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ORIGINAL ARTICLE

The effect of pelvic floor muscle training and intravaginal electrical stimulation on urinary incontinence in women with incomplete spinal cord injury: an investigator-blinded parallel randomized clinical trial

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Abstract

Introduction and hypothesis Urinary incontinence is a prevalent problem in women with spinal cord injury. The aim of this study was to examine the effect of pelvic floor muscle training (PFMT) alone and combined with intravaginal electrical stimulation (IVES) on urinary incontinence in women with incomplete spinal cord injury.

Methods In this investigator-blinded randomized clinical trial, we recruited women aged 18–75 with incomplete spinal cord injury and urinary incontinence from a single spinal cord injury clinic in Denmark. Women were randomly assigned to either PFMT or PFMT combined with IVES daily at home for 12 weeks. All women were trained by a physiotherapist using vaginal palpation and electromyography biofeedback. Outcome measures were recorded at baseline (week 0), post-intervention (week 12) and follow-up (week 24) and included change in the total score on the International Consultation on Incontinence Questionnaire urinary incontinence short form (ICIQ-UI-SF) and daily episodes of urinary incontinence.

Results From 27 April 2015−9 September 2016, we randomly assigned 36 women (17 in the PFMT group and 19 in the PFMT+IVES group); 27 completed the interventions (13 in the PFMT group and 14 in the PFMT+IVES group). The results showed no difference between the groups on ICIQ-UI-SF or episodes of urinary incontinence at 12 and 24 weeks. Only the PFMT group had a significant change from baseline on ICIQ-UI-SF [−2.4 (95% CI -4.3−−0.5), $p = 0.018$] and daily episodes of urinary incontinence [−0.4 (95% CI -0.8−−0.1), $p = 0.026$] at 12 weeks.

Conclusions PFMT+IVES is not superior to PFMT alone in reducing urinary incontinence in women with incomplete spinal cord injury.

Keywords Urinary incontinence · Spinal cord injury · Pelvic floor muscle training · Electrical stimulation · Neurogenic bladder

Introduction

Urinary incontinence (UI) is a prevalent problem in persons with spinal cord injury (SCI), affecting approximately 52% [1]. The characteristics of UI in persons with SCI vary according to the type of neurogenic bladder dysfunction: neurogenic detrusor overactivity (NDO) can result in urgency UI, acontractile bladder can result in overflow UI, and underactive urethral sphincter as well as weakness of the pelvic floor muscles (PFMs) can result in neurogenic stress UI [2]. Studies have shown that urinary incontinent SCI persons experience reduced quality of life (QoL) compared with their urinary continent counterparts. In addition, UI has been reported to be one of the primary physical problems affecting the sexuality of SCI women [3].

Pelvic floor muscle training (PFMT) is a well-established first-line conservative treatment of stress UI in able-bodied women [4]. Moreover, studies have shown that PFMT can decrease urgency UI because of inhibition of bladder contractions [5, 6]. Another conservative treatment of UI is electrical stimulation (ES). The mechanism of action is unclear; however, it has been suggested that ES at high frequencies (40–

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50 Hz) stimulates the efferent motor fibers of the pudendal nerve, facilitating PFM contraction. This may lead to muscle hypertrophy and increased urethral pressure. Conversely, ES at low frequencies (5–10 Hz) stimulates the afferent fibers of the pudendal nerve, promoting bladder relaxation by inhibiting the parasympathetic vesical motor neurons [7]. The evidence of using high-frequency ES to reduce stress UI in able-bodied women is contradictory, and most studies find no additional effect of high-frequency intravaginal ES compared with PFMT alone [8–10]. Nevertheless, there is a lack of studies investigating high-frequency ES in persons with neurologic disorders. On the other hand, low-frequency ES applied intravaginally has shown good results on urgency UI comparable or superior to anticholinergic medication [11, 12]. It could be hypothesized that a combination of high- and low-frequency ES is beneficial particularly in SCI persons with NDO and reduced strength and sensibility of the PFMs given the threefold effect of the stimulation: relaxation of the bladder, strengthening of the PFMs and increased awareness of the PFMs. However, the effect of non-invasive ES in persons with UI due to neurologic disorder has been sparsely examined, and the literature includes only two randomized clinical trial studies [13]. These studies showed promising results on UI in persons with stroke or multiple sclerosis [14, 15]. To our knowledge, no studies have investigated the effect of PFMT alone or combined with intravaginal electrical stimulation (IVES) on UI in women with SCI. Hence, the aim of this investigator-blinded parallel randomized clinical trial was to examine the effect of PFMT and PFMT combined with IVES on UI in women with incomplete SCI.

Materials and methods

Study participants

This was an investigator-blinded parallel-group randomized clinical trial. Eligible participants were women aged 18–75 years with incomplete SCI and UI with a total score of ≥ 8 on the International Consultation on Incontinence Questionnaire UI short form (ICIQ-UI-SF). Exclusion criteria were motor completeness of injury (A or B on the American Spinal Injury Association Impairment Scale) [16], lack of ability to contract the PFMs examined by the investigator, vesical botulinum toxin injection within the last year, pregnancy and use of a pacemaker. The use of bladder-relaxant drugs was allowed if the dose was not changed during the study. To describe the urodynamic detrusor function, the most recent cystometry and pressure-flow study was searched for in the medical records. If not available, a cystometry and pressure-flow study was to be performed in our department. As the occurrence of stress UI was not investigated in the cystometry and pressure-flow studies conducted prior to this study, the type of UI was defined by the ICIQ-UI-SF questionnaire. Participants were recruited from a single SCI center in Denmark during April 2015–January 2017.

Study design

Recruited women attended a screening visit where a digital vaginal and rectal examination was conducted by the primary investigator to examine if the women were able to perform a voluntary PFM contraction. In addition, the ICIQ-UI-SF questionnaire was filled out and evaluated according to the exclusion criteria.

If eligible, participants were randomized 1:1 to one of two groups: (1) PFMT or (2) PFMT combined with IVES. We used a computer-generated randomization list in a block size of four. Allocation was conducted by a research-assistant according to the order of inclusion. Whereas the research assistant, physiotherapists and study participants were aware of the allocated arm, the primary investigator who assessed the outcomes and analyzed data was blinded. The study was approved by the National Committee on Health Research in Denmark, and the study was registered at clinicaltrials.gov, NCT02427230.

Shortly after enrollment, the participants attended a second visit during which all women received an individual physiotherapeutic standardized consultation [17]. With the woman in a supine position, the examination included visual inspection, digital vaginal and rectal palpation and electromyography biofeedback (U-Control EMG Biofeedback®, NMKimport, Værløse, DK) with a vaginal or anal sensor as visual and auditory guidance tools. All physiotherapists had been trained in PFMT and IVES during a 5-day course held by a specialized pelvic floor physiotherapist. Instructions for PFMT included approximately 30 near-maximal contractions of 5–10-s duration followed by 10 s of pause, adjusted to the woman's pelvic floor muscle function. In addition to the PFMT instructions, the PFMT+IVES group received instructions on how to use an electrical stimulation device, Cefar Peristim Pro® (NMKimport, Værløse, DK), with a vaginal probe. Instructions included the daily use of two stimulation programs. First, an intermittent stimulation (frequency 40 Hz, pulse width 250 μs) was applied for 7.5–10 min, during which 30 stimulation cycles were given, each including 5–10 s of stimulation followed by 10-s breaks. The women were instructed to perform the active PFMT program concurrent with the IVES, using the electrical device as guidance on how and when to contract the muscles. Second, a continuous stimulation (frequency 10 Hz, pulse width 250 μs) was applied for 10–20 min, during which the women were instructed to relax their PFMs. Both stimulation programs should be delivered at the women's maximum tolerated intensity. Women in both groups were asked to train daily for 12 weeks and to keep a daily training diary. During the active training period, the women attended two additional consultations with

the physiotherapist at week 4 and 8 where the training diary was evaluated, the PFMT was assessed using vaginal palpation and electromyography biofeedback, and the training instructions were adjusted according to the patient's improvements. To enhance motivation, participants were also offered a phone consultation with the physiotherapist at week 2, 6 and 10. At the 12-week visit, the IVES device was handed in, and all participants were encouraged to continue PFMT.

Outcomes

Outcomes were measured during the first visit after enrollment (week 0) after the 12-week intervention period (week 12) and after 12 additional weeks of follow-up (week 24). The primary outcome measure was change in total score on the validated questionnaire, ICIQ-UI-SF, developed by the International Consultation on Incontinence [18], which was translated into Danish and tested for content validity and test-retest reliability in a study investigating urinary incontinence during and after pregnancy [19]. The questionnaire contains questions regarding the frequency, severity and the impact of UI on QoL, providing a total score ranging from 0 to 21 with a higher score indicating worse symptoms and greater impact on QoL.

Secondary outcomes included change in opening urethral pressure (OUP) during PFM contraction and at rest measured with urethral pressure reflectometry (UPR) [20]. UPR measures the pressure and cross-sectional area in the urethra simultaneously using a thin polyurethane bag placed in the urethra. The bag is inflated with air, and the cross-sectional area is measured with acoustic reflectometry. The method has proven to be highly sensitive in detecting changes in the OUP caused by drugs reducing stress UI [21]. To prevent urinary tract infection caused by the UPR, all women were given a prophylactic antibiotic treatment (400 mg pivmecillinam and 500 mg amoxicillin-clavulanic acid), which was administered 1 h prior to the investigation and in the evening.

Other secondary outcomes included change in 3-day bladder diary parameters (daily episodes of UI, mean bladder capacity, maximal functional bladder capacity and number of daily voiding episodes), a 24-h pad test, total score on the International Consultation on Incontinence Questionnaire overactive bladder (ICIQ-OAB), in which the total score range is 0–56, with a higher score indicating worse symptoms [22], and total score on the International SCI QoL Basic Data Set (SCI-QoL) in which the total score range is 0–30, with a higher number meaning greater satisfaction [23]. At week 12 and 24, the Patient Global Impression of Improvement scale (PGI-I) was applied [24].

Sample size and statistical methods

To detect a change in total score on ICIQ-UI-SF of 5 (SD 4), which is in accordance with the study of Sirls et al. [25], with a two-sided 5% significance level and a power of 80%, a sample of ten women per group was necessary. To compensate for possible dropouts, we aimed at including 20 women in each group.

We analyzed data only for those women who completed the study (per protocol). Parametric, nonparametric and categorical baseline parameters were presented as mean (± SD), median (interquartile range) or numbers (%) and analyzed using Student's t-test, Mann-Whitney-U test or Fisher's exact test, respectively. Changes from baseline at 12 and 24 weeks were analyzed using analysis of covariance (ANCOVA) in parametric data, presenting results as mean (95% confidence interval), and Mann-Whitney-U test in nonparametric data, presenting results as median (interquartile range). The ANCOVA analysis included the baseline value of the parameter as a fixed effect, when the effect of intervention group was examined. In each group, change from baseline was analyzed using a paired t-test in the parametric data or Wilcoxon signed rank test in nonparametric data. The statistical analyses were repeated in two subgroups as post-hoc analyses after excluding: (1) participants who trained < 50% of the days in the intervention period or (2) participants with stress or undefined UI. All statistical analyses were performed in SAS version 7.1, and $p < 0.05$ was considered statistically significant.

Results

The Consolidated Standards of Reporting Trials flow diagram is presented in Fig. 1. From 27 April 2015−9 September 2016, we included and randomized 36 women. One woman in the PFMT+IVES group was excluded after enrollment but prior to the first session with the physiotherapist as the investigators found that polyuria and excessive daily fluid intake (> 4 l) were the main causes of the woman's frequency and UI symptoms. Four women in each group discontinued the study. The time of dropout during the study was the same in the two groups: One dropped out prior to the active intervention period, two dropped out after 0–4 weeks of the active intervention period and one dropped out after 4–8 weeks of the active intervention period in both groups. One woman in the PFMT+IVES group was excluded after 12 weeks because of vesical botulinum toxin injections.

Table 1 lists baseline characteristics of the study groups. The women in the PFMT+IVES group were significantly older, had a lower mean and maximum functional bladder capacity, used more pads, had a lower daily fluid intake and daily diuresis, and had a higher score on the ICIQ-OAB compared with the women in the PFMT group. Three women (one in the PFMT and two in the PFMT+IVES group) reported UI symptoms prior to the SCI. Only four women (two in the PFMT and two in the PFMT-IVES group) had a normal

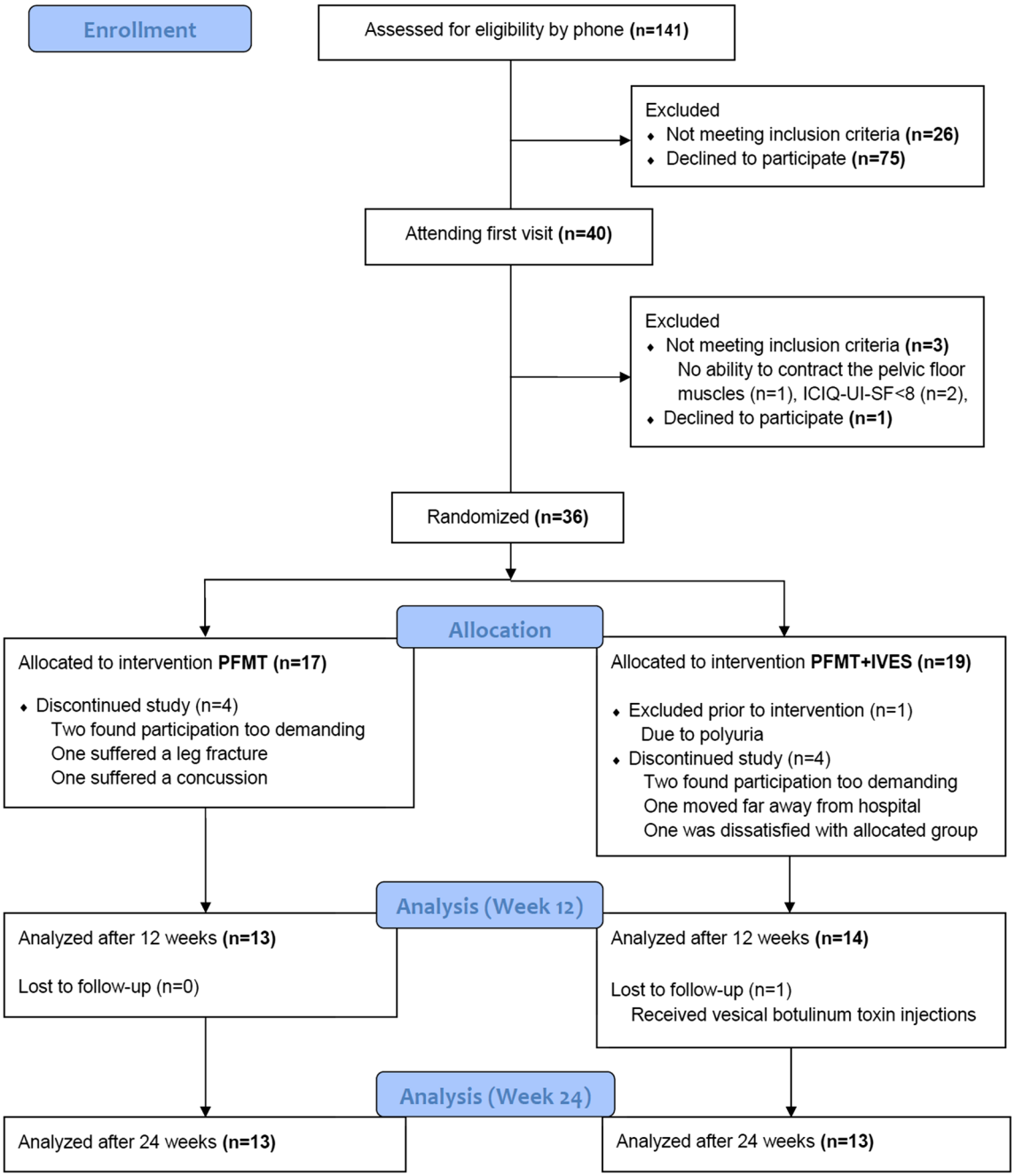

Fig. 1 Consolidated Standards of Reporting Trials (CONSORT) flow diagram

sensation by pin prick and light touch in the S3 and S4-S5 dermatomes.

The changes from baseline in outcome measures after intervention at week 12 or 24 are shown in Tables 2 and 3 and Fig. 2. There were no significant between-group differences at week 12, except for the change in OUP-resting, which showed a 5.7 cmH2O larger increase in pressure in the PFMT group compared with the PFMT+IVES group. The within-group analyses showed a significant change from baseline at 12 weeks (marked with an *) in the PFMT group regarding the total score on ICIQ-UI-SF [−2.4 (95% CI -4.3−−0.5), p = 0.018], OUP-squeezing [7.7 cmH2O (95% CI 1.7–13.8), p = 0.017], OUP-resting [3.9 cmH2O (95% CI 0.5–7.3), p = 0.030] and daily incontinence episodes [−0.4 (95% CI -0.8−−0.1), p = 0.030]. The PFMT+IVES group only improved significantly on the 24-h pad test [median − 32.5 g (IQR −112–3), p = 0.045].

At week 24 (Table 3), there were no significant between-group differences in change in outcome measures from baseline. The within-group analysis showed a significant change from baseline in the PFMT group on the ICIQ-UI-SF [−2.5 (95% CI -4.5−−0.6), p = 0.016], number

Table 1 Baseline characteristics and outcome measures

Characteristics	All ($n = 27$)	PFMT ($n = 13$)	PFMT+IVES ($n = 14$)	*P*
Age, years	55 (47–61)	47 (36–56)	59 (49–67)	**0.027**
Parity	2 (1–2)	2 (0–2)	2 (1–2)	0.4
Body mass index, kg/m^2	24.5 (20.8–31.4)	24.7 (21.6–27.7)	22.5 (18.4–32.0)	0.8
Etiology of injury				1.0
Spinal cord injury	24 (89%)	11 (85%)	13 (93%)	
Myelomeningocele	3 (11%)	2 (15%)	1 (7%)	
Level of injury[a]				0.4
Cervical	6 (23%)	4 (31%)	2 (14%)	
Thoracic	8 (31%)	5 (38%)	3 (21%)	
Lumbar	12 (46%)	4 (31%)	8 (57%)	
Completeness[b]				1.0
C	6 (22%)	3 (23%)	3 (21.5%)	
D	20 (74%)	10 (77%)	10 (71.5%)	
E	1 (4%)	0	1 (7%)	
Follow-up after injury, years	11 (3–21)	13 (4–26)	10 (3–19)	0.7
Urinary incontinence[c]				0.2
Stress	4 (15%)	3 (23%)	1 (7%)	
Urgency	8 (30%)	4 (31%)	4 (29%)	
Mixed	13 (48%)	4 (31%)	9 (64%)	
Undefined	2 (7%)	2 (15%)	0	
Detrusor function[d]				0.6
Normal	8 (30%)	5 (38%)	3 (21%)	
Detrusor overactivity	13 (48%)	6 (46%)	7 (50%)	
Acontractile/underactive	6 (22%)	2 (15%)	4 (29%)	
Clean intermittent catheterization	16 (59%)	6 (46%)	10 (71%)	0.3
Use of bladder-relaxant drugs	6 (22%)	2 (15%)	4 (29%)	0.7
Use of muscle-relaxant drugs[e]	10 (37%)	4 (31%)	6 (43%)	0.7
Reflectometry				
OUP-squeezing, cmH_2O	51.9 (± 15.1)	56.5 (± 16.5)	47.7 (± 12.9)	0.13
OUP-resting, cmH_2O	46.7 (± 14.4)	50.7 (± 13.5)	42.9 (± 14.7)	0.17
3-Day bladder diary				
Daily incontinence episodes	1.5 (0.5–3)	1 (0–2)	2 (1–4)	0.07
Mean bladder capacity, ml	252 (± 87)	313 (± 58)	200 (± 72)	**0.001**
Max bladder capacity, ml	443 (± 174)	558 (± 154)	344 (± 125)	**0.001**
Daily voiding episodes	7 (± 2)	6 (± 2)	7 (± 2)	0.19
Daily used pads	2 (1–4)	1 (0–3)	2 (2–4)	**0.022**
Daily fluid intake, ml	1681 (± 412)	1901 (± 345)	1492 (± 376)	**0.008**
Daily diuresis, ml	1716 (± 511)	1976 (± 506)	1493 (± 413)	**0.013**
24-h pad test, g	33 (11–164)	34 (7–70)	32 (13–174)	0.6
Questionnaires				
ICIQ-UI-SF	13 (11–16)	11 (10–16)	13.5 (12–16)	0.2
ICIQ-OAB	30 (16–39)	18 (16–30)	36.5 (29–43)	**0.018**
SCI-QoL	19 (15–24)	18 (17–20)	20 (15–24)	0.5

PFMT, pelvic floor muscle training; IVES, intravaginal electrical stimulation; OUP, opening urethral pressure; ICIQ-UI-SF, International Consultation on Incontinence Questionnaire Urinary Incontinence Short Form, ICIQ-OAB, International Consultation on Incontinence Questionnaire Overactive bladder; SCI-QoL, International Spinal Cord Injury Quality of Life Basic Data Set. Data are presented as number (%), mean (±SD) or median (interquartile range). [a] Excluding one patient with no level of injury because of completeness E. [b] Completeness is classified according to the American Spinal Injury Association Impairment Scale. [c] Urinary incontinence is classified according to ICIQ-UI-SF; urgency if yes to "leaks before you can get to the toilet." Stress if yes to "leaks when you cough or sneeze" or "leaks when you are physically active/exercising." Mixed if yes to both categories and undefined if no to both categories. [d] Detrusor function on the most recent cystometry and pressure-flow study. [e] Including benzodiazepine (n = 1), per oral baclofen ($n = 3$), baclofen pump (n = 1) and gabapentin ($n = 7$), which was used in the treatment of neurogenic pain, but also has an anti-spasmolytic effect

of daily incontinence episodes [−0.6 (95% CI -1.0−−0.2), $p = 0.010$], the maximal functional bladder capacity [−120 ml (95% CI -227−−13), $p = 0.031$] and the 24-h pad test [median − 11 g (IQR −84−−2), $p = 0.020$]. The PFMT+IVES group improved on ICIQ-OAB (−5.8, [95% CI -9.0−−2.7], $p = 0.002$).

According to the training diary, women in the PFMT group performed the intervention daily in a median of 76 days (range 31–91). Women in the PFMT+IVES group performed the intervention daily in a median of 67 days (range 14–95) (Mann-Whitney-U, $p = 0.2$). On the days when the intervention was carried out, compliance with the training instruction

was generally good. The mean number of contractions was 28 (range 22–30) with a mean duration of 8 s (range 5–10) in the PFMT group, and the mean stimulation time was 9 min (range 8–10) with the intermittent stimulation and 15 min (range 15–20) with the continuous stimulation in the IVES+PFMT group. Four women (one in the PFMT group and three in the PFMT+IVES group) did not perform the assigned intervention more than 50% of the days during the 84-day intervention period. When excluding the four women from the study population in a sub-analysis (supplementary Table A), there was no difference between the groups in any parameters, and the within-group results at week 12 did not differ from those found in the complete study population.

In a second sub-analysis (supplementary Table B), only the women with urgency or mixed UI according to the ICIQ-UI-SF answers were included ($n = 21$). The results showed no differences between the groups in any parameters.

One woman in the PFMT group reported soreness in the pelvic floor area, but no other adverse events were reported.

Discussion

This is the first randomized clinical trial investigating the effect of PFMT and IVES in women with neurogenic UI after SCI. The trial demonstrates that IVES combined with PFMT is not superior to PFMT alone in reducing UI and improving QoL. After a 12-week training period, only the PFMT group showed significant improvement of the ICIQ-UI-SF score, daily UI episodes and the OUP during contraction and at rest. A significant effect on daily UI episodes and ICIQ-UI-SF was also found at week 24, demonstrating a persistent effect 3 months after the intensive PFMT program had ended.

Given the novelty of the study, a comparison with results from other studies conducted in SCI persons is not possible. However, our findings differ from the findings in a similar study by McClurg et al. that included 74 multiple sclerosis patients [15]. The authors found that 9 weeks of daily intravaginal/intra-anal electrical stimulation (40 and 10 Hz) in addition to PFMT was more effective than PFMT alone on lower urinary tract dysfunction. The mean number of daily UI episodes was reduced

Table 2 Change in outcome measures after intervention at 12 weeks

Outcome measures	*n*	PFMT	*n*	PFMT+IVES	IVES+PFMT − PFMT *(adjusted)*[a]	*P*
ICIQ-UI-SF	*13*	−2.4 (−4.3—0.5)*	*14*	−2.2 (−4.8—0.4)	0.4 (−2.8–3.6)	0.8
ICIQ-OAB	*13*	1.6 (−6.9–10.1)	*14*	−3 (−10.3–4.3)	2.4 (−8.6–13.3)	0.7
Reflectometry						
OUP-squeezing, cmH_2O	*13*	7.7 (1.7–13.8)*	*14*	1.4 (−2.4–5.2)	−5.2 (−12.3–1.8)	0.14
OUP-resting, cmH_2O	*13*	3.9 (0.5–7.3)*	*14*	−1.3 (−4.6–1.9)	−5.7 (−10.4—1.1)	**0.018**
3-Day bladder diary						
Daily incontinence episodes	*11*	−0.4 (−0.8—0.1)*	*12*	0.1 (−0.6–0.8)	0.6 (−0.2–1.4)	0.14
Mean bladder capacity, ml	*12*	22 (−43–87)	*13*	−3 (−20–15)	−23 (−117–70)	0.6
Max bladder capacity, ml	*12*	−67 (−175–41)	*13*	−9 (−56–38)	−46 (−172–80)	0.5
Daily voiding episodes	*12*	−0.6 (−1.8–0.7)	*13*	−0.5 (−1.6–0.7)	0.9 (−0.5–2.2)	0.18
24-h pad test, g	*12*	−6.0 (IQR −54 − 5)	*12*	−32.5 (IQR −112–3) [$]	–	0.6
SCI-QoL	*13*	2 (IQR 0–6)	*14*	1 (IQR −3 − 6)	–	0.7
PGI-I	*13*	3 (IQR 2–3)	*14*	3 (IQR 3–4)	–	0.7

PFMT, pelvic floor muscle training; IVES, intravaginal electrical stimulation; ICIQ-UI-SF, International Consultation on Incontinence Questionnaire Urinary Incontinence Short Form; OUP, opening urethral pressure; ICIQ-OAB, International Consultation on Incontinence Questionnaire Overactive bladder; SCI-QoL, International Spinal Cord Injury Quality of Life Basic Data Set; PGI-I, Patient Global Impression of Improvement, where 1 = very much better, 2 = much better, 3 = a little better, 4 = no change, 5 = a little worse, 6 = much worse and 7 = very much worse

Results are calculated by subtracting post-treatment values (week 12) from pre-treatment values (week 0) and presented as mean (95% confidence interval) or median (IQR, interquartile range). [a] Analysis of covariance (ANCOVA) was adjusted for the baseline value. *Significant change by paired t-test. [$] Significant change by paired Wilcoxon signed rank test

Table 3 Change in outcome measures after follow-up at 24 weeks

Outcome measures	*n*	PFMT	n	PFMT+IVES	IVES+PFMT – PFMT *(adjusted)*[a]	*P*
ICIQ-UI-SF	*13*	−2.5 (−4.5—0.6)*	*13*	−2.5 (−5.5–0.4)	0.3 (−3.1–3.7)	0.8
ICIQ-OAB	*13*	1.2 (−5.8–8.1)	*13*	−5.8 (−9.0—2.7)*	−4.2 (−12.4–4.1)	0.3
Reflectometry						
OUP-squeezing, cmH_2O	*13*	6.4 (−0.2–13.0)	*13*	1.5 (−2.5–5.4)	−3.9 (−11.8–3.9)	0.3
OUP-resting, cmH_2O	*13*	1.9 (−2.7–6.4)	*13*	0.1 (−3.3–3.4)	−1.0 (−6.9–4.9)	0.7
3-Day bladder diary						
Daily incontinence episodes	*10*	−0.6 (−1.0—0.2)*	*11*	−0.1 (−1.1–0.9)	−0.6 (−0.6–1.7)	0.3
Mean bladder capacity, ml	*12*	−25 (−71–21)	*13*	12 (−17–42)	12 (−55–79)	0.7
Max bladder capacity, ml	*12*	−120 (−227—13)*	*13*	−3 (−50–44)	17 (−101–135)	0.8
Daily voiding episodes	*12*	0 (−1.4–1.4)	*13*	−0.4 (−1.3–0.5)	0.2 (−1.0–1.4)	0.7
24-h pad test, g	*11*	−11.0 (IQR −84—2) [$]	*12*	−13.5 (IQR −101 − 17)	–	0.7
SCI-QoL	*13*	3 (IQR 0–6)	*13*	1 (IQR −2 − 3)	–	0.3
PGI-I	*13*	3 (IQR 3–4)	*13*	3 (IQR 3–4)	–	0.9

PFMT, pelvic floor muscle training; IVES, intravaginal electrical stimulation; ICIQ-UI-SF, International Consultation on Incontinence Questionnaire Urinary Incontinence Short Form; OUP, opening urethral pressure; ICIQ-OAB, International Consultation on Incontinence Questionnaire Overactive bladder; SCI-QoL, International Spinal Cord Injury Quality of Life Basic Data Set; PGI-I, Patient Global Impression of Improvement, where 1 = very much better, 2 = much better, 3 = a little better, 4 = no change, 5 = a little worse, 6 = much worse and 7 = very much worse

Results are calculated by subtracting follow-up values (week 24) from pre-treatment values (week 0) and presented as mean (95% confidence interval) or median (IQR, interquartile range). [a] Analysis of covariance (ANCOVA) was adjusted for the baseline value. *Significant change by paired t-test. [$] Significant change by paired Wilcoxon signed rank test

by 85% in the electrical stimulation group and 47% in the PFMT group. In comparison, the reduction in UI episodes was 25% in the PFMT group and 3% in the PFMT+IVES group in our study. In fact, PFMT+IVES was less effective than PFMT in most parameters, which could be due to suboptimal performance of PFMT while handling an electrical device and holding a vaginal probe in place simultaneously. The increase in OUP after intervention represents an objective measure of improved strength of the PFMs, which is known to reduce stress UI. The superior effect of PFMT compared with PFMT+IVES on OUP is in agreement with studies showing that the effect of IVES is inferior [8] or equal to PFMT [9] in able-bodied women with stress UI.

Some studies conducted in able-bodied women with urgency UI have shown that low-frequency IVES effectively reduces urgency UI/symptoms and increases bladder capacity, comparable to the effect of anticholinergic medication [11–13]. In a study by Ozdedeli et al., IVES reduced daily UI episodes from 1.7 to 0.3, reduced the number of urgency episodes from 4.7 to 1.7 and increased the maximal cystometric bladder capacity from 329 ml to 442 ml with an effect comparable to trospium hydrochloride [12]. In our study, we found no significant changes from baseline in the number of daily voiding episodes in the mean and maximal bladder capacity or in the ICIQ-OAB score in the IVES+PFMT group, demonstrating a lack of effect of IVES on the urgency-associated outcomes. A significant reduction of the ICIQ-OAB score was found in the IVES group at the 24-week follow-up compared with baseline, but given the fact that there was no effect at the 12-week follow-up and that IVES was not applied from week 12–24, this was more likely due to effective post-intervention PFMT.

It could be argued that the effect of IVES was obscured by the heterogeneity in the study population regarding types of UI. Consequently, we conducted a sub-analysis including only the women with urgency or mixed UI, but no differences between the groups or changes from baseline at 12 weeks in urgency-associated outcomes were found in the IVES+PFMT group.

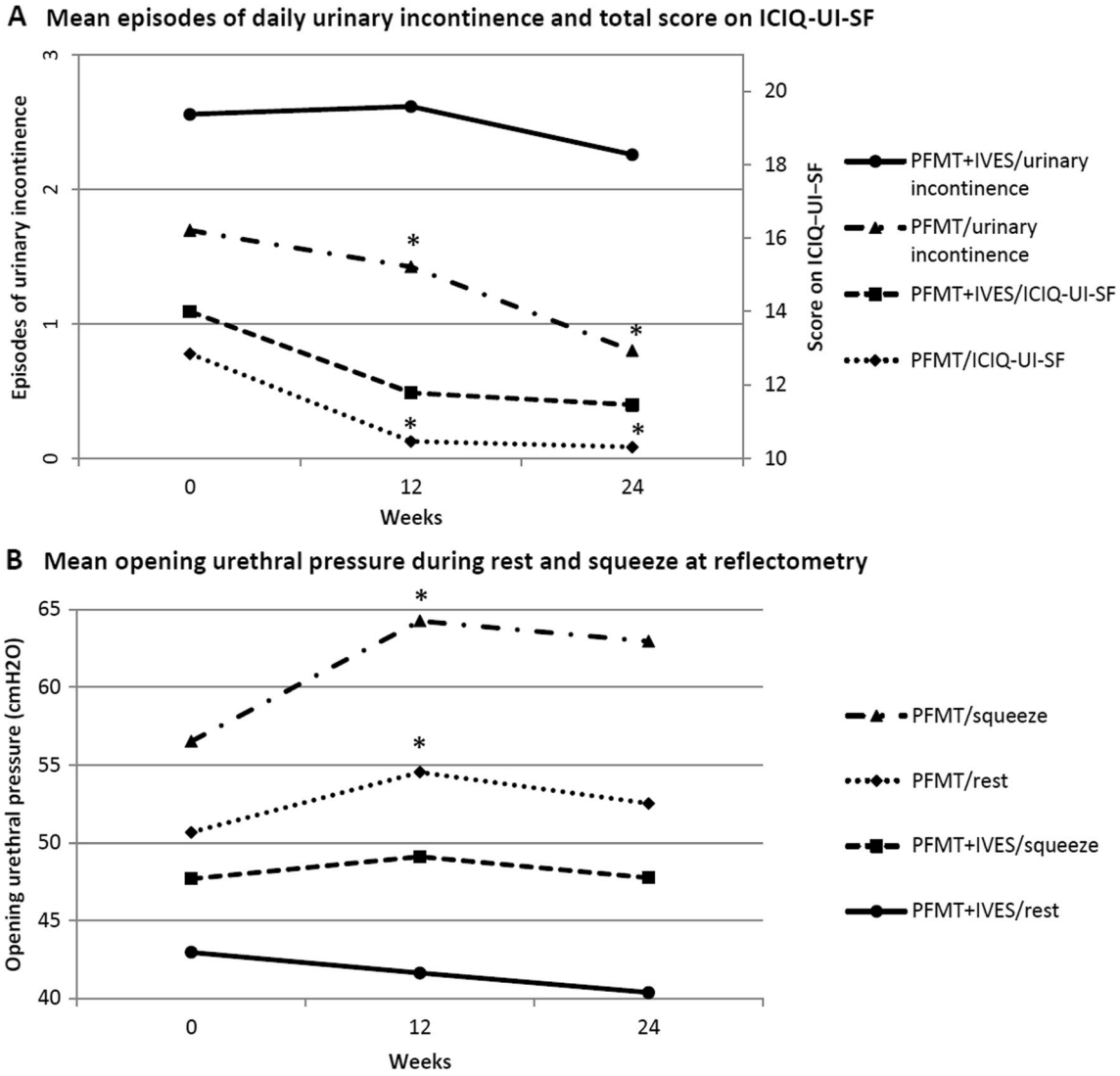

Fig. 2 Mean outcome measures at week 0, 12 and 24. Data are analyzed with paired t-test, comparing outcome measures at week 0 with week 12 and 24 according to intervention group. *$p < 0.05$. ICIQ-UI-SF, International Consultation on Incontinence Questionnaire urinary incontinence short form; PFMT, pelvic floor muscle training; IVES, intravaginal electrical stimulation

IVES is a more time-consuming treatment than PFMT, requiring 17–30 min of dedication daily compared with 7.5–10 min of PFMT. In addition, PFMT is a more accessible treatment than IVES, which requires removal of clothes to insert the vaginal probe, a private setting and good hand function to operate the devices. Further, the costs of IVES are higher than the costs of PFMT. Given these circumstances and the fact that there were no additional effects of IVES on UI compared with PFMT alone, the authors of this study cannot recommend the use of IVES in incomplete SCI women.

The statistically significant difference of 2.4 points at 12 weeks and 2.5 points at 24 weeks on the primary outcome, ICIQ-UI-SF, after PFMT was much lower than the estimated minimally important difference (MID) of 5 points used in the sample size calculation. However, the MID was suggested in a study evaluating midurethral sling operations in stress UI women [25], which would be expected to have a greater effect than a conservative treatment like PFMT. A study published after the sample size calculation was conducted suggests an MID of 2.52 (SD 2.56) after PFMT in stress UI women [26], which is comparable to the difference found in our study. When conducting a sample size calculation with an MID of 2.52 (SD 2.56), 17 women in each group should be included to detect a relevant change in ICIQ-UI-SF, which is more than we included in the study. However, as the significant difference between the groups in resting OUP and the nonsignificant differences between the groups in almost all parameters were in favor of the PFMT group, and not the IVES+PFMT group as expected, a true benefit of PFMT+IVES was not overlooked in this study because of a small sample size. Nevertheless, a significant reduction of 2.5 points on ICIQ-UI-SF and approximately 0.5 UI episodes after PFMT is a

limited effect, which should be considered when advising a woman with SCI about PFMT as treatment of UI.

The strengths of this study are its novelty and the randomized investigator-blinded design. Other strengths include the use of the validated and standardized questionnaire, ICIQ-UI-SF, and the use of the objective outcome measure, UPR.

A limitation of this study is the fact that the effect of PFMT was not compared with a placebo group. Due to a limited number of SCI women with UI living in Denmark, the authors decided not to include a placebo group in the study. Another limitation of this study is the differences in the baseline parameters between the two groups, despite the randomized design of the study. To minimize the differences, parametric data were analyzed with ANCOVA, adjusting for the baseline values. Finally, as the training interventions were conducted at home without supervision, compliance with the training program could have been lower than reported in the training diaries.

Conclusion

IVES with PFMT is not superior to PFMT alone in reducing UI, and PFMT should be recommended as the first-line conservative treatment of UI in women with incomplete SCI.

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Compliance with ethical standards

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