EFFECTS OF FARINELLI BREATHING EXERCISE ON RESPIRATORY FUNCTION AND SYMPTOMS IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Running title: FARINELLI BREATHING EXERCISE IN COPD PATIENTS

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Abstract:

Background: Farinelli breathing (FB) exercise is a typical breathing exercise used by singers. This study aimed to investigate and compare the effects of FB exercise with diaphragmatic breathing (DB) exercises on respiratory function and symptoms in patients with chronic obstructive pulmonary disease (COPD).

Methods: Sixteen patients aged 51–80 years with mild and moderate COPD severity were recruited for the study. They were divided into two groups: the DB (n=8) and FB groups (n=8). Both groups received complete breathing exercise training five times/week for 8 weeks. The respiratory function, effects on COPD symptoms, cytokine level, and oxidative stress variables were analyzed during the pre- and post-tests. The dependent variables between the pre- and post-tests were analyzed using paired t-tests. An independent t-test was used to compare the variables between the groups. Differences were considered significant at p < 0.05.

Results: The maximal expiratory pressure (MEP), maximum oxygen consumption (VO2max), and COPD Assessment Test (CAT) scores changed significantly in the DB group after the 8-week intervention compared to the pre-test, whereas force vital capacity, forced expiratory volume in the first second, maximum voluntary ventilation, maximal inspiratory pressure (MIP), MEP, VO2max, CAT score, tumor necrosis factor-alpha, and malondialdehyde level changed significantly in the FB group in the post-test. Moreover, both MIP and MEP in the FB group were significantly higher than those in the DB group.

Conclusion: FB exercise improves respiratory function and COPD symptoms in patients with COPD, and may provide an alternative intervention for breathing exercises in pulmonary rehabilitation programs.

Keywords: Farinelli breathing, chronic obstructive pulmonary disease patients, respiratory function, COPD questionnaire scores
Introduction

Chronic obstructive pulmonary disease (COPD) is the third leading cause of death globally. COPD is a common, treatable, and preventable disease characterized by airflow limitation and persistent respiratory system infections resulting from exposure to noxious gases and particles. Airflow limitation, caused by irreversible airway restriction and emphysema, is the hallmark of COPD, which leads to a decrease in maximum oxygen consumption. Chronic cough, sputum production, and dyspnea are the most important symptoms in patients with COPD. Its mechanism can be explained by decreased oxygen with increased hydrogen ions (H+) and carbon dioxide in the aorta, leading to the sensation of respiratory discomfort and a feeling of breathlessness. At this point, the medulla oblongata fires respiratory drive signals to the receptors in the lungs and respiratory muscles, resulting in breathing. Thus, breathing exercises improve gas exchange, decrease gas trapping, and alter the breathing pattern.

Patients with COPD use their accessory respiratory muscles due to air trapping (hyperinflation), abnormal thoracic movement, and sarcomere shortening of the diaphragm, which results in labored breathing that impairs their daily activities and exercise tolerance. Pathophysiological changes in the pulmonary tissue, airways, and pulmonary blood vessels, are associated with inflammatory cytokines and oxidative stress in patients with COPD. Reactive oxygen species (ROS) and reactive nitrogen species production, initiated by inflammatory processes and mitochondrial respiration, result in membrane and DNA damage. Moreover, the release of inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 in patients with prolonged inflammation, is associated with disease progression.

Breathing exercises, such as low-intensity aerobic exercise, improved exercise tolerance, increased respiratory muscle strength and endurance, and corrected abnormal chest and abdominal movements, overall diminish hyperinflation. Several types of breathing exercises, such as deep breathing, pursed-lip breathing, and diaphragmatic breathing (DB), are a fundamental part of comprehensive pulmonary rehabilitation programs for patients with COPD. Zhang et al. studied the effects of conventional breathing exercises in patients with COPD; for 8 weeks, the patients practiced inhaling quickly (0.8 to 1 s), holding their breath, and exhaling slowly (3 to 4 s). They found that the
maximal inspiratory muscle pressure (MIP), maximal expiratory pressure (MEP), and 6-minute walk distance (6-MWD) increased. Moreover, a previous study demonstrated that 4 weeks of incentive spirometry in patients with COPD not only increased pulmonary function and respiratory muscle strength but also reduced inflammatory cytokines and oxidative stress\(^1\). In singers, the benefits of breathing exercises include breath control and improved respiratory muscle strength, which can improve vocal efficiency. Farinelli breathing (FB) exercise is a traditional breathing exercise in singers that consists of three phases: inhalation, suspension, and expiration. The principle of this breathing exercise is to inhale slowly through the nasal cavity with the activation of the diaphragm and exhale slowly with a pursed lip. To the best of our knowledge, this is the first study to apply singers’ breathing exercises in patients with COPD. Interestingly, a previous study showed that singers had superior pulmonary function than non-singers\(^{21-22}\). Furthermore, the effects of these FB and DB exercises on respiratory function and symptoms in patients with COPD were compared, which is something that should be considered in pulmonary rehabilitation for patients with COPD. DB is a classic breathing exercise with the goal of improving gas exchange and chest expansion. Previous studies have indicated that DB improves lung volumes, respiratory motion, oxygen saturation (SpO2), respiratory rate, sensation of dyspnea, and reduces fatigue during exercise in patients with COPD\(^{23-25}\). Thus, the objective of this study was to investigate the effect of the FB exercise and compare FB and DB exercises on pulmonary function, respiratory muscle strength, aerobic capacity, effects on COPD symptoms, cytokine levels, and oxidative stress in patients with COPD.

Materials and Methods

Study design and subjects

This study utilized a pre-test/post-test interventional research design and was approved by the Institutional Review Board of the Royal Thai Army Medical Department, Thailand (Study Code: IRBRTA 1347/2562). This study was registered as a clinical trial with clinicaltrials.gov (no. NCT04869033). The sample size of participants was calculated by the G*Power program (3.1.9.2) with an alpha error of 0.05, and a power of 0.80; a minimum of six participants in each group was required for this study. Nineteen patients with COPD were recruited to this study from Phramongkutklao
All participants gave written informed consent prior to participation in the study. The patients were assigned to the FB and DB groups using random allocation by the investigators and stratified by sex (male and female), age (51–60, 61–70, and 71–80 years old), and severity (mild and moderate). The severity was determined after repeated pulmonary function tests based on the predicted forced expiratory volume in the first second (FEV₁,%) and FEV₁/FVC ratio, according to the 2021 Global Initiative for Chronic Obstructive Lung Disease. The inclusion criteria were as follows: 1) patients with COPD who were treated at Phramongkutklao Hospital; 2) having a history of smoking; 3) predicted FEV₁ of more than 50% after bronchodilator; 4) no change in medication in 4 weeks preceding the study; 5) no history of acute exacerbations in 4 weeks; 6) no history of cardiac disease. The exclusion criteria were as follows: 1) recurrent acute exacerbations; 2) inability to participate in at least 80% of the training program (≤ 32 sessions of 40 sessions); 3) unwillingness to continue performing the exercises.

Participants were contacted and underwent a 2-hour orientation, which included assessment training, after their main healthcare practitioner granted them medical clearance to participate (after blood collecting, physiological characteristics, pulmonary function, respiratory muscle strength, 6-MWD, and COPD questionnaires) in the intervention procedures (breathing exercises). At the hospital, there is a confidentiality and privacy room where data is collected. The health history and COPD questionnaires (including the modified Medical Research Council Dyspnea Scale [mMRC] and COPD Assessment Test [CAT]) were investigated by interviews on the pre-experimental day, and characteristics, such as age, weight, body mass index (BMI), blood pressure, percentage of body fat, and SpO₂, were recorded. Blood was collected in sterile Ethylenediaminetetraacetic acid (EDTA) tubes from the cubital vein by a nurse at Phramongkutklao Hospital and analyzed by a medical technologist. EDTA blood was centrifuged at 3000 rpm for 10 min to obtain the plasma. All plasma samples were stored at -80°C before their use in the different assays. Pulmonary function was assessed repeatedly before evaluating respiratory muscle strength and the 6-MWD. All participants were randomly assigned to the DB or FB group and continued to receive their regular medication.

Following the initial examination, participants were given a breathing exercise manual notebook, including program instructions and an activity diary, to evaluate program adherence. Each
participant was given a personalized home breathing exercise regimen (5 days per week for 8 weeks), which was closely monitored by the researchers. Participants were monitored during the breathing exercise sessions and continued to take their prescribed bronchodilator medications. Furthermore, the researchers called all participants twice a week to correct the performance of the breathing exercises as needed, as well as to inquire about any barriers that the participants encountered during the sessions and to verify the correct performance of the breathing exercises.

**FB and DB exercise programs**

This study was designed with two different types of breathing exercises: DB and FB. These groups were differentiated by the route and time in seconds of inhalation, suspension, and exhalation. Both groups were instructed to practice in a seated position on a chair with back support, starting with normal breathing (NB) for 1 min, followed by a different breathing pattern.

In the DB group, patients **inhaled through the nose and exhaled through the mouth**; after 1 min of NB, the patients inhaled for 2 seconds and exhaled for 2 seconds through the nasal airway. This pattern was continued for 4 min, and then the patients returned to NB for 1 min. One minute of NB and 4 minutes of DB was considered one set. The participants were asked to perform six sets/day for 5 days/week (Monday–Friday) for weeks 1–4, and to increase the duration to eight sets/day for 5 days/week for weeks 5–8.

In the FB group, patients **inhaled through the nose, held their breath, and exhaled using pursed lips**. After 1 minute of NB, the patients followed a set of instructions: 1) inhaled for 2 seconds, suspended for 2 seconds, exhaled for 2 seconds; 2) inhaled for 3 seconds, suspended for 3 seconds, exhaled for 3 seconds; 3) inhaled for 4 seconds, suspended for 4 seconds, exhaled for 4 seconds; 4) inhaled for 5 seconds, suspended for 5 seconds, exhaled for 5 seconds; and 5) inhaled for 6 seconds, suspended for 6 seconds, exhaled for 6 seconds.

This cycle lasted for 1 min and was repeated a total of four times. One minute of NB and 4 minutes of FB was considered one set. The participants were asked to perform six sets/day for 5
Pulmonary function test

Pulmonary function and breathing pattern were assessed using the predicted value and liter of force vital capacity (FVC), vital capacity (VC), and the maximum voluntary ventilation (MVV) maneuver analyzed in a computerized spirometer (SpirobankG) as per the guidelines from the American Thoracic Society pulmonary function test. The participants were asked to wear a nose clip while sitting on a chair, and the researcher gave the participants the step-by-step protocol to prevent incorrect maneuvers. For the FVC maneuver, three cycles of slow NB were performed before demonstrating forced inspiration and expiration and returning to NB. For the VC maneuver, NB inhalation and exhalation were performed until the signal of the device sounded, followed by deep and slow inhalation and exhalation. For the MVV maneuver, the participants were asked to inhale and exhale quickly and forcefully for 10 seconds.

Respiratory muscle strength test

Respiratory muscle strength was assessed by measuring the MIP and MEP in a seated position using a portable handheld mouth pressure meter (i.e., MicroRPM) with a nose clip. For the MIP measurement, the participants were asked to exhale until they felt no air remaining in their lungs (starting with the functional residual capacity (FRC) point), then held the device on their mouth and inhaled forcefully for 1-2 seconds. For the MEP measurement, the participants were asked to inhale until their lungs were completely filled with air (starting with the total lung capacity [TLC] point), then they kept the device on their mouth and exhaled forcefully for 1–2 seconds.

Aerobic capacity evaluation

Aerobic capacity was assessed using the 6-MWD, following the guidelines of the 2002 ATS. A modified settlement of the 25 m straight walking test with turning points was performed on the 4th floor next to the Critical Pulmonary Division. Participants were asked to wear comfortable clothes and shoes during the test, and their vital signs (e.g., resting heart rate and blood pressure) were evaluated before
and after the test. The participants were asked to walk at a comfortable pace for 6 minutes under the supervision of a nurse and were permitted to terminate and rest during the test if they sensed heavy dyspnea. The researchers collected the data and calculated maximum oxygen consumption (VO₂ max) using the following formula:

\[
\text{VO₂ max (ml/kg/min) = [0.02 x distance (m)] - [0.191 x age (year)] - [0.07 x weight (kg)] + [0.09 x height (cm)] + [0.26 x heart rate (bpm)] x systolic blood pressure (mmHg) x (10^{-3}) + 245}
\]

**Effects on COPD symptoms**

The effects on COPD symptoms were assessed using the mMRC and the CAT scores. The mMRC is a questionnaire used to evaluate the level of disability in the daily life of patients with COPD. The mMRC has a 5-point (0–4) scale based on the severity of dyspnea, whereas the CAT is a patient-completed instrument to assess and quantify the quality of life and burden of the symptoms in patients with COPD. It consists of eight questions, each of which has a semantic 6-point (0–5) differential scale, providing a total score of up to 40 points. The scores 0–10, 11–20, 21–30, and 31–40 represented mild, moderate, severe, and very severe clinical impact, respectively.

**Statistical analysis**

All data were statistically analyzed for their normal distribution using the Shapiro–Wilk test before calculating the mean and standard deviation (SD). The characteristic data, pulmonary function, respiratory muscle strength, inflammatory cytokines, oxidative stress, aerobic capacity, and effects on COPD symptoms were analyzed by independent t-tests to compare groups. A paired t-test was used to compare the results before and after breathing exercises. All statistical analyses were performed using the SPSS software program (version 17.0; SPSS Inc., Chicago, IL, USA) for Windows. The tests were considered to be significant for a p-value < .05.

**Results**

The eligible participants were allocated into two groups (Figure 1): DB (n = 9) and FB (n = 10). Three participants dropped out of the study because of scheduling difficulties. Due to the corona virus disease 2019 pandemic, hospital visits are limited, and patients are concerned. Therefore, the DB and FB groups
were comprised of 8 (Men, 7; Women, 1) and 8 (Men, 7; Women, 1) patients, respectively. The medication information of the participants was identical in both groups; the majority of them had COPD Stage II and were given a bronchodilator inhaler.

Physiological characteristic data

None of the variables were statistically different at baseline in either group (p > 0.05). The data were expressed as means and SDs. (Table 1).

Pulmonary function

The FB group showed significant changes in FVC (p = 0.026), FEV₁ (p = 0.012), and MVV maneuver (p = 0.000), but there was no significant difference between the groups (Figure 2.).

Respiratory muscle strength and aerobic capacity

In the DB group, only MEP changed significantly (p = 0.013), while the FB group changed significantly in MIP (p = 0.000) and MEP (p = 0.000). Both MIP and MEP were significantly higher in the FB group than in the DB group when comparing them with the post-test (p = 0.016 and p = 0.039, respectively). Moreover, after 8 weeks of breathing exercises in the DB and FB groups, the 6-MWD (p = 0.005 and p = 0.002) and VO₂max (p = 0.010 and p = 0.035) increased significantly when compared with the pre-test, although there was no significant difference between the groups (Figure 3.).

Inflammatory cytokine and oxidative stress

There was no statistical change in any variables in the DB group, whereas TNF-α (p = 0.027) and malondialdehyde (MDA) levels (p = 0.015) were significantly reduced in the FB group, although there was no significant difference between the groups in the post-test (Figure 4.).

Effects on COPD symptoms

Regarding the effects on COPD symptoms, both groups showed significantly reduced CAT scores (p = 0.017 and p = 0.005), although there was no significant difference between the groups in the post-test (Figure 5.).
Discussion

The main finding of this study indicates that respiratory function and COPD symptoms in stable (Stage I and Stage II) COPD were improved, which was a novel finding. Since respiratory function and dyspnea symptoms worsened in patients with COPD, there are two main pathophysiological characteristics—chronic bronchitis and emphysema—leading to excessive sputum production and narrowing of the airways, resulting in an insufficient capacity for gas exchange. Moreover, patients with COPD have hyperinflation-induced respiratory muscle dysfunction and limited tidal volume and inspiratory reserve volume resulting in an abnormal breathing pattern. COPD patients in the FB group had significantly higher MIP and MEP than those in the DB group, which emphasizes the activation of the diaphragm. The suspension phase is similar to the sustained maximal inspiration breathing technique, where the inhalation forms the FRC until the TLC has been reached in order to increase the alveolar distension. Its use results in lung stretching and increased the VC. Additionally, the exhalation phase resembles the Pursed-lip breathing technique, where the patient exhales through pursed lips, resulting in reduced gas trapping. Performing the FB exercise, participants breathed in slowly to activate the diaphragm muscle while in the suspension phase until achieving the struggle phase. This increased the magnitude and frequency of respiratory muscle contraction, resulting in enhanced gaseous exchange efficiency and improvements in respiratory muscle strength, represented by increased MIP and MEP. Moreover, this breathing exercise increased the MVV maneuver, which represents respiratory muscle endurance. This suggests that the FB exercise can improve respiratory function in patients with COPD.

The better COPD patient’s respiratory function, the greater the health benefits. Immune responses play an important role in respiratory function; cytokines and oxidative stress are elevated, and ROS have the ability to change biological molecules, signaling pathways, and antioxidant molecule activity, all of which have been implicated in the pathogenesis of COPD. The repetitive breathing cycle of FB, resulting in an alteration in the immune response of respiratory muscles by downregulating inflammatory cytokines and decreasing TNF-α production from macrophages. This mechanism not only decreases the TNF-α level but also reduces ROS generation, which may result in decreased MDA levels. These findings indicate that FB exercise can increase respiratory muscle strength and minimize
air trapping, as well as decrease TNF-α and MDA levels, which affect pulmonary fibrosis and emphysema, leading in decreased pulmonary obstruction, improved FEV₁, and reduced cardinal symptoms.

The important respiratory symptom present in COPD is dyspnea caused by a decrease in O₂ levels in the aorta. Increased H⁺ and CO₂ levels in the arteries cause respiratory discomfort and breathlessness triggering the medulla oblongata to initiate inspiratory neural drive in the lung receptors and respiratory muscles to instruct breathing³², where breathing exercises enable efficient gas exchange. Reduced air retention in the lungs modifies the efficacy of breathing patterns to reduce dyspnea³¹,³⁰,³³. Our results indicate that the FB group had decreased CAT scores after eight weeks of breathing exercise sessions, and improved ventilatory functions, dyspnea, health status, and physical activity in patients with COPD. Decreased CAT scores after treatment indicate that FB can reduce dyspnea and general symptom perception in patients with COPD.

The aim of the study was to find the differences in effectiveness between FB and DB exercises on respiratory function and symptoms in patients with COPD. We have the following areas to consider when interpreting the results of this study. First, the number of enrolled participants was small. Future research in patients with COPD is needed to validate the possible applications of these findings in patients using combined medication and with varying severity, as well as bigger sample sizes and comparisons with other breathing exercises. Second, we discovered that patients with COPD are overweight (the average BMI of the participants was above 25 kg/m²) and have decent lung function, which differs from prior studies. The rationale is that the patients in this study had COPD Stages I (mild) and II (moderate), thus their appetite and dyspnea were not severe enough to cause weight loss and decreased lung function. More advanced recruitment in various stages of COPD, we believe, is feasible.

In conclusion, for COPD patients, the FB exercise can open up airways sufficiently enough to allow more air to pass through and aids in the control of shortness of breath. FB exercise is a quick and easy technique that reduces the patient's breathing rate making each breath more efficient. Although this breathing technique is somewhat complex, if practiced on a regular basis, it may become habitual. This exercise enhanced pulmonary function, respiratory muscle strength, aerobic capacity, and reduced
inflammatory cytokines, oxidative stress, and COPD symptoms. Healthcare practitioners, such as nurses, physicians, and exercise therapists play important roles in promoting this beneficial exercise as a useful an alternative tool for COPD patients by incorporating it into their advice, patient manuals, and practical guidelines for improving health status and quality of life.

**Author contribution:** S.I. designed and performed the experiments, data collection, and analyzed the data and drafted the manuscript. N.W. designed and performed the experiments, contributed to sample preparation, data collection and aided in interpreting the results. D.S. contributed to sample preparation and data collection. W.T. conceptualized and designed the study, assisted with the implemented of the intervention, data collection, interpreting the results, discussion and conclusion, and revised/reviewed the manuscript.

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**References**


**Figure 1.** CONSORT 2010 flow diagram of participant allocation, follow-up and analysis.
Data are presented as mean (SD). * p < 0.05 vs. Pre-test.

FVC = Forced Vital Capacity, FEV₁ = Forced Expiratory Volume in the first second, MVV = Maximal Voluntary

**Figure 2.** The comparison of pulmonary function between pre- and post-breathing exercise and between FB and DB groups.
Data are presented as mean (SD). * p < 0.05 vs. Pre-test, † p < 0.05 vs. DB group

MIP = Maximal Inspiratory Pressure, MEP = Maximal Expiratory Pressure, 6-MWD = 6-minute walk distance, VO2max = Maximal oxygen consumption

**Figure 3.** The comparison of respiratory muscle strength and aerobic capacity between pre- and post-breathing exercise and between FB and DB groups.
* p < 0.05 Vs. Pre-test

TNF-α = Tumor necrosis factor-alpha, IL-6 = Interleukin-6, MDA = Malondialdehyde

**Figure 4.** Inflammatory cytokine (TNF-α and IL-6) and oxidative stress (MDA) between pre- and post-breathing exercise and between FB and DB groups.
* $p < 0.05$ Vs. Pre-test

mMRC = modified Medical Research Council, CAT = COPD assessment test

**Figure 5.** The effects on COPD symptoms (mMRC and CAT) between pre- and post-breathing exercise and between FB and DB groups.
**Table 1.** Physiological characteristic data in the DB and FB groups.

<table>
<thead>
<tr>
<th>Variables</th>
<th>DB (n=8)</th>
<th>FB (n=8)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>66.63 ± 9</td>
<td>67.63 ± 7.93</td>
<td>0.82</td>
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<tr>
<td>Sex, M:F</td>
<td>7:1</td>
<td>7:1</td>
<td>-</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>70.78 ± 15.62</td>
<td>70.65 ± 14.02</td>
<td>0.99</td>
</tr>
<tr>
<td>RHR (bpm)</td>
<td>83.75 ± 20.23</td>
<td>86.00 ± 16.13</td>
<td>0.80</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.86 ± 5.99</td>
<td>26.31 ± 4.21</td>
<td>0.86</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>116.38 ± 23.31</td>
<td>127.88 ± 4.57</td>
<td>0.19</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>73.50 ± 10.98</td>
<td>80.75 ± 4.52</td>
<td>0.10</td>
</tr>
<tr>
<td>PBF (%)</td>
<td>29.69 ± 8.15</td>
<td>30.35 ± 7.91</td>
<td>0.92</td>
</tr>
<tr>
<td>SpO₂ (%)</td>
<td>96.63 ± 1.69</td>
<td>95.25 ± 1.98</td>
<td>0.16</td>
</tr>
<tr>
<td>FVC (L)</td>
<td>2.47 ± 0.49</td>
<td>2.34 ± 0.69</td>
<td>0.68</td>
</tr>
<tr>
<td>FEV₁ predicted (%)</td>
<td>73.36 ± 8.81</td>
<td>72.01 ± 11.37</td>
<td>0.80</td>
</tr>
<tr>
<td>FVC predicted (%)</td>
<td>78.38±17.80</td>
<td>74.25±20.82</td>
<td>0.68</td>
</tr>
</tbody>
</table>

Data are presented as number or mean ± SD.

DB = diaphragmatic breathing, FB = Farinelli’s breathing, HRR = Resting heart rate, BMI = Body Mass Index, SBP = Systolic Blood Pressure, DBP = Diastolic Blood Pressure, BF = percent of body fat, SpO₂ = Oxygen saturation.