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ORIGINAL ARTICLE

Randomized trial of a comparison of rehabilitation or drug therapy for urgency urinary incontinence: 1-year follow-up

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Abstract
Introduction and hypothesis Our goal was to compare the long-term efficacy of bladder training (BT), pelvic floor muscle training (PFMT), combined pelvic floor rehabilitation (CPFR), and drug therapy (DT) in patients with urgency urinary incontinence (UUI).
Methods This multicenter single-blind randomized controlled trial compared the efficacy of BT, PFMT, DT, and CPFR at baseline and 3- and 12-month follow-ups. Outcome measures included number of voids/24 h, number of UUI episodes, Quality of Life related to UUI (QOL-rUI), urogynecologic visual analog scale, and self-reported function and disability.
Results A significant improvement was found for all treatment groups at 3 and 12 months in urinary frequency, UUI episodes, QOL-rUI, and number of daily pads. Only CPFR showed a significant decrease of 4 voids/24 h and a significant increase in self-reported function.
Conclusions The study demonstrated long-term benefits of DT, BT, PFMT, and CPFR in the treatment of UUI with a slight advantage for CPFR.

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Keywords Bladder training · Drug therapy · Long-term efficacy · Pelvic floor rehabilitation · Pelvic floor muscle training · Urgency urinary incontinence

Abbreviations

DT	Drug therapy
BT	Bladder training
CPFR	Combined pelvic floor rehabilitation
LLFDI	Late-Life Function and Disability Instrument
PFMT	Pelvic floor muscle training
QOL-rUI	Quality of Life related to UUI
SUI	Stress urinary incontinence
UI	Urinary incontinence
UUI	Urgency urinary incontinence

Introduction

Urgency urinary incontinence (UUI) is defined as a complaint of involuntary loss of urine associated with urgency [1]. Women with UUI tend to suffer a decrease in quality of life (QOL) more than those with stress urinary incontinence (SUI) because the leakage is unexpected, sudden, and often of large volume. UUI is associated with worse QOL and depression, poorer quality of sleep, worse sexual function, and lower work productivity compared to matched controls [2]. The prevalence of UUI increases with age [3] and in the geriatric age group is associated with increased social isolation, functional decline, risk of falls, and admission to long-term care facilities [4].

Efforts have been made to find an optimal long-term treatment for UUI that would reduce symptoms and show minimal side effects. Bladder training (BT) and drug therapy (DT) have shown better results than no treatment or placebo treatment for UUI [5, 6]. BT lasting for a minimum of 6 weeks is recommended as first-line treatment for women with UUI, and DT is recommended if BT has been

ineffective [7]. Voluntary pelvic floor muscle (PFM) contractions may be used to control urgency and UUI by inhibiting the detrusor contraction and thus reducing the patient's urgency to void [8]. Previous studies found no differences in outcomes between various protocols of DT with and without BT and PFM training (PFMT) [9, 10]. Only one study which compared short-term outcomes of DT to BT and PFMT for women aged over 55 with UUI and SUI found that BT and PFMT were more effective [11]. Short- and long-term outcomes were compared between DT and pelvic floor rehabilitation that combines BT and PFMT in treating UUI and found that combined rehabilitation was more effective [12, 13]. The question whether a PFMT protocol [14], BT [15], or DT treatments [9] for women with UUI are clinically effective in the short, medium, and long term remains unanswered. Therefore, the purpose of this study was to compare long-term clinical efficacy of four conservative treatment protocols: DT, BT, PFMT, and combined pelvic floor rehabilitation (CPFR). Based on a previous study [12] we hypothesized that CPFR that includes BT, PFMT, and behavioral advice would be more effective in the long term than the other protocols investigated in treating women with UUI symptoms.

Materials and methods

Women with overactive bladder (OAB) symptoms who showed an interest in participating in this randomized single-blind controlled trial were recruited from Maccabi Healthcare Services (Maccabi). Women were recruited through invitation letters that were sent to 30,000 potential candidates randomly selected from a population of 520,000 women aged 45–75. Only women with UUI symptoms who were diagnosed by healthcare professionals and fulfilled the inclusion and exclusion criteria were recruited. The UUI definition was based on that of Coyne et al. [16] in which women were asked about episodes of urinary frequency, degree of bother, and incidence of incontinence. Inclusion criteria were: women aged 45–75 who experienced at least three episodes of UUI that were not completely explained by SUI symptoms over the previous 4 weeks [16]. Exclusion criteria were: not being independent, contraindications to DT, current urinary tract infection, neurological disease, diagnosed with psychiatric or depressive disorder, previous pelvic floor surgery, and previous pelvic floor physical therapy.

All subjects provided informed consent in accordance with procedures approved by the Institutional Review Board of Maccabi (Clinical Trials Registration number NCT00498888). Women who showed an interest in participating in the study underwent a brief telephone interview regarding their urinary incontinence and health status before further testing was performed. Woman found eligible to participate following the interview received the study's protocol and bladder diary by regular mail or by electronic mail. Eligible candidates who agreed to participate were asked to obtain a referral for physical therapy from their physician, as requested by Maccabi regulations, followed by individual assessment and vaginal digital palpation by the principle investigator (RK). Inclusion criteria were: PFM contraction, Oxford strength scale ≥2 [8], and no vaginal prolapse. Patients also underwent ultrasound bladder scan (BladderScan® BVI 6400, Diagnostic Ultrasound, Bepex Ltd., Herzliya, Israel) to verify residual urine volume, which according to inclusion criteria was less than 100 ml [7]. Women who did not match these criteria were excluded from the study and offered standard treatment.

Procedures

The study was comprised of baseline examination (t0), post-testing examination after 3 months of treatment (t1), and 12-month follow-up (t2). Patients from the BT, PFMT, and CPFR groups had four visit appointments, once every 3 weeks, with 1 of 20 female physical therapists who specialized in pelvic floor rehabilitation. These therapists were from 15 different physical therapy clinics from 5 geographical districts of Maccabi. Each visit lasted 50 min. To ensure standardization of all study procedures, training meetings were conducted by the principle investigator for all participating therapists before and during the trial.

Randomization and blinding

After baseline examination, patients were randomly allocated to one of the four study groups by randomly permuted blocks of four, with random assignment concealed in tamper-proof envelopes. The assignment was enclosed in sequentially numbered sealed envelopes by a person not involved in the study. The examiner was blinded to the participant's allocation; however, the participants were not blinded to the group allocation. To minimize the likelihood of assessor bias [17], participants were asked not to discuss their treatment and/or reveal any information on group allocation to the principal investigator doing the assessments.

Intervention

The four treatment protocols (DT, BT, PFMT, or CPFR) were based on previously conducted research, representing "real-life" care [7, 9]. To test the study procedures, a pilot study of 20 patients was conducted by RK without blinding.

Drug therapy (DT)

Women were provided a 3-month free of charge supply of tolterodine SR 4 mg (Detrusitol SR 4 mg, Pfizer

Pharmaceuticals Israel Ltd.) [5]. The compliance with taking medication was tracked by collecting the blister packs that were used during the trial.

Bladder training (BT)

The BT protocol [6] aimed at increasing the time interval between voids, either by a predetermined or self-adjusted schedule, so that incontinence was ultimately avoided. BT was comprised of three components: (1) patient education on bladder function and on how continence is usually maintained; (2) scheduled voiding using a prefixed or flexible timetable, guiding participants to increase intervals between voids—the aim was to achieve an interval of 3–4 h between voids; and (3) positive reinforcement through psychological support and encouragement [6]. A frequency volume chart [18] was completed between appointments to record time and volume of voids per 24 h.

Pelvic floor muscle training (PFMT)

The PFMT protocol was based on the National Institute for Health and Clinical Excellence recommendations [7]. At each appointment, the women practiced 3 sets of 8–12 slow maximal contractions sustained for 6–8 s in different functional body positions, progressing from lying to standing. The maximum prescribed PFMT duration progressed to 10 s of contractions followed by 10 s of relaxation. Participants then continued a daily PFMT home-based program and recorded their home exercise sessions using an exercise log. Participants were also taught to contract these muscles repeatedly to diminish urgency and prevent UI as suggested by Burgio et al. [19] and perform contractions prior to and during physical stress [7].

Combined pelvic floor rehabilitation (CPFR)

The CPFR protocol included BT, PFMT, and behavioral advice, including bowel education to avoid constipation, advising modification of fluid intake, daily activity, and ergonomic consultation [7, 20]. Bladder diaries were completed between appointments to record time and volumes of voids per 24 h [18].

Outcome measures

Primary outcome measures were number of voids per 24 h, voided volume, incontinence episodes and fluid intake as recorded in the bladder diary [2, 18, 21], and self-recording of UUI episodes during the previous week [12, 13]. Secondary outcome measures were improvement in QOL, as measured by the QOL related to UUI (QOL-rUI) questionnaires [12, 22]. QOL-rUI instruments were:

1. Incontinence Quality of Life (I-QOL), a condition-specific instrument designed to measure the QOL effects of UI in women. The I-QOL contains 22 items with a 5-point Likert-type response scale yielding a total score and three subscale scores (i.e., avoidance and limiting behaviors, psychosocial impacts, and social embarrassment) with good to excellent test-retest reliability [intraclass correlation coefficient (ICC) 0.83–0.93] [23].
2. Visual analog scale (VAS) in urogynecologic research, which requires the respondent to place a mark on a 100-mm line to indicate the degree to which a certain attribute is present. The VAS has been well studied in the context of pain and found to be valid and reliable (ICC 0.78–0.94) [24, 25].
3. Incontinence Severity Index (ISI), consisting of two questions regarding frequency (four levels) and amount (three levels) of leakage. The validity of the ISI has been demonstrated for different types of UI and has received the highest recommendation from the 2nd and 3rd International Consultation on Incontinence [26].
4. Information on number of pads used during the past week, and a selection from a list of ten symptoms that are known to be related to UI or DT: dry mouth, constipation, sleepiness, fatigue, vision disturbances, dizziness, difficulties in urination, difficulties in breathing, headache, and low back pain.
5. Self-reported Late-Life Function and Disability Instrument (LLFDI), a self-reported scale specifically designed to assess two distinct outcomes: function and disability. Test-retest ICCs ranged from good to excellent (0.77–0.90) for the function component and fair to good for the disability component (0.63–0.83) [27]. The term function refers to a person's ability to perform specific activities with the lower and upper extremities that require gross or fine motor actions. Disability refers to the person's limitations in the performance of socially defined life tasks which are expected of an individual within a typical sociocultural and physical environment. Women with UUI are known to have decreased lower extremity function scores compared to healthy controls [22].

Sample size estimation

The sample size was calculated based on the primary outcome measure: the reduction of voids per 24 h. The median reduction of 3 voids/24 h was suggested to be clinically important for treating OAB symptoms [21]. The number of subjects required to detect a reduction of 3 voids/24 h was calculated. A significance level of 0.05 and 80 % power was

chosen for a clinically meaningful result, with estimation performed two-sided, resulting in a need for 45 women in each group for a total of 180 women and an expectancy of attrition rate of about 10 % [5].

Statistical analysis

Baseline characteristics of all study groups were compared using one-way analysis of variance (ANOVA) or Kruskal-Wallis U test when data were not normally distributed (Shapiro-Wilk statistic). To test the hypothesis that the CPFR program was beneficial (1) during the first 3 months (t0 to t1) and (2) during the 12-month follow-up in comparison with baseline measurements (t0 to t2), we applied mixed effect models for repeated measures to evaluate within group and between group differences. We applied a separate model where the dependent variables were: number of voids per 24 h, self-recording of UUI episodes during the previous week and the QOL-rUI and LLFDI questionnaires (a continuous one), while the independent variables were categorical: the study groups (DT vs BT vs PFMT vs CPFR), time (t0, t1, and t2), and the interaction effect between group and time. A within-group comparison between treatment and control periods (change in scores from t0 to t1 and t0 to t2) was performed using a Wilcoxon signed rank test if clinical benefit was found for one of the groups over time. The *p* values reported are based on two-sided comparisons. A *p* value of 0.05 was considered statistically significant.

For the primary outcomes, effect size (ES) of Hedge's *g* was calculated by dividing the difference between the means of CPFR and DT groups by the t0 standard deviation of 83 women of these two groups. The following guidelines were used when interpreting ES magnitudes: 0.0–0.2, 0.2–0.5, and 0.5–0.8 were considered small, moderate, and large, respectively [28]. All data were analyzed by intention to treat methodology. For participants who dropped out from

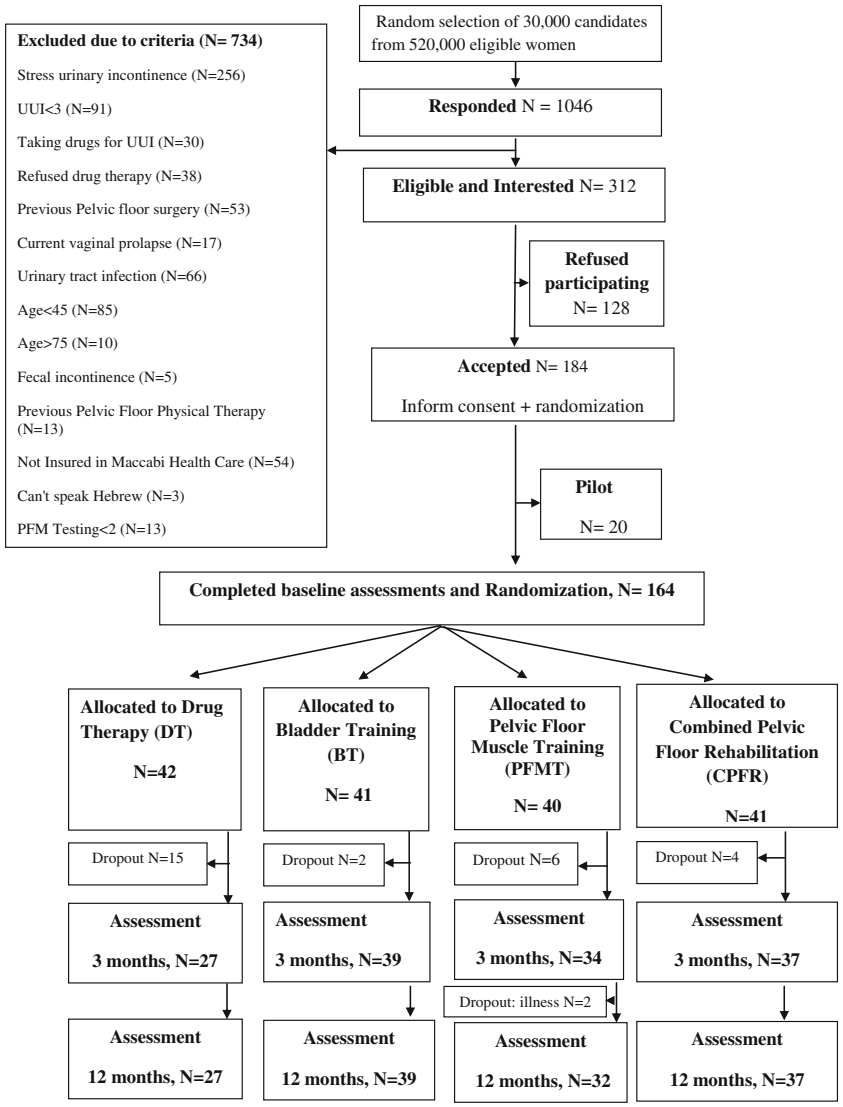

Fig. 1 Study design and flow of participants through each stage of the trial

the study, the last value available was carried forward to account for missing data [11]. Statistical analyses were performed using SPSS Statistics version 15 (SPSS Inc., Chicago, IL, USA).

Results

Recruitment

Of the 30,000 women to whom invitation letters were sent, 1,046 were interested in participating in the study and were screened for the trial; 734 were excluded because they did not meet the inclusion criteria. Of the remaining 312 women that were eligible for the study, 128 refused to participate in the randomized controlled trial protocol, resulting in 184 who signed the informed consent prior to treatment (Fig. 1). Comparison of age between women who received invitations and participated (n=184, age=56.7, SD=8.0, range=45–75) to those who did not participate in the study (n=29,816, age=56.0, SD=7.9, range=45–75) yielded no significant difference (p=0.638). The first 20 women who were recruited and participated in the pilot study were not included in the final analyses, leaving 164 valid cases for final analysis. The retention rate was 83.5 % at 3 months and 82 % at the 1-year follow-up.

Baseline data

No statistically significant differences were found between the four treatment groups in baseline demographic and health characteristics (Table 1). Baseline variables, including age, parity, body mass index, and number of UUI per week were not significantly associated with retention of participants at 3 months, but number of voids per 24 h (p=0.048) and number of pads per week (p=0.031) were significantly lower in retained subjects.

Outcome data

All four treatment groups showed significant improvement over the study period with a significant main effect for time for all primary and secondary outcomes. No significant interaction effects between group and time were found for all primary and secondary outcomes, suggesting similar trends of change over time between all four treatment groups (Table 2). However, between-group comparison showed that a decrease of more than 3 voids/24 h occurred only in the CPFR group (−3.4 at t1 and −4 at t2) (Table 3), with a moderate ES (0.35) compared with the DT group.

Also, although the time × treatment groups interaction effect was not significant for the number of UUI-related

Table 1 Patient characteristics at baseline (n=164)

Characteristics	Full sample, n=164	DT, n=42	BT, n=41	PFMT, n=40	CPFR, n=41	p value
Demographic characteristics						
Age	56.7±8.0	57.1±9.0	57.2±8.2	56.4±7.1	56.2±7.8	0.963
Education (years)	14.4±3.0	14.1±3.3	14.6±3.2	14.8±2.7	14.2±2.9	0.605
Number of births	2.7±1.5	2.6±1.7	2.8±1.4	2.4±1.3	2.9±1.3	0.371
Married	121 (73.8 %)	32 (76.2 %)	30 (73.2 %)	29 (72.5 %)	30 (73.2 %)	0.892
Health characteristics						
Body mass index	28.2±5.8	28.0±5.8	28.9±6.3	27.0±3.6	29.0±6.8	0.694
Smoking	18 (11 %)	6 (14.3 %)	5 (12.2 %)	5 (12.5 %)	2 (4.9 %)	0.537
Diabetic drug use	8 (4.9 %)	1 (2.4 %)	2 (4.9 %)	2 (5 %)	3 (7.3 %)	0.781
High blood pressure drug use	25 (15.2 %)	7 (16.7 %)	7 (17.1 %)	7 (17.5 %)	4 (9.8 %)	0.735
Previous abdominal surgery	77 (47 %)	24 (57.1 %)	22 (53.7 %)	13 (32.5 %)	18 (43.9 %)	0.923
Postmenopausal	120 (73.2 %)	31 (73.8 %)	29 (70.7 %)	29 (72.5 %)	31 (75 %)	0.967
Hormone replacement therapy	7 (4.3 %)	1 (2.4 %)	1 (2.4 %)	2 (5 %)	3 (7.3 %)	0.642
Physically active	110 (67.1 %)	25 (59.5 %)	28 (68.3 %)	24 (60 %)	33 (80.5 %)	0.149
Fall last year	24 (14.6 %)	3 (7.1 %)	8 (19.5 %)	7 (17.5 %)	6 (14.6 %)	0.377
Dry mouth	60 (36.6 %)	12 (28.6 %)	14 (34.1 %)	15(37.5 %)	19 (46.3 %)	0.400
Constipation	36 (22 %)	6 (14.3 %)	11 (26.8 %)	11 (27.5 %)	8 (19.5 %)	0.410
Fatigue	105 (64 %)	23 (54.8 %)	26 (63.4 %)	28 (70 %)	28 (68.3 %)	0.470
Headache	45 (27.4 %)	8 (19 %)	13 (31.7 %)	15 (37.5 %)	9 (22 %)	0.210
Low back pain	59 (36 %)	11 (26.2 %)	13 (31.7 %)	18 (45 %)	17 (41.5 %)	0.262

Values represent mean ± SD for continuous data and n (%) for categorical data. All p values are based on the Kruskal-Wallis test for continuous variables and chi-square test for categorical variables

Table 2 Outcome measures by time and treatment groups

Outcome measures	Treatment group	Measurements			ANOVA (t0-t2)	
		t0	t1	t2	Time	Time × treatment group
Number of voids/24 h	DT	12.6±4.4	11.3±4.4	10.5±5.6	F=32.915 (p<0.001)	F=1.657 NS (p=0.131)
	BT	11.7±3.8	9.7±3.1	10.0±4.4		
	PFMT	11.5±3.7	9.6±3.9	9.5±4.3		
	CPFR	12.6±6.3	9.2±3.2	8.6±3.4		
Number of UUI episodes/week	DT	9.2±11.9	3.6±5.0	5.2±11.4	F=18.496 (p<0.001)	F=0.889 NS (p=0.503)
	BT	5.7±6.1	3.9±5.2	2.8±3.9		
	PFMT	6.3±7.9	3.8±6.6	3.0±6.2		
	CPFR	6.5±7.5	2.8±3.8	3.0±4.7		
I-QOL instrument	DT	66.1±21.1	82.5±23.1	86.5±22.3	F=91.912 (p<0.001)	F=0.981 NS (p=0.438)
	BT	76.3±20.6	89.6±21	88.1±24.3		
	PFMT	72.7±22.0	87.4±22.6	90.1±20.6		
	CPFR	71.9±21.2	89.1±17.8	89.4±19.1		
Visual analog scale	DT	7.2±2.0	4.8±3	4.0±3.1	F=114.232 (p<0.001)	F=1.233 NS (p=0.289)
	BT	7.3±2.0	4.8±3.4	4.3±3.3		
	PFMT	6.7±2.5	4.3±3.3	4.1±3.3		
	CPFR	7.2±2.6	3.6±3	3.3±2.9		
Number of UUI-related symptoms	DT	2.0±1.9	2.2±2.0	1.7±1.4	F=8.759 (p<0.001)	F=1.177 NS (p=0.318)
	BT	2.5±2.0	1.9±1.8	1.7±1.6		
	PFMT	2.7±1.8	2.3±1.9	2.2±1.8		
	CPFR	2.7±1.5	2.0±1.7	2.1±1.5		
Number of pads/week	DT	17.7±16.0	13.6±15.4	13.2±13.1	F=15.102 (p<0.001)	F=0.378 NS (p=0.893)
	BT	12.4±11.1	10.4±10.4	9.9±11.1		
	PFMT	17.8±31.6	15.1±31.8	13.2±31.7		
	CPFR	13.7±13.6	9.7±8.9	8.3±8.3		
ISI	DT	6.5±3.5	3.8±3.2	4.1±3.0	F=57.782 (p<0.001)	F=0.294 NS (p=0.939)
	BT	6.7±3.3	4.3±3.3	4.3±3.8		
	PFMT	5.4±3.6	3.4±3.6	2.9±3.0		
	CPFR	6.4±3.3	3.7±3.2	3.9±3.4		
Disability component-overall limitation	DT	75.6±16.9	77.4±15.9	79.7±21.6	F=14.374 (p<0.001)	F=0.797 NS (p=0.573)
	BT	71.7±13.3	75.7±13.8	77.0±14.6		
	PFMT	71.4±17.7	78.1±17.3	77.4±16.8		
	CPFR	68.3±12.7	76.8±15.0	75.3±17.1		
Function component-overall function	DT	72.0±7.7	72.7±9.2	75.4±3.0	F=8.252 (p<0.001)	F=1.370 NS (p=0.226)
	BT	71.3±10.9	72.1±12.5	73.1±13.8		
	PFMT	69.6±10.2	71.7±12.1	70.6±12.2		
	CPFR	66.4±10.1	70.4±12.6	70.3±13.9		

ANOVA with repeated measures for all outcomes measures with main effects of treatment groups (DT, BT, PFMT, and CPFR) and time (t0, t1, and t2) and the interaction effect between group and time. Values are means ± SD. Statistical significance was set at p<0.05

t0 baseline, *t1* 3 months, *t2* 12 months, *DT* drug therapy, *BT* bladder training, *PFMT* pelvic floor muscle training, *CPFR* combined pelvic floor rehabilitation, *I-QOL* Incontinence Quality of Life, *ISI* Incontinence Severity Index, *NS* not significant

symptoms (p=0.318), a significant decrease in symptoms was found in the BT and CPFR groups at t1 and t2 (Table 3). Other outcomes that had within-group differences with time (even while the overall time × group interaction effect was not significant) were identified. The overall limitation disability component of the LLFDI showed a significant improvement for all physical therapy groups (BT, PFMT, and CPFR) but not for DT. Self-reported function related to improvement in lower extremity function was identified at t1 and t2 in the CPFR group only (Table 3). The maximum bladder void, from the 24-h bladder diary was normal in all groups (mean range of 325–420 ml) with no significant differences between and within groups.

Table 3 Changes from baseline to t1 and t2 for outcome measures

Outcome measures	Treatment group	t1	t2
Number of voids/24 h	DT	−1.3[a]	−2.1[b]
	BT	−2.0[a]	−1.7[b]
	PFMT	−1.9[a]	−2.0[b]
	CPFR	−3.4[a]	−4.0[b]
Number of UUI episodes/week	DT	−5.6[a]	−4.0[b]
	BT	−1.8[a]	−2.9[b]
	PFMT	−2.5[a]	−3.7[b]
	CPFR	−3.3[a]	−3.5[b]
Number of UUI-related symptoms	DT	+0.2	−0.3
	BT	−0.6[a]	−0.8[b]
	PFMT	−0.4	−0.5
	CPFR	−0.7[a]	−0.6[b]
Disability component-overall limitation	DT	+1.8	+4.1
	BT	+4.0[a]	+5.3[b]
	PFMT	+6.7[a]	+6.0[b]
	CPFR	+8.5[a]	+7.0[b]
Function component-overall function	DT	+0.7	+3.4
	BT	+0.8	+1.8
	PFMT	+2.1[a]	+1.0
	CPFR	+4.0[a]	+3.9[b]

Values are mean ± SD. A decrease in outcome scores indicates an improvement in status. Within-group analyses were performed only on those measures for which a clinical benefit was found for one of the groups. Statistical significance was set at $p<0.05$

DT drug therapy, *BT* bladder training, *PFMT* pelvic floor muscle training, *CPFR* combined pelvic floor rehabilitation

[a] Significant differences within groups comparing post-intervention (t1) and baseline periods (t0) (Wilcoxon signed rank test)

[b] Significant differences between follow-up (t2) and baseline periods (t0) (Wilcoxon signed rank test)

Treatment adherence and adverse effects

The reported adherence to physical therapy treatment (BT= 85 %, PFMT=90 %, and CPFR=95 %) was significantly higher than the compliance in DT (64 %) (p=0.01) at 3-month follow-up assessment. Dropouts were defined as participants who took either less than three monthly packs of DT or attended less than three appointments with the physical therapist [19]. Reasons for dropout from the DT group included 13 women who were unsatisfied with their group allocation; acute back pain (1 woman) and dizziness (1 woman). Two women withdrew from BT because of their medical condition (one woman) and no response to treatment (one woman). Six women withdrew from PFMT due to their medical condition (one woman) and no response to treatment (five women), with an additional two women withdrawing because of their medical condition at 1 year. Four women withdrew from the CPFR because of no response to treatment (Fig. 1).

Discussion

The main purpose of this study was to compare the clinical effectiveness of four conservative treatment protocols including drug therapy and three different types of pelvic floor rehabilitation. Our findings partially support our main hypothesis. Although all four treatment groups showed significant improvements over time in UUI episodes, 24 h frequencies, and measures related to UUI QOL, the CPFR that includes BT, PFMT, and behavioral advice showed a slight advantage in voiding frequency, number of UUI-related symptoms, and self-reported function compared to other protocols. We consider the decrease of more than 3 voids/24 h seen in the CPFR group to be clinically relevant [21]. To the best of our knowledge, this is the first study to report concurrent improvements in the CPFR group at the end of 3 and 12 months of follow-up in voiding frequency, number of UUI-related symptoms, and self-reported function of daily life.

At the present time, our results cannot be supported by studies on populations with OAB [10] or UUI with SUI [9, 11, 19, 29], but are consistent with the follow-up results of our first parallel clinical trial [12]. In addition, our rigorous standardized treatment protocols are reproducible compared to previous studies that varied in drug treatment dosage [9, 11, 29], behavioral protocol which depended on achieving at least 50 % reduction in frequency [11], or schedule which was determined jointly by the patient and therapist [9]. A Cochrane Review [14] suggested that more attention in terms of time has a positive effect on treatment outcomes. In the present study all participants received similar exposure to physical therapy or to their physician. Thus, our protocols addressed several potential biases which affected previous studies.

Our study found no significant interaction effects of group and time for all primary and secondary outcomes, suggesting occurrence of similar changes over time between all four treatment groups. The observed findings could be interpreted in two ways: (1) improved UUI symptoms may represent natural recovery or (2) all four interventions are equally effective. The first explanation cannot be completely excluded, although a recent study [11] utilizing the same treatment concepts based on 8 weeks of behavioral or drug treatment determined they were more effective than placebo control and in another study PFMT was more effective than placebo in the treatment of urinary incontinence at the 1-year follow-up postpartum [30], supporting the interpretation of equally effective treatments.

The position of the National Institute for Health and Clinical Excellence and the International Continence

Society [1, 2, 7] is that idiopathic UUI women require treatment to relieve their symptoms; thus not treating UUI patients would be an ethically problematic approach. Based on recent Cochrane Reviews [6, 8, 14] that found very little data available regarding long-term benefits of BT, PFMT, or DT [5] in treating UUI, our data support the guidelines [2, 7] of behavioral therapy including PFMT and BT as first-line treatment for UUI symptoms.

The dropout rate in this study of 29/164 (18 %) during 1 year of follow-up is similar to the 19 % dropout rate reported earlier [9]. The DT group had a significantly higher dropout rate of 35 % compared with all rehabilitation treatments (15/42, $p=0.01$), which is higher than reported by Burgio et al., i.e., 17.9 % [11]. This further supports the advantages of physical intervention as compared with drug therapy in which side effects are common (e.g., dry mouth and constipation) [2].

This study has several limitations: first, we were unable to include a control group, due to the aforementioned ethical considerations. A non-treatment group would provide further information regarding the pure influence of time. Second, we assessed volunteers; it is well known that volunteer participants tend to have higher compliance in studies that require physical activity when compared with the general population; thus the external validity of the study should be treated with caution. Third, in the present study we did not perform a global evaluation of the treatment; in some patients frequency or urgency is the most bothersome symptom, and in others UUI is the most bothersome symptom. For that reason the effect of CPFR may be overestimated as it performed best in reduction of micturition episodes rather than having an effect on the most bothersome symptoms.

In conclusion, the present study demonstrated long-term benefits of DT, BT, PFMT, and CPFR in the treatment of UUI with a small advantage for CPFR. Based on our results, CPFR can be recommended as first-line treatment to women with pure UUI, showing long-term benefits with a lower number of UUI-related symptoms. Further research is needed to examine cost-effectiveness and patient acceptability of the various treatment approaches.

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Conflicts of interest None.

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