Protocol

1. Name of the research

: Comparison of effectiveness between Active cycle of breathing techniques (ACBT) and Oscillating positive expiratory pressure (OPEP, Aerobika) device assisted treatment in patients with bronchiectasis in Korea : Randomized Controlled Trials

Document date : May-22-2025

2. Name and address of clinical trial institution

Chungbuk National University Hospital, 776, 1sunhwan-ro, Seowon-gu, Cheongju-si, Chungcheongbuk-do, Republic of Korea

3. Name and title of principal investigator, and co-investigators

Principal investigator: **Bumhee Yang**, Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Associate professor

Co-investigator: **Sun-Hyung Kim**, Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Assistant professor

4. Name and address of the referral (support) organization

N/A

5. Drugs and Devices for the research

Aerobika (Trudell Medical International, London, ON)

6. Background of the research

Bronchiectasis is a chronic lung disease characterized by permanent dilation of the bronchus, often accompanied by chronic respiratory symptoms and recurrent lung infections and inflammation. It is one of the most common chronic respiratory diseases worldwide, and its prevalence has been steadily increasing in recent years. Patients with bronchiectasis experience a significant disease burden, with lower quality of life and more frequent access to health care compared to the general population.

Our findings showed that the prevalence of bronchiectasis in Korea is higher than that in the United States and Europe (Germany, United Kingdom, etc.), and given the high incidence of tuberculosis in Korea, the disease burden of bronchiectasis, one of the major complications of

tuberculosis, is significant for both patients and the country. In particular, the disease burden of bronchiectasis is strongly associated with acute exacerbations.

Acute exacerbations of bronchiectasis can be caused by a variety of factors, including fine dust, bacteria, and non-tuberculous antibacterial infections, and can result in worsening sputum and dyspnea symptoms, requiring hospitalization or, in severe cases, intensive care unit treatment. Most patients with bronchiectasis will experience at least one acute exacerbation in their lifetime, and the main goals of treatment are to reduce acute exacerbations and infections, reduce airway inflammation, and facilitate sputum clearance to improve the patient's quality of life.

The British Thoracic Society guideline for bronchiectasis in adults, published in the journal Thorax in 2019, recommends that patients with bronchiectasis should be offered individualized airway management. Airway management techniques include using the Active Cycle of Breathing Technique and Oscillating PEP (OPEP), which are known to be effective in clearing sputum and have a positive impact on improving patients' quality of life. When applied to bronchiectasis patients with frequent acute exacerbations, OPEP has been shown to improve symptoms and reduce acute exacerbations. However, previous study was a pilot study, which have been limited by the small number of patients enrolled and the lack of a control group.

7. Research Objective

To evaluate the effectiveness of active cycle of breathing techniques alone versus active cycle of breathing techniques therapy plus an Oscillating Positive Expiratory Pressure (OPEP) device in reducing the occurrence of acute exacerbations and improving symptoms in patients with bronchiectasis who have experienced 3 or more acute exacerbations within 1 year.

8. Risk and Benefit

: For patients who experience frequent acute exacerbations more than three times per year, the use of OPEP in addition to active cycle of breathing techniques may improve quality of life and reduce acute exacerbations.

On the other hand, rare side effects of OPEP use include hemoptysis and pneumothorax, but these are very rare (<0.1% in existing reports) and the risk can be reduced by selecting patients with fewer side effects.

9. Selection and Exclusion Criteria for Subjects

Total Subject: 100 patients

control group : 50 patients with bronchiectasis using active cycle of breathing techniques

experimental group : 50 patients with bronchiectasis using ACT and OPEP simultaneously

The control and test groups will be randomly assigned by the research nurse, and neither the physician nor the patient will be aware of this.

Selection criteria:

- 18 years of age or older
- Patients diagnosed with bronchiectasis involving one or more lobes on chest computed tomography (CT)
- Patients experiencing frequent exacerbations (with 3 or more exacerbations) within 1 year
- Patients able and willing to use the Aerobika device (OPEP)

Exclusion criteria :

- diagnosis of bronchiectasis due to cystic fibrosis
- traction bronchiectasis due to interstitial lung disease (ILD)
- pregnant patients
- patients with a history of OPEP device use
- patients who cannot tolerate increased breathing work
- hemodynamic instability (e.g., unstable blood pressure)
- patients with a past or current history of hemoptysis (pulmonary bleeding) and untreated pneumothorax

10. Basis for calculating the number of target group

: Based on a pilot study previously conducted at our institution to determine the number of eligible participants

11. Methods of recruiting subjects and consent procedures

: Patients attending the outpatient department of respiratory internal medicine for bronchiectasis at Chungbuk National University Hospital who have experienced 3 or more acute exacerbations within 1 year will be selected and informed consent will be obtained after explaining the study in person.

12. Safeguards for recruiting vulnerable populations

- Patients who are classified as vulnerable research subjects will not be solicited to participate in the study, and only those who voluntarily agree to participate in the study will be included.
- Only for individuals who have read and understood the informed consent document and have voluntarily signed an informed consent form (guardian consent if patient is unable to consent)
- There will be no impact regarding the relative threat to the patient's care from participation or non-participation in the study
- Ensure that consent is obtained from both the subject and their legal representative.

13. Screening test methods

Not necessary because it targets patients already diagnosed with bronchiectasis

14. Research design and methods

Patients will be randomized to one of the study groups at the baseline visit (time = 0 weeks), followed by follow-up visits at 1 month, 3 months, 6 months, 9 months, and 12 months.

The following are collected on the first visit only

- age, gender, BMI, smoking history
- History of previous exacerbation
- Underlying medical conditions (including gastroesophageal reflux disease (GERD))

The following are collected on every visit

- Patient symptoms: modified Medical Research Council (mMRC), validated Korean version of the Bronchiectasis Health Questionnaire (BHQ), COPD Assessment Score (CAT Score)
- Laboratory findings: CBC, ESR, CRP, albumin, NE, MPO
- Sputum volume and color

The following are only collected on follow-up visits

- Frequency of adverse events (AEs), defined as worsening of three or more major symptoms for 48 hours or more, requiring a change in treatment
- Includes monthly phone consultation
- Frequency of adverse events

PFT will be measured at the first visit and at 12 months.

Chest computed tomography (CT) and radiologic findings (modified Reiff score) will be measured at Visit 1 and 12 months.

Bronchiectasis severity score is measured at Visit 1 and 12 months.

15. Standard treatment of target disease

There is currently no established standard treatment.

16. Validity assessment methods

Improvement of patient symptoms and quality of life through mMRC, BHQ, CAT score, and PFT

Measuring the frequency of acute exacerbations during the study period

17. Statistical analysis methods

Continuous variables were analyzed using t-test or Mann-Whitney U test. Categorical variables were compared using Pearson Chi-square test, Fisher's Exact test.

18. Clinical study drop-out criteria

N/A

19. Predicted side effects and precautions for use

Rare cases of hemoptysis and pneumothorax have been reported, and patient education will include instructions on how to start and blow with lower pressure

20. Criteria, methodology, and reporting of safety, including adverse events

N/A

21. Estimated study duration

2 years from IRB approval date

22. Protecting privacy and confidentiality of research data

: The information collected is from patient's medical record, or information such as the type, date, procedures and results of various tests. This information may include information from the subject's medical record and information created or collected during the clinical study. However, all information collected will be processed with code numbers and initials so that it is not recognizable as information about the subject, and relevant documents will be stored in a locked file cabinet.

No personal information will be collected

.

23. Managing, storing, and disposing of human remains when collected

Human derived materials Research Consent Process

Because we will be collecting human derived materials, respiratory samples and blood directly from human subjects, we will obtain written informed consent and human derived materials research consent from those who provide human derived materials.

It is provided in accordance with 「Personal Information Protection Act, Article 15 - Collection and Use of Personal Information and Bioethics-related Laws」including the purpose of collecting and using personal information, items collected, period of collection and use, provision of information to third parties, and refusal of consent to collection and use.

Clarify that consent is given on a voluntary basis, without coercion, and that there will be no adverse consequences to the subject if the subject refuses to participate in the research or discontinues participation during the research.

Method to use and dispose of human derived materials

Human derived materials will be analyzed as anonymous coded data without personal identifiers and will be stored for 3 years after the end of the study before being disposed. On the other hand, specific information identified during the analysis will be shared with co-investigator and used for reporting results and papers without recording personal information.

After testing, the remaining samples will be stored in the refrigerator in their original state considering the possibility of retesting, and after all test results and analysis are completed, they will be classified and disposed of according to Article 4 (Kinds of Medical Waste).

24. A plan for statistical analysis of the study, including a plan for interim analyses and scope for early termination of the study if necessary.

: N/A

25. Continuous Safety Monitoring Plan and Material Safety Monitoring Plan

: The results of the data safety monitoring exercise should be reported to the appropriate IRB at the time of the interim report or end/outcome report.

26. Methods to ensure the research is ethical

We will conduct research in accordance with approved protocols and investigator compliance, and will ensure compliance with the Declaration of Helsinki and ICH-GCP standards and all applicable regulations.

The research will be conducted in accordance with the approved research protocol and researcher compliance, and all data from research subjects will be anonymized, kept strictly confidential, password protected, in separate files, and not identifiable through the research data.

27. Data storage

Data obtained from this study will be kept for up to 10 years after the end of the study and then destroyed immediately.

28. Research plan (timeline)

Duration (month)	1	2	3	4	5	6	7	8	9	10	11	12
IRB review												
Patient Registration												

Patient f/u debrief												

29. Reference

1. Hill AT, Sullivan AL, Chalmers JD, et al. British Thoracic Society Guideline for bronchiectasis in adults. *Thorax* 2019: 74(Suppl 1): 1-69.

2. Chalmers JD, Chang AB, Chotirmall SH, et al. Bronchiectasis. *Nature reviews Disease primers* 2018; **4**(1): 45.

3. Yang B, Choi H, Lim JH, et al. The disease burden of bronchiectasis in comparison with chronic obstructive pulmonary disease: a national database study in Korea. *Annals of translational medicine* 2019; **7**(23).

4. Kim, S. R., Kim, S. H., Kim, G. H., et al. Effectiveness of the use of an oscillating positive expiratory pressure device in bronchiectasis with frequent exacerbations: a single-arm pilot study. Frontiers in medicine. 2023; 10, 1159227