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【 ORIGINAL ARTICLE 】

Antitussive Effect of a Chest Band in Patients with Interstitial Lung Disease: The Preliminary Results from a Pre-post Intervention Study

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Abstract:

Objective Evidence supporting the efficiency of clinically administered therapies against interstitial lung disease (ILD)-related cough is limited. Thus, we conducted a study to evaluate the efficacy of short-term use of chest bands on cough in patients with ILD.

Methods This pre-post intervention study was performed at two university hospitals between April 2017 and August 2020. Scores of the visual analog scale (VAS) for cough severity (in terms of frequency and intensity), Leicester Cough Questionnaire (LCQ)-acute, and frequency scale for symptoms of gastroesophageal reflux disease (FSSG) were assessed before and after the use of the chest band (24/48 hours).

Patients The study included patients with idiopathic interstitial pneumonias (IIPs) or connective tissue disease-associated interstitial lung disease (CTD-ILD).

Results Four patients with IIPs and seven with CTD-ILD were included in the analysis. The cough intensity and LCQ-acute total score improved significantly after the use of the chest band (p=0.007 and p=0.005, respectively), although the cough frequency showed no significant reduction (p=0.074). Furthermore, the FSSG total and acid-reflux symptom scores improved (p=0.018 and p=0.027, respectively), and a negative correlation between the change in LCQ-acute total score and that in FSSG score for acid-reflux symptoms was observed (Spearman rho =-0.841, p=0.001).

Conclusion The results of the current study suggest that chest bands might be useful for treating chronic refractory cough in patients with ILD and gastroesophageal reflux disease. However, these results should be interpreted with caution due to methodological limitations associated with this study.

Key words: chest band, cough, interstitial lung disease

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Introduction

Awareness about the essentiality of palliative care for patients with interstitial lung disease (ILD) is increasing (1). Suppression of cough in patients with ILD is a crucial component of palliative care, as chronic cough in such patients leads to impairment of the health-related quality of life (HRQoL) (2, 3).

In addition to impairing the HRQoL, coughing in patients with ILD may be related to disease progression (4-7). Studies on patients with scleroderma-related ILD reported a relationship between the frequency of cough and extent of fibrosis on high-resolution computed tomography (HRCT) images (4, 5). In our previous study, the patient-reported cough intensity and frequency were reported to be associated with

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clinical indices representing disease severity [e.g., the composite physiology index (CPI)] in patients with idiopathic interstitial pneumonias (IIPs) (7). Another study found that both the intensity and frequency of mechanical stress-related breathing led to the activation of transforming growth factor beta-1 in fibrotic tissues of rats (8). Therefore, treatments that suppress the intensity and frequency of cough are needed, but evidence supporting the antitussive effect of clinically administered therapies against ILD-related cough is limited (9).

Jones et al. reported that percussion stimulation over the posterior lung base, where fibrosis is highly extensive, induced cough in more patients with idiopathic pulmonary fibrosis (IPF) than at the upper anterior chest or manubrium sternum (10). In addition, Sumitani et al. found that the use of a chest band at the lower rib cage level decreased the visual analog scale (VAS) score for cough frequency in an ILD patient with refractory cough (11). Therefore, the inhibition of the thoracic cage's mechanical stimulation may be a novel method of treating ILD-related cough. However, the antitussive effect of such a chest band has not been well documented.

The present study was therefore conducted to evaluate the efficacy of short-term use of a chest band for controlling cough in patients with ILD.

Materials and Methods

Study design

This study was conducted at two university hospitals from April 2017 to August 2020 as a pretest-posttest experimental design (Trial registration ID: UMIN000025001), and all procedures followed were in accordance with the Declaration of Helsinki.

Subjects

The eligibility criteria for this study were as follows: patients with IIPs or connective tissue disease-associated interstitial lung disease (CTD-ILD), age ≥20 years old, and VAS scores for the intensity and frequency of cough >10 mm. Eligible patients were approached by researchers in the outpatient department and invited to take part in the study. IIPs were diagnosed as described previously (12-14). IPF was diagnosed based on the biopsy patterns and HRCT findings according to the guidelines (15). The exclusion criteria were as follows: (i) absence of cough; (ii) a diagnosis of respiratory tract infections <1 month before the study; (iii) a history of rhinitis or catarrhal symptoms, asthma, and atopic cough; (iv) inability to answer questions; (v) arterial oxygen saturation of ≤90% at rest; (vi) use of oxygen therapy; (vii) presence of orthopedic disease that precluded the attachment and removed a chest band; and (viii) presence of skin disease on the chest.

Written informed consent was obtained from each patient, and the study was approved by the Ethics Committee of the Kyoto University Graduate School of Medicine and Kanazawa University School of Medicine.

Intervention

The intervention was performed using a chest band (RIB BAND; Nippon sigmax, Tokyo, Japan). This product was designed for rib support in patients with rib fractures. The chest circumference was measured to ensure the selection of a band of appropriate size, and the patients were instructed on how to use the chest band before the intervention. We advised patients to exhale in order to achieve the resting expiratory level before wrapping the product around the lower part of the chest. Participants were asked to continuously wear the chest band over their underwears for 24 or 48 hours, except when they took a bath.

Data collection

Before the session, anthropometric data and data on the smoking history, medical history, treatment drug, dyspnea, and findings of pulmonary function tests were obtained from computer-based patient records and patient-completed questionnaires. Dyspnea was evaluated using the modified Medical Research Council (mMRC) chronic dyspnea scale, which yields scores ranging from 0 (breathless with strenuous exercise) to 4 (too breathless to leave the house or breathless when dressing or undressing). Pulmonary function tests were conducted using the CHESTAC system (Chest M.I., Tokyo, Japan), and the diffusing capacity of the lung for carbon monoxide (DL_{CO}) was measured using the single-breath technique. The CPI was employed to predict the extent of fibrosis on HRCT, with the following formula: CPI= 91.0-(0.65×percent predicted DL_{CO})-[0.53×percent predicted forced vital capacity (FVC)]+[0.34×percentage of predicted forced expiratory volume in 1 second (FEV_1)] (16).

In the pre- and post-intervention periods, the cough severity, cough-specific HRQoL, and symptoms of gastroesophageal reflux disease (GERD) were assessed. We defined cough severity according to the frequency and intensity of cough. The assessment of both the intensity and frequency of cough has been reported to be essential for understanding its impact and related factors (7, 17). The frequency and intensity of cough were assessed using a 100-mm VAS [range: 0, (no cough) to 100 (unbearable)], which is the most commonly used scale to evaluate subjective cough severity in studies (17). The VAS was used in a standardized manner, as recommended by the CHEST Expert Cough Panel in 2015 (18). The cough-specific HRQoL was assessed using the Japanese version of the Leicester Cough Questionnaire (LCQ)-acute (19). The Japanese version of the LCQ-acute was developed by the first author (RS), Dr. Satoru Ebihara (Toho University), Dr. Akio Niimi (Nagoya City University), and Dr. Haruhiko Ogawa (Kanazawa University) (20). These researchers and the developer of the original version hold the copyright for the questionnaire. The total score for this questionnaire ranges from 3 to 21; the higher the score, the better the cough-specific quality of life. The LCQ is an ade-

quate tool for conducting clinical trials on ILD because it shows good feasibility and sensitivity (21). The frequency scale for symptoms of GERD (FSSG), which was developed by Kusano et al., was used to assess the symptoms of GERD (22). FSSG, which involves acid-reflux and dysmotility symptom domains, has previously been used in studies focused on cough (23, 24). The total score ranges from 0 to 48; the higher the scores, the greater the severity of GERD symptoms.

The primary endpoint was the change in cough severity. To determine whether or not the chest band elicits side effects, we measured the uncomfortable feeling score using a five-point Likert scale [range: 1 (not at all) to 5 (extreme)], the VAS score of dyspnea, and percutaneous oxygen saturation (SpO_2) using a finger pulse oximeter (Ubi-x ST/BL; Ubi-X, Tokyo, Japan).

Statistical analyses

The sample size was determined according to the cough severity determined using the VAS. Data from our first 5 pilot patients were used to calculate the sample size (effect size of 31 mm) for an alpha level of 5% and a power of 90%. Considering a possible 30% dropout rate, a sample of 8 participants was required. The normality of the data was first investigated using the Shapiro-Wilk test and histogram. Differences between pre- and post-intervention within the group were tested using Wilcoxon's signed rank test, as the variables were non-normally distributed. The chi-square test for goodness of fit (with Fisher's exact test if data were sparse) was used for categorical variables. Spearman's rank correlation coefficient was calculated to explore the interrelationship between the modulation of cough and the changes in FSSG scores. Data are expressed as numbers with percentages or medians with the interquartile range (IQR).

All analyses were performed using the SPSS software program, version 25.0 (IBM, Armonk, USA). P values <0.05 were considered statistically significant.

Results

Patients' characteristics

Two of the 13 patients registered for this study were excluded from the analysis (1 patient with rhinitis, adult asthma, and atopic cough and 1 patient with atopic cough). Data on four and seven patients with IIPs and CTD-ILD, respectively, were subjected to the analysis in this study. Drugs used by these patients were as follows: antifibrotic agents in one patient (with IIPs), glucocorticoids in seven patients (one with IIPs and six with CTD-ILD), proton pump inhibitors (PPIs) in nine patients (three with IIPs and six with CTD-ILD), and antitussive drugs in six patients (one with IIPs and five with CTD-ILD). None of the patients used angiotensin-converting enzyme inhibitors or were current smokers.

Table 1 shows the characteristics of patients with IIPs and of those with CTD-ILD. The patients included 4 men (36%), and the median patient age was 75 years old. The median DL_{CO} and CPI were 38.4% and 53.9, respectively, in these patients.

Effects of a chest band

Fig. 1 shows the effects of using a chest band on the VAS scores of intensity and frequency of cough and LCQ-acute total score. The cough intensity improved from 63 mm (IQR: 35-79 mm) to 30 mm (IQR: 23-42 mm), and the LCQ-acute total score improved from 13.4 (IQR: 11.0-14.9) to 15.8 (IQR: 14.4-17.6). Six patients (54.5%) showed an improvement of >2.5 points in the LCQ-acute total score. Furthermore, scores in all domains of the LCQ-acute improved (all $p<0.05$) (data not shown). Although the VAS score of cough frequency tended to decrease after the use of a chest band ($p=0.074$), no significant changes were noted. Fig. 2 shows the changes in FSSG scores after the use of a chest band. The FSSG total score improved from 4 (IQR: 2-18) to 2 (IQR: 0-3), and the acid-reflux symptom score improved from 2 (IQR: 0-8) to 0 (IQR: 0-2). The dysmotility symptom score tended to decrease ($p=0.057$).

No significant bias was found in the uncomfortable feeling score [not at all, 0 (0%); none, 4 (36%); moderate, 2 (18%); quite, 5 (46%); and extreme, 0 (0%)] ($p=0.648$). There were also no significant changes in either the VAS score of dyspnea or SpO_2 [13 mm (IQR: 0-30 mm) to 22 mm (IQR: 3-32 mm), $p=0.767$ and 95% (IQR: 94%-96%) to 96% (IQR: 94%-96%), $p=0.730$, respectively]. The median of patient-reported chest band usage time was 23.5 hours in patients.

Finally, we examined the interrelationship between the modulation of cough and changes in FSSG scores (Table 2). There was a highly significant correlation between the change in the LCQ-acute total score [ΔLCQ-acute (total)] and that in the FSSG score for acid-reflux symptoms (ΔFSSG acid-reflux symptoms) (Spearman rho =-0.841, p= 0.001). In addition, there was a positive correlation between the change in the VAS score of cough frequency (ΔCough frequency) and the ΔFSSG acid-reflux symptoms, albeit only a marginal one (Spearman rho =0.588, p=0.057).

Discussion

To our knowledge, this is the first study to indicate the antitussive effect of a chest band in a group of patients with ILD. The patient-reported cough intensity and LCQ-acute total score improved significantly after the use of the chest band, although the cough frequency (VAS score) showed no significant reduction. The FSSG total and acid-reflux symptom scores also improved after the use of the chest band. Furthermore, a negative correlation between the ΔLCQ-acute (total) and ΔFSSG acid-reflux symptoms was observed. There was no significant bias in the uncomfortable feeling score after the use of the chest band, and no significant changes in both the VAS score of dyspnea and SpO_2 were

Table 1. Characteristics of Patients with Interstitial Lung Disease (n=11).

Characteristics	Values
Male sex, n (%)	4 (36)
Type of interstitial lung disease, n (%)	
IIPs	
Idiopathic pulmonary fibrosis	2 (18)
Unclassifiable idiopathic interstitial pneumonia	2
CTD-ILD	
Systemic sclerosis	2
Sjögren's syndrome	2
Rheumatoid arthritis	2
Systemic sclerosis and rheumatoid arthritis	1 (9)
Age, years, median (IQR)	75.0 (64.0–77.5)
Body mass index, median (IQR)	22.4 (21.1–23.3)
mMRC chronic dyspnoea scale, median (IQR)	2 (2–2.5)
Pulmonary function tests, % predicted, median (IQR)	
FEV_1	77.5 (70.1–87.4)
FVC	77.8 (63.9–88.1)
TLC	61.3 (56.0–88.8)
DL_{CO}	38.4 (34.7–44.3)
Composite Physiologic Index, median (IQR)	53.9 (48.4–57.8)

CTD-ILD: connective tissue disease-associated interstitial lung disease, DLco: diffusing capacity of the lung for carbon monoxide, FEV_1: forced expiratory volume in 1 s, FVC: forced vital capacity, IIPs: idiopathic interstitial pneumonias, IQR: interquartile range, mMRC: modified Medical Research Council, TLC: total lung capacity

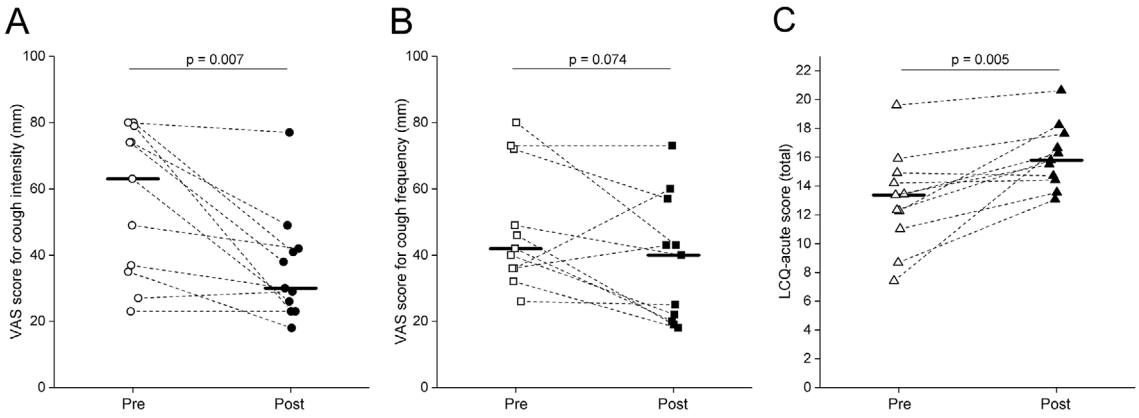

Figure 1. Changes in the cough parameters after the use of a chest band. Individual values of the visual analog scale (VAS) score for cough intensity (A), VAS score for cough frequency (B), and Leicester Cough Questionnaire (LCQ)-acute total score (C) recorded before and after the use of a chest band. The patient-reported cough intensity and LCQ-acute total score improved significantly after the use of the chest band (p=0.007 and p=0.005, respectively), although the cough frequency showed no significant reduction (p=0.074). Bars represent median values. LCQ: Leicester Cough Questionnaire, VAS: visual analog scale

found.

Sumitani et al. reported that the use of a chest band in an ILD patient with refractory cough reduced the VAS score for cough frequency from 79 mm to 34 mm (11). In the present study, the VAS score for cough frequency tended to decrease; however, this decrease was not significant (p= 0.074). This discrepancy may be due to different subtypes of ILD being explored in these studies. The median VAS score for cough intensity decreased significantly from 63 mm to 30 mm after the use of a chest band in this study. The median LCQ-acute total score also improved from 13.4 to 15.8 after the use of this product; 6 patients (54.5%) showed an improvement of >2.5. The clinical minimal important difference (MID) is 2.5 for the LCQ-acute total score (19). Thus,

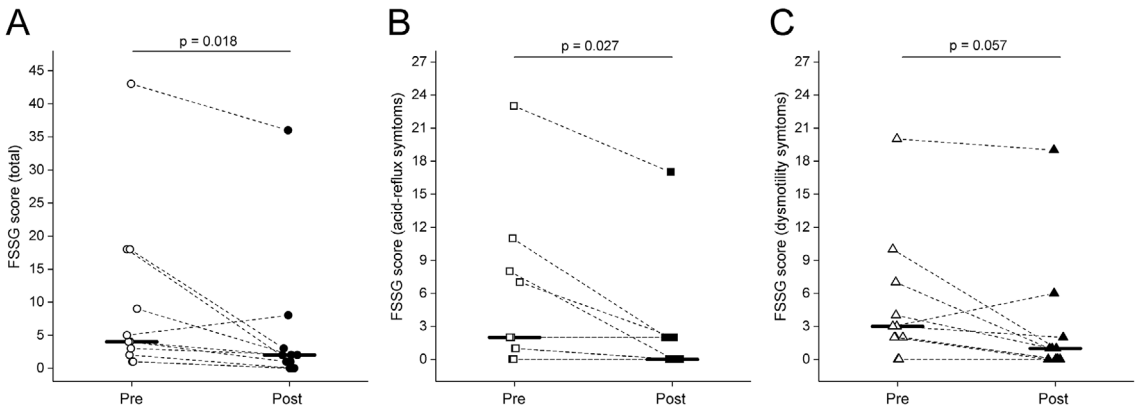

Figure 2. **Changes in the FSSG scores after the use of a chest band. Individual values of the frequency scale for symptoms of gastroesophageal reflux disease (FSSG) total score (A), FSSG acid-reflux symptom score (B), and FSSG dysmotility symptom score (C) recorded before and after the use of a chest band. The FSSG total and acid-reflux symptom scores improved after the use of the chest band (p=0.018 and p=0.027, respectively), although the FSSG dysmotility symptom score showed no significant improvement (p=0.057). Bars represent median values. FSSG: frequency scale for symptoms of gastroesophageal reflux disease**

Table 2. **Relationships between the Changes in VAS Scores for Intensity and Frequency of Cough or LCQ-acute Total Score and Those in FSSG Scores in Patients with Interstitial Lung Disease.**

	ΔCough intensity		ΔCough frequency		ΔLCQ-acute (total)	
	ρ	p value	ρ	p value	ρ	p value
ΔFSSG						
Total	-0.152	0.655	0.041	0.904	-0.498	0.119
Acid-reflux symptoms	0.120	0.726	0.588	0.057	-0.841	0.001
Dysmotility symptoms	-0.266	0.430	-0.244	0.469	-0.180	0.597

The Spearman rank correlation coefficient was used to assess correlations between the data. FSSG: frequency scale for symptoms of gastroesophageal reflux disease, LCQ: Leicester Cough Questionnaire, VAS: visual analog scale

the improvement of the LCQ-acute total score in the present study reached the MID level. Taken together, these findings suggest that subjective symptom severity scores for chronic cough in patients with ILD may be improved after the use of a chest band.

The chest band's effect on chronic cough in patients with ILD in the present study might be due to two reasons. First, mechanical stimulation of the thoracic cage may be inhibited by the chest band. The activation of rapidly adapting receptors (RARs) by architectural distortion of the bronchial tree (i.e., traction bronchiectasis) is suspected to be the mechanism underlying the occurrence of cough in patients with IPF (25, 26). It was also found that RARs discharge was inversely related to dynamic lung compliance in dogs (27). Patients with ILD have been reported to show a decline in both dynamic and static lung compliance (28). Furthermore, low-frequency (i.e., 20 Hz) percussion stimulation over the posterior lung base, where fibrosis is highly extensive, was shown to cause cough in patients with IPF (10). Hence, the chest band, which attenuates the movement of the thoracic cage, was suspected to prevent cough evoked by mechanical stimulation in patients with ILD showing RARs activity. Second, the symptoms of GERD were relieved by the chest band. In the present study, the FSSG total and acid-reflux symptom scores improved after the use of the chest band, and a highly significant correlation was noted between the ΔLCQ-acute (total) and ΔFSSG acid-reflux symptoms. GERD is associated with cough in ILD (29), particularly in patients with CTD-ILD (7). A study on anti-reflux treatment in patients with GER-associated cough reported that the ΔLCQ and ΔCough VAS scores were correlated with the ΔFSSG total and acid-reflux symptom scores (30). Because the chest band can limit chest wall excursion (31), this product appeared to inhibit excessive negative intrathoracic pressure, which may prevent acid-reflux from the stomach. Unfortunately, we were unable to measure the intrathoracic or esophageal pressure and acid-reflux times. In this study, which showed an antitussive effect, 9 out of 11 patients (81.8%) were using PPIs. A systematic review reported insufficient evidence to conclude that PPIs are universally beneficial for cough associated with GERD in adults (32). A chest band may be useful in reliev-

ing cough symptoms in PPI-resistant GERD [e.g., patients who have reflux of a mixed (liquid-gas) composition (33)].

The CHEST guideline and expert panel report do not recommend prescription drugs (e.g., pirfenidone, corticosteroids, thalidomide, cromolyn sodium, cyclophosphamide, and mycophenolate) for ILD-associated cough because of side effects or insufficient effect verification (9). Although several studies have reported the efficacy of non-pharmacological interventions, such as speech pathology therapy (34, 35) and physiotherapy, speech therapy, and language therapy (36), in patients with unexplained chronic cough, no studies have evaluated the efficacy of these interventions in patients with ILD. In the present study, no significant bias in the uncomfortable feeling score after the use of a chest band was observed, and there were no significant changes in the VAS score of dyspnea or SpO_2 after the use of the product, with an antitussive effect of the chest band noted in patients with ILD. Therefore, the chest band's short-term use appears to be a safe new non-pharmacological intervention for improving chronic cough in patients with ILD. In the present study, the short-term use of a chest band or wearing it at the resting expiratory level may have prevented side effects, such as discomfort and changes in the VAS score of dyspnea or SpO_2. However, restriction of the chest wall is known to affect the pulmonary function (37). Further research is therefore needed to determine if such long-term limitation of chest wall excursion causes side effects (e.g., elevation of the carbon dioxide level in the blood).

Several important methodological limitations associated with the present study warrant mention. First, the absence of a control group may have led to exposure to a regression to the mean effect and a placebo effect. The findings should therefore be considered preliminary. We selected a pre-post design in the present study because we expected to experience trouble recruiting patients. Second, we were unable to eliminate selection bias. Patients might easily perceive improvement because the selection criteria for the intensity and frequency of cough were set to >10 mm. Third, because the number of samples that could be counted and analyzed by the cough monitor was low, we used subjective tools for the data collection and evaluation. Future studies that include both subjective and objective tools are needed. Fourth, the small sample size of our study may have impaired the generalization of our findings. Finally, because this was a short-term study, the long-term efficacy of the device, side effects associated with long-term limiting chest wall excursion, and the possibility of masking disease deterioration could not be evaluated. Future long-term studies with a control group or large sample size must be conducted using both subjective and objective tools to validate the current results and confirm this intervention's safety.

Conclusion

The short-term use of a chest band may effectively and safely reduce the cough intensity and improve the cough-specific HRQoL in patients with ILD; however, our results should be interpreted with caution due to methodological limitations associated with this study. The FSSG score also improved after the use of a chest band, and a negative correlation between the ΔLCQ-acute (total) and ΔFSSG acid-reflux symptoms was observed. A chest band might be useful for treating chronic refractory cough in patients with ILD and GERD; however, the long-term efficacy of such a device in those patients is still unclear and requires further examinations.

The authors state that they have no Conflict of Interest (COI).

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