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Original article

Lung sound analysis can be an index of the control of bronchial asthma

Terufumi Shimoda [a,*], Yasushi Obase [b], Yukio Nagasaka [c], Hiroshi Nakano [a], Reiko Kishikawa [a], Tomoaki Iwanaga [a]

[a] Clinical Research Center, Fukuoka National Hospital, Fukuoka, Japan
[b] Second Department of Internal Medicine, School of Medicine, Nagasaki University, Nagasaki, Japan
[c] Kyoto Respiratory Center, Otowa Hospital, Kyoto, Japan

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Abbreviations:
FeNO, fractional exhaled nitric oxide; FEV_1, forced expiratory volume in one second; FVC, forced vital capacity; V_{50} and V_{25}, maximal expiratory flow at 50% and 25%; ICS, inhaled corticosteroid; LSA, lung sound analysis; LF, low frequency; PC20, provocative concentration of acetylcholine causing a 20 % fall in FEV_1; E/I LF, the expiration-to-inspiration sound power ratio in a low-frequency range

A B S T R A C T

Background: We assessed whether lung sound analysis (LSA) is a valid measure of airway obstruction and inflammation in patients with bronchial asthma during treatment with inhaled corticosteroids (ICSs).
Methods: 63 good adherence patients with bronchial asthma and 18 poor adherence patients were examined by LSA, spirometry, fractional exhaled nitric oxide (FeNO), and induced sputum. The expiration-to-inspiration lung sound power ratio at low frequencies between 100 and 200 Hz (E/I LF) obtained by LSA was compared between healthy volunteers and bronchial asthma patients. Next, post-ICS treatment changes were compared in bronchial asthma patients between the good adherence patients and the poor adherence patients.
Results: E/I LF was significantly higher in bronchial asthma patients (0.62 ± 0.21) than in healthy volunteers (0.44 ± 0.12, $p < 0.001$). The good adherence patients demonstrated a significant reduction in E/I LF from pre-treatment to post-treatment (0.55 ± 0.21 to 0.46 ± 0.16, $p = 0.002$), whereas the poor adherence patients did not show a significant change. The decrease of E/I LF correlated with the improvement of FEV_1/FVC ratio during the ICS treatment ($r = -0.26$, $p = 0.04$). The subjects with higher pre-treatment E/I LF values had significantly lower FEV_1/FVC and $V_{50,\%pred}$ ($p < 0.001$), and significantly higher FeNO and sputum eosinophil percentages ($p = 0.008$ and $p < 0.001$, respectively).
Conclusions: The E/I LF measurement obtained by LSA is useful as an indicator of changes in airway obstruction and inflammation and can be used for monitoring the therapeutic course of bronchial asthma patients.

Introduction

Bronchial asthma is a chronic inflammatory disease characterized by airway infiltration of inflammatory cells, including eosinophils, mast cells, macrophages, neutrophils, and lymphocytes, as well as airway narrowing and increased bronchial hyperresponsiveness (BHR).[1]

Lung sound auscultation with a stethoscope is routinely performed in clinical practice.[2] Adventitious sounds that are audible on auscultation, such as rhonchi and wheezes, play an important role in the diagnosis of bronchial asthma.[3,4] However, wheezes due to airway obstruction are not as sensitive a diagnostic indicator as changes in lung sounds. When airway obstruction is mild, wheezes are often inaudible on auscultation with a stethoscope. Lung sound analysis (LSA) is useful for examining the pathophysiology of bronchial asthma because it is more sensitive than auscultation with a stethoscope. Furthermore, LSA is non-invasive and repeatable. We previously reported that the expiration-to-inspiration sound power ratio in a low-frequency range, between 100 and 195 Hz (E/I LF), was increased in bronchial asthma patients with airway inflammation and obstruction.[5]

* Corresponding author. Clinical Research Center, Fukuoka National Hospital, 4-39-1 Yakatabaru, Minami-ku, Fukuoka 811-1394, Japan.
E-mail address: t-shimoda@mfukuoka2.hosp.go.jp (T. Shimoda).
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In this study, we examined airway obstruction, inflammation, and BHR to evaluate whether E/I LF is useful for monitoring the effect of ICS therapy on the clinical course of bronchial asthma.

Methods

Subjects

Our study included 79 patients with mild persistent bronchial asthma who were examined before and after 6 months of ICS therapy (800 μg/day as CFC-BDP equivalent). Of these patients, 63 (82%) used ICS regularly as prescribed (90–100% adherence; according to the concordance rate between the asthma diary and the inhalation usage) were classified in the good adherence group. 14 subjects (18%) used ICS irregularly (30–50% adherence) were classified in the poor adherence group. There were 2 patients with 50–90% adherence and no patients with less than 30% adherence. Bronchial asthma was diagnosed according to the Global Initiative for Asthma Guidelines.[1] All subjects had to present values less than or equal to 8000 mcg/mL in a test of BHR to inhaled acetylcholine, and they had to have a history of wheezing and/or dyspnea. At the initial visit, 80% of the subjects showed positive reversibility (reversible with at least 12% and 200 mL improvements in FEV_1 after bronchodilator therapy), whereas the remaining 20% had negative reversibility with normal respiratory function at the visit and were diagnosed with bronchial asthma based on positive BHR and medical history.

At the enrollment, no patients were treated with inhaled or systemic corticosteroids. The use of anti-asthma drugs, including bronchodilators, was discontinued for at least 24 h prior to the examination. Subjects with a history of chronic obstructive pulmonary disease, any cardiovascular diseases, or with a current viral or bacterial infection were excluded from the study. The healthy control subjects ($n = 27$) had no respiratory symptoms, no overt illnesses, and exhibited no abnormalities in their lung function tests and chest radiographies. The ethics committee of Fukuoka National Hospital approved the study protocol (protocol No. 20-12), and all participants received verbal and written study information before providing their informed consent.

Lung sound analysis

Lung sounds were recorded for ≥30 s over the base of the left lung using a hand-held microphone. The patients took a deep breath through a disposable mouthpiece to synchronize their breath cycles while the breath sounds were recorded. The recording system consisted of an electro-stethoscope containing a wide-range audio sensor that was adhered inside a diaphragm (Bio-Sound Sensor BSS-01; Kenz Medico, Saitama, Japan), a signal processing system, and a personal computer. The sensor had a band-pass filter range of 40–2500 Hz and a sound-collecting ability in the 40–2000 Hz range. The recorded sounds were analyzed using a sound spectrometer (Easy LSA-2008; Nakano, Fukuoka National Hospital). The recorded sounds were re-sampled to 10,000 Hz and analyzed by 1024-point fast Fourier transformation (FFT) with 60% overlap into adjacent segments, using a Hanning data window. The results are presented as a sound spectrograph with frequencies in Hz on the vertical axis and time on the horizontal axis. On the display, the vertical axis displays the cycles per minute in kilohertz, and the horizontal axis displays the time in seconds. The intensity (dBSPL) of the sound is depicted by the color and brightness (Fig. 1). The recording system was calibrated with a reference sound pressure (1 kHz; 94 dB [0 dB = 20 μPa]). We defined low frequencies (LF) as frequencies of 100–200 Hz, and we determined inspiration sound pressure, expiration sound pressure, and inspiration-to-expiration sound pressure ratio in the low-frequency range (E/I LF). E/I LF data were converted from logarithmic values (dBSPL) to real values.[5]

Measurement of flow–volume curves

Lung function was measured using a spirometer (Chest Graph HI-701, Chest M.I., Tokyo, Japan). The results are expressed as a

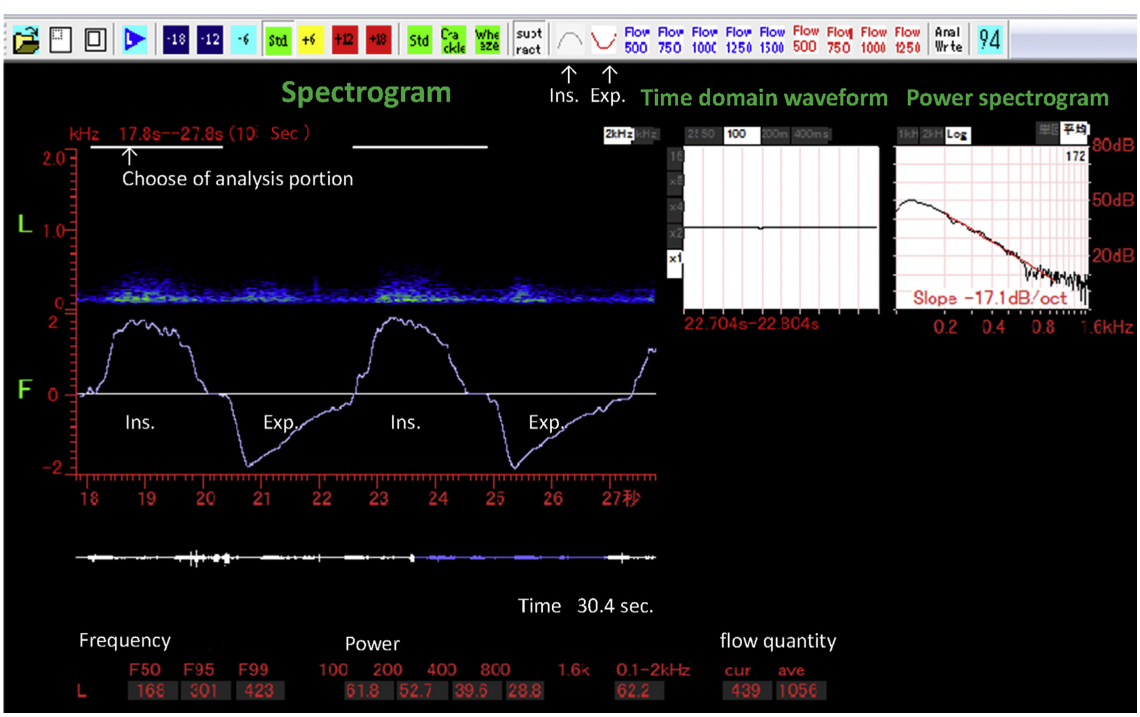

Fig. 1. Sound spectrogram display of lung sounds in a patient (Easy LSA). The recorded sound was analyzed by fast Fourier analysis and displayed as a spectrograph with the frequency shown in Hz on the vertical axis and time on the horizontal axis. The sound intensity is presented by color and brightness. Selected portion of the analysis. Selected range of inspiratory or expiratory position. Calculation of the average sound pressure level (dBSPL) at a low frequency (100–200 Hz).