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Original Article

The effectiveness of additional long-term use of bottle-positive expiratory pressure in chronic obstructive pulmonary disease: A single-blind, randomized study

Özge Keniş-Coşkun[1], Derya Kocakaya[2], Sefa Kurt[1], Büşranur Fındık[1], İlker Yağcı[1], Emel Eryüksel[2]

[1]Department of Physical Medicine and Rehabilitation, Marmara University Faculty of Medicine, Istanbul, Türkiye
[2]Department of Pulmonology, Marmara University Faculty of Medicine, Istanbul, Türkiye

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ABSTRACT

Objectives: This study aimed to investigate the long-term use of bottle-positive expiratory pressure (PEP) in addition to breathing exercises as a home-based rehabilitation aid on exercise capacity, spirometric parameters, and quality of life in chronic obstructive pulmonary disease (COPD) patients.

Patients and methods: From a total of 30 patients with stable moderate-to-severe COPD, 24 (22 males, 2 females; mean age: 62.4+7.2 years; range, 40 to 75 years) were included in the final study and randomized into two groups: the group that performed breath retaining techniques and the group that was instructed to use the bottle-PEP in addition to these techniques. Patients were evaluated with modified Medical Research Council scale, COPD assessment test (CAT), spirometry, St. George's Respiratory Questionnaire (SGRQ), and 6-min walk distance (6MWD) before, three months and six months after the initiation of the program.

Results: In the bottle-PEP group, patients' mean 6MWD increased from 380.6±67.6 to 444.1±22.0 m (p=0.002), the mean CAT score decreased from 17.8±36.8 to 12.9±6.2 (p=0.03), and the mean SGRQ total score significantly decreased from 57.1±23.1 to 47.6±21.9 (p<0.05) after three months. The improvement in 6MWD continued in six months but disappeared in SGRQ and CAT scores. In the exercise group, only the 6MWD improved, and there were no significant improvements in other parameters regardless of time. There were no significant differences between the groups in any of the parameters at any follow-up session.

Conclusion: While bottle-PEP does not significantly contribute when added to breathing exercises in patients with moderate-to-severe COPD in improving function and quality of life, it can be used as a safe choice in patients' home rehabilitation programs.

Keywords: Chronic obstructive pulmonary disease, quality of life, randomized trial, rehabilitation, positive expiratory pressure.

Chronic obstructive pulmonary disease (COPD) is a preventable disease characterized by an inflammatory response due to various harmful particles and gases, particularly smoking. It is characterized by irreversible and progressive airflow limitation. In COPD, airflow limitation develops as a result of small airway disease and parenchymal destruction.[1] The Global Burden of Disease Study reports a prevalence of 251 million cases of COPD globally in 2016, with deaths primarily in low and middle-income countries.[2]

In recent years, the beneficial effects of pulmonary rehabilitation programs in addition to the current medical treatments in patients with COPD have been emphasized.[3,4] Pulmonary rehabilitation is often prescribed to delay progression and provide relief

Corresponding author: Özge Keniş-Coşkun, MD. Marmara Üniversitesi Tıp Fakültesi Fiziksel Tıp ve Rehabilitasyon Anabilim Dalı, 34899 Pendik, İstanbul, Türkiye.
e-mail: ozgekenis@gmail.com

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of symptoms.[4] Various therapeutic interventions are applied to improve lung function, facilitate mucus clearance, and reduce the frequency of acute exacerbations.[5] One of the main components of the rehabilitation program in patients with COPD is airway cleaning techniques, which include conventional therapy (postural drainage, percussion, and vibration), airway cleaning through breathing techniques (cycle of active breathing techniques, autogenic drainage), positive expiratory pressure (PEP) devices (masked, mouthpiece, and oscillating), and high-frequency chest wall oscillation.[6] Positive expiratory pressure therapy applies resistance during expiration to provide PEP,[7] which improves collateral ventilation, secretion clearance, aerosol distribution, and functional residual capacity.[8] Positive expiratory pressure prevents the collapse of small airways, contributes to better gas distribution, and increases expiratory time and volume.[9] Currently, many commercial PEP devices are available. However, bottle-PEP can be used as an alternative to manufactured and marketed PEP devices since it can easily be made with low-cost parts.[10] Although there are many studies in the literature on airway clearance techniques in other pulmonary diseases with different devices, the use and effectiveness of bottle-PEP devices as a home-based rehabilitation aid in patients with COPD has not been previously investigated. Moreover, there are no data to show whether using bottle-PEP supplies additional benefit when added to an exercise program that includes breathing retaining techniques.

This study aimed to investigate the long-term use of bottle-PEP as an addition to breathing exercises as a home-based aid to improve exercise capacity, spirometry, and quality of life in the rehabilitation of patients with moderate-to-severe stable COPD.

PATIENTS AND METHODS

This single-center study was conducted between January 2019 and January 2020 in the Pulmonology and Physical Medicine and Rehabilitation Departments of Marmara University Faculty of Medicine. Thirty patients who were diagnosed with stable moderate-to-severe COPD according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria were included in the single-blind, randomized study. After recruitment, patients were randomized into two parallel groups using a computerized list that randomly allocated the patients into one of the two groups with a 1:1 ratio. However, three patients from each group could not finish the study; thus, 12 patients in each group were included in the final analyses for a total of 24 patients (22 males, 2 females; mean age: 62.4+7.2 years; range, 40 to 75 years). The patient flow chart is given in Figure 1. The exclusion criteria were receiving treatment for exacerbation of COPD, the presence of a more pronounced respiratory pathology other than COPD (for example, bronchiectasis, lung cancer), confused mental state, or neurologic disease that would prevent cooperative operation, a history of acute coronary disease or cardiac arrhythmia in the past three months, pneumothorax in the last six months, or abdominal or thoracic surgery in the previous six months, the presence of significant musculoskeletal pathology preventing the patients from performing the six-minute walk distance (6MWD) test, other conditions that might hinder the use of PEP, such as lung transplantation or orofacial surgery in the past six months, and patient refusal to participate in the study. Patients' age, sex, height, weight, body mass index, smoking history, and the time since COPD was diagnosed were recorded at recruitment.

All interventions were instructed by a trained physiotherapist at the initial visit and repeated at each control checkpoint. Patients in the first group were instructed to perform breath retaining techniques that consist of diaphragmatic breathing and thoracic expansion, each with 15 repetitions three times per day. For diaphragmatic breathing, the following verbal instructions were given during inhalation and exhalation: "perform a slow maximal inspiration allowing the air to go to your belly," and "perform a normal expiration without forcing abdominal retraction." For thoracic expansion, patients were instructed to relax their shoulders and performed a deep inspiration from resting end-expiratory volume, followed by a breath-hold of 2-3 sec and, finally, relaxed expiration. During the period of instruction, the physiotherapist gave manual pressure to the lateral chest wall to encourage the expansion of the lower chest, and patients were instructed to do the same after the initial instruction.[11,12] Patients in the bottle-PEP group were instructed to use the bottle-PEP in addition to the breath retaining techniques. The bottle-PEP is a device used in a plastic bottle with a volume of 1.5 L, by filling with water to form pressure of about 10 cmH_2O and expiration with an 80 cm tube about 8 mm thick and placed in the bottle (Figure 2). This design has been previously shown to produce the 10 cmH_2O pressure provided by the water column.[10] Bottle-PEP is used in the supine position and the lateral decubitus position in both

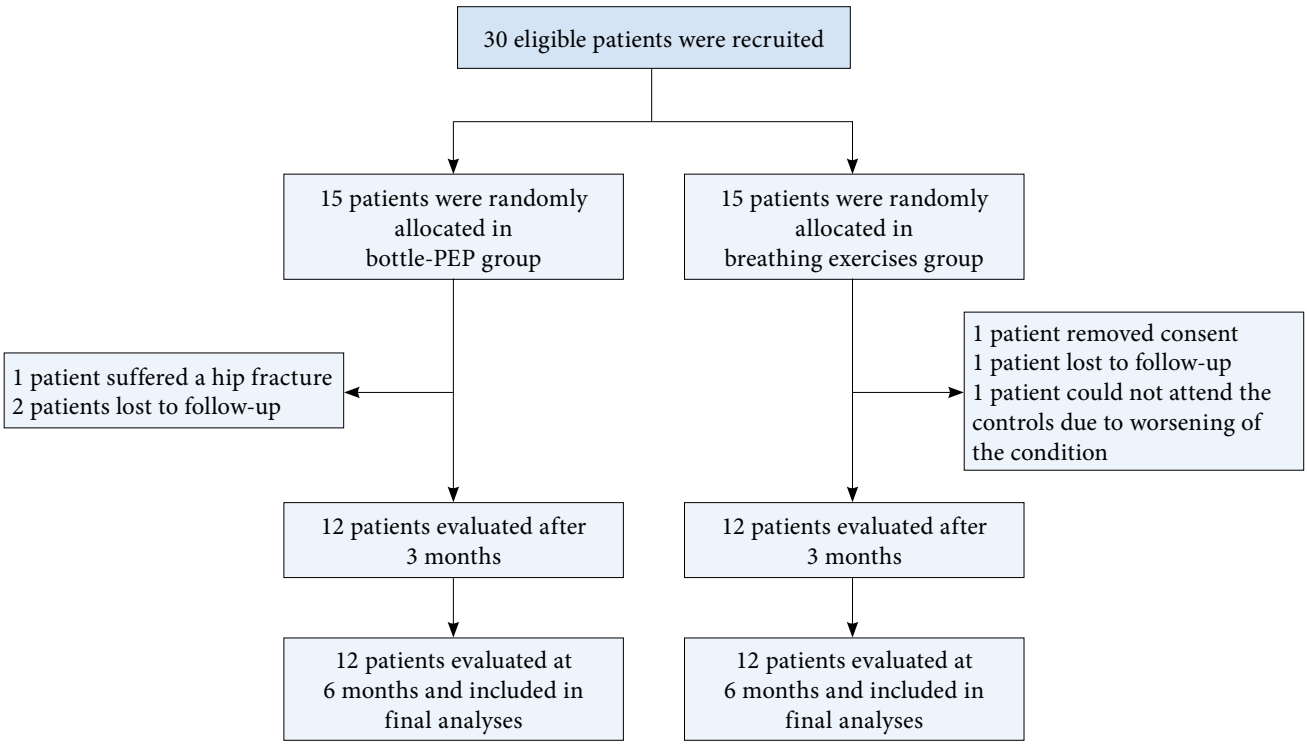

Figure 1. Patient flow chart.
PEP: Positive expiratory pressure.

directions, and five expirations are recommended in each position. Patients are recommended to use it twice every day. Patients were weekly called to be reminded about bottle-PEP use to ensure continuous application of the exercises and bottle-PEP. These weekly sessions were also used to detect any acute exacerbations during the treatment, and patients were instructed to come to the hospital if they observed signs of exacerbation during or after their exercises.

All evaluations were performed and recorded by a blinded investigator. Patients were evaluated using the modified Medical Research Council scale (mMRC), COPD assessment test (CAT), spirometry, St. George's Respiratory Questionnaire (SGRQ), and the 6MWD test before the initiation of the program and after three and six months . If any of the patients were having an exacerbation during their follow-up, their assessments were postponed for four weeks. Spirometry was performed by a flow-sensitive device (Jaeger Masterscope PC; Hoechberg, Germany) according to the American Thoracic Society/European Respiratory Society (ATS/ERS) criteria.[13] Dyspnea levels of patients were graded from 0 to 4 by using mMRC,[14] and the Turkish version of the CAT was

Figure 2. Bottle-PEP device.
PEP: Positive expiratory pressure.

applied to the patients to evaluate the degree of symptoms.[15] The 6MWD test was performed according to the ATS/ERS criteria.[16] The patients were guided to walk back and forth in a 30-m-long corridor. The total walking distance was recorded in meters. The SGRQ is a standardized self-completed questionnaire for measuring impaired health and perceived well-being (quality of life) in COPD. The total score was calculated from subcategory scores (symptoms, activity, and impact). Its scores range from 0 (no impairment) to 100 (maximum impairment). It has been previously translated to and validated in Turkish.[17]

Statistical analysis

Power analyses were performed using G*Power version 3.1, software (Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany). There are no previous studies with the exact primary outcome measurements; therefore, a similarly designed study that used 6MWD test as a secondary outcome measurement was followed as an example;[18] 11 volunteers in both groups were calculated to reach 95% power when alpha = 0.05, and the effect size was calculated as 1.47. Considering a potential drop-out rate of 20%, 15 patients were recruited for each group.[19] Other statistical analyses were performed using IBM SPSS version 22.0 software (IBM Corp., Armonk, NY, USA). There were no missing data. Basic methods were used for descriptive analyses. The distribution of the data was assessed using the Shapiro-Wilk test and Q-Q plots. The data were distributed normally. For the assessment of the effects within each group, repeated-measures analysis of variance (ANOVA) with Bonferroni correction was used. For group differences, two-way mixed ANOVA was used. A p value of <0.05 was accepted as statistically significant other than repeated measures analyses. After Bonferroni correction, a p value of <0.01666 was considered statistically significant.

RESULTS

All of the patients had chronic bronchitis phenotype except two patients in each group who had emphysema phenotype. There were no significant

TABLE 1
Demographic properties of the patients

	Bottle-PEP group (n=12)			Breath retaining group (n=12)		
	n	%	Mean±SD	n	%	Mean±SD
Mean age (year)			65.6±7.3			60.7±6.7
Mean BMI (kg/m^2)			27.0±4.3			27.1±5.4
Sex						
Male	11	91		11	91	
GOLD classification						
Class 2	6	50		5	41.6	
Class 3	6	50		3	58.4	
Initial mMRC						
mMRC 1	5	41.6		8	66.6	
mMRC 2	4	33.3				
mMRC 3	3	25		4	33.3	
Mean CAT score			17.8±6.8			16.5±11.8
Mean history of cigarette smoking (packyears)			41.1±14.2			46.8±22.4
Mean FEV_1 (%)			54.4±19.8			54.9±22.2
Mean FVC (%)			80.0±17.4			86.9±24.9
Mean FEV_1/FVC (%)			61.2±20.4			58.3±15.4
Mean six minute walk test (meter)			380.6±67.6			417.2±60.2
Mean time since diagnosis (year)			10.0±6.8			12.5±5.8
Mean time since final exacerbation (month)			11.5±18.5			14.4±24.5

PEP: Positive expiratory pressure; SD: Standard deviation; BMI: Body-mass index; GOLD: Global Initiative for Chronic Obstructive Lung Disease; mMRC: Modified Medical Research Council scale; CAT: Chronic obstructive pulmonary disease assessment test; FEV_1: Forced expiratory volume in 1 sec; FVC: Forced vital capacity.

TABLE 2
Changes within each group in three and six months

			Month 0			Month 3			Month 6		Mean difference within group			
											0 *vs.* 3 months		0 *vs.* 6 months	
	Group	Mean±SD	Mean	95% CI	Mean±SD	Mean	95% CI	Mean±SD	Mean	95% CI	Mean	95% CI	Mean	95% CI
6-minute walk test (meters)	Bottle	380.6±67.6			444.1±22.0			458.9±23.4			63.44	25.12-101.75	78.25	34.32-122.19
	P value													
	Breath retaining	417.2±60.2			445.4±52.2			446.4±56.5			28.18	14.25-42.11	29.18	10.21-48.17
	P value													
	Mean difference between groups		38.32	14.90-91.55		9.73	45.68-65.15		12.53	49.08-74.16				
	P value		0.15			0.71			0.67					
CAT score	Bottle	17.8±6.8			12.9±6.2			13.6±8.4			4.91	0.29-9.54	4.25	-1.49- 9.99
	P value											0.003*		0.18
	Breath retaining	16.5±11.8			11.8±9.3			13.5±9.6			4.72	-0.72-10.17	3.00	-4.3-10.30
	P value											0.09		0.79
	Mean difference between groups		0.41	-7.50 – 8.34		0.42	-6.29 – 7.11		-1.65	-9.51 – 6.21				
	P value		0.91			0.90			0.66					
SGRQ-total	Bottle	57.1±23.1			47.6±21.9			44.9±22.7			9.48	0.74-18.89	12.14	-1.2-25.50
	P value											0.005*		0.08
	Breath retaining	47.3±26.8			38.3±25.2			40.3±24.6			9.03	-3.13 – 21.20	7.00	-5.16 – 19.17
	P value											0.18		0.39
	Mean difference between groups		9.34	-11.47 – 30.15		7.61	-12.23 – 27.46		1.85	-18.86 – 22.57				
	P value		0.36			0.43			0.85					
SGRQ-symptoms	Bottle	72.1±19.6			65.9±19.6			66.3±19.9			6.26	-4.64 – 17.17	5.79	-5.72 – 17.30
	P value											0.4		0.55
	Breath retaining	58.0±30.3			53.3±28.2			56.4±23.2			4.67	-7.05 – 16.40	1.55	-15.03-18.14
	P value											0.83		1
	Mean difference between groups		10.88	-10.42- 32.18		10.69	-9.48 – 30.8		8.07	-10.94 – 27.09				
	P value		0.30			0.38			0.28					
SGRQ-activity	Bottle	64.7±22.8			55.6±25.2			52.9±28.0			9.13	-4.22 – 22.48	11.82	-2.85 – 26.48
	P value											0.24		0.13
	Breath retaining	54.5±22.1			46.1±20.5			49.2±18.6			8.42	-0.85 – 17.70	5.31	-8.10 – 18.72
	P value											0.08		0.84
	Mean difference between groups		10.32	-8.29 – 28.95		9.39	-9.8 – 28.59		3.11	-17.87 – 24.09				
	P value		0.26			0.32			0.76					

TABLE 2
Continued

		Month 0			Month 3			Month 6			Mean difference within group: 0 *vs.* 3 months		Mean difference within group: 0 *vs.* 6 months	
	Group	Mean±SD	Mean	95% CI	Mean±SD	Mean	95% CI	Mean±SD	Mean	95% CI	Mean	95% CI	Mean	95% CI
SGRQ impact	Bottle	48.0±26.0			37.3±23.8			33.7±23.6			10.66	-0.55-21.88	14.28	-2.52-31. 08
	P value											0.06		0.10
	Breath retaining	36.7±30.4			28.2±28.4			29.2±29.6			11.49	-6.04-29.04	10.47	-4.08-25.03
	P value											0.26		0.20
	Mean difference between groups		8.26	-15.32-31.85		6.45	-15.69-28.60		0.25	-23.10-23.62				
	P value		0.47			0.55			0.98					
FEV_1 percent	Bottle	54.4±19.8			55.3±20.7			51.5±24.0			0.95	-2.71-0.81	3.79	-14.82-22.42
	P value											0.47		1
	Breath retaining	54.9±22.2			53.0±22.9			51.5±19.5			1.87	-1.26-5.00	2.65	-6.87-14.12
	P value											0.35		1
	Mean difference between groups		2.31	-13.79-18.41		2.33	-16.12-20.79		2.08	-17.31-21.47				
	P value		0.76			0.80			0.82					
$MMEF^{25-75}$ percent	Bottle	27.7±16.8			28.0±16.7			26.3±13.7			0.30	-3.78-94.73	1.33	-2.93-5.26
	P value											0.87		0.5
	Breath retaining	22.8±14.9			22.2±15.0			25.6±15.5			0.65	0.11-1.42	2.78	2.69-8.25
	P value											0.08		0.28
	Mean difference between groups		4.35	-9.24-17.94		7.37	-5.92-20.62		3.35	-9.91-16.61				
	P value		0.50			0.28			0.60					

CI: Confidence interval; SD: Standard deviation; CAT: Chronic obstructive pulmonary disease assessment test; SGRQ: St. George's Respiratory Questionnaire-Revised * denotes significant changes. FEV1: Forced expiratory volume in 1 sec; MMEF: Maximal mid-expiratory flow; For the assessment of the effects within each group, repeated-measures ANOVA with Bonferroni correction was used. For group differences, two-way mixed ANOVA was used.

differences between the demographic properties of the groups, which can be seen in Table 1.

In the bottle-PEP group, patients' mean 6MWD increased from 380.6±67.6 to 444.1±22.0 m (p=0.002), the mean CAT score decreased from 17.8±36.8 to 12.9±6.2 (p=0.03), and the mean SGRQ total score significantly decreased from 57.1±23.1 to 47.6±2.9 (p<0.05) after three months. The improvement in 6MWD continued at six months; however, improvements in SGRQ and CAT scores did not persist. In the exercise group, only the 6MWD improved (417.2±60.2 to 445.4±52.2, p=0.001), with no significant improvements in other parameters. In the results of two-way mixed ANOVA, there were no significant interactions between the addition of bottle-PEP and 6MWD, CAT scores, SGRQ scores, or the forced expiratory volume in 1 sec (FEV_1) (p>0.05 for all parameters). Similarly, the main effect of the group did not demonstrate a significant change in these parameters (p>0.05 for all parameters). The change in parameters within each group and group comparisons at every checkpoint are given in

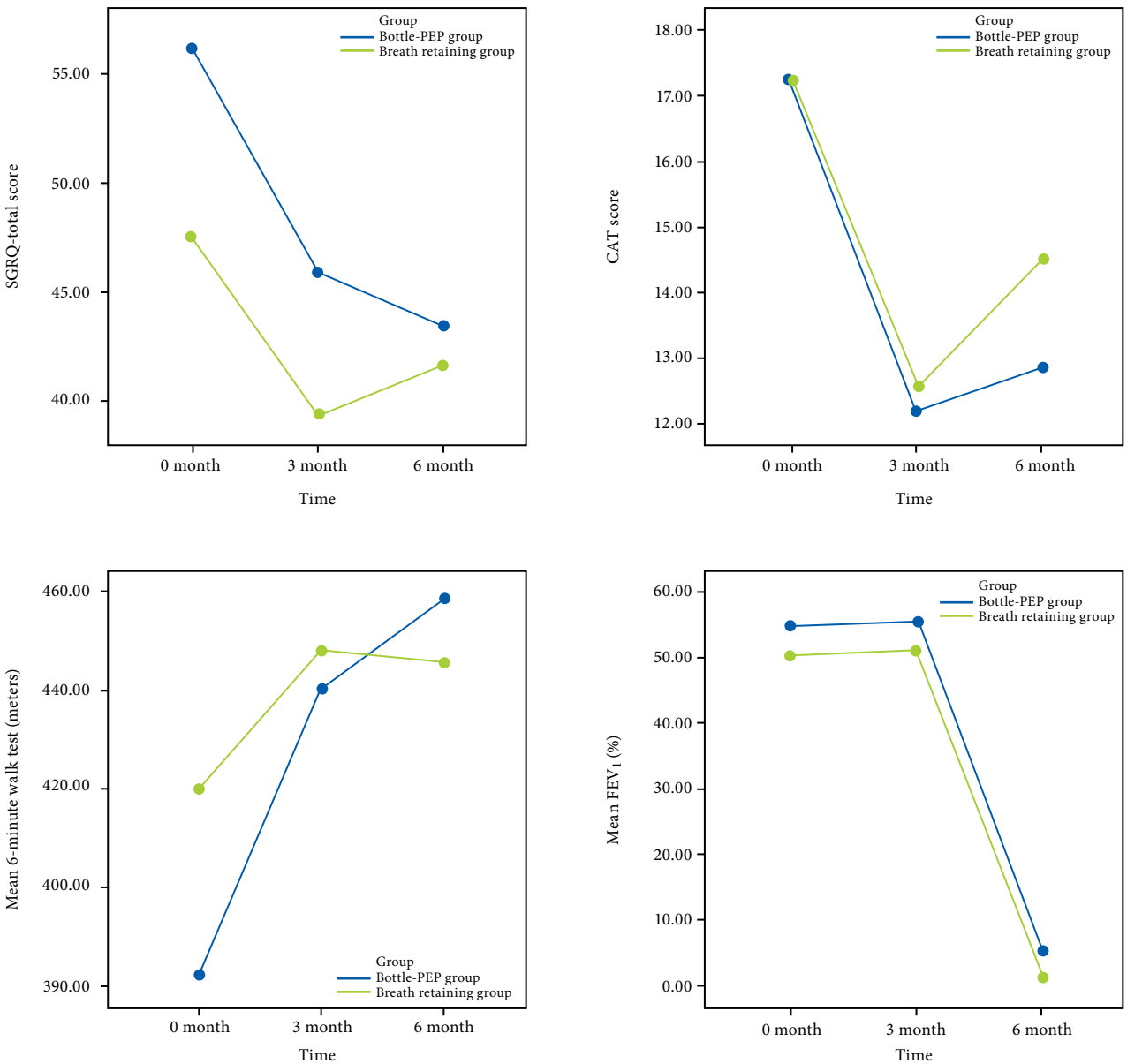

Figure 3. Graph depicting changes in main parameters in each group within the time frame of the study.

SGRQ: St. George's Respiratory Questionnaire-Revised; CAT: Chronic obstructive pulmonary disease assessment test; FEV1: Forced expiratory volume in 1 sec.

Table 2. These changes have also been visualized in Figure 3.

One patient in each group had an infective exacerbation during the study period. None of the patients experienced any adverse or unwanted effects due to the therapies implemented during the study. The patients' medications were optimized at the beginning of the study. The patients who had exacerbations received antibiotic therapy during the exacerbation period, and they all returned to their baseline therapies after the treatment.

DISCUSSION

This study showed that a long-term home program including bottle-PEP as a rehabilitation intervention improved symptoms and quality of life; however, it was not superior to a breathing retaining exercise regimen. Nevertheless, they were both effective in improving functional outcomes. The changes in symptoms and quality of life were sustained for a short period for some measurements, and functional improvement was sustained for six months. None of the treatments exhibited any significant changes in spirometric parameters.

Positive expiratory pressure techniques are already widely implemented in pulmonary rehabilitation in a variety of conditions. The main problem is that in countries that have populations with lower socioeconomic status or insurance policies that do not cover PEP devices, they may not be acquired by the patients and cannot be used. Bottle-PEP is easily assembled by a physician and can be administered as an alternative to commercially available devices, therefore, constituting a valuable choice.[20] Previous surveys among physical therapists showed that it was used daily in a variety of situations.[21] A recent review demonstrated that there were only seven articles that implemented bottle-PEP, and most of the existing literature was about the technical properties of the device rather than long-term results.[22] In patients with COPD, only one study investigated the postexercise effects of bottle-PEP, and it revealed that it could reduce postexercise dyspnea.[23] Similarly, other studies that implemented PEP used it during acute exacerbations for a short period and followed up the patients after the treatment had ended, rather than trying to implement PEP therapy as a long-term option. These studies reported short-term results, displaying PEP therapies' advantages compared to usual medical care.[18,24,25] To the best of our knowledge, this is the first study to implement and evaluate bottle-PEP as a home-rehabilitation therapy in patients with stable COPD.

The results of the present study did not show a significantly favorable outcome for bottle-PEP compared to breathing retaining techniques alone. However, the changes within the bottle-PEP group were statistically significant, whereas they were not in the other group. These results indicate that although the difference was negligible between the groups, bottle-PEP can constitute an important addition in patients who have trouble cooperating with breathing techniques or find them too abstract without a device to guide them. In addition, the short-term changes in the bottle-PEP group signify that it may be more helpful in motivating patients' participation in pulmonary rehabilitation treatments. There was only one exacerbation in each group, and no further complications were observed due to bottle-PEP, confirming that it can be a safe alternative when used in stable patients. It must be kept in mind that, in study conditions, these patients were closely monitored, and infection control may not be adequate during circumstances of daily practice. The lack of significant differences between groups can help us determine that breathing techniques can be solely implemented for a safer approach if there are doubts about proper device use and cleaning.

There are several limitations of this study. First, although sample sizing was implemented, the population of the single-centered study was narrow and lacked female participants, making it hard to generalize to the wider population of patients with COPD. Second, the mechanisms of the implemented techniques were not investigated since they were considered beyond the scope of this study; further research may also be warranted on this issue. Lastly, the actual usage by the patients could not be monitored directly since both approaches were implemented as home rehabilitation programs. Although the patients were checked on via phone calls, we cannot be certain that they implemented the therapies as they were instructed. However, this design might also be helpful in simulating daily life conditions more realistically.

In conclusion, bottle-PEP can constitute a safe and low-cost alternative to other PEP devices; however, it does not significantly contribute when added to breath retaining techniques in patients with moderate-to-severe COPD in improving function and quality of life.

Ethics Committee Approval: The study protocol was approved by the Marmara University Faculty of Medicine Ethics Committee (Number: 09.2019.052) and was registered to the Clinical Trials system (Number: NCT03900195). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from the patients.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Was involved in background and research design, patient recruitment, data analyses, writing and editing of the manuscript: Ö.K.C., İ.Y. E.E.; Patient recruitment, writing and editing of the manuscript: D.K., S.K., B.F.

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