Asthma in Adventure Travelers

A Prospective Study Evaluating the Occurrence and Risk Factors for Acute Exacerbations

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Background: Exacerbation of asthma during travel to remote regions may lead to devastating consequences. The course of asthma in travelers and the risk factors for disease exacerbation during travel have not been studied.

Methods: We screened 5835 consecutive travelers and identified 203 patients with asthma. Before travel, all enrollees were assessed for presumed risk factors for asthma exacerbation by means of an interview and an exercise test combined with spirometry. After travel, data regarding travel characteristics and asthma severity were recorded by means of a structured telephone interview.

Results: The 203 enrollees visited 56 countries for a median duration of 13 weeks, 147 were engaged in high-altitude trekking, and 88 had asthma attacks. Among these, 40 reported worsening asthma during travel, 32 experienced the worst asthma attack ever, and 11 reported a life-threatening asthma attack. Two independent risk factors for attacks during travel were identified: frequent use (≥3 times weekly) of inhaled bronchodilators before travel (relative risk [RR], 3.35; 95% confidence interval [CI], 1.75-6.39) and participation in intensive physical exertion during treks (RR, 2.04; 95% CI, 1.04-3.98). When both risk factors were present, the RR for asthma attacks increased to 5.52 (95% CI, 2.81-10.84).

Conclusions: Asthma frequently worsens during travel and should not be ignored as a potentially life-threatening condition requiring pretravel consideration. Asthmatic travelers who frequently use inhaled bronchodilators before travel or participate in intensive trekking during travel are at increased risk to develop asthma attacks. Therapy should be intensified to achieve better disease control; intensive trekking should be discouraged.

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in the travel plans and precautions taken before and during travel.

**METHODS**

**STUDY DESIGN AND POPULATION**

This was a prospective cohort study. All patients 18 years or older who visited a single travel clinic in Tel Aviv, Israel, for pretravel consultation during 1995 were asked to fill out a questionnaire regarding their health status. Travelers were asked specifically about history of asthma. Those who declared themselves as “active asthmatic” were eligible for the study. All study participants underwent a pretravel and posttravel evaluation. Patients were excluded if they did not agree to participate in the evaluation, could not be located after travel, or did not travel.

**PRETRAVEL EVALUATION**

A single physician (Y.G.) interviewed eligible patients. Demographic variables, general medical history, detailed allergy and asthma history, and patient’s self-expectations for the impact of asthma on travel were recorded on a structured questionnaire. The patient’s expected date of return from travel was also recorded. After the interview, patients underwent lung auscultation (results were categorized as no wheezing, minimal wheezing, or significant wheezing) and spirometry (Compact Spirometer; Vitalograph, Inc, Lenexa, Kan). Patients were encouraged to perform at least 3 maneuvers to meet the American Thoracic Society criteria for acceptability and reproducibility. The largest forced expiratory volume in 1 second (FEV1) was used for analysis. All patients with an FEV1 greater than 65% of the predicted value who had not used bronchodilators during the preceding 4 hours were examined by an exercise test. Patients who had used bronchodilators during this period were rescheduled for a later test. Those with an FEV1 equal to or lower than 65% of the predicted value were not tested. The exercise test was executed on a treadmill slope of 15° with a gradual increase in speed to 8 km/h within 3 minutes, for a total of 10 minutes of exercise. The workload increased the heart rate to 80% to 90% of the age-predicted maximum (calculated as 220−age). Lung auscultation and spirometry were repeated 8 to 10 minutes after termination of exercise. An FEV1 reduction of 15% or greater compared with the preexercise value was defined as a positive test result. Test results were reported to the patient without any further intervention.

**POSTTRAVEL EVALUATION**

On the basis of the expected date of return, patients were located after travel, and structured telephone interviews were conducted by a single physician (Y.G.). Data regarding travel characteristics, allergies, episodes of asthma attacks, and possible risk factors for asthma exacerbation during travel were recorded. Travelers were asked whether they had experienced asthma attacks (1 or more), which were defined as the acute occurrence of wheezing and dyspnea. Mild dyspnea of a nonepisodic nature and without wheezing was not considered an attack. Travelers were also asked to compare asthma during travel with that in the pretravel period by answering the following 3 questions: “Compared with a similar duration of time prior to travel, was your asthma severity during travel better, the same, or worse? Compared with a similar duration of time prior to travel, was the frequency of your asthma attacks less, the same, or more? Compared with the worst asthma attack before travel, was the worst attack during travel less severe, the same, or the worst attack in your life?”

**STATISTICAL ANALYSIS**

Travelers were divided into 2 groups according to the occurrence or nonoccurrence of asthma attacks during travel. Univariate and multivariate logistic regression analyses were used to measure the association between each variable and the risk to develop asthma attacks during travel. In the univariate analysis, differences between groups were analyzed with the χ² test for categorical variables and the t test for continuous variables, except for the length of travel, for which the Mann-Whitney rank sum test was used. A 2-sided P value of less than .05 was used to indicate statistical significance. Relative risk for continuous variables was calculated for increments of 1 year for age, increments of 0.1 L and 1% for FEV1, and increments of 1 month for length of travel. Variables significantly associated with asthma attacks in the univariate analyses (P<.05) were eligible for inclusion in the multivariate models. To retain sufficient statistical power, the presence of wheezing after exercise was excluded from the model because data were missing for 23 patients who did not perform the exercise test. In the multivariate analysis all variables were dichotomized. To control for time, analysis of covariance was used with length of travel as a continuous covariate. Statistical analysis was performed with SPSS software, version 8.0 (SPSS Inc, Chicago, Ill).

**RESULTS**

Of 5835 travelers who visited the travel clinic during 1995, 220 (3.8%) were eligible for the study. Of these, 17 were excluded for the following reasons: 8 refused to participate, 8 could not be located for posttravel evaluation, and 1 canceled the trip. All 203 enrollees were white, the mean age was 23.9 years, and 50% were female.

**PRETRAVEL CHARACTERISTICS**

Table 1 summarizes the pretravel characteristics. The typical enrollee had seasonal asthma (76%); had other allergies (75%); was diagnosed before the age of 10 years (59%); and used bronchodilators during the year preceding travel (83%). Exercise was reported as a trigger for asthma attacks by 138 (68%), but only 5 reported that asthma limited their daily activities.

**POSTTRAVEL EVALUATION**

Of the 203 travelers, 193 were interviewed within 10 days and 10 within 2 months after travel. Table 3 summarizes travel characteristics. The enrollees visited 56 countries, of which Thailand, India, and Nepal were the most frequently visited, for a median duration of 13 weeks (range, 2-123 weeks). Intensive high-altitude trekking, defined as difficult walking in altitudes above 1500 m, was common overall (125 travelers [65%]) and also among travelers with positive exercise tests (65%).
Asthma attacks during travel were reported by 88 (43%) of 203 travelers. Table 4 summarizes the characteristics of these travelers. Of the 88, 40 (45%) reported worsened asthma during travel; 32 (37%) had experienced the “worst asthma attack in their life”; and 11 (13%) reported having life-threatening attacks during travel. Only 18 (20%) of the 88 with attacks and 5 (13%) of the 40 with worsened asthma had modified their itinerary before traveling to avoid what they expected to be risky routes. Thirty-six (90%) of the 40 with worsening asthma and 10 (91%) of the 11 with life-threatening asthma had failed to foresee this outcome when asked before travel.

**UNIVARIATE ANALYSIS**

Univariate analyses identified 6 variables significantly associated with developing asthma attacks during travel, 4 of which were pretravel variables (Tables 1 and 2): frequent pretravel use of inhaled bronchodilators, emergency department treatment for asthma during the year preceding travel, presence of preexercise wheezing, and presence of significant wheezing after exercise. The 2 significant intratravel variables were participation in intensive physical exertion while trekking, and traveling for a period longer than 6 months (Table 3). Other variables, including pretravel history of exercise-induced asthma, glucocorticoid use, low FEV1 values before and after exercise test, and positive exercise test, were not significantly associated with having asthma attacks during travel.

**MULTIVARIATE ANALYSIS**

In the complete multivariate model, after controlling for the length of travel, inhaled bronchodilator use 3 or more times weekly (relative risk, 3.35; 95% confidence interval, 1.75-6.39; \( P < .001 \)) and participation in intensive physical exertion during treks (relative risk, 2.04; 95% confidence interval, 1.04-3.98; \( P = .04 \)) remained the only independent variables. The relative risk for developing asthma attacks during travel among patients with these 2 risk factors increased to 5.52 (95% confidence interval, 2.81-10.84; \( P < .001 \)).
This is the first study to describe the course of asthma in travelers. The study population included young adults who traveled to developing countries for an average period of 4 months. Most enrollees had features of allergic asthma: family history of asthma, other allergies (hay fever and eczema), seasonal (rather than perennial) attacks, and positive reaction to immediate-type skin allergy tests. Almost 4% of the travelers who visited our...
travel clinic had asthma, similar to the prevalence of asthma previously reported among young adults. 3,7,8

According to the Global Initiative for Asthma classification, 9 most of our patients with asthma would have been classified as having mild or moderate disease. Travelers with severe asthma were less likely to participate in rigorous travel because it involves physical exertion and staying in medically inaccessible areas. However, being diagnosed as having mild or moderate disease does not protect one from developing near-fatal or fatal attacks. In a series of asthma deaths among children and young adults from Australia, 33% had a history of mild asthma. 10 Several studies 11,12 have reported that variables such as duration of asthma, sex, smoking status, ethnicity, presence of atopy, and degree of airway obstruction or bronchial hyperresponsiveness were similar among patients with near-fatal or fatal asthma as compared with patients with mild exacerbation. The disease characteristics that place patients at risk for fatal or near-fatal asthma attacks remains ill defined. Of those previously suggested, only a history of recurrent hospitalization or need for ventilatory assistance are specific enough to be helpful. These characteristics, however, are found in only 36% of fatal cases and 6% of near-fatal cases 13-14 and, as expected, were uncommon among our travelers. Sudden catastrophic episodes of asthma are well described but are very rare. 15,16 In nearly 85% of deaths due to asthma, the final episode lasts at least 12 hours. 17,18 Most asthma deaths are the result of an uncontrolled progressive attack. 19,20 Therefore, we chose acute asthma attacks as the primary outcome measure in the present study. The identification of pretravel and intratravel risk factors for developing asthma attacks during travel, and thus identification of a population at risk, was the major aim of this study.

With multivariate analysis, 2 variables were identified as independent risk factors for developing acute asthma attacks during travel. The first was the frequent use of inhaled bronchodilators before travel. Asthmatic travelers who had used inhaled bronchodilators 3 or more times weekly during the year preceding travel were 3 times more likely to develop asthma attacks during travel when compared with their counterparts who had used bronchodilators less frequently or not at all. Excessive use of inhaled bronchodilators, especially in the absence of use of inhaled corticosteroids, was reported to confer an increased risk of severe, “near-fatal,” and fatal asthma attacks regardless of whether it was directly responsible or served as a marker for more severe or poorly controlled disease. 21,22 Underuse of inhaled corticosteroids was observed in our study population in both frequent and infrequent users of inhaled bronchodilators and could not explain the different outcomes. Undertreatment is commonly reported among patients with asthma. 23,24

The second variable was participation in intensive physical activity in treks during travel. Travelers performing such activity doubled their risk of developing asthma attacks in comparison with travelers who participated in less demanding physical exertion. This finding raises the question of whether a pretravel history of exercise-induced asthma or a pretravel evaluation with an exercise test may help pretravel identification of patients at risk. Our results, however, failed to support these assumptions. A history of exercise-induced asthma before travel, although common in our study population (68% of all travelers), was found in similar proportions among the groups with and without asthma attacks during travel. Furthermore, no significant association was found between positive exercise test or a poor pretest FEV1 result and the occurrence of asthma attacks during travel. This lack of association may be related to the fact that an apparent asthmatic response after exercise challenge may represent a diurnal fluctuation in pulmonary mechanics that develops spontaneously in persons with asthma. Indeed, several studies demonstrated low reproducibility of pulmonary response to exercise. 25,26 The mechanism of exercise-induced asthma is incompletely understood. It is generally agreed that the initial event in the induction of exercise-induced asthma relates to the degree of heat loss from airways on exercise. The amount of heat loss depends on minute ventilation as well as on temperature and humidity of the inspired air. Airway obstruction is maximized when the inspired air is cold or dry and minimized when it is warm and humid. In fact, inhalation of cold dry air has been suggested as a strong stimulus for the release of inflammatory mediators and subsequent bronchoconstriction. 27 We hypothesize that it was not only physical exertion but also a combination

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. (%) of Travelers</th>
</tr>
</thead>
<tbody>
<tr>
<td>No change or improvement</td>
<td>48 (55)</td>
</tr>
<tr>
<td>Worsening</td>
<td>40 (45)</td>
</tr>
<tr>
<td>No change from pretravel year</td>
<td>39 (44)</td>
</tr>
<tr>
<td>Less than pretravel year</td>
<td>27 (31)</td>
</tr>
<tr>
<td>More than pretravel year</td>
<td>22 (25)</td>
</tr>
<tr>
<td>Asthmatic attacks as severe as previous</td>
<td>41 (48)</td>
</tr>
<tr>
<td>Less than previous</td>
<td>13 (15)</td>
</tr>
<tr>
<td>“The worst ever”</td>
<td>32 (37)</td>
</tr>
<tr>
<td>Experienced life-threatening asthma</td>
<td>11 (13)</td>
</tr>
<tr>
<td>Treated by a physician because of asthma</td>
<td>11 (13)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. (%) of Travelers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trekking</td>
<td>38 (43)</td>
</tr>
<tr>
<td>Exercise</td>
<td>36 (41)</td>
</tr>
<tr>
<td>Air pollution</td>
<td>24 (27)</td>
</tr>
<tr>
<td>Dust</td>
<td>22 (25)</td>
</tr>
<tr>
<td>Cold weather</td>
<td>18 (20)</td>
</tr>
<tr>
<td>Respiratory tract infection</td>
<td>18 (20)</td>
</tr>
<tr>
<td>Heights</td>
<td>16 (18)</td>
</tr>
<tr>
<td>Heat and humidity</td>
<td>10 (11)</td>
</tr>
<tr>
<td>Plants</td>
<td>10 (11)</td>
</tr>
<tr>
<td>Laughter</td>
<td>9 (10)</td>
</tr>
<tr>
<td>Excitement</td>
<td>8 (9)</td>
</tr>
<tr>
<td>Smoking</td>
<td>8 (9)</td>
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*Data were available for 86 travelers.
†Travelers may have had more than 1 trigger for exacerbation.
of other factors associated with trekking—high altitude, cold dry air, and exposure to new allergens—that triggered asthma attacks during physically demanding trekking. Identification of travelers at risk for the development of asthma attacks during trekking is particularly important since the primary aim of therapy in patients with exercise-induced asthma is prophylaxis. Inhalation of β-agonists, particularly long-acting compounds, has been shown to prevent obstruction if used before exertion.

Of the 88 travelers who reported acute asthma attacks, almost half assessed the severity of the asthma attacks during travel to be worse than the attacks during the length-equivalent period before travel, 37% experienced “the worst asthma attack in their life,” and 12% had life-threatening attacks. These data suggest that a significant number of travelers were in a potentially dangerous situation during travel. Nevertheless, many travelers underestimated the risk of developing a life-threatening asthma attack during travel, failed to predict this outcome in the pretravel interview, and did not modify their original plans to minimize the risk of asthma attacks. The ability to prepare for future exacerbation or to respond to worsening asthma was shown to be crucial in the prevention of severe attacks. The dependence on the emergency department for initial care was found to be prevalent among patients experiencing a near-fatal attack before its development. Such an approach is particularly prone to failure whenever emergency care is not provided, delayed, or inappropriate, as might be the case in remote areas in Third World countries.

The first step in attempting to decrease morbidity of asthma during travel is to increase the awareness of both physicians and patients to the possibility that asthma might dangerously worsen during travel. Asthmatic travelers should be assessed for active disease. Optimal asthma control before travel should be achieved by adequate use of medications in any patient with active disease. Travelers who have used inhaled β-agonist bronchodilators 3 times weekly or more during the year preceding travel should be advised to postpone travel to developing countries until better asthma control is achieved. Travel planning to avoid triggers for exacerbation, especially intensive exercise during trekking, is important. Clinicians should ensure that all asthmatic travelers are aware of optimal maintenance management, can recognize deteriorating asthma, and can follow a clear individual crisis plan. An intervention trial is needed to assess the efficacy of these measures for the prevention of asthma exacerbation during travel.

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REFERENCES