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Pilot randomized controlled trial of a hypnosis intervention for women with bladder pain syndrome

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Abstract

Aims: To evaluate the feasibility and acceptability of a randomized controlled trial of a hypnosis intervention for the treatment of bladder pain syndrome/interstitial cystitis (BPS/IC) in women.

Methods: We conducted a parallel arm, non-blinded, pilot randomized controlled trial of standardized hypnosis sessions including a hypnosis web tool versus usual care in adult women with BPS/IC. Pilot study outcomes included feasibility domains: process, resources and management, safety, and acceptability. Clinical outcomes of lower urinary tract symptoms and quality of life were measured using validated questionnaires at baseline and at the end of the 4-week intervention.

Results: We randomized 29 out of 30 (96.7%) eligible women. In the hypnosis group, 12 of 15 (80.0%) subjects completed the 4-week intervention and follow up, and 13 of 14 (92.9%) in the usual care group. In the hypnosis group, adherence to the standardized sessions was 80% and participants used the web-based tool for an average of 5.6 ± 2.7 times per week. Scores for emotional distress, relaxation, pain severity and expected bladder symptoms significantly improved during the first two of three planned hypnosis sessions (all $p < 0.05$). Improvement in quality of life scores was greater in the hypnosis group than the usual care group (-2.6 ± 2.3 vs. -0.9 ± 1.1, $p = 0.04$). There were no significant between-group differences in urinary symptoms or bladder pain. No adverse events were reported.

Conclusions: A hypnosis intervention for the treatment of bladder pain syndrome/interstitial cystitis is feasible, acceptable, safe, and may improve quality of life.

KEYWORDS
bladder pain syndrome, hypnosis, interstitial cystitis, mind-body therapy

Julie B. Schnur, Heidi S. Harvie, Guy H. Montgomery, and Lily A. Arya are contributed equally to this work.

1 | INTRODUCTION

Bladder pain syndrome/interstitial cystitis (BPS/IC) is a complex multidimensional condition that affects eight million women in the United States.[1] Chronic pelvic pain and urinary symptoms in BPS/IC are frequently associated with affective symptoms such as anxiety and depression.[2] Though BPS/IC has an immense impact on quality of life,[3] effective treatment options are lacking.

Central augmentation of pain processing is a key element of BPS/IC pain. Animal and human studies suggest that the chronic pain of BPS/IC is the result of how afferent signals from the bladder are processed in the brain rather than solely a result of somatosensory input from the bladder.[4–6] Therefore, therapies that focus on the central processing of pain rather than bladder-targeted treatments may improve BPS/IC symptoms.

Hypnosis is defined as an agreement between a hypnotist and patient, to participate in a psychotherapeutic technique based on the hypnotist providing suggestions for changes in sensation, perception, cognition, affect, mood, or behavior.[7] Hypnosis can reduce pain by changing how patients think and feel, and may also modify brain processes underlying the pain experience.[7,8] Prior studies have demonstrated the efficacy of hypnotic analgesia for acute postoperative pain, chronic low back pain, chronic prostatitis/pelvic pain in men, and chronic pain associated with neurologic conditions.[9–12] Hypnosis interventions are brief, easy to teach patients, have no specific side effects of their own, and have been shown to be cost-effective.[10,11] Thus, hypnosis may be useful for the management of BPS/IC.

We conducted a pilot randomized controlled trial to evaluate the feasibility and acceptability of hypnotic analgesia for the treatment of BPS/IC in women.

2 | METHODS AND MATERIALS

2.1 | Design

We conducted a two-arm, non-blinded, randomized controlled pilot trial of a 4-week hypnosis intervention versus usual care in women with BPS/IC between October 2019 to October 2020 (clinicaltrials.gov ID: NCT04010513). Institutional Review Board (IRB) approval, including changes imposed due to COVID-19 research restrictions, were obtained from the University of Pennsylvania.

2.2 | Participants and recruitment

Adult women from the Urogynecology and Urology clinics of the University Pennsylvania were recruited. Included participants were at least 18 years old with a diagnosis of BPS/IC based on AUA criteria and score of ≥8 on the Interstitial Cystitis Symptom Index and Problem Index.[13,14] Additional inclusion criteria were: negative urine culture within 1 month of enrollment, no changes in BPS/IC treatments within 4 weeks before enrollment, and fluent in English. We excluded women who were treatment naïve, women who had received fourth line or higher therapy based on the AUA treatment algorithm,[13] women currently undergoing physical therapy for pelvic pain, current pregnancy or lactation, unevaluated hematuria, urinary retention, prior cystectomy, urinary diversion or augmentation cystoplasty, known bladder calculus, a primary diagnosis of another chronic pain condition, and severe psychiatric or cognitive impairments that prevented participation in hypnosis.

All participants completed validated questionnaires in an electronic database at baseline and at the end of the 4-week study. In addition, subjects in the hypnosis group completed a Visual Analogue Scale (VAS) regarding symptoms immediately before and after each hypnosis session. Subjects completed the questionnaires on a tablet during in-person visits and remotely through a web-based application following COVID-19 restrictions.

2.3 | Interventions

The hypnosis intervention included: (1) three standardized 18-min one-on-one hypnosis sessions with a trained hypnotist over 4 weeks and (2) a web tool for daily home self-hypnosis practice. Sessions were initially in-person in the Urogynecology practice. Following COVID-19 restrictions from May 2020 to the end of the study, the one-on-one hypnosis sessions were conducted on a virtual video conference platform. The content (described below) and timing of the sessions were identical for the in-person and virtual sessions. The first and second sessions were 1 week apart while the second and third session were 2 weeks apart. At the end of the first session, each participant received instructions on how to practice self-directed hypnosis by playing a 16-min hypnosis recording on a study web app. Participants were instructed to listen to the hypnosis recording at least twice weekly. All participants were allowed to continue their usual BPS/IC medications.

A standardized script was used for each hypnosis session. The first session included a *debunking* script that outlined and defined hypnosis, explained what to expect with hypnosis, and dispelled common misconceptions regarding hypnosis. A standardized script was used for

hypnotic induction, deepening, suggestions, post-hypnotic suggestions, and awakening.[15] The script included relaxing imagery followed by suggestions for reduced bladder symptoms, pain and distress. Each session concluded with a reminder to use the self-directed hypnosis web tool.

A visual analog scale (VAS) from 0 (low) to 100 (high) was administered before and after each hypnosis session to measure acceptability of the intervention (see below).

The usual care group was instructed to continue routine appointments and treatments with the provider managing their BPS/IC symptoms. At the completion of the study, participants in the usual care group were offered access to the web tool.

2.4 | Feasibility outcomes

We measured feasibility and acceptability consistent with published guidelines for pilot studies.[16] Our primary outcome was randomization rate. Our secondary outcomes were study completion rate, acceptability of hypnosis, and change in symptoms on validated questionnaires. To assess *process*, we monitored recruitment, eligibility, and retention rates in the trial. To assess *resources and management*, we evaluated the impact of transition from in-person to virtual conference visits.

2.5 | Acceptability and efficacy of hypnotic analgesia

To assess acceptability of hypnosis, we measured five symptoms: current emotional distress, current relaxation, current pain severity, expected pain severity, and expected bladder symptoms using VAS questions (0–100) immediately before and after each hypnosis session. Our hypothesis was that women who found the hypnosis intervention acceptable would report less emotional distress and greater relaxation following the hypnosis session. Change in current pain severity, expected pain severity, and expected bladder symptoms served as a short-term measure of the efficacy of hypnotic analgesia.

We also evaluated weekly use of the hypnosis web recording throughout the 4-week study. The web tool allows measurement of the number of times the recording is used by all participants per week, however per participant data was not available. We calculated average utilization of the web tool per week by dividing the total utilization per week by the total number of participants for that week. We defined successful web tool utilization a priori as minimum of two uses per participant per week.

2.6 | Clinical outcomes

Data on adverse events was collected at each hypnosis session and at end of study visit. Response to treatment was measured using the Global Response Assessment. Participants reporting that they were at least "moderately improved" were classified as responders. Non-responders included participants who reported slight improvement, no change in symptoms, worsened symptoms or withdrew before end of study. Our secondary outcome were change in the following validated symptom questionnaires from baseline to after the four week treatment intervention.

The Female Genitourinary Syndrome Index (F-GUPI), is a nine-item validated questionnaire developed to assess bladder-specific pain. Total score ranges from 0 to 45 with subscales of pain (0–23), urinary symptoms (0–10), and quality of life (0–12).[17] The Interstitial Cystitis Symptom Index (ICSI) and the Interstitial Cystitis Pain Index (ICPI) are validated indices that measure severity and impact of urinary urgency, frequency, nocturia and bladder pain. Total score for the ICSI ranges from 0 to 20 and for the ICPI from 0 to 16 with higher scores indicating worse symptoms and greater negative impact on quality of life.[14]

Prior studies report that pain and urinary symptoms should be reported separately in women with BPS/IC.[18] We therefore also calculated a composite pain severity score and a composite urinary severity score as previously validated by Stephens-Shields et al.[19] The composite pain severity score (0–28) is the sum of the F-GUPI pain subscore and item 4 of the ICSI. The composite urinary severity score (0–25) is the sum of the F-GUPI urinary subscore and items 1–3 of the ICSI.

2.7 | Changes implemented due to COVID-19 restrictions

Following COVID-19 restrictions, participants were recruited and enrolled via telemedicine and the hypnosis intervention was administered via video visits. Participants completed validated questionnaires in the electronic database remotely.

2.8 | Statistical analysis

Statistical analysis was performed using Stata v15.1 (Stata Corp.). Demographic data were compared using Mann–Whitney U test for continuous variables and χ^2 with Fisher exact test for categorical variables. Acceptability (change in VAS for emotional distress and

relaxation) and efficacy of hypnotic analgesia (change in VAS for pain and urinary symptoms) before and after each hypnosis session were analyzed using paired t test. Proportion of responders was compared between groups using χ^2 test. Symptom scores on validated questionnaire were compared between groups using the two-sample t test with Satterwaite's correction for unequal variance. We evaluated the effect of changes in study design imposed by COVID-19 pandemic by comparing acceptability and efficacy measures between in-person and virtual hypnosis sessions using Mann–Whitney U test. A $p = 0.05$ was used as threshold for statistical significance.

3 | RESULTS

Of the 30 eligible participants, 29 women underwent randomization yielding a randomization rate of 96.7% (Figure 1). Study completion rates were 80% (12/15) for the hypnosis group and 93% (13/14) for the usual care group. Lost to follow up rates were 20% ($n = 3$) and 7% ($n = 1$) for the hypnosis and usual care groups, respectively.

Baseline characteristics of the two groups are described in Table 1. There were no significant differences in age, race, body mass index, and duration since BPS/IC diagnosis for the two groups. Duration of BPS/IC symptoms was significantly shorter for hypnosis group ($p < 0.05$). Women in the hypnosis group had a higher rate of cesarean delivery ($p = 0.02$). Four participants in the usual care group practiced mindfulness/meditation compared to none in the hypnosis group.

3.1 | Feasibility outcomes

3.1.1 | Process

In the hypnosis group, six women (40%) received all hypnosis sessions via in-person visits. Following COVID-19 restrictions, eight women (53%) received all hypnosis sessions via virtual video visits with one subject receiving a combination of virtual and in-person hypnosis visits. Of a total of 42 hypnosis sessions administered, 18 (43%) were administered in-person while 24 (57%) were administered virtually.

3.1.2 | Resource and management

There were no reported difficulties in scheduling in-person or virtual conference visits. There were no missed

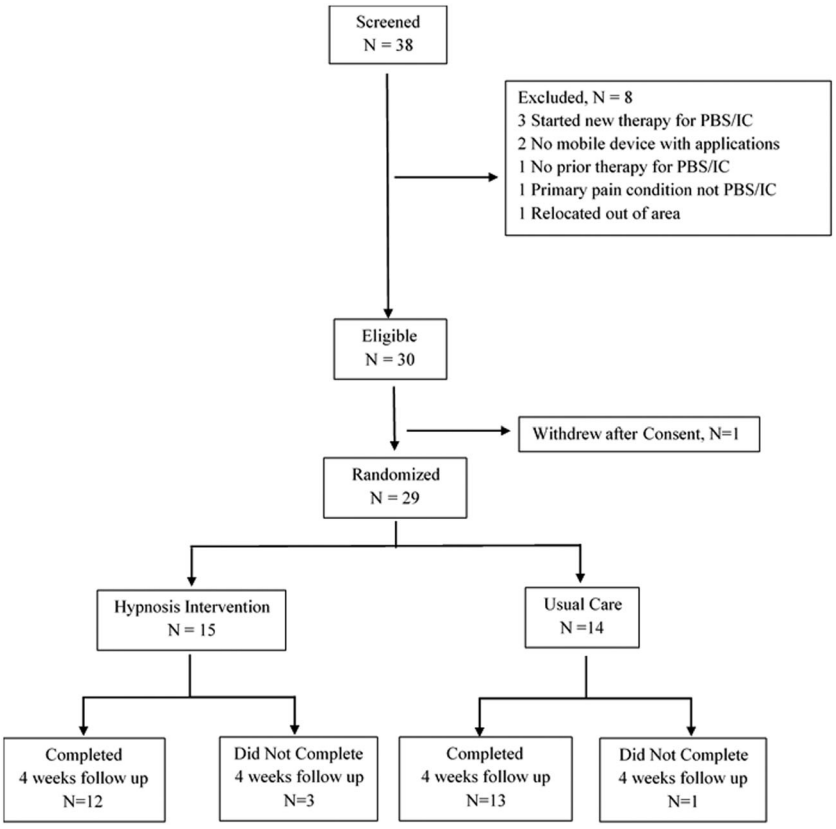

FIGURE 1 Study participant flow chart

TABLE 1 Baseline characteristics

	Hypnosis group ($N = 15$)	Usual care group ($N = 14$)	p value
Age, years (SD)	40.1 (17.0)	44.9 (20.0)	0.50[a]
Race (N, %)			0.53[b]
Caucasian	13 (86.7)	10 (71.4)	
African American	2 (13.3)	2 (14.3)	
Hispanic/Latino	0 (0.0)	1 (7.1)	
Asian American	0 (0.0)	1 (7.1)	
BMI, kg/m^2 (SD)	25.1 (6.1)	27.3 (6.0)	0.41[a]
Education level (N, %)			0.74[b]
Some High School	1 (6.7)	0 (0.0)	
High School Diploma	2 (13.3)	2 (14.3)	
Some College	8 (53.3)	6 (42.9)	
College Degree	4 (26.7)	5 (35.7)	
Graduate Degree	0 (0.0)	0 (0.0)	
Time since IC diagnosis in years (range)	4.4 (1–14)	9.1 (1–34)	0.19[a]
Time with IC symptoms in years (range)	5.9 (1–17)	13.8 (1–37)	**0.04**[a]
Number of prior surgeries (median, range)	2 (0–4)	2 (0–4)	0.55[c]
Cesarean deliveries (median, range)	0 (0–3)	0 (0–0)	**0.02**[c]
Hysterectomy (N, %)	2 (13.3)	3 (21.4)	0.64[d]
Medical conditions (N, %)			
Myofascial pelvic pain/pelvic floor dysfunction	8 (53.3)	5 (35.7)	0.43[b]
Endometriosis	1 (6.7)	3 (21.4)	0.31[d]
Vulvodynia	3 (20.0)	3 (21.4)	0.99[d]
Irritable bowel disease	7 (46.7)	4 (28.6)	0.46[d]
Chronic back pain	2 (13.3)	6 (42.9)	0.10[d]
Migraine headaches	3 (20.0)	4 (28.6)	0.67[d]
Fibromyalgia	2 (13.3)	0 (0.0)	0.48[d]
Anxiety disorder	6 (40.0)	4 (28.6)	0.71[d]
Depression	4 (26.7)	4 (28.6)	0.99[d]
Current treatments for BPS/IC (median, range)	1 (0–4)	1 (0–3)	0.92[c]
Dietary modifications (N, %)	1 (6.7)	3 (21.4)	0.31[d]
Pelvic floor physical therapy (N, %)	2 (13.3)	0 (0.0)	0.48[d]
Phenazopyridine (N, %)	3 (20.0)	1 (7.1)	0.60[d]
Pentosan polysulphate (N, %)	0 (0.0)	2 (14.3)	0.21[d]
Tricyclic antidepressants (N, %)	5 (33.3)	2 (14.3)	0.40[d]
Bladder instillations (N, %)	0 (0.0)	1 (7.1)	0.46[d]
Number of prior treatments for BPS/IC (median, range)	2 (1–5)	2 (1–2)	0.57[c]

(Continues)

TABLE 1 (Continued)

	Hypnosis group ($N = 15$)	Usual care group ($N = 14$)	p value
Prescription opioids (N, %)	4 (26.7)	3 (21.4)	0.68[d]
Marijuana use (N, %)	4 (26.7)	2 (14.3)	0.41[d]

Note: The bold values indicate the significance of $P < 0.05$.

Abbreviations: BMI, body mass index; BPS/IC, bladder pain syndrome/interstitial cystitis.

[a]t test.

[b]χ^2 test.

[c]Wilcoxon rank sum.

[d]Fisher-exact test.

sessions due to technology issues or participant inability to access virtual video conferences. One trained hypnosis interventionist provided all of the hypnosis sessions.

3.1.3 | Adverse events

No adverse events were reported in the hypnosis or usual care groups during the study.

3.1.4 | Acceptability and short-term efficacy of hypnotic analgesia

Women in the hypnosis group reported an increase in relaxation and a decrease in emotional distress on VAS items following each hypnosis session indicating the acceptability of intervention (Table 2). VAS questions on current and expected pain severity levels and expected urinary symptoms also improved after each hypnosis session indicating short-term efficacy of hypnotic analgesia. Changes were statistically significant following the first and second hypnosis session but not after the third session, possibly because baseline symptom scores had already improved by the beginning of the third session. Despite this trend, pre-hypnosis scores were not significantly different from the beginning of session 1 to session 3.

3.1.5 | Adherence to hypnosis

In the hypnosis group, 12 (80%) participants completed all three structured hypnosis sessions. Utilization of the hypnosis web tool was high with participants accessing the web app 5.6 (±2.7) times per week on average. Adequate utilization of the web application (defined a priori as 2 or more uses per participant per week) was achieved in 96.9% (29/30) of the weeks during the study. There was no difference in adherence rates for in-person versus video sessions with 18 of 19 (94.7%) in-person sessions completed and 24 of 26 (92.3%) video sessions completed ($p = 0.75$).

3.1.6 | Effect of changes due to COVID-19

There was no difference in mean change in emotional distress, degree of relaxation, pain severity or expected bladder symptoms between in-person or virtual video conference visits for the hypnosis sessions (Table 3) ($p > 0.18$). There was no difference in adherence rates for in-person versus video sessions (see above).

3.1.7 | Clinical outcomes

Based on Global Response Assessment, 26.7% (4/15) subjects in the hypnosis group and 7% (1/14) women in the usual care group were classified as responders ($p = 0.16$). An additional 6 subjects (40%) in the hypnosis group and 1 subject (7%) in the usual care group reported "slight" improvement. The proportion of participants who reported "no change" was higher in the usual care group than the hypnosis group (71% vs. 13%, $p < 0.01$). Worsening of symptoms during the study period was reported by one participant in the usual care group and none in the hypnosis group.

On validated symptom questionnaires, women in the hypnosis group reported significant improvement in quality of life (Table 4) ($p < 0.05$). Improvement in pain and urinary symptom scores was greater for the hypnosis group than the usual care group however, these changes were not statistically significant.

4 | DISCUSSION

The study demonstrated that it is feasible to implement a hypnosis intervention that combines standardized hypnosis sessions with a patient-directed hypnosis web tool

TABLE 2 Acceptability of hypnosis intervention based on visual analog scales (0–100) of current and expected symptoms

Clinical symptoms	Hypnosis session 1 ($N = 15$)			Hypnosis session 2 ($N = 15$)			Hypnosis session 3 ($N = 12$)		
	Pre-hypnosis[a]	Post-hypnosis[a]	p value[b]	Pre-hypnosis[a]	Post-hypnosis[a]	p value[b]	Pre-hypnosis[a]	Post-hypnosis[a]	p value[b]
Current emotional distress, mean (SD)	35.1 (25.2)	19.5 (23.8)	**0.003**	37.4 (23.2)	23.0 (14.6)	**0.04**	32.0 (31.0)	16.9 (17.6)	0.13
Current relaxation[c], mean (SD)c	36.4 (21.2)	67.9 (23.2)	**0.01**	36.5 (18.2)	61.5 (23.4)	**0.02**	48.4 (26.3)	73.1 (19.5)	**0.04**
Current pain severity, mean (SD)	38.1 (24.3)	23.4 (19.6)	**0.01**	33.0 (22.2)	17.6 (18.8)	**0.01**	28.9 (10.1)	22.9 (24.3)	0.09
Expected pain severity, mean (SD)	38.3 (29.0)	31.6 (23.0)	0.21	37.6 (21.4)	30.8 (22.4)	0.11	27.6 (23.1)	22.6 (19.2)	0.08
Expected bladder symptoms, mean (SD)	45.9 (21.4)	33.3 (22.5)	**0.002**	46.5 (17.6)	37.6 (21.6)	**0.03**	34.9 (19.7)	27.0 (15.4)	0.18

Note: Current symptoms were defined as symptom severity at the time the questionnaire was administered expected symptoms were defined as symptom severity expected 1 week following hypnosis session. The bold values indicate the significance of $P < 0.05$.

Abbreviation: SD, standard deviation.

[a]Visual analog scales were completed by participants immediately before and after all three hypnosis sessions.

[b]Paired t test.

[c]Higher relaxation score reflects a greater degree of relaxation.

for the treatment of BPS/IC in women. We also demonstrated that it is feasible to conduct a randomized clinical trial of hypnosis versus usual care in women with BPS/IC. Interest in the hypnosis intervention was high with randomization rate of 96.7% and dropout rates were low. Acceptability of the hypnosis intervention, as measured by objective improvement in emotional distress and relaxation with each session, was also high. Adherence to hypnosis was high with 80% of women in the hypnosis arm completing all three sessions. Utilization of the patient-directed hypnosis web tool was an average of five times per week and exceeded the recommended minimum of two times per week. Finally, though overall response rates were not significantly different between groups, quality of life improved significantly in the hypnosis group and improvement in pain and urinary symptoms also modestly favored the hypnosis group. Taken together, these findings suggest that hypnosis may be a useful adjunctive treatment for the management of BPS/IC symptoms.

Mind-body interventions are gaining increasing attention as useful techniques that promote self-management of chronic pain and have few adverse effects. In a prior study of 11 BPS/IC participants, Kanter et al. reported that women who participated in a mindfulness-based stress reduction intervention reported feeling empowered to control symptoms.[20] Unlike mindfulness, during which patients are taught to focus one's concentration and awareness on the present moment,[21] hypnosis often involves escaping the present moment. Hypnotic participants are asked to focus on, and become absorbed in, imaginal scenes (e.g., a day at the beach) which are often separate and distant from "the present moment." Furthermore, hypnotic goal-directed suggestions are made to help change patients' thoughts, feelings, sensations, and/or behaviors to improve quality of life. That is, hypnosis more directly targets reducing, eliminating, or helping patients overcome what is bothering them. In our study, during hypnosis, patients were given specific suggestions for reduced pain and urinary symptoms, which in turn may directly lead to reduction in the patients' experience of pain, consistent with prior research.[22] An additional advantage of hypnosis is that each hypnosis session is brief, in this case lasting only 18 min. The efficacy of the hypnosis intervention was noted by significant improvement in VAS measurements of emotional distress, relaxation, current pain, and expected pain and urinary symptoms immediately after each hypnosis session. In this preliminary study, we did not assess participants' levels of hypnotic suggestibility (hypnotizability) as such an assessment would add significantly to patient burden ("gold standard" measures of hypnotizability often take

TABLE 3 Comparison of in-person versus virtual hypnosis intervention

	In-person hypnosis sessions ($N = 18$)	Virtual hypnosis sessions[a] ($N = 24$)	p value[b]
Current emotional distress, mean change (SD)	−17.1 (20.5)	−8.5 (20.6)	0.27
Current relaxation[c], mean change (SD)	34.1 (31.9)	17.8 (31.8)	0.18
Current pain severity, mean change (SD)	−14.5 (17.6)	−10.3 (16.2)	0.50
Expected pain severity, mean change (SD)	−8.7 (17.7)	−4.3 (11.2)	0.39
Expected bladder symptoms, mean change (SD)	−5.4 (11.2)	−11.2 (13.4)	0.23

Note: Current symptoms were defined as symptom severity at the time the questionnaire was administered expected symptoms were defined as symptom severity expected one week following hypnosis Mean change was the difference in visual analog scale (0–100) from before to after hypnosis intervention.

Abbreviation: SD, standard deviation.

[a]Virtual hypnosis sessions started after COVID-19 restrictions limited in-person visits and were conducted on a video conference platform.

[b]Mann–Whitney U test.

[c]Higher relaxation score reflects a greater degree of relaxation.

TABLE 4 Change in pain and urinary symptoms in hypnosis versus usual care in women with BPS/IC

	Baseline, mean (SD)		Four-week follow up, mean (SD)		Change in scores, mean (SD)		
	Hypnosis	Control	Hypnosis	Control	Hypnosis	Control	p value
Composite Pain Score	14.1 (6.6)	16.4 (4.2)	11.3 (5.2)	14.4 (5.2)	−3.5 (2.3)	−2.0 (4.4)	0.32
Composite Urinary Symptom Score	14.6 (6.3)	14.6 (4.6)	10.3 (7.6)	13.3 (6.0)	−2.1 (2.3)	−1.3 (2.9)	0.63
F-GUPI total	28.2 (7.2)	27.7 (6.0)	20.3 (7.5)	25.3 (7.5)	−6.3 (3.3)	−2.4 (6.1)	0.08
Pain Subscale	12.7 (4.1)	13.0 (3.4)	9.6 (3.9)	12.2 (4.0)	−2.5 (1.9)	−0.8 (3.7)	0.94
Urinary Subscale	6.6 (2.4)	6.8 (1.9)	4.6 (3.0)	6.2 (2.5)	−1.4 (1.8)	−0.6	0.27
Quality of Life Subscale	9.4 (2.3)	7.9 (2.8)	6.1 (2.5)	7.0 (2.9)	−2.6 (2.3)	−0.9 (1.1)	**0.04**
Interstitial Cystitis Symptom Index	11.3 (4.6)	11.2 (3.3)	8.6 (5.4)	9.4 (4.2)	−1.7 (2.8)	−1.8 (2.5)	0.91
Interstitial Cystitis Problem Index	9.8 (4.6)	10.1 (3.5)	8.3 (4.9)	8.6 (3.5)	−1.2 (2.4)	−1.5 (1.9)	0.75

Note: Satterthwaite t test. The bold value indicates the significance of $P < 0.05$.

Abbreviation: SD, standard deviation.

longer than administering the intervention itself[23,24]), previous meta-analyses indicate that the vast majority of patients can benefit from hypnosis interventions, and meta-analysis also indicates that hypnotizability accounts for a relatively small portion of the variance in clinical hypnosis outcomes.[23,25,26]

The COVID-19 pandemic unexpectedly provided us with a unique opportunity to compare in-person hypnosis to virtual video hypnosis sessions. In our study, more than half (57%) of sessions were conducted virtually as compared to 43% through in-person visits. Although patients were not randomized to these conditions, improvement in emotional distress and relaxation scores demonstrated that virtual video hypnosis sessions were as acceptable as in-person sessions. The effect of hypnotic analgesia, as measured by change in current pain, expected pain, and expected bladder symptoms, was also similar for in-person and video visits. Prior studies also suggest that women with pelvic floor disorders increasingly prefer remote telemedicine to in-person visits since they minimize barriers caused by difficulty in transportation and time way from work and family.[27] Future studies will be required to more formally determine if there are significant differences in the clinical effectiveness of in-person versus virtual hypnosis sessions for BPS/IC.

Our pilot and feasibility study was not powered to compare clinical outcomes between groups. Clinical outcomes favored the hypnosis group though most differences were not statistically significant, likely due to small sample size. The response rate, defined as at least "moderate improvement" on the Global Response Assessment was 26% for the hypnosis group and 7% for the usual care group. Conversely, a larger proportion of

women in the usual care group than the hypnosis group reported "no change" in symptoms (71% vs. 13%). Pain and urinary symptom severity scores showed greater improvement in the hypnosis than the usual care group, though differences were not statistically significant likely due to small sample size. Despite the small sample size, women in the hypnosis group reported significantly greater improvement in quality of life than the usual care group. Since patients in the hypnosis group were allowed to continue their ongoing BPS/IC treatments, our findings suggest that hypnosis may be a promising adjuvant treatment for BPS/IC. Our study also provides critical data for estimating effect sizes and subsequently calculating sample size for a larger clinical trial.

Limitations of our study include a small sample size and a short duration of follow-up. The majority of our participants were of white race and this may limit the generalizability of our findings, although our previous work did not report modification of clinical effects based on race.[7,11] Duration of BPS/IC symptoms was significantly shorter for the hypnosis group, however, there was wide variability in reported duration, possibly due to recall bias. For future large-scale clinical trials, stratification based on symptom duration could be considered. Inescapable changes in study design due to the COVID-19 pandemic may also have influenced our findings.

5 | CONCLUSIONS

A hypnosis intervention consisting of structured hypnosis sessions and a self-administered hypnosis web tool is feasible and acceptable for women with BPS/IC. Efficacy of hypnotic analgesia was similar for virtually administered and in-person hypnosis sessions. Our high recruitment and retention rate demonstrate the feasibility of conducting a large-scale randomized trial. Clinical outcomes modestly favor the hypnosis intervention suggesting that hypnosis may be a useful adjunctive treatment for the management of BPS/IC.

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CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

Study design, data collection, data analysis, manuscript preparation: Alex J. Soriano. *Study design, data analysis, manuscript preparation*: Julie B. Schnur. *Study design, data analysis, manuscript preparation*: Heidi S. Harvie. *Study design, manuscript preparation*: Diane K. Newman. *Study design, data analysis, manuscript preparation*: Guy H. Montgomery. *Study design, data analysis, manuscript preparation*: Lily A. Arya.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author.

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