable consequences and would have ethical implications. Moreover, this study is valid because of its originality and its relevance by aiming to introduce new perspectives for the treatment of NB in HTLV-1–infected subjects. Additionally, it extends previous observation that physiotherapy for lower of urinary tract dysfunction is safe, cost-effective, simple to perform, and well accepted by the patients.

**CONCLUSION**

Physiotherapy for urinary incontinence was effective in the treatment of NB in HTLV-1–infected individuals, reducing urinary complaints and increasing the strength of the perineal muscles, which reflected positively on the QoL of the patients. However, long-term follow-up and experience are required to determine the details of the techniques used, as well as their periodicity, limits, and the adequacy of this indication for the treatment of NB in HTLV-1–infected individuals.

**Acknowledgment.** We thank Cristiano Sampaio and students Milena Andrade, Talita Miranda, Camila Melo, Daniela Sena, and Joseane Anunciação for their contribution in the preparation of this paper. This study was supported by the Brazilian National Research Council and the Science Technology Minister of Brazil (CNPQ/MCT 573839/2008-5).

**Table 2.** Quality of life characteristics before and after urological physical therapy for HTLV-1 patients. Salvador, Bahia, Brazil 2014.

<table>
<thead>
<tr>
<th>Variables (n = 21)</th>
<th>Before</th>
<th>Median (IQ)</th>
<th>After</th>
<th>Median (IQ)</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>General perception of health</td>
<td>50.00(50)</td>
<td>50.00(25)</td>
<td></td>
<td></td>
<td>.148</td>
</tr>
<tr>
<td>Impact on incontinence</td>
<td>67.00(33)</td>
<td>01.00(50)</td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Limitation of daily life</td>
<td>50.00(50)</td>
<td>00.00(50)</td>
<td></td>
<td></td>
<td>.001</td>
</tr>
<tr>
<td>Physical limitation</td>
<td>33.00(51)</td>
<td>00.00(59)</td>
<td></td>
<td></td>
<td>.016</td>
</tr>
<tr>
<td>Social limitation</td>
<td>33.00(72)</td>
<td>00.00(22)</td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Personal relationships</td>
<td>00.00(67)</td>
<td>00.00(33)</td>
<td></td>
<td></td>
<td>.082</td>
</tr>
<tr>
<td>Emotions</td>
<td>44.00(62)</td>
<td>00.00(44)</td>
<td></td>
<td></td>
<td>.002</td>
</tr>
<tr>
<td>Sleep and disposition</td>
<td>33.00(50)</td>
<td>17.00(42)</td>
<td></td>
<td></td>
<td>.005</td>
</tr>
<tr>
<td>Gravity measures</td>
<td>33.00(43)</td>
<td>13.00(44)</td>
<td></td>
<td></td>
<td>.144</td>
</tr>
</tbody>
</table>

IQ, interquartile range.
Wilcoxon signed rank test.
*P values lower than .05 were considered statistically significant.

**References**


**EDITORIAL COMMENT**

Human T-cell lymphotropic virus 1–associated myelopathy or tropical spastic paraparesis (HAM or TSP) is a rare condition encompassing lower extremity weakness, bowel and bladder dysfunction, and dermatologic manifestations. The ultimate goals of treating the urologic sequelae of HAM or TSP are the same as for other constellations of storage or voiding symptoms resulting from neurologic insult: (1) preserve the upper urinary tracts, (2) identify ways to empty the bladder efficiently, (3) minimize urinary tract infections, (4) maintain continence, and (5) preserve quality of life. Optimizing low pressure urinary storage by decreasing detrusor overactivity and improving compliance may directly contribute to the achievement of several of these goals. Behavioral modifications and pharmacotherapy typically constitute the initial steps of the treatment algorithm; however, the use of muscarinic receptor antagonists may exacerbate concomitant bowel dysfunction and may be associated with cognitive sequelae. More invasive options such as intravesical orabotulinumtoxin A injection or neumodulation are also available; however, chemodenervation may exacerbate emptying dysfunction and sacral neumodulation often necessitates several surgical procedures and revisions. Of all the potential options, pelvic floor muscle training (PFMT) may be associated with essentially no significant adverse sequelae and may confer a benefit in urinary emptying, as well.

The authors describe promising outcomes after PFMT with electrical stimulation in this small group and they are to be applauded for their efforts. We can take several things away from this study. First, there is no downside to PFMT, save for lacking the physical ability to engage the regimen faithfully and regularly. Second, outcomes are durable as long as the patient is able to perform the therapy. One only needs to look at the multiple sclerosis literature for a comparable benchmark. Lucio et al randomized women with multiple sclerosis to PFMT vs sham group and found that the women in the active treatment group had a significant reduction in pad weight, daily pad use, and nocturia episodes. Additionally, McClurg et al found that the addition of active neuromuscular electrical stimulation to PFMT and biofeedback was associated with a significantly greater reduction in daily incontinence episodes in another randomized clinical trial. Finally, Lucio et al showed that the improvement in lower urinary tract symptoms after PFMT in their cohort was positively associated with improvement in quality of life. The final takeaway is that the benefits of PFMT seem to be limited to women with mild disability. Indeed, women in the current study who had suspected HAM or TSP required fewer sessions to achieve benefit. It is also presumed that these patients had lesser physical impairment. Ultimately, the disease may progress and additional therapeutic options may be incorporated, especially those with higher risk to benefit ratios. It is reassuring to know that, given the right circumstances, a treatment modality such as PFMT can provide a benefit in both storage and emptying symptoms in this challenging population.

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**References**


The human T-cell lymphotropic virus type 1 (HTLV-1) was identified earlier than the human immunodeficiency virus, but until now there is no specific therapy for the infection of HTLV-1. HTLV-1 infection has been neglected mainly due to the misconception that it is a low morbidity infection. Actually, only 5% of HTLV-1–infected subjects develop HTLV-1–associated myelopathy (HAM) or adult T-cell lymphoma leukemia, the main diseases associated with the virus. However, recent evidence has shown that more than 50% of infected subjects who do not fulfill the criteria for HAM present a variety of diseases, including sicca syndrome, periodontal disease, HTLV-1–associated arthropathy, and neurogenic bladder.

Urinary manifestations may occur in virtually all patients with HAM, as well as in up to 20% of individuals previously considered HTLV-1 carriers. The main urinary manifestations are nocturia, urgency, and incontinence. In such cases, urodynamic studies have documented detrusor overactivity and detrusor dysymmetry as the main abnormal findings. When areflexia bladder occurs, the use of intermittent catheters is necessary. As stated in the letter to the editor, this picture resembles conditions found in patients with multiple sclerosis. However, severe urinary complaints, including areflexia bladder, have been observed in patients who do not fulfill the criteria for definitive HAM, and the majority of patients with HTLV-1–associated neurogenic bladder do not develop HAM. Recently, these individuals have been classified as probable myelopathy, but because urinary manifestations are not a step toward HAM, and because its pathogenesis differs from patients with HAM or tropical spastic paraparesis, patients with neurogenic bladder but without HAM should be considered to have a distinct clinical form of the HTLV-1 infection. As urinary manifestations have a great impact on the quality of life of HTLV-1–infected subjects, and because there is no therapy for HTLV-1 infection, measures that can attenuate manifestations related to the virus are highly relevant.

An open clinical trial performed with a small number of patients, described in the article by the authors, had highly positive results. Future controlled trials with a high number of subjects should be encouraged.

In the published manuscript, the sample was formed with patients who had substantial urinary symptoms. Urologic dysfunctions were documented through urodynamic studies and all patients failed to respond to anticholinergic drugs. In addition to the improvement observed in all patients who had storage symptoms, the patients who had areflexia bladder were able to discontinue the use of vesical catheters after electrophysiotherapy. Because HTLV-1–related diseases occur predominantly in poor populations, the cost-benefit relationship is very important. In such cases, floor electrophysiotherapy is a safe, cost-effective alternative that can be self-performed.

The study provided evidence that the use of pelvic floor muscle training in association with electrical stimulation enhanced perineal muscle strength and significantly improved all urinary manifestations, and consequently, the quality of life of patients with HTLV-1–associated neurogenic bladder.

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http://dx.doi.org/10.1016/j.urology.2015.09.038

UROLOGY 89: 39, 2016. © 2016 Published by Elsevier Inc.