Randomized Multicenter Clinical Trial of Myofascial Physical Therapy in Women With Interstitial Cystitis/Painful Bladder Syndrome and Pelvic Floor Tenderness


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Purpose: We determined the efficacy and safety of pelvic floor myofascial physical therapy compared to global therapeutic massage in women with newly symptomatic interstitial cystitis/painful bladder syndrome.

Materials and Methods: A randomized controlled trial of 10 scheduled treatments of myofascial physical therapy vs global therapeutic massage was performed at 11 clinical centers in North America. We recruited women with interstitial cystitis/painful bladder syndrome with demonstrable pelvic floor tenderness on physical examination and a limitation of no more than 3 years’ symptom duration. The primary outcome was the proportion of responders defined as moderately improved or markedly improved in overall symptoms compared to baseline on a 7-point global response assessment scale. Secondary outcomes included ratings for pain, urgency and frequency, the O’Leary-Sant IC Symptom and Problem Index, and reports of adverse events. We compared response rates between treatment arms using the exact conditional version of the Mantel-Haenszel test to control for clustering by clinical center. For secondary efficacy outcomes cross-sectional descriptive statistics and changes from baseline were calculated.

Results: A total of 81 women randomized to the 2 treatment groups had similar symptoms at baseline. The global response assessment response rate was 26% in the global therapeutic massage group and 59% in the myofascial physical therapy group (p = 0.0012). Pain, urgency and frequency ratings, and O’Leary-Sant IC Symptom and Problem Index decreased in both groups during followup, and were not significantly different between the groups. Pain was the most common adverse event, occurring at similar rates in both groups. No serious adverse events were reported.
Conclusions: A significantly higher proportion of women with interstitial cystitis/painful bladder syndrome responded to treatment with myofascial physical therapy than to global therapeutic massage. Myofascial physical therapy may be a beneficial therapy in women with this syndrome.

Key Words: pelvic pain; cystitis, interstitial; physical therapy modalities

The treatment of IC/PBS remains suboptimal and its clinical course can be highly variable. However, most patients display tension and tenderness of the pelvic floor musculature and other somatic tissues. Frequently found abnormalities include muscular tenderness and connective tissue restrictions of muscle, fascia and subcutaneous tissues of the pelvic floor, hip girdle and abdominal wall. These somatic abnormalities may contribute to the pain of IC/PBS. There is suggestive evidence that treatment of these tissue abnormalities using myofascial physical therapy techniques can significantly relieve the symptoms of IC/PBS.

We previously reported the findings of a multicenter, randomized feasibility study comparing specialized pelvic floor myofascial physical therapy to treatment with nonspecific global therapeutic massage for the relief of symptoms in patients with IC/PBS or chronic prostatitis/chronic pelvic pain syndrome. In that study the benefit of MPT compared to GTM was most marked in patients with IC/PBS or chronic prostatitis/chronic pelvic pain syndrome. In that study the benefit of MPT compared to GTM was most marked in patients with IC/PBS or chronic prostatitis/chronic pelvic pain syndrome. In that study the benefit of MPT compared to GTM was most marked in patients with IC/PBS or chronic prostatitis/chronic pelvic pain syndrome.

METHODS

We conducted a single-blind, randomized clinical trial comparing pelvic floor MPT to GTM. The design and methods of this randomized trial are identical to those described previously for our feasibility study, with the exception that in this study the recruitment was limited to women.

Female patients were eligible for study inclusion if they had a clinical diagnosis of IC/PBS, and recorded ratings for bladder pain, frequency and urgency each at a usual level of at least 3 on a 0 to 10 scale, present for at least 3 months but not for longer than 3 years. Baseline symptom ratings were recorded twice, 2 weeks apart, and the average rating of symptom severity was used to determine study eligibility. An additional eligibility requirement was the finding of pelvic floor tenderness during vaginal examination by the study physician and confirmed by the study physical therapist.

Women were excluded from study if they had not previously undergone at least 1 course of a standard therapy for IC/PBS or if they had previously received treatment with pelvic floor MPT. Those who met the eligibility criteria at baseline screening were randomized equally to MPT or to GTM. The goal of randomizing 88 subjects (44 per treatment arm) at 11 clinical centers, with 4 to 5 participants at each center, was chosen to provide 80% power to detect a difference of 30% in the response rates, assuming a rate for GTM of 10% as shown in our pilot study. Those randomized to MPT received targeted internal and external tissue manipulation, focusing on the muscles and connective tissues of the pelvic floor, hip girdle and abdomen. The MPT methodology has been described in detail previously. The GTM treatment followed a traditional full body Western massage program. Physical therapists from each site were centrally trained and certified in the performance of both interventions to standardize treatment. Subjects received up to 10, 60-minute treatment sessions during a 12-week period. Subjects were not informed whether the treatment they were receiving was MPT or GTM. No other changes in urological care occurred during the course of the study.

Physician examiners and research nurses collecting outcome data were masked to treatment assignment. Outcomes related to symptom improvement were assessed at 12 weeks (at the completion of the treatment phase) and were planned again 3 months later during a followup
RESULTS

We recruited at a rate that was slower than expected, and with limited funding we closed the study before reaching the recruitment goal of 88 patients. A total of 81 patients were recruited between July 2008 and May 2009. The majority were white with a median age of 43 years (range 18 to 77). There were no statistically significant differences between the treatment groups in terms of demographic characteristics.

The 2 baseline symptom severity scores were averaged to provide an overall baseline score. Although the entry criteria only required a score of 3 or more on the 0 to 10 point severity scales for pain and frequency, 46% of subjects presented with severe pain (rating greater than 7) and 56% with severe frequency (rating greater than 7). Of the subjects 74% self-reported at least 11 voids daily at both baseline visits. There were also no statistically significant differences in baseline symptoms between the groups.

Of the 81 randomized patients 78 (96%) completed the 12 weeks of study. Three patients withdrew from the study during the first 12 weeks, including 2 (5%) in the GTM group and 1 (3%) in the MPT group (see figure). Of the withdrawals 2 had the primary reason for withdrawal as personal constraints, and 1 as dissatisfaction with treatment. Among the 78 subjects who completed the study 72 (92%) received at least 7 of the 10 assigned treatments. Of the subjects 21 (55%) in the MPT group and 15 (38%) in the GTM group completed all 10 assigned treatments in the 12-week study period. All subjects who withdrew from the study received fewer than 5 assigned treatments.

Overall 59% in the MPT group and 26% in the GTM group reported moderate or marked improvement (p = 0.0012), and were classified as responders (table 1). Interestingly 43% in the GTM group reported no improvement while the corresponding rate was only 18% in the MPT group.

Both treatment groups demonstrated improvement in the secondary outcomes of pain, urgency, frequency and quality of life (table 2). While improvements tended to be greater in the MPT group, the differences were modest and none were statistically significantly different.

Overall 62% (50 of 81) of participants reported at least 1 adverse event, classified as mild in 12% (10 of 81), moderate in 35% (28 of 81) or severe in 15% (12 of 81). The adverse event rate was 60% for GTM (25 of 42) vs 64% for MPT (25 of 39), with no statistically significant difference between the treatment arms (exact ordered categorical test p = 0.73). The most
common adverse event in both treatment groups was pain, primarily in the bladder or pelvis, which was reported by 14% of the participants. Pain was also the most common adverse event rated in the severe category. These reports most likely represent not only symptoms related to treatment but also the variable nature of the disorder. Less common adverse events were infection (12%), constitutional symptoms (11%) and gastrointestinal disturbances (10%). All other adverse events were infrequent and no serious adverse events were reported.

Unfortunately there was considerable loss to followup during the 3-month period after the initial 12 weeks of treatment. After the followup phase of the study (during the 3 months after the initial 12 weeks of treatment) we had partial followup information on just 30 (77%) of the 39 patients assigned to MPT and on 28 (67%) of the 42 assigned to GTM. Of the 30 patients initially treated with MPT 4 (13%) had elected to continue MPT during the 3-month followup. Of the 28 patients initially treated with GTM 8 (29%) had elected to receive MPT during the 3-month followup. At the end of the followup phase the final outcome of interest (GRA) was completed by just 11 of 42 (26%) in the GTM group and 23 of 39 (59%) in the MPT group. Therefore, we are unable to draw any conclusions about the durability of treatment outcomes in either group.

### DISCUSSION

This study supports the concept of pelvic floor MPT for the treatment of IC/PBS, with nearly 60% of women experiencing moderate or marked improvement in overall symptoms compared to only a 26% response rate in the active control group. While there were no statistically significant differences in symptom subscales of pain and quality of life, change from baseline to week 12 in symptom severity and frequency favored MPT over GTM. These results support the findings from our pilot study, and the results of other case series describing the results of manual therapies for the relief of urological pelvic pain conditions. We believe these results justify the clinical use of MPT in the treatment of IC/PBS and other pelvic pain conditions.

The etiology of the somatic abnormalities in patients with urological pain syndromes is not known. It is possible that the somatic abnormalities found in the lumbosacral dermatomyotomes in patients with IC/PBS are secondary, i.e., referred from a primary pelvic visceral abnormality. It is equally possible that these somatic abnormalities are a primary phenomenon and may themselves give rise to secondary visceral hypersensitivity. The latter possibility is supported by recent animal studies demonstrating induction of visceral (bladder) hypersensitivity by experimental injury to a somatic (sciatic) nerve that shares innervation with the viscus.

### Table 1. Primary outcome: GRA after 12-week treatment phase

<table>
<thead>
<tr>
<th></th>
<th>GTM (42)</th>
<th>MPT (39)</th>
<th>Totals</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. subjects randomized</td>
<td>42</td>
<td>39</td>
<td>81</td>
</tr>
<tr>
<td>No. response based on GRA at 12 wks (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Responders</td>
<td>11 (26.2)</td>
<td>23 (59.0)</td>
<td>34 (42.0)</td>
</tr>
<tr>
<td>Nonresponders</td>
<td>31 (73.8)</td>
<td>16 (41.0)</td>
<td>47 (58.0)</td>
</tr>
<tr>
<td>No. GRA:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Markedly improved</td>
<td>5</td>
<td>10</td>
<td>15</td>
</tr>
<tr>
<td>Moderately improved</td>
<td>6</td>
<td>13</td>
<td>19</td>
</tr>
<tr>
<td>Slightly improved</td>
<td>13</td>
<td>9</td>
<td>22</td>
</tr>
<tr>
<td>No change</td>
<td>14</td>
<td>5</td>
<td>19</td>
</tr>
<tr>
<td>Slightly worsened</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Moderately worsened</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Markedly worsened</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Missing or withdrawn</td>
<td>3</td>
<td>1</td>
<td>4</td>
</tr>
</tbody>
</table>

### Table 2. Secondary outcomes

<table>
<thead>
<tr>
<th></th>
<th>Mean ± SD Baseline</th>
<th>Mean ± SD Week 12</th>
<th>Mean ± SD Change From Baseline to Week 12</th>
<th>Difference in Change (p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain (0–10 Likert scale)</td>
<td>5.6 ± 1.7</td>
<td>6.1 ± 1.7</td>
<td>−1.5 ± 2.1</td>
<td>−2.2 ± 2.2 (0.27)</td>
</tr>
<tr>
<td>Urgency (0–10 Likert scale)</td>
<td>6.0 ± 1.7</td>
<td>6.1 ± 1.7</td>
<td>−1.4 ± 2.6</td>
<td>−2.1 ± 2.6 (0.16)</td>
</tr>
<tr>
<td>Frequency (0–10 Likert scale)</td>
<td>6.2 ± 1.7</td>
<td>6.5 ± 1.8</td>
<td>−1.3 ± 2.1</td>
<td>−2.2 ± 2.3 (0.17)</td>
</tr>
<tr>
<td>24-Hr frequency (urinary diary)</td>
<td>12.4 ± 4.8</td>
<td>13.6 ± 6.3</td>
<td>−1.3 ± 3.6</td>
<td>−2.0 ± 3.7 (0.49)</td>
</tr>
<tr>
<td>ICSI (max range 0–20)</td>
<td>11.4 ± 3.5</td>
<td>11.9 ± 3.4</td>
<td>−2.2 ± 3.2</td>
<td>−3.2 ± 3.7 (0.31)</td>
</tr>
<tr>
<td>ICP (max range 0–16)</td>
<td>10.7 ± 3.0</td>
<td>10.5 ± 2.8</td>
<td>−2.4 ± 2.6</td>
<td>−3.6 ± 3.6 (0.09)</td>
</tr>
<tr>
<td>SF-12 physical component summary (max range 0–100)*</td>
<td>45.4 ± 10.0</td>
<td>41.5 ± 10.0</td>
<td>0.3 ± 6.9</td>
<td>4.1 ± 9.2 (0.08)</td>
</tr>
<tr>
<td>SF-12 mental component summary (max range 0–100)*</td>
<td>45.8 ± 8.8</td>
<td>40.1 ± 8.9</td>
<td>4.9 ± 8.5</td>
<td>45.0 ± 10.8 (0.86)</td>
</tr>
<tr>
<td>FSP (range)*</td>
<td>20.7 ± 7.9</td>
<td>18.7 ± 8.2</td>
<td>2.2 ± 8.7</td>
<td>20.5 ± 8.5 (0.67)</td>
</tr>
<tr>
<td>FSQ (max range 0–43)*</td>
<td>28.1 ± 6.9</td>
<td>29.8 ± 6.0</td>
<td>−5.9 ± 7.9</td>
<td>−8.9 ± 9.1 (0.22)</td>
</tr>
</tbody>
</table>

* For these measures higher values represent better functioning and thus, positive changes from baseline represent improvement.
Clinically the somatic abnormalities associated with IC/PBS are obvious and have been recognized for some time.\textsuperscript{1–8} It is appropriate that the role of the short, painful and/or hypertonic pelvic floor in the development of chronic genitourinary conditions has now begun to inform physiotherapeutic interventions aimed at rehabilitation.\textsuperscript{15} Whether the somatic abnormalities are primary or secondary, our studies suggest that it is clinically valuable to address and relieve them, as demonstrated here using specialized MPT.

The strengths of our study include its prospective, multicenter, randomized design with a standardized protocol for pelvic floor MPT and a positive control. Limitations include the fact that only 81 of the expected 88 women were enrolled in the study due to slow recruitment and loss of funding to complete the study. However, the study was still adequately powered to identify significant differences in the primary outcome of the study. The enrolled subjects also represent a select population drawn from academic medical centers, and recruitment was limited to subjects with pelvic floor tenderness on examination and duration of symptoms of less than 3 years. In addition, all subjects were treated by highly trained, experienced physical therapists, and we had a large number of patients ineligible to participate. Therefore, the results may not be generalizable to the IC/PBS population at large, and we do not know whether MPT would benefit patients who have IC/PBS symptoms but no pelvic floor tenderness. Nevertheless, the findings encourage further investigation of MPT as a treatment modality for IC/PBS, and suggest that it could become a highly acceptable and clinically meaningful first line therapy.

An important area for further study is the durability of the responses to this therapy. Although the original design of this study including followup beyond the 12-week active treatment period, there was considerable loss to followup during the following 3 months. Therefore, we were unable to draw any conclusions about the durability of treatment outcomes in either group. Some other important areas for further study include the determination of the elements of an optimal MPT regimen, the duration of treatment necessary for durable response, a clinical algorithm for the identification of patients most likely to respond to treatment and finally, the development and refinement of an optimal training program to expand the population of physical therapists who can deliver effective pelvic floor MPT.

**APPENDIX**

**Interstitial Cystitis Collaborative Research Network Membership**

In addition to the authors, the Interstitial Cystitis Collaborative Research Network Study Group includes the following institutions and individuals. The number of subjects randomized at each center is given in parentheses.

**University of Washington** – Jane Miller, Charles H. Muller, Jean Kalhoff, James Bassuk, Sharon Downing, Robert F. Bale, Jr. (9)

**Stanford University** – Rajesh Shinghal, Rodney Anderson, Debra Clay, Anna Ramakrishnan (8)

**University of California, San Diego** – James Porter, Solomon Hargraves, Martin Rubenstein, Mary O’Dwyer (8)

**William Beaumont Hospital** – Eleanor Anton, Cheryl Wolfert, Loni Lampkins (8)

**University of Maryland** – Susan Kean, Rosanna Dinh, Rupali Sangramapurkar (8)

**Queen’s University** – Alvaro Morales, Laurel Emerson, Lesley Carr, Joseph Downey, Janet Clark-Pereira, Sylvia Robb (8)

**Loyola University Medical Center** – Linda Bruhaker, Janet Rindels, Grace Bucher (7)

**University of Pennsylvania Health System** – Diane K. Newman, Sylvia Salazar, Jennifer Milado, Louis Moy (7)

**University of Iowa** – Michael O’Donnell, Susan Lutgendorf, Mary Eno, Kelly O’Barry (6)

**Henry Ford Hospital** – Kandis Rivers, Samina Romero, Michelle Peabody (6)

**University of Rochester** – Edward Messing, Elizabeth Betty Smith, Kay Rust, Jay Reeder (6)

**University of Pennsylvania School of Medicine (Data Coordinating Center)** – Keith Mickelberg, Ted Barrell, Shannon Chuai

**The National Institute of Diabetes and Digestive and Kidney Diseases** – Christopher Mullins, Mary Harris

**Interstitial Cystitis Association** – Vickie Ratner

**REFERENCES**


