A randomized, double-blind, placebo-controlled trial of onabotulinumtoxin A trigger point injections for myofascial pelvic pain

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BACKGROUND: Pelvic pain is estimated to effect 15% of women, and onabotulinumtoxin A is used to treat a variety of pain disorders. However, the data on the use of onabotulinumtoxin A for the treatment of women with myofascial pelvic pain are limited.

OBJECTIVE: The objective of the study was to compare the effect of onabotulinumtoxin A vs placebo injections to the pelvic floor muscles in women with myofascial pelvic pain.

STUDY DESIGN: This was a double-blind, randomized, placebo-controlled trial in women with myofascial pelvic pain. Women ≥18 years were eligible if they reported pain ≥6 on a 10 point visual analog scale ≥50% of the time and had pain on palpation ≥6 on the visual analog scale in ≥1 of 6 pelvic floor muscle groups. Participants were randomly allocated to a pelvic floor injection of 200 units of onabotulinumtoxin A or 20 mL of saline. All participants started 8 weeks of physical therapy 4 weeks after the injection. Participants completed validated questionnaires at baseline, 2, 4, and 12 weeks after injection. At each visit, a urogynecologist who was blinded to treatment arm performed a clinical examination with palpation of the left and right sides of 6 pelvic floor muscle groups. The primary outcome was change in participant-reported pain on palpation of the most painful pelvic floor muscle at 2 weeks. Analyses were intention to treat.

RESULTS: We consented 60 women. One participant was lost to follow-up after she was consented; therefore, we randomized 59 women. The groups had similar demographic and clinical characteristics. With regard to the primary outcome, there was no significant difference between the intervention and placebo groups in the change in participant-reported pain on palpation of the most painful pelvic floor muscle at 2 weeks. There were no significant differences in participant-reported pain on palpation for any muscle group at 4 or 12 weeks. At 4 and 12 weeks, participants in the intervention group reported greater declines in overall pelvic pain on the visual analog scale compared with the placebo group, although these differences were not statistically significant (both $P = .16$). Using the Patient Global Impression of Improvement index, participants in the intervention group were more likely to report their symptoms were improved at 4 and 12 weeks compared with the placebo group, although this difference was significant only at 4 weeks ($P = .03$ and $P = .10$, respectively). At 2 weeks, the placebo group had a significant improvement in the Pelvic Floor Distress Inventory score compared with the intervention group ($P = .01$); however, this difference did not persist at 4 ($P = .19$) or 12 weeks ($P = .11$). At 2 weeks, the most common adverse event was constipation in the intervention and placebo groups, with 10.1% reporting de novo constipation. This was followed by urinary incontinence in the intervention group (22%) and urinary tract infection (9%) in the placebo group.

CONCLUSION: Pelvic floor onabotulinumtoxin A injections for myofascial pelvic pain were not more effective than saline injections at decreasing muscle pain on palpation. Despite this, participants who received onabotulinumtoxin A were more likely than those who received saline to report improvement, albeit not statistically significant, in their overall pelvic floor pain at 4 and 12 weeks.

Key words: myofascial pain, onabotulinumtoxin A, pelvic pain, trigger point injections

Chronic pelvic pain is estimated to affect approximately 15% of women with a significant impact on quality of life and health care costs.[1] Chronic pelvic pain is a complex and often multifactorial condition affecting more than just the pelvis. Research from laparoscopic findings in women with chronic pelvic pain, epidemiological studies on chronic pelvic pain, and evaluation of women with functional somatic syndrome have supported this notion.[2]

Women with chronic pelvic pain frequently have other conditions such as irritable bowel syndrome, fibromyalgia, painful bladder syndrome, vulvodynia, and myofascial pain. Up to 23% of women with chronic pelvic pain have myofascial pain that is characterized by short, tight, tender pelvic floor muscles with hypersensitive trigger points.[3,4] Myofascial pelvic pain has been associated with several other pain disorders, including interstitial cystitis, dyspareunia, and chronic pelvic pain disorders.

Similarly, functional lower urinary pathology, such as overactive bladder and stress urinary incontinence, has been associated with pelvic floor muscle dysfunction.[5] Management of the myofascial component of chronic pelvic pain is multidisciplinary, and treatment strategies include use of steroids, nonsteroidal antiinflammatory drugs, muscle relaxants, antidepressants, pelvic floor physical therapy/exercise, and trigger point injection of various substances, including local anesthetic agents, steroids, and onabotulinumtoxin A.[6]

The use of onabotulinumtoxin A (Botox A; Allergan, Dublin, Ireland) has been described in the treatment of myofascial pain in addition to a variety of other pain conditions, including focal dystonia, spasticity, and headaches.[7,8] Other studies have reported that onabotulinumtoxin A injections in patients with vaginismus and vestibulodynia were associated with improved pain and

Cite this article as: Dessie SG, Von Bargen E, Hacker MR, et al. A randomized, double-blind, placebo-controlled trial of onabotulinumtoxin A trigger point injections for myofascial pelvic pain. Am J Obstet Gynecol 2019;221:517.e1-9.

0002-9378/$36.00

https://doi.org/10.1016/j.ajog.2019.06.044

AJOG at a Glance

Why was this study conducted?

This study was conducted to determine the effect of onabotulinumtoxin A vs placebo injections to the pelvic floor muscles in women with myofascial pelvic pain.

Key findings

Onabotulinumtoxin A injections into the pelvic floor for myofascial pelvic pain were not more effective in decreasing muscle pain than saline injections. Adverse events from onabotulinumtoxin A were limited and similar to those from placebo.

What does this add to what is known?

This study provides evidence that effects of onabotulinumtoxin A injections on pelvic pain are not clearly understood and need further exploration.

quality of life and reduced use of oral pain medications from 8 to 14 weeks.[7,9,10]

A randomized, placebo-controlled study in patients with chronic pelvic pain reported a reduction in resting tension and pelvic floor muscle pressure, which translated to a reduction in pelvic pain and dyspareunia, in patients who received pelvic floor injections of onabotulinumtoxin A compared with saline. However, the difference between the treatment and placebo groups was not statistically significant.[11]

In our practice, we have had substantial clinical experience with the use of onabotulinumtoxin A injection to the pelvic floor. In a prior retrospective study, we found that onabotulinumtoxin A injections were associated with decreased pain; however, that study had only 31 patients and limited follow-up.[12]

The objective of this randomized, double-blind, placebo-controlled trial was to compare the change in participant-reported pelvic pain among women with myofascial pelvic pain treated with a pelvic floor injections of onabotulinumtoxin A vs placebo.

Materials and Methods

This investigator-initiated, randomized, double-blind, placebo-controlled trial was approved by the Institutional Review Board at Mount Auburn Hospital (Cambridge, MA) and was registered with ClinicalTrials.gov (NCT01905137).

Study population

We approached potentially eligible women for study participation from January 2013 through December 2017. Women were eligible if they were at least 18 years of age, reported persistent pelvic pain of 6 or more on a 10 point visual analog scale at least 50% of the time over the past 3 months and on examination had a short, tight pelvic floor and pain on palpation of at least 6 on a 10 point visual analog scale in at least 1 muscle group (coccygeus, piriformis, obturator internus, iliococcygeus, puborectalis, or pubococcygeus).

Women were not eligible if they were pregnant, breastfeeding, had a preexisting neurological or neuromuscular condition that precluded them from onabotulinumtoxin A injections, had a sensitivity or allergy to onabotulinumtoxin A, were using aminoglycosides or any other medication that may potentiate neuromuscular weakness, had prior treatment of onabotulinumtoxin A injections to the pelvic floor, had a mass or lesion on physical examination, had pelvic organ prolapse greater than stage II, were planning pelvic floor surgery within the next 3 months, or changed pain medication within the past 3 months.

All participants had to be willing to complete pelvic floor physical therapy starting 4 weeks after the injection at a designated physical therapy provider. All participants provided written informed consent.

Randomization and blinding

Participants were randomly allocated to pelvic floor onabotulinumtoxin A injections with concurrent pelvic floor physical therapy or to pelvic floor saline injections with concurrent pelvic floor physical therapy in a 1:1 ratio. Block randomization was generated by a computer, and allocation was concealed in opaque envelopes until the time of randomization. The participant and treating physician were blinded to the treatment arm. Participants who were randomized to the placebo group were offered onabotulinumtoxin A injections at no cost after their study participation was complete.

Study protocol

Participants had a pelvic floor evaluation by a physical therapist, who was specifically trained in pelvic floor dysfunction and myofascial release techniques, to establish a baseline of pelvic floor findings for each participant prior to their injection in an outpatient office setting.

A study staff member who did not treat or evaluate the participants drew 200 units of onabotulinumtoxin A diluted in 20 mL of preservative-free saline or 20 mL of saline into a syringe. The treatment and placebo injections were performed by 1 of 4 fellowship-trained female pelvic medicine and reconstructive surgery specialists.

The participant was placed in the dorsal lithotomy position and asked to verbally quantify tenderness on digital muscle palpation of the following muscle groups: coccygeus, piriformis, obturator internus, iliococcygeus, puborectalis, and pubococcygeus using the Wong-Baker FACES Pain Rating Scale. During muscle assessment, examiners applied enough pressure on palpation that would blanch a fingernail. This was used as benchmark to allow for consistency between examiners.

All participants received 100 mg of 2% topical lidocaine hydrochloride jelly in the vagina for 15 minutes prior to the injections. A pudendal block kit with trumpet guide that allows for a depth of 1 cm needle penetration through vaginal mucosa into the muscle fibers was used

for the injections. The syringe was withdrawn before each injection to avoid intravascular injection. The index finger was used for palpation because the 20-gauge pudendal block kit needle was advanced to target sites piercing through the vaginal mucosa to the intended muscle groups.

The physician performed 20 injections of 1 mL of either onabotulinumtoxin A (10 units) or saline; injections were distributed bilaterally and based on areas of participant-reported pain. Intravaginal pressure was applied for a few minutes as required for hemostasis.

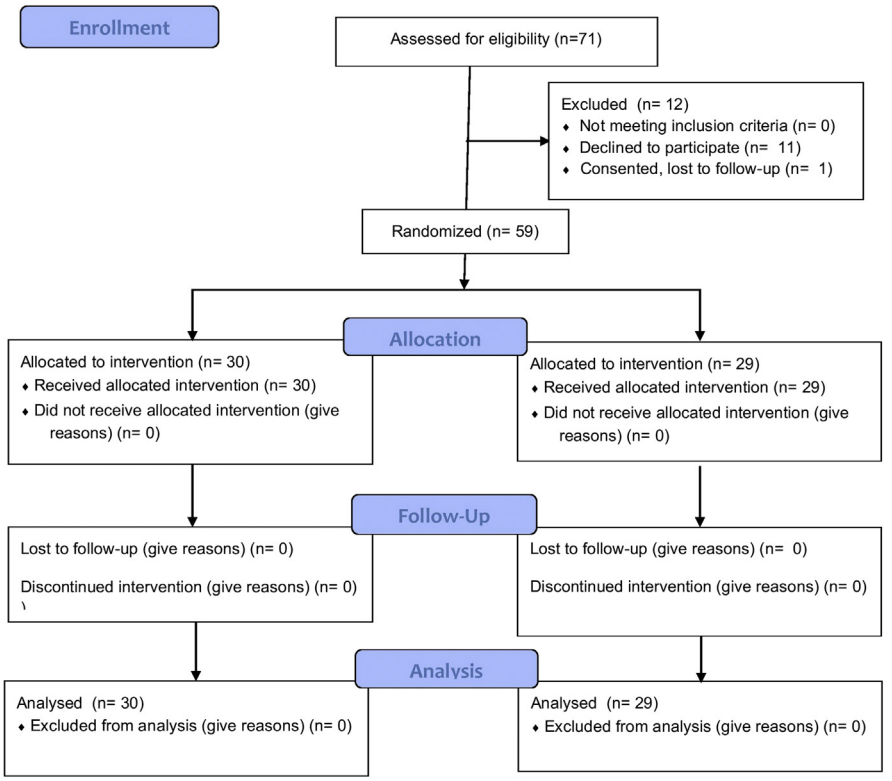
Participants had additional study visits 2, 4, and 12 weeks after the injection. At all visits, a study physician performed a clinical examination with palpation of pelvic floor muscle groups and asked participants to rate their pain on a 10 point visual analog scale for each muscle group. Participants also were asked to complete 3 validated quality-of-life questionnaires.

We used the Pelvic Floor Distress Index (PFDI-20) to assess pelvic floor symptoms and associated bother; the PFDI-20 has 3 subscales: the Pelvic Organ Prolapse Distress Inventory; the Colorectal-Anal Distress Inventory; and the Urinary Distress Inventory-6.[13]

Participants also completed the Patient Global Impression of Severity and Global Impression of Improvement tool to quantify overall perception of their pain condition and response to treatment, for which lower scores indicate more improvement,[14] and the Pelvic Pain and Urinary Urgency Frequency scale[15] to quantify bladder pain and voiding symptoms.

In addition, all participants started pelvic floor physical therapy 4 weeks after the injection for a total of 8 weekly sessions. These sessions were 45−60 minutes in length and consisted of individualized combinations of intravaginal and external pelvic and abdominal soft and connective tissue−targeted manual therapy as well as education and exercise regarding movement, biopsychosocial pain concepts, alignment, and respiration. Treatments were tailored to the patient as the physical therapist determined appropriate.

FIGURE 1
Consort flow diagram



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The primary outcome was the change from baseline to 2 weeks in participant-reported pelvic pain on palpation of the most painful pelvic floor muscle group. Secondary outcomes included changes in pain on palpation at 4 and 12 weeks, change in overall self-assessment of pain on the visual analog scale (VAS), and changes on the quality-of-life questionnaires. We also assessed medication use, compliance with physical therapy, and incidence of adverse events at each study visit.

Sample size

Based on results from our retrospective study, we estimated that participants in the treatment arm would have a 6 point reduction in pelvic pain score from baseline to 2 weeks after the injection.[12] Given the possible placebo effect, we estimated a mean pelvic pain score reduction of 3.5 points in the placebo arm. Assuming a 2-sided alpha of 0.05, we needed 24 evaluable participants per arm to have 80% power to detect the specified effect. Given that the data were likely to have a nonnormal distribution, we inflated the sample size by 15%, yielding a required sample size of 28 participants per group for a total sample size of 56 participants. Allowing for 10% loss to follow-up or withdrawal, we aimed to enroll 32 women per group.

Statistical analysis

We conducted an intention-to-treat analysis. Given nonnormal distributions, continuous data are presented as median (interquartile range); categorical data are presented as frequency (percentage). We compared continuous data with the Wilcoxon rank sum test and categorical data with the χ^2 or Fisher exact test. For

TABLE 1
Baseline demographics and clinical characteristics

Characteristics	Intervention (n = 30)	Placebo (n = 29)
Age at enrollment, y	43 [30, 55]	40 [31, 54]
Body mass index	23 [22, 27]	27 [24, 29]
Race/ethnicity		
Non-Hispanic white	27 (90)	26 (90)
Other	3 (10)	3 (10)
Nulliparous	11 (37)	17 (59)
Postmenopausal	13 (43)	10 (34)
Vaginal estrogen use	6 (20)	6 (21)
History of pelvic floor physical therapy	23 (77)	20 (69)
Sexually active	17 (57)	8 (28)
Urinary incontinence	11 (37)	17 (59)
Years of pain	7 [3, 10]	5 [3, 10]
Number of current pain medications	2 [1, 4]	2 [2, 3]
Constipation	19 (63)	21 (72)
Dyspareunia	23 (77)	13 (45)
Dysmenorrhea	11 (37)	10 (34)
Recurrent urinary tract infections	5 (17)	4 (14)
Urinary Incontinence	12 (40)	14 (48)
Fecal Incontinence	1 (3)	7 (24)
Other pain disorders	22 (73)	23 (79)

Data are presented as median [interquartile range] or n (percentage).

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each study visit, we calculated change in pain in each muscle group compared with baseline and compared the median changes between the 2 treatment arms.

To compare participant perceptions of symptom improvement at each time point, we collapsed responses on the Patient Global Impression of Improvement into better (very much better, somewhat better) and not better (no change, somewhat worse, very much worse). All tests were 2 sided and values of $P < .05$ were considered to be statistically significant. All analyses were conducted using Statistical Analysis System (SAS 9.4; SAS Institute, Cary, NC).

Results

We consented 60 women. One participant was lost to follow-up after she was consented; therefore, we randomized 59 women: 30 to the intervention group and 29 to the placebo group (Figure 1). Overall, the 2 groups were similar with regard to demographic and clinical characteristics such as age, body mass index, race, and years of pain; however, participants in the intervention group were more likely to be sexually active and have dyspareunia and less likely to have fecal incontinence.

The majority of participants were premenopausal, were non-Hispanic white, and had multiple pain disorders (Table 1). Most participants also had a history of pelvic floor physical therapy treatment and constipation. The intervention group had more participants rating their pain as severe or moderate at baseline compared with the placebo group. Compliance to physical therapy during the trial was similar in both groups, with 62% of participants in the placebo gtoup completing all 8 scheduled physical therapy sessions and 70% of those in the intervention group.

Participants in the intervention group demonstrated improvement in pain for all muscle groups at each follow-up visit. This was true for participants in the placebo group as well, except that they had no improvement in pain scores at 2 weeks in 3 muscle groups: the left and right puborectalis and the right piriformis. With the exception of the left coccygeus, none of these changes were statistically significantly different between the 2 groups. At 2 weeks, there was a 1 point decrease in pain for the left coccygeus in the intervention group and a 3 point decrease in the placebo group ($P = .046$). This difference was no longer present at 4 weeks (Table 2).

With regard to overall impression of disease severity, patient global impression of severity improved more in the placebo group compared with the intervention group, with 63.0% of participants in the placebo group rating their severity as normal or mild at 12 weeks compared with 48.1% in the intervention group, although this difference was not statistically significant ($P = .59$, Figure 3).

Using the Patient Global Impression of Improvement index, participants in the intervention group were more likely to report their symptoms were improved at 4 and 12 weeks compared with the placebo group ($P = .03$ and $P = .10$, respectively), although the difference was statistically significant only at 4 weeks (Figure 4).

There was a greater decline in median self-reported overall pelvic floor pain on the VAS at 4 weeks after injections among participants in the intervention group (−1 [−4, 0]) compared with the placebo group (−0.2 [−1, 1]). The same was true when comparing VAS at 12 weeks (−1 [−4, 0] and 0 [−4, 1], respectively) (Figure 2). However, neither difference between the groups was significant (both $P = .16$, Table 3).

Two weeks after the injections, there was a worsening in scores for the PFDI among women in the intervention group

TABLE 2
Changes in pain on palpation for each muscle group at 2, 4, and 12 weeks after injection compared with baseline

	Left muscle groups			Right muscle groups		
Variables	Intervention (n = 30)	Placebo (n = 29)	*P* value	Intervention (n = 30)	Placebo (n = 29)	*P* value
Coccygeus						
Two weeks	−1 [−2, −1]	−3 [−4, −1]	.046	−2 [−3, 0]	−1 [−3, 0]	.50
Four weeks	−2 [−4, −1]	−2 [−4, −1]	.72	−3 [−4, −1]	−2 [−3, 0]	.19
Twelve weeks	−3 [−5, −1]	−2 [−5, −1]	.390	−3 [−4, 0]	−2 [−4, 0]	.54
Iliococcygeus						
Two weeks	−2 [−3, −1]	−2 [−5, −1]	.12	−1 [−3, 0]	−1 [−3, 0]	.85
Four weeks	−1 [−3, 0]	−1 [−4, 0]	.92	−1 [−5, 0]	−3 [−4, 0]	.77
Twelve weeks	−3 [−5, −1]	−2 [−4, −1]	.46	−3 [−5, −1]	−1 [−3, 0]	.28
Obturator onternus						
Two weeks	−1 [−3, 0]	−1 [−5, 0]	.84	−1 [−3, 0]	−1 [−4, 0]	.54
Four weeks	−2 [−4, 0]	−2 [−4, −1]	.82	−2 [−3, 0]	−2 [−4, 0]	.77
Twelve weeks	−3 [−5, −3]	−3 [−3, 0]	.22	−3 [−6, 0]	−2 [−5, 1]	.45
Piriformus						
Two weeks	−1 [−3, 0]	−2 [−4, −1]	.12	−2 [−3, −1]	0 [−3, 1]	.10
Four weeks	−2 [−3, 0]	−2 [−4, 0]	.79	−2 [−4, −1]	−1.0 [−3, 0]	.20
Twelve weeks	−2 [−4, 0]	−2 [−6, 0]	.85	−3 [−4, 0]	−1 [−4, 0]	.42
Pubcoccygeus						
Two weeks	−1 [−3, 0]	−1 [−5, 0]	.44	−1 [−3, 1]	−2 [−3, 0]	.44
Four weeks	−1 [−3, 1]	−2 [−4, 0]	.29	−2 [−3, 0]	−1 [−4, 0]	.80
Twelve weeks	−3 [−6, 0]	−3 [−5, 2]	.55	−3 [−5, 0]	−1 [−3, 2]	.18
Puborectalis						
Two weeks	−1 [−3, 1]	0 [−1, 1]	.39	−1 [−3, 1]	0 [−2, 1]	.37
Four weeks	−3 [−4, −1]	−1 [−3, 0]	.31	−2 [−4, 0]	−1 [−3, 1]	.54
Twelve weeks	−2 [−6, −1]	−1 [−3, 0]	.21	−2 [−5, −1]	−1 [−4, 0]	.22

Data are presented as median [interquartile range]. Negative numbers reflect reduced pain.

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that was significantly different from the placebo group ($P = .01$). However, at 4 and 12 weeks, the median PFDI score was not significantly different between the 2 groups (both $P \geq .23$, Figure 5A). The same was true for median Colorectal-Anal Distress Inventory-8 and median Urinary Distress Inventory-6 scores at 2, 4, and 12 weeks ($P > .17$ for all; Figure 5C). All participants demonstrated a decrease in Pelvic Pain and Urinary Urgency Frequency scores from baseline to 12 weeks; however, there was no significant difference between the 2 groups ($P = .23$, Figure 5D).

Constipation was the most common adverse effect reported in both groups. Six participants (10.2%) reported de novo constipation 2 weeks after injections (4 in the onabotulinumtoxin A group and 2 in the placebo group, $P = 1.0$). The second most common complication was urinary incontinence, with 4 women in the intervention group and 1 in the placebo group reporting this complication at 2 weeks ($P = .3$). Other complications included recurrent urinary tract infection, fecal incontinence, and urinary retention, each occurring in fewer than 4 participants.

Comment

Onabotulinumtoxin A injection into the pelvic floor for patients with myofascial pelvic pain was not more effective at decreasing muscle pain 2 weeks after injection than saline in the most painful muscle group. Secondary outcomes, such as PFDI and Pelvic Pain and Urinary Urgency Frequency scores, demonstrated that onabotulinumtoxin A injection into the pelvic floor was not more beneficial than an injection of saline. Despite this, a higher percentage of participants who received onabotulinumtoxin A injection into the pelvic floor were more likely to report their

FIGURE 2
Self-reported overall pain on visual analog scale (0–10) over time

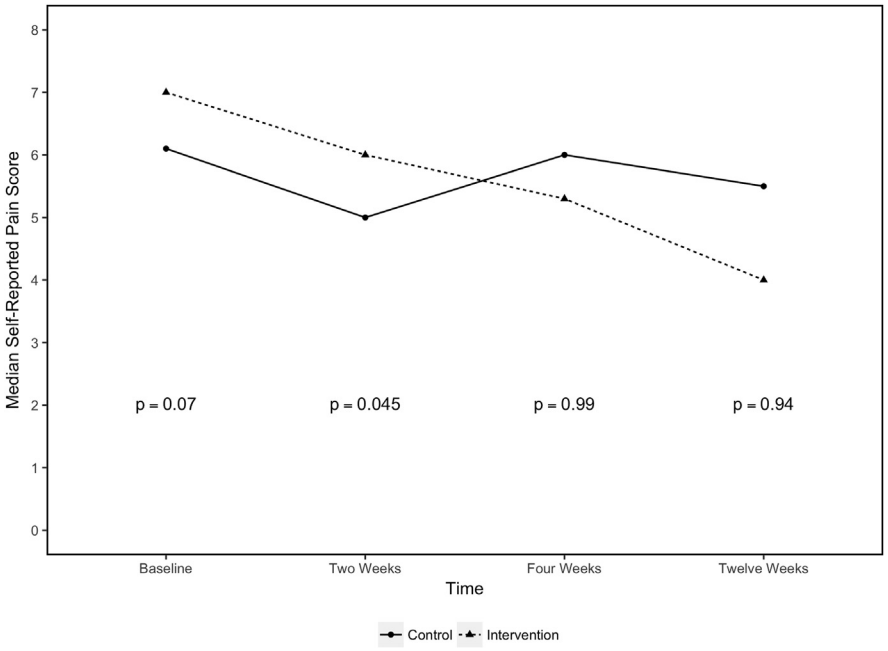

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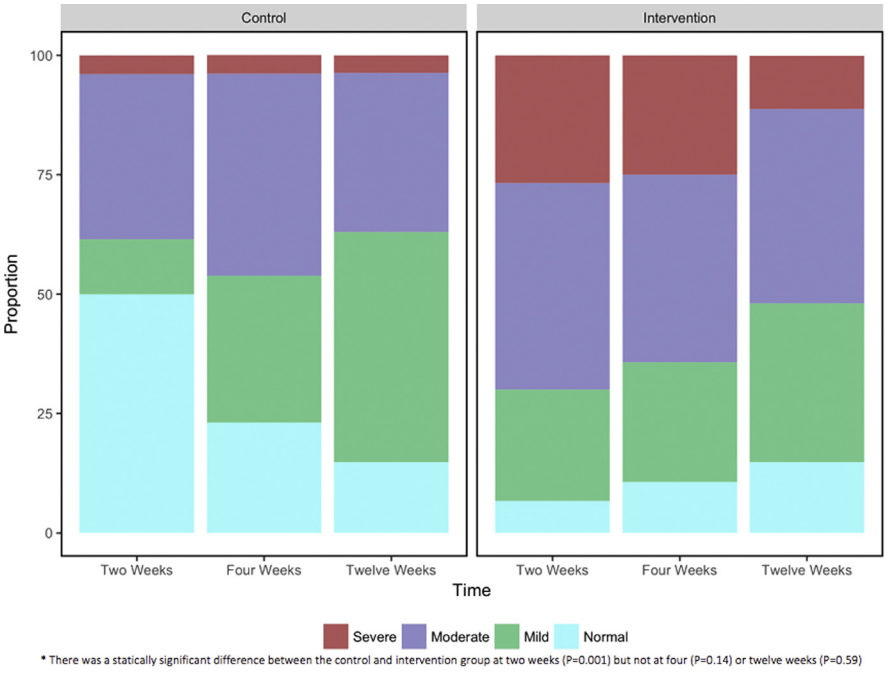
FIGURE 3
Patient global impression of severity



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overall pelvic pain as improved than those who received saline injections at 4 and 12 weeks after their injection, although this was statistically significant only at 4 weeks.

Onabotulinumtoxin A injection appears to have minimal risks with few side effects noted among participants enrolled in the trial. Participants in the intervention arm did not have more adverse events than women in the placebo arm.

Similar to our findings, Rao et al[16] performed a randomized trial evaluating the effect of 100 units of onabotulinumtoxin A vs placebo injections into the anal sphincter among 12 patients with levator ani syndrome. The authors found no improvement in pain at 90 days; however, they had complete data on only 7 participants.[16]

Another randomized, placebo-controlled study comparing 80 units of onabotulinumtoxin A to saline similarly found improvement in pain scores in both treatment arms. The treatment arm of this study saw a significant decrease in VAS score for dyspareunia and non-menstrual pelvic pain. The placebo group saw a significant decrease in VAS score for only dyspareunia. However, there was no difference between the placebo and intervention arms, similar to our results. The authors attributed this to a small sample size, and the possible pain relief women in the placebo arm may have felt from the placebo injections and increased medical attention.

These factors may have contributed to the improvement in symptoms seen in our placebo group as well. Despite the similar results, this study differed from our study in the amount of onabotulinumtoxin A injected (80 vs 200 units) and the duration of follow-up (6 months vs 3 months).[11]

Small observational studies have demonstrated improvement in symptoms among patients who received onabotulinumtoxin A for their pelvic pain. Morrissey et al[17] enrolled 28 women in a prospective, open-label pilot study to examine the effect of onabotulinumtoxin A injections on women with high-tone pelvic floor

dysfunction. These participants reported a significant improvement in pain symptoms; however, the participants were not blinded to their treatment and the injections were done via electromyography guidance, rather than palpation as in this study, which may have helped target the most contracted muscle group.[17]

Similarly, a study conducted with 12 participants in Australia demonstrated improvement in pelvic pain symptoms after onabotulinumtoxin A injections into the puborectalis muscle, but participants were not blinded to treatment.[18]

The motivation for this randomized trial came from the retrospective study at our institution, which demonstrated a significant improvement in pain scores after onabotulinumtoxin A injections into the pelvic floor. In our prior study, the majority of patients were injected with 300 units of onabotulinumtoxin A, while we used 200 units in the study presented here.[12] We chose this amount based on clinical experience after the retrospective study and to minimize adverse effects. However, this lower dose may have contributed to the lack of benefit observed in this trial. In addition, the participants in the retrospective study were not blinded to treatment, and their course of physical therapy was not controlled. This may have also contributed to the increased effect of onabotulinumtoxin A compared with our study.

There were several strengths to our study. The randomization minimized confounding, and the blinding and placebo control minimized observer bias and reporting bias. Physical therapy was started 1 month after injections, allowing time to evaluate the effect of onabotulinumtoxin A injections alone and with the addition of physical therapy.

Weaknesses of our study include the possibility of a type II error. Although we met our small sample size requirement, the power calculation was based on a pilot study and the assumption of a minimal response from the placebo group. However, the placebo effect may have resulted in participants experiencing pain relief from the saline injections.

There are data to support the positive effect of saline injections on myofascial pain, and this may have contributed to the lack of difference noted in this study between the intervention and placebo groups.[19] Dry needling itself has been shown to decrease muscle spasm for some patients.[20] It would have been beneficial to have a no-treatment arm to the study to control for this.

FIGURE 4
Patient global impression of improvement

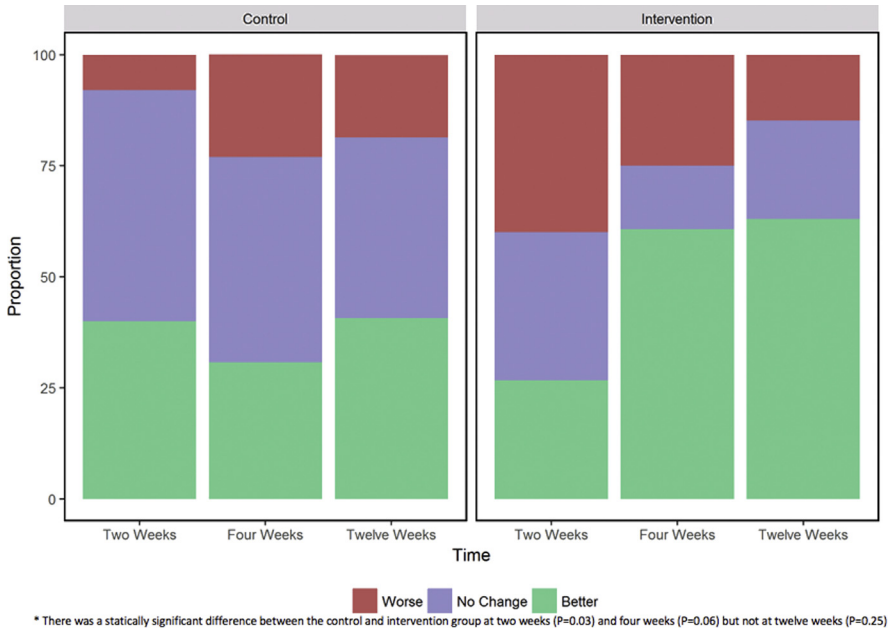

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TABLE 3
Changes in PFDI-20 and pain, as measured by VAS at 2, 4, and 12 weeks after injection compared with baseline

Variables	Intervention (n = 30)	Placebo (n = 29)	*P* value
Pelvic Floor Distress Inventory			
Two weeks	3 [−14, 22]	−10 [−27, −4]	.01
Four weeks	−3 [−22, 6]	−18 [−38, −2]	.19
Twelve weeks	−7 [−21, 11]	−21 [−64, −2]	.11
Visual analog scale pain			
Two weeks	−0.3 [−3, 1]	−0.3 [−2, 0.1]	.65
Four weeks	−1 [−4, 0]	−0.2 [−1, 0.8]	.16
Twelve weeks	−1 [−4, 0]	0 [−4, 1]	.16

Data are presented as median [interquartile range]. Negative numbers reflect reduced pelvic floor symptoms/bother.

Negative numbers reflect reduced pain.

PFDI, Pelvic Floor Distress Index-20; *VAS*, visual analog scale.

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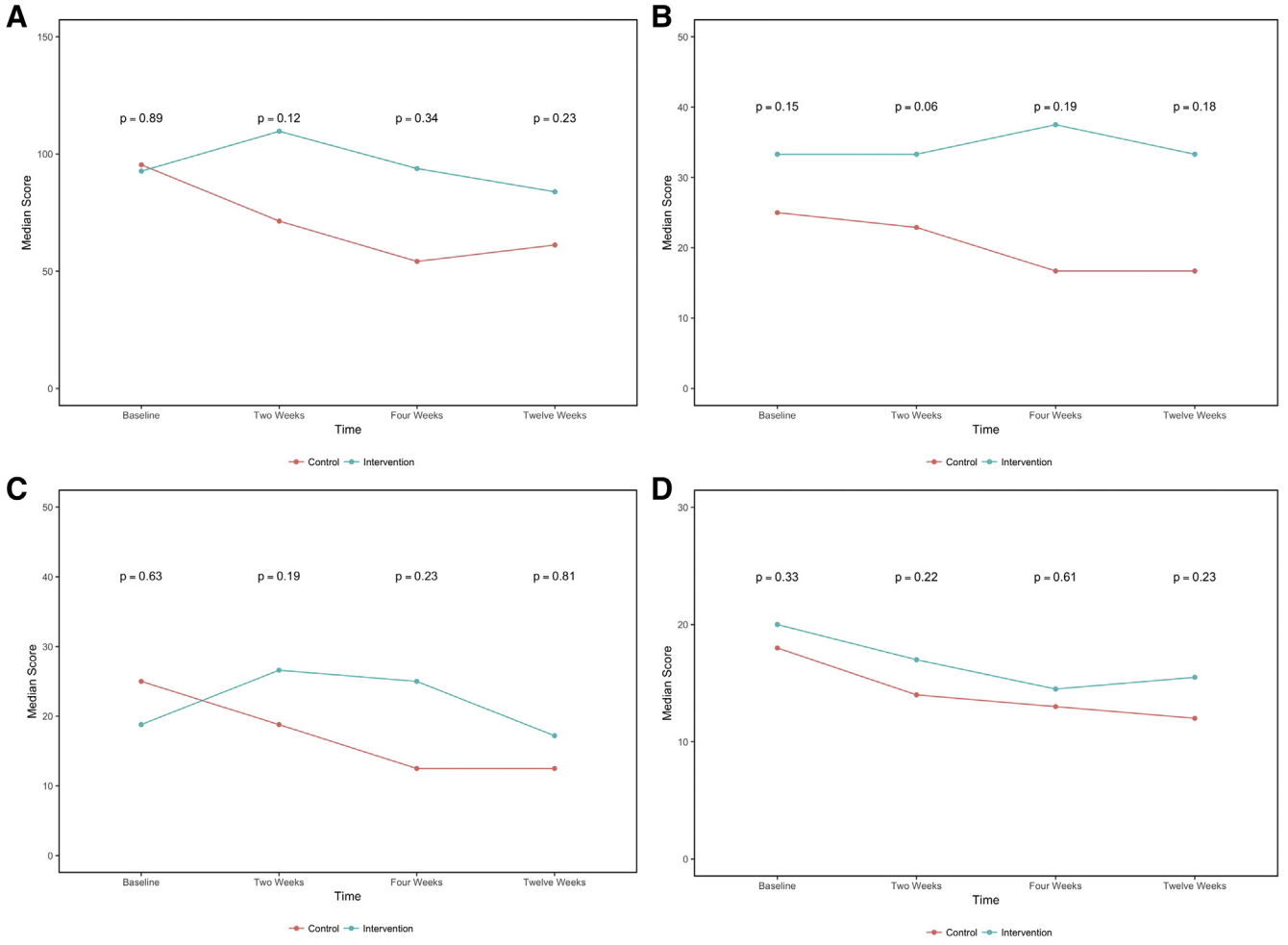
FIGURE 5
Symptom scores



A, Median Pelvic Floor Distress Inventory score. **B,** Median Pelvic Organ Prolapse Distress Inventory score. **C,** Median Colorectal-Anal Distress Inventory (CRAD-8) score. **D,** Pain urgency frequency score.

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Furthermore, this study may have limited generalizability because we restricted our study population to women with severe pain, given that in our clinical practice, we reserve onabotulinumtoxin A injections for patients with severe refractory pain. It is possible that the effect of the onabotulinumtoxin A may be different among women with less severe symptoms.

We also had 4 clinicians administering the injections; therefore, reproducibility between providers may have been variable. Additionally, follow-up was limited to 12 weeks; therefore, there may have been other outcomes not captured because of the lack of follow-up time.

The majority of participants in this trial had multiple pain disorders. Although we asked participants to keep their pain medication stable during the study, there may have been patients undergoing various treatments for their other pain disorders during the 12 week study period that was not controlled for in the results.

Lastly, because pain disorders profoundly affect quality of life, multiple measures of disease severity and response to treatment might be necessary to truly assess response to interventions.

This study provides insufficient evidence to support the use of onabotulinumtoxin A injections for patients with myofascial pelvic pain. Larger studies are needed with possible higher doses of onabotulinumtoxin A and different nonplacebo control arms. Given the positive effects seen in previous studies, further research is needed to examine the role of trigger point injections and onabotulinumtoxin A in this patient population. Onabotulinumtoxin A treatment for myofascial pelvic pain appears to be relatively safe with few complications; however, its place in the treatment line for myofascial pelvic pain

needs further investigation. Future studies could try to identify potential subgroups of patients who could benefit from the addition of pelvic injections of onobotulinumtoxin A. ■

Acknowledgments

We acknowledge Kathleen Rogers for her assistance with managing study funding, the institutional review board, and patient recruitment; Jessica McKinney PT, MS, CMPT, for her assistance with all aspects of pelvic floor physical therapy for study participants; and William Winkelman, MD, for his data management work. Clinical trial information includes the following: date of registration was July 23, 2013; and the date of initial participant enrollment was Sept. 18, 2013. The clinical trial identification number was NCT01905137, and the registration site was https://clinicaltrials.gov/ct2/show/NCT01905137?term=NCT01905137&rank=1.

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Received Jan. 3, 2019; revised May 20, 2019; accepted June 20, 2019.

This study was supported by a grant from Allergan and Harvard Catalyst; the Harvard Clinical and Translational Science Center (National Center for Advancing Translational Sciences, National Institutes of Health award UL 1TR002541); and financial contributions from Harvard University and its affiliated academic health care centers. The sources of funding had no role in study design; collection, analysis, and interpretation of data; writing of the report; or the decision to submit for publication.

The authors report no conflict of interest.

Presented at the 45th annual meeting of the Society of Gynecologic Surgeons March 31 through April 3, 2019, Tucson, AZ.

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