

Research Article

Pulmonary Function Testing of Patients with Chest Tightness Relieved with Bronchodilator

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Abstract

Background: It has been hypothesized that some patients with chest tightness of unknown origin can be successfully treated with a bronchodilator.

Methods: Forty patients diagnosed with recurrent chest tightness that improves in response to treatment with a bronchodilator and without characteristic attacks of bronchial asthma were retrospectively studied. These patients were diagnosed as having chest pain variant asthma. The flow volume curve patterns of pulmonary function tests were classified as one of three types: an “upper-airway obstruction pattern,” “obstruction pattern,” or “normal pattern.” The patients with chest tightness during the first examination were administered a bronchodilator via inhalation. We counted the patients who had an improved peak expiratory flow rate after inhalation, which was defined as an increase of greater than 1.5-fold in forced expiratory volume in one second.

Results: Among the patients with chest tightness, the flow volume curve patterns in the pre-treatment pulmonary function tests exhibited upper-airway obstruction patterns in 16 patients (40%). The sixteen patients (61.5%) administered a bronchodilator via inhalation at the first examination demonstrated improved peak expiratory flow rates greater than the forced expiratory volume in one second after the bronchodilator inhalation.

Conclusions: This phenomenon suggests that chest tightness that improves in response to treatment with a bronchodilator is triggered by a constriction of large airways.

Keywords: Chest Tightness; Chest Pain Variant Asthma; Bronchial Asthma; Bronchodilator; Pulmonary Function Test; Upper-Airway Obstruction Pattern

Introduction

Chest tightness is a common symptom of diverse diseases. Many patients who experience chest tightness consult their physicians, and they are usually diagnosed with cardiovas-

cular or gastrointestinal disease. However, many patients remain undiagnosed and untreated. We hypothesize that some patients with chest tightness of unknown origin can be successfully treated with a bronchodilator or other asthma drugs [1].

The Global Initiative for Asthma (GINA) is a medical guidelines organization that works with public health officials and health care professionals around the world to reduce asthma prevalence, morbidity, and mortality. The GINA states that chest tightness is an asthma symptom [2]. Chest tightness is more likely muscle tightness or a physical difficulty moving air that is sensed through proprioception and not through pain pathways. Chest tightness of patients with bronchial asthma sometimes improves with a bronchodilator [1].

Whitney and co-workers reported on three patients who presented with chest tightness that was relieved with a bronchodilator. These patients were diagnosed with asthma [3]. Specifically, this disease was termed “chest pain variant asthma,” and several articles in the medical literature have addressed this disease [1, 4-6, 7]. No clear diagnostic criteria have been established for chest pain variant asthma, but it should be defined as chest tightness without characteristic attacks of bronchial asthma that improves with the use of a bronchodilator [1]. Chest pain variant asthma is difficult to diagnose because it is poorly characterized disease. The mechanism of chest tightness remains unexplained.

A pulmonary function test is an extremely useful method for diagnosing bronchial asthma [2]. Because pulmonary function testing in patients with chest tightness relieved with bronchodilator has been relatively unexplored, we examined forty cases of chest tightness relieved with a bronchodilator and without characteristic attacks of bronchial asthma.

Methods

Study design and subjects

Forty patients diagnosed as having recurrent chest tightness that improved in response to treatment with a bronchodilator and without characteristic attacks of bronchial asthma at the Toyama Prefectural Central Hospital between 2006 and 2013 were retrospectively studied.

We proposed that the chest tightness experienced by these patients and relieved by asthma drugs was classified into one of the following three types: “chest pain variant asthma,” “bronchial asthma with chest pain,” and “non-asthmatic allergic chest pain” [1]. No clear diagnostic criteria have been established for chest pain variant asthma. We hypothesized that chest pain variant asthma was defined as chest tightness relieved with a bronchodilator and without characteristic attacks of bronchial asthma [1]. The patients who presented with characteristic signs of bronchial asthma with chest tightness, which improved following the administration of a leukotriene receptor antagonist, systemic corticosteroid, or bronchodilator, were diagnosed with bronchial asthma with chest pain. We defined an asthma attack as recurrent episodes of wheezing

and breathlessness that are reversible spontaneously or with treatment. The patients who presented with recurrent chest tightness that was relieved with a bronchodilator and without characteristic attacks of bronchial asthma in this study were diagnosed as having chest pain variant asthma.

None of the patients in this study had been diagnosed with bronchial asthma before the first examination, and they had no other lung diseases. All of the patients complained primarily of chest tightness. Most of the patients underwent chest X-rays, laboratory diagnostics, electrocardiograms, pulmonary function testing, and upper gastrointestinal endoscopy to verify the absence of a pneumothorax, infection, coronary disease, or gastrointestinal disease. The patients were administered a bronchodilator via inhalation for chest tightness. The patients were diagnosed following a recurrent positive response to inhaling a bronchodilator and not presenting with characteristic attacks of bronchial asthma. The patients with chest tightness at the first examination were administered a bronchodilator via inhalation and underwent pulmonary function tests before and after inhalation.

For comparison, we randomly enrolled forty patients diagnosed with typical bronchial asthma at the Toyama Prefectural Central Hospital between 2006 and 2013. An asthma diagnosis was based on guidelines from the GINA [2]. None of the patients in this study were diagnosed with bronchial asthma before being examined, and they had no other lung diseases. At the first examination, all of the patients had either a mild asthma attack or no attack and were administered a bronchodilator (0.03 mg of procaterol hydrochloride, a short acting beta2-stimulant) via inhalation. They underwent pulmonary function testing before and after the inhalation.

For all eighty patients, the flow volume curve patterns of the pulmonary function tests before the bronchodilator treatment were classified into one of the following three types: an “upper-airway obstruction pattern,” “obstruction pattern,” and “normal pattern.” The classification was determined by a subjective judgment by a conference of authors.

Among the patients who were administered a bronchodilator via inhalation, those with improved rates of less than 5% in both peak expiratory flow rate (PEFR) and forced expiratory volume in one second (FEV1) were considered unreliable. We counted the patients with improved PEFRs after inhalation, which was defined as an increase of more than 1.5-fold in the FEV1. We also counted the patients with an improved FEV1 rates after inhalation, which was defined as an increase of more than 1.5-fold in the PEFR.

Statistics

The data are expressed as the means \pm SDs. The between-group

differences were determined using a chi-squared test.

Ethics

This retrospective study was approved by the ethics committee at the Toyama Prefectural Central Hospital.

Results

Among the forty patients diagnosed as having chest pain variant asthma, the average age of the onset of chest tightness was 36.7 ± 17.9 years; the average age at diagnosis of this disease was 40.7 ± 19.6 years; and the male:female ratio was 11:9. Among the forty patients diagnosed with bronchial asthma, the average age at the first examination and diagnosis of chest pain variant asthma was 52.8 ± 16.5 years, and the male:female ratio was 1:3.

Of the patients with chest pain variant asthma, 26 experienced chest tightness at the first examination, and 14 did not experience tightness (Figure 1). In the pulmonary function tests of the patients with chest tightness, the pre-treatment flow volume curve pattern revealed 12 of the patients (46.2%) had upper-airway obstruction patterns, 5 (19.2%) had obstruction patterns, and 9 (34.6%) had normal patterns. The twenty-six patients presenting with chest tightness at the first examination were administered a bronchodilator via inhalation. Then, 16 of these patients (61.5%) showed improvements in the rates of PEFRs that were more than 1.5-fold greater than the FEV1 (see Figure 2).

In the patients diagnosed with bronchial asthma, the flow volume curve patterns in the pulmonary function tests before the treatment revealed that 2 of the patients (5%) had upper-airway obstruction patterns, 30 of the patients (75%) had obstruction patterns, and 8 of the patients (20%) had normal patterns (Figure 1). After being administered a bronchodilator via inhalation, 18 of the patients (45%) showed improved PEFRs 1.5-fold greater than the FEV1; 13 of the patients (32.5%) showed improved rates of FEV1 that were greater than the PEFRs.

The most common flow volume curve pattern in the pulmonary function tests of the patients with chest pain variant asthma before treatment was the upper-airway obstruction pattern. The percentage of upper-airway obstruction patterns in the patients diagnosed with recurrent chest tightness was significantly more than that in the patients diagnosed with bronchial asthma ($p < 0.001$). In the pulmonary function tests of the patients diagnosed with recurrent chest tightness who were administered a bronchodilator via inhalation, the most common change observed was an improved rate of PEFR that was than 1.5-fold greater than the FEV1. The percentage of this change in the patients diagnosed with recurrent chest tightness was significantly greater than in the patients diagnosed with bronchial asthma ($p = 0.037$).

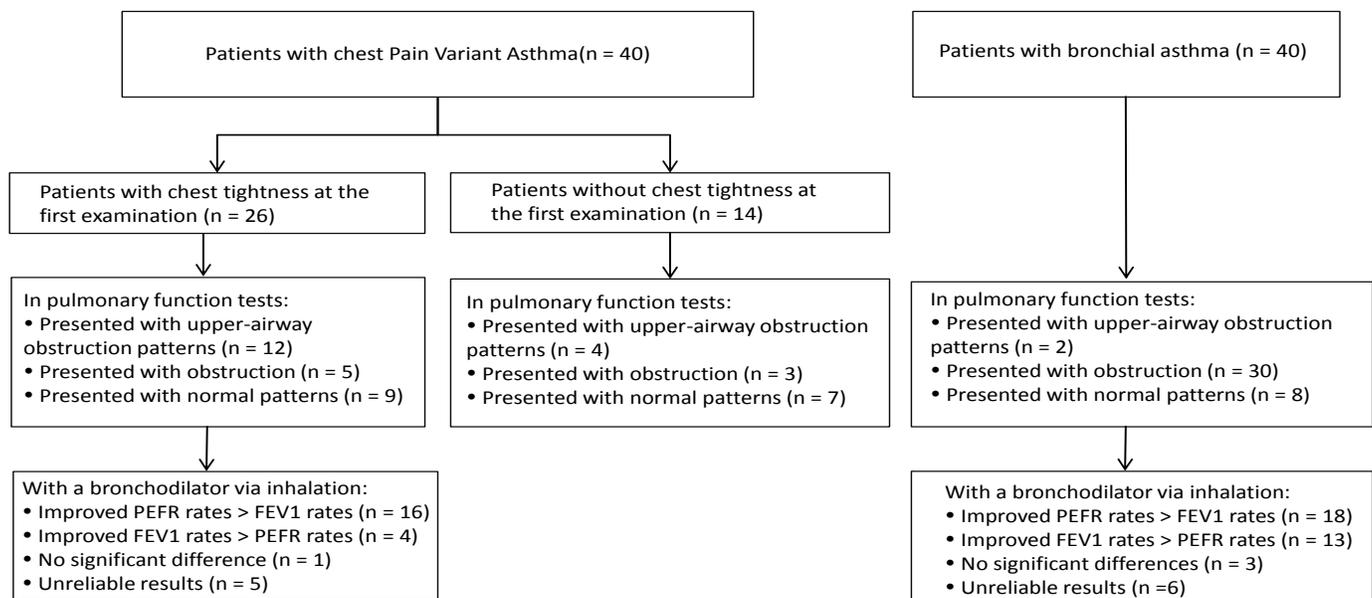
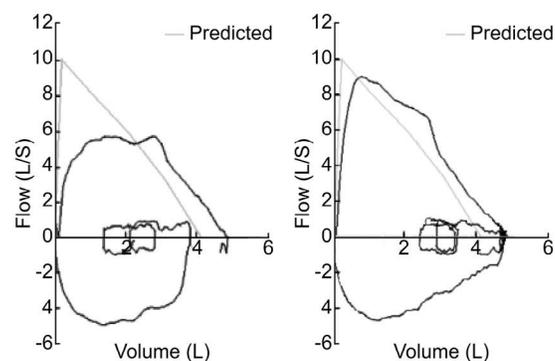


Figure 1. Patient enrollment and outcomes. PEFR: peak expiratory flow rate, FEV1: forced expiratory volume in one second.



	Before inhalation of procaterol hydrochloride	After inhalation of procaterol hydrochloride	Improvement rate (%)
FVC(L)	4.91	4.88	- 0.6
FEV1(L)	4.41	4.44	0.7
PEF(L/sec)	5.60	8.88	57.3

Figure 2. A practical example of a patient diagnosed with chest pain variant asthma. The patient experienced chest pain only at the first examination. He received a bronchodilator (0.03 mg of procaterol hydrochloride, a short acting beta2-stimulant) via inhalation and pulmonary function tests before and after the inhalation. In the pre-treatment pulmonary function test, the flow volume curve pattern was indicative of upper-airway obstruction. The upper-airway obstruction pattern improved after the patient was administered a bronchodilator via inhalation. PEFr: peak expiratory flow rate, FEV1: forced expiratory volume in one second.

Discussion

Treating patients with an inhalation of a bronchodilator during an attack of chest tightness can be useful in diagnosing chest pain variant asthma [1]. Most likely, chest pain variant asthma is a subtype of bronchial asthma [5]. Typical bronchial asthma patients present with recurrent episodes of wheezing, breathlessness, dyspnea, and cough from airway constriction, but chest pain variant asthma patients present with recurrent episodes of chest tightness from airway constriction [1].

A typical symptom of chest pain variant asthma is a retrosternal tightness or a heavy sensation in the chest. It is sometimes associated with cough, sputum, or tightness radiating to one side of the head, back, or chest [1]. The severity, frequency, duration, and onset time of a chest tightness attack can vary in different patients. Patients with chest pain variant asthma should be treated in the same manner as those with typical asthma. Upon clinical examination, we realized that many of the patients diagnosed with chest pain variant asthma showed an upper-airway obstruction pattern in the pulmonary function tests, which improved with a bronchodilator via inhalation [1,6].

In this study, we analyzed the pulmonary function tests of pa-

tients diagnosed with chest pain variant asthma. Many of the patients with chest tightness had a flow volume curve with upper-airway obstruction patterns in the pre-treatment pulmonary function tests. The rates of PEFr improved after treatment and were greater than that of the FEV1 after inhalation, which indicated an upper-airway condition. An upper-airway obstruction pattern may be caused by a disease of the oral cavity, thyroid enlargement, or a comparatively large airway [8]. We hypothesize that the upper-airway obstruction pattern reveals that chest tightness is induced in constriction of comparatively large airways, such as the trachea and main bronchi. Thus, the patients with chest tightness showed no wheezing during the chest tightness attack, and many of them demonstrated retrosternal tightness. However, it is doubtful that tracheal and main bronchial muscle constriction leads to an upper-airway obstruction pattern of the flow volume curve because these airways have cartilage. An upper-airway obstruction pattern may be not caused by poor expiration due to chest tightness because some patients had a flow volume curve with upper-airway obstruction patterns without chest tightness. We are planning an analysis of these clinical conditions using different study methods.

Some of patients with chest pain variant asthma during chest tightness had a flow volume curve with normal patterns in the pre-treatment pulmonary function tests [7]. They showed mild or no improvements in the PEFr and FEV1 of their pulmonary function tests between before and after inhalation of bronchodilator. We suspected that their chest tightness results from mild airway constriction.

There is a need for increased knowledge of chest tightness relieved with a bronchodilator or other asthma drugs and without characteristic attacks of bronchial asthma. Thus, this clinical condition should be further investigated. We are engaged in several prospective studies analyzing patients with chest pain variant asthma (clinical trial registration number: UMIN13994), the proportion in causative disease with chronic or recurrence chest tightness (UMIN13992), and patients with non-asthmatic allergic chest pain (UMIN13998). We hope to reveal the epidemiology, pathology, pathophysiology, and clinical characteristics of chest pain variant asthma and its relative disease in these studies.

Conflicts of interest: The authors have reported no significant conflicts of interest regarding any companies/organizations whose products or services may be discussed in this article.

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