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Original Article

Pulmonary Function Tests in Thunderstorm-associated Respiratory Symptoms: A Cross-sectional Study

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What's Known

- Most previous studies of thunderstorm asthma were applied to environmental and meteorological variables. Several patients with asthma-like symptoms during thunderstorms had no previous history of asthma.

What's New

- To the best of our knowledge, this is the first study to evaluate the pulmonary function and bronchial hyperresponsiveness test characteristics in thunderstorm-associated respiratory symptoms. Most of the patients with thunderstorm-associated respiratory symptoms had no obvious evidence of airflow limitation in spirometry, but most of them with normal baseline spirometry had positive provocation tests.

Abstract

Background: Epidemic thunderstorm asthma is an observed increase in cases of acute bronchospasm following thunderstorms. This study aimed to compare the frequency of obstructive airway disease or bronchial hyperresponsiveness in subjects with thunderstorm-associated respiratory symptoms with subjects with similar symptoms presented at other times.

Methods: A cross-sectional study from June to November of 2013 was conducted on subjects with thunderstorm-associated respiratory symptoms living in Ahvaz City, Iran. Thunderstorm-associated subjects were presented with asthmatic symptoms in thunderstorms, and other patients presented with similar symptoms at other times. Baseline spirometry was performed on patients to examine the presence of obstructive airway disease. In all patients with normal spirometry, a provocation test was applied. A comparison of qualitative and quantitative variables was made using the Chi-square and independent *t* test, respectively. All analyses were carried out using SPSS Statistics Version 22. A P value less than 0.05 was considered statistically significant.

Results: Out of 584 subjects, 300 and 284 participants were in thunderstorm-associated and non-thunderstorm-associated groups, respectively. After the final analysis, 87 (30.6%) and 89 (33.3%) of the thunderstorm-associated subjects and non-thunderstorm-associated group, respectively, had pieces of evidence of airflow limitation (P=0.27). Among the patients with normal spirometry, 161 (81.72%) of the thunderstorm-associated patients and 100 (56.17%) patients of the non-thunderstorm-associated symptoms group had a positive methacholine challenge test result (P<0.001).

Conclusion: Most of the patients with thunderstorm-associated respiratory symptoms had no obvious evidence of airflow limitation in spirometry.

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Keywords ● Asthma ● spirometry ● Thunderstorm ● Methacholine chloride ● Respiratory function tests

Introduction

Asthma is one of the chronic inflammatory diseases of the airways that causes reversible limitation of airflow in spirometry tests. According to the World Health Organization report, there will probably be 400 million asthma patients in the world by 2025.[1]

The term "Thunderstorm Asthma Epidemic" refers to the increase in the number of cases with bronchospasm symptoms following thunderstorms.[2] Although thunderstorm asthma (TA) epidemics are rare, they are significant public health problems in some countries.[3] Current evidence suggests that TA results from the interaction of environmental factors with individual susceptibility factors.[4]

Most previous studies on TA focused on environmental and meteorological variables.[5-8] In other studies, several patients experiencing asthma-like symptoms during thunderstorms did not have a previous history of asthma or may have only suffered from seasonal rhinitis.[9, 10] Baseline spirometry or bronchoprovocation tests are the essential methods to identify asthma.[11, 12]

This study was conducted in Ahvaz, Iran. Ahvaz is an industrial city that has petrochemical, silk textile, carbon black, sugarcane, and steel companies. Several dust storms occur in this city annually. According to the report of the World Health Organization (WHO) in 2011, it was the most polluted city in the world. After a seasonal rainfall occurred on 2nd November 2013 in Ahvaz, 2996 patients were referred to Ahvaz Jundishapur Medical University emergency departments (ED) with dyspnea or cough after about two hours of rainfall initiation. The asthma epidemic lasted for around three weeks, and its peak occurred through the first three days after rainfall. We have already reported the burden of the epidemic and the basic characteristics of most of these patients. What is noteworthy here is that the asthma definition is not based on pulmonary function tests but only on the symptoms described by the patients.[13]

This study aimed to assess the pulmonary functions after seasonal thunderstorms among patients with asthma-like symptoms including spirometry and provocation test in Ahvaz, Iran to evaluate objective evidence of obstructive airway disease or bronchial hyperresponsiveness. To the best of our knowledge, this is the first study to evaluate pulmonary function test results in seasonal rainfall-associated respiratory symptoms.

Participants and Methods

A cross-sectional study was conducted on the people living in Ahvaz City, Iran, from June to November of 2013, to evaluate the presence and frequency of obstructive airflow limitation or bronchial hyperresponsiveness, measured by the spirometric or provocation tests, respectively, in patients with respiratory symptoms associated with the first seasonal rainfalls in November 2013 in comparison with subjects presented with similar symptoms at other times.[9]

Following the sudden onset of the epidemic, about one day after its initiation, a data gathering form, which consisted of a brief history, was distributed in nine hospitals. A nurse practitioner or a physician interviewed the patients who had respiratory symptoms (dyspnea, wheezing with or without cough) during thunderstorms.

After three weeks, the subjects who had completed the primary questionnaire were called to complete a secondary questionnaire with more details. Out of about 2500 patients, 1800 provided their contact information, but ultimately only 800 patients accepted to fill out the secondary questionnaire. Of this population, 284 thunderstorm-associated subjects (TAS) and 267 participants who presented with similar symptoms not related to thunderstorms, referred to as non-thunderstorm-associated subjects (NTAs), were included. They filled out similar questionnaires and underwent pulmonary function tests. [Sample size formula: $n=(N(z^2)\times pq)/(d^2(N-1)+z^2 pq)$. P=0.71 (considering positive pulmonary function test results of 0.51, according to a study by Cheraghvandi and colleagues, q=0.2, d=0.05, z=1.96)].[14]

Participants

TAS had asthma-like symptoms and was referred to the hospital during or shortly after the early autumn rainfall regardless of whether they also attended at other times. NTAS refers to individuals who had previously presented with similar respiratory symptoms during previous winter, spring, and summer seasons before the epidemic. All the participants were not asthmatic (had no definite asthma according to objective data, spirometry, or provocation test). The patients with hemoptysis, current pregnancy, suspicion of acute coronary syndrome, and poor cooperation to do spirometry maneuvers were excluded. This study was approved by Ahvaz Jundishapur University of Medical Sciences ethics committee (code: IR.ajums.Rec.1393.167). Written informed consent was obtained from all participants.

Variables

The primary outcomes were to evaluate obstructive pattern frequency in spirometry tests (based on $FEV1/VC_{max}$ or FEV1/FVC≤70% or positive methacholine challenge test frequency in subjects with normal baseline spirometry). Each participant performed spirometry according to American Thoracic Society (ATS) and European Respiratory Society (ERS) guidelines with a

standard spirometer (Ganshorn, Germany). If there was no evidence of airflow limitation (FEV1/VC_{max} or FEV1/FVC more than 70%), a provocation test with methacholine was done according to ATS guidelines with considering contraindications and withholding drugs that could interfere with test results. We used the two-min tidal breathing method. The subjects inhaled aerosolized normal saline, followed by aerosolized saline containing methacholine in doubling doses from 0.0125 mg/mL to 16 mg/mL at each interval. Doubling doses were administered in this manner until either FEV1 fell by 20% of baseline or until the final dose was administered. The Methacholine challenge test result was defined as positive, if the provocation concentration causing a 20% fall in FEV1 (PC20) was less than 16 mg/mL. In this study, definition of asthma was based on FEV1/VC_{max} or FEV1/FVC≤70% predicted or positive methacholine challenge test result in the presence of asthma symptoms. Secondary outcomes were associated with probable risks of thunderstorm-associated respiratory symptoms including age, sex, previous asthma or rhinitis history, and smoking history.

Statistical Analysis

All analyses were carried out using SPSS Statistics Version 22. Categorical variables were expressed as numbers and percentages. The continuous variables were expressed as mean values and standard deviations. A comparison of qualitative variables among groups of subjects was made by the Chi-square test. We used an independent *t* test to compare quantitative variables. A P-value less than 0.05 was considered statistically significant.

Results

A total of 584 patients aged 15-65 years, were enrolled in the study. The flowchart of the study (figure 1) and the basic characteristics of the participants are shown (table 1). Most of the patients in the two groups were middle-aged (mean age of 36 years old). There were no significant sex differences between the two groups; male sex numbers and percentages were 155 (54.5%) and 146 (54.6%) in TAS and NTAS, while female sex numbers and percentages were 129 (45.4%) and 121 (45.3%) in TAS and NTAS, respectively (P≤0.98). Previous asthma history was less frequent in TAS (P<0.001). Smoking history was more prevalent in NTAS than TAS (P=0.02). Previous and current rhinitis histories were more frequent in TAS (P<0.001). There was no statistically significant difference in obstructive airway pattern in basic spirometry between the two groups (P=0.27). According to FEV1, moderate to severe obstructive patterns were more prevalent in TAS than NTAS (P=0.01 and P=0.04, respectively). Normal baseline spirometry was similar in the two groups (P=0.52). According to the methacholine challenge test result, bronchial hyperresponsiveness was significantly more frequent in TAS (P<0.001) (table 2).

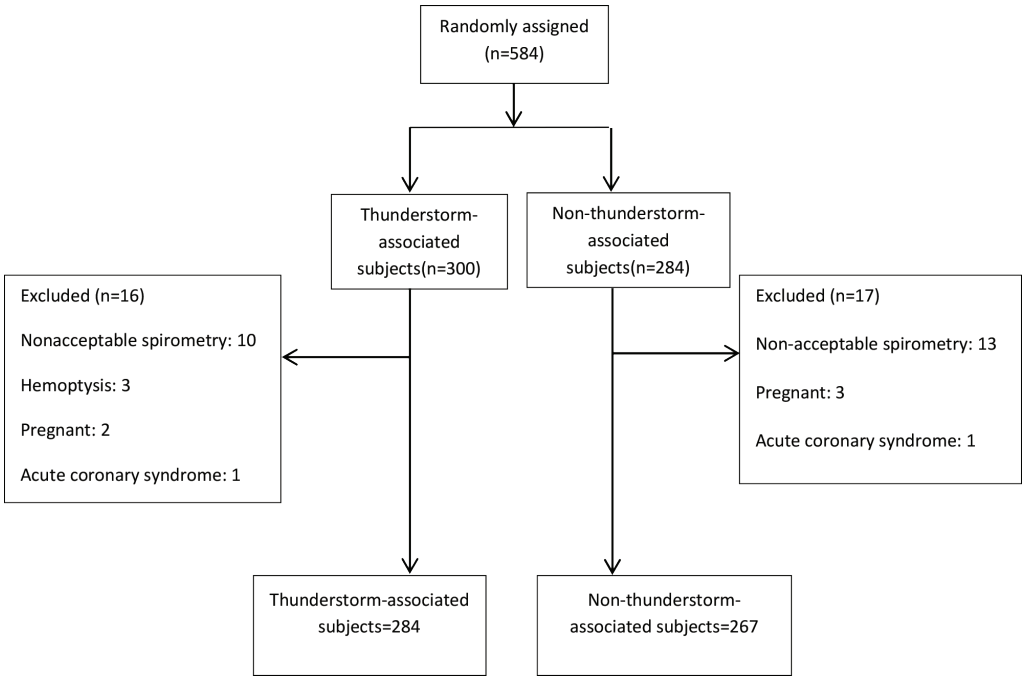

Figure 1: The flow chart of the study. A total of 584 patients were randomly assigned to participate. Of this population, 284 participants were thunderstorm-associated subjects, and 267 participants who presented with similar symptoms at other times were non-thunderstorm-associated subjects.

Table 1: Basic characteristics of thunderstorm-associated and non-thunderstorm-associated subjects

Characteristics		Thunderstorm-associated subjects	Non-thunderstorm-associated subjects	P value
Age(year, Mean ±SD)*		36±12	36±11	0.66
Sex n (%)	Male	155 (54.5)	146 (54.6)	0.98
	Female	129 (45.4)	121 (45.3)	
Previous asthma history, n (%)		53 (18.6)	94 (35.2)	<0.001
Smoking history, n (%)		39 (13.7)	56 (20.9)	0.02
Previous history of rhinitis		95 (33.4)	56 (20.9)	<0.001
Current history of rhinitis		135 (47.5)	81 (30.3)	<0.001

*Comparison of qualitative variables among groups of subjects was made by the Chi square test. A P value less than 0.05 was considered statistically significant.

Table 2: The results of spirometry and provocation tests in thunderstorm-associated and non-thunderstorm-associated subjects

Pulmonary function test data	Thunderstorm associated subjects n=284	Non-thunderstorm-associated subjects n=267	P value
FEV_1/FVC ≤70%*	87 (30.6)	89 (33.3)	0.27
FEV_1≥80%	9 (10.34)	23 (25.84)	0.01
FEV_1 60-79%	42 (48.27)	33 (37.07)	0.01
FEV_1<60%	36 (41.37)	33 (37.07)	0.04
FEV_1/FVC>70%	197 (69.36)	178 (66.66)	0.52
Positive MCT	161 (81.72)	100 (56.17)	<0.001
Negative MCT	36 (18.27)	78 (43.82)	<0.001

FEV_1: Forced Expiratory Volume in one second; FVC: Forced Vital Capacity; MCT: Methacholine Challenge Test; *Independent *t* test used to compare quantitative variables. A P value less than 0.05 was considered statistically significant.

Discussion

Around one-third of the TAS had spirometry evidence of airflow limitation (FEV1/VC_{max}≤70%) and most of the others had positive provocation test results. This study showed that the prevalence of spirometry findings with obstructive patterns is similar in thunderstorm-associated and non-thunderstorm patients with asthma symptoms, but airflow limitation is more severe in thunderstorm-associated subjects. It may be due to recent exposure to allergens in thunderstorm conditions, which could exacerbate or trigger asthma. This recent allergen exposure may also explain more frequent positive bronchial provocation tests in some cases.[15] This result showed that most of the thunderstorm-associated respiratory symptoms are related to bronchial hyperresponsiveness without evidence of an obvious obstructive pattern in spirometry. We did not find any previous studies on conducting pulmonary function tests in individuals experiencing thunderstorm-associated respiratory symptoms.

There were no sex or age differences between cases and controls, and most of the participants in both groups were middle-aged men. These results were compatible with the results of previous studies on thunderstorm-associated respiratory symptoms.[4, 10, 16]

Most of the TAS and NTAS in our study did not have previous history of asthma according to self-reporting data, and asthma was more frequent in TAS than NTAS. The accuracy of asthma diagnosis increases by objective measurement of airway hyperresponsiveness. In s study by Thien, only 28% of patients had current doctor-diagnosed-asthma.[4] Moreover, in a study by Rangamuwa, 58% of participants had no asthma diagnosis.[10] The results of these studies are concurrent with ours.

A significant percentage of TAS had a history of allergic rhinitis, which is in accordance with literature- reported Melbourne epidemic.[10] Allergic rhinitis could induce bronchial hyperresponsiveness without asthma presence. The low prevalence of smoking among cases is compatible with the finding of Rangamuwa and colleagues with a low prevalence of smoking among patients presented with respiratory symptoms in thunderstorms. Besides, in the Melbourne epidemic on 21 November 2016, most of the patients were non-smokers.[10] Recent exposure to allergens in thunderstorm conditions increases the likelihood of asthma and may also affect smokers in the NTAS group who have chronic obstructive airway disease.

Our hypothesis for these results is that thunderstorm-associated cases represent a distinct subgroup of asthma. This may be a kind of seasonal asthma that is triggered by specific allergens and often presented in climatic changes related to thunderstorms without consistent objective evidence of asthma

in spirometry tests. These triggers have been shown in several studies as a complex of climatic changes and organic air pollutants such as pollens or spores.[6, 7]

This study had some limitations. Pulmonary function tests were done about three weeks after the respiratory attack. Bronchial hyperresponsiveness may diminish after sometimes with avoidance of triggers, and this may justify the normality of spirometry and provocation test results among some of the participants. We did not stop inhaled corticosteroids before pulmonary function tests. Inhaled corticosteroids may also decrease the threshold of bronchial hyperresponsiveness, and this may be another reason for the negative results of provocation tests in some patients.

Conclusion

Most of the patients with thunderstorm-associated respiratory symptoms had no obvious evidence of airflow limitation in spirometry, but most of them with normal baseline spirometry had positive provocation tests. Most of the subjects with thunderstorm-associated respiratory symptoms are middle-aged patients with allergic rhinitis and without previous history of asthma.

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Authors' Contribution

M.HS: Study design, interpretation, and manuscript revision; S.A: Data collection and drafting; SH.B: Data collection and manuscript revision; H.R: Data interpretation and manuscript revision; E.I: Data interpretation and manuscript revision. All authors have read and approved the final manuscript and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflict of interest: None declared.

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