Research Article

Air travel can be safe and well tolerated in patients with clinically stable pulmonary hypertension

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ABSTRACT

Our aim was to determine what proportion of patients with pulmonary hypertension (PH) has undertaken air travel contrary to the general medical advice and to characterize these patients according to disease severity and medical treatment. In cooperation with Pulmonale Hypertonie e.V., the German patient organization, a questionnaire was distributed. In total, 430 of 720 questionnaires were returned completed. Of the 179 patients who travelled at least once by air, the distribution of New York Heart Association functional classes I/ II/ III/ IV was 2/ 77/ 74/ 8, respectively; 83 patients were receiving monotherapy; 58 patients were receiving a combination of two or more therapies; 57 patients were on long-term ambulatory oxygen treatment; and 29 patients used supplemental oxygen while travelling. Overall, 20 adverse events were reported, mostly of mild to moderate severity (i.e., peripheral edema, dyspnea), with need of medical intervention in only 7 cases. The 251 patients who did not travel by air were, on average, in more advanced stages of disease and/or clinically unstable. In conclusion, a majority of patients (159 out of 179) did not experience any complications during or directly after the flight even though no special precautions were taken. Thus we conclude that for patients with PH in a stable clinical condition, air travel can be safe and well tolerated.

Key Words: air travel, high altitude, hypoxic pulmonary vasoconstriction, pulmonary hypertension, safety

INTRODUCTION

Pulmonary hypertension (PH) is defined as a resting mean pulmonary arterial pressure ≥25 mmHg.[1] The subgroup of patients with pulmonary arterial hypertension (PAH) is defined by the additional criterion of a pulmonary capillary wedge pressure ≤15 mmHg.[1] PH may be associated with underlying diseases or may affect only the small pulmonary arterial vessels, which leads to vasoconstriction and vascular remodeling. Irrespective of its etiology, PH is a serious and often progressive disorder that results in right ventricular dysfunction and impairment of exercise tolerance, and may lead to right-heart failure and death. Advances in treatment that have occurred over the past two decades have led to substantial improvements in quality of life in patients with PAH.[2] These improvements encourage patients with PH to live as less restrictive as possible, which often involves air travel.

More than 1 billion individuals worldwide travel on commercial aircraft each year, and there are a reported 0.31 in-flight deaths per million passengers carried.[3] Cardiovascular events represent the major cause of in-flight deaths.[4] Due to engineering and financial constraints, the ambient in-flight cabin pressure is maintained to the equivalent of a maximum altitude of 2438 m.[5,6] This reduction in cabin pressure is the equivalent of breathing 15% oxygen (compared with 21% oxygen at sea level).[7] In patients with PH, the hypobaric environment during air travel leads to a general hypoxic vasoconstriction in the lung, which exacerbates

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pulmonary resistance and right ventricular load, and may lead to acute right-heart decompensation. Thus, in addition to typical flight-associated risks, such as deep vein thrombosis, lung embolism and alterations in fluid balance, individuals with cardiovascular disease also risk worsening of their underlying condition during air travel.

Hypoxic pulmonary vasoconstriction is a fundamental physiological mechanism that optimizes perfusion–ventilation matching in periods of regional hypoventilation of the lung. However, during global alveolar hypoxia, whether due to lung disease or environmental conditions such as high altitude, hypoxic pulmonary vasoconstriction results in increased pulmonary resistance and enhanced right-heart load.[8] Wide variations exist in individual responses to a hypobaric environment and the underlying mechanisms are not clearly understood. Thus, it is not known whether it is safe for patients with PH to travel by air and whether such travel is well tolerated. The aim of this retrospective survey was to evaluate the outcome and experiences of patients with PH who have travelled by air.

MATERIALS AND METHODS

We conducted an anonymized survey in cooperation with Pulmonale Hypertonie e.V. (PH e.V.), a German patient self-care organization, concerning air travel in patients with PH, and the experiences of those who had undertaken air travel since their initial diagnosis.

Patient population

We contacted 720 patients with pulmonary hypertension who were members of PH e.V. and/or were routinely followed by the pulmonary hypertension department of the University Hospital of Giessen and Marburg (Giessen, Germany). The inclusion criteria were adult patients with a confirmed diagnosis of pulmonary arterial hypertension, which includes idiopathic PAH, familial PAH, chronic thromboembolic pulmonary hypertension, or PAH associated with congenital heart defects, collagen vascular diseases, or chronic lung diseases, on stable PH-specific therapy regimens, which means without changes in specific therapy at least for 3 months prior to air travel. Exclusion criteria were severe lung diseases without secondary PH, left ventricular diseases (i.e., dilated cardiomyopathy, ischemic cardiomyopathy, significant coronary heart disease or valvular diseases) and other chronic diseases affecting tolerance of air travel (for example, severe renal failure).

Study design

We sent the postal questionnaire to all patients with pulmonary hypertension who were members of PH e.V. and/or were routinely followed by the pulmonary hypertension department of the University Hospital of Giessen and Marburg. A short explanatory section and a written consent form were distributed with the questionnaire. Response to the questionnaire was anonymous. If patients provided their contact details, these were documented separately. The questionnaire consisted of multiple-choice questions, free text and yes/no questions.

Analysis

The returned questionnaires were checked for completeness and any incomplete or illegible ones were discarded. The number of respondents who had flown since initial diagnosis and their air travel experiences were recorded following descriptive analysis.

RESULTS

In total, 430 of 720 patients completed the anonymized questionnaire (response rate: 60%). All responders provided their written consent. Of the 430 respondents, 179 (42%) had undertaken one or more flights since the initial diagnosis of PH and 251 respondents (58%) had not flown since the diagnosis. In all, 159 (89%) patients who had travelled by air since their diagnosis of PH experienced no adverse events during or directly after flying, whereas 20 (11%) reported having had one or more adverse events during or directly after at least one of their flights. Patient characteristics, including disease etiology, functional class, therapy and supplemental oxygen status, are shown in Table 1 for non-flyers, flyers and flyers with adverse events.

The most common disease etiology was idiopathic PAH, which was reported in a similar proportion of non-flyers and flyers (30% vs. 35%). Most patients were in New York Heart Association (NYHA) functional class II or III (73% of non-flyers and 84% of flyers). However, more non-flyers than flyers were in NYHA functional class IV (11% vs. 4%). A similar proportion of non-flyers and flyers used PH-specific monotherapy (40% vs. 46%). However, the use of PH-specific combination therapy and supplemental oxygen was more common among non-flyers than flyers (53% vs. 32% and 59% vs. 32%, respectively), and fewer non-flyers than flyers were using only basic therapies such as diuretics and oral coagulation (7% vs. 15%). Of the flyers only four patients used supplemental oxygen during the flight at least, but seven patients stated that they normally have supplemental oxygen therapy. Among non-flyers, severely reduced exercise capability, the need for supplemental oxygen even at sea level, advice from their medical practitioners and fear of worsening of their disease, including to the extent of death, were described as the most important factors in deciding not to fly.

Of the 20 flyers who reported adverse events during or shortly after flying, 10 (50%) had flown at least three times since their diagnosis. 12 patients travelled by air more than three hours, 8 patients less than 3 hours. The most prevalent adverse events were dyspnea and peripheral edema, followed by exhaustion (Table 2). Most adverse events were of mild or moderate severity. Seven patients required medical intervention, one of whom needed to be referred to intensive care; the remaining six required diuretics (n=2), cardioversion for atrial fibrillation (n=1), psychological intervention for fear of flying (n=1), physical rest (n=1) and referral for further diagnostic work-up (n=1). Patient characteristics were similar for flyers overall, for flyers without adverse events and for those with adverse events. A similar proportion of all flyers and those with adverse events used supplemental oxygen during the flight (16% vs. 20%). However, 30% of patients with adverse events were using only basic therapy alone, compared with 15% of all flyers. But in total 73% of the flyers (130 of 179 patients) as well as 73% of the non-flyers (185 of 251 patients) had a basic therapy with Coumadin, so that there is no difference in the use of Coumadin, which might have affect the outcome. Only three patients of the "flyers" did not have any basic therapy, but the had at least a combination therapy of two or more specific drugs.

Our retrospective study of 430 patients with PH shows that air travel is common in this patient population, with almost half (42%) having undertaken one or more flights since the initial diagnosis of their disease. Furthermore, air travel was generally safe and well tolerated, with only a minority (11%) of patients who had travelled by air reporting that they had experienced adverse events during or shortly after their travels and only one of these patients requiring transfer to intensive care. Patients who did not travel by air were generally in poorer physical health than those who did fly. The proportion of patients who were in NYHA functional class IV was more than twice as high in the group of non-flyers than in the group of flyers. Similarly, the proportion of patients who required routine supplemental oxygen was almost twice as high in the non-flyer as in the flyer group. The proportion of flyers who were not on PH-specific therapy (30% vs. 15%) was twice as high in the group of flyers with adverse events as in those without adverse events.

DISCUSSION

Hypoxic pulmonary vasoconstriction contributes to ventilation–perfusion matching in the lung by diverting blood flow to oxygen-rich areas. However, during conditions of general hypoxia, such as those present at high altitude or during air travel, hypoxic pulmonary

Table 1: Clinical characteristics of patients with pulmonary hypertension who were non-flyers, flyers and flyers with adverse events

	Non-flyers (*n*=251)	All flyers (*n*=179)	Flyers with adverse events (*n*=20)
Etiology, n (%)*			
Pulmonary arterial hypertension			
IPAH	75 (30)	63 (35)	10 (50)
CHD	23 (9)	22 (12)	2 (10)
CVD	9 (4)	7 (4)	2 (10)
PH owing to lung disease	36 (14)	18 (10)	3 (15)
CTEPH	43 (17)	36 (20)	3 (15)
NYHA class, n (%)*			
I	1 (0.4)	2 (1)	0 (0)
II	79 (31)	77 (43)	7 (35)
III	106 (42)	76 (42)	10 (50)
IV	27 (11)	8 (4)	1 (5)
Supplemental oxygen, n (%)			
Yes	148 (59)	57 (32)	7 (35)
Duration, hours/day	18–24	8–12	8–12
> 16 hours/day	117 (46)	19 (11)	3 (15)
Therapy*			
Basic therapy only†	18 (7)	26 (15)	6 (30)
PH-specific monotherapy, n (%)‡	100 (40)	83 (46)	6 (30)
PH-specific combination therapy§, n (%)	133 (53)	58 (32)	8 (40)
Oxygen taken during flight, n	–	29 (16)	4 (20)

CHD: congenital heart disease; **CTEPH:** chronic thromboembolic pulmonary hypertension; **CVD:** collagen vascular disease; **IPAH:** idiopathic pulmonary arterial hypertension; **NYHA:** New York Heart Association. *Numbers presented may not add up to total in some variables due to missing values. †Basic therapy includes diuretics and oral anticoagulation. ‡Monotherapy includes endothelin receptor antagonists, phosphodiesterase inhibitors, prostanoids or calcium channel blockers. §Defined as ≥two PH–specific drugs

Table 2: Adverse events in the group of 179 patients with pulmonary hypertension (PH) who were flyers

Adverse event	Number of flyers with particular adverse event* (%)
Dyspnea	6 (3.4)
Peripheral edema	6 (3.4)
Exhaustion	3 (1.7)
Heart palpitations	2 (1.1)
Chest pain	2 (1.1)
Headache	2 (1.1)
Worsening of general condition	2 (1.1)
Fear of flying	1 (0.6)

*In total, 20 flyers (11.2%) reported having had one or more adverse events during or directly after at least one of their flights.

vasoconstriction may be disadvantageous because it leads to an increase in pulmonary vascular resistance and pulmonary arterial pressure, which may aggravate right-heart loading.[9] The consequences of acute hypoxia are increases in heart rate, myocardial contractility and cardiac output. In healthy individuals, the response to hypobaric hypoxia, such as occurs during air travel, is a mild tachycardia with increased myocardial oxygen demand.[10] In patients with significant impairment of myocardial function or of coronary flow reserve, symptoms or complications such as acute cardiac arrest, or atrial or ventricular fibrillation may occur. Increased sympathetic activity at altitudes of 1,500–3,000 m produces lower workload tolerances and a decreased work capacity that may cause worsening of an underlying disease. In addition, the general flight environment, which is characterized by inactivity, and includes an air humidity of 3–10% (compared with 70% at sea level in Europe) and increased perspiration of up to 90 ml/h (compared with 40 ml/h at sea level), increases the risk for other in-flight medical issues. A fluid ingestion of 100 ml/h is thus recommended to avoid deleterious circulatory effects such as thrombosis.[11]

There are no data from controlled trials regarding air travel safety for patients with PH. Guidelines for PH by the American College of Cardiology Foundation and the American Heart Association recommend supplemental oxygen on commercial aircraft for patients with a pre-flight pulse oximetry saturation of less than 92%.[12] The European Society of Cardiology and European Respiratory Society guidelines for PH recommend in-flight supplemental oxygen for patients with PH in functional class III or IV and those with arterial blood oxygen pressure consistently below 8 kPa (60 mmHg).[13] A flow rate of 2 L/min is recommended to bring the inspired O_2 pressure to the levels seen at sea level.[13] In the present study, a substantial proportion of flyers did not adhere to these guidelines: although 45% of flyers were in functional class III or IV, only 16% used supplemental oxygen in-flight. The focus on functional class III and IV patients in the European guidelines is interesting in light of the small difference in the rate of adverse events observed in the current study between functional class II (about 9%) and functional class III or IV (about 13%).

For patients with chronic lung disease who are planning to travel by air, the European Respiratory Society advises a minimum vital capacity of 3 liters, a forced expiratory volume in 1 second (FEV_1)>70% of reference, a minimum oxygen saturation of 85% and a minimum partial pressure of oxygen in arterial blood (paO_2) of 70 mmHg, as well as a stable state of health.[14] The British Thoracic Society guidelines recommend a hypoxic challenge test similar to the high altitude simulation test (HAST) for adults who have a resting oxygen saturation of 92–95% at sea level together with an additional risk factor, as the resting oxygen saturation on its own is not a good predictor of desaturation at high altitude.[10] The Air Emergency Task Force of the American Medical Association recommends that patients with emphysema, lung fibrosis and cystic fibrosis should use supplemental oxygen therapy during air travel, especially if paO_2 is expected to be less than 55 mmHg without supplemental oxygen.[14] In Germany, there is no obligatory regulation concerning the pre-flight assessment of travellers with chronic diseases. In general, individuals are considered capable of flying if they can achieve a workload of 50 watt on a treadmill without discomfort or if they are able to walk the gangway of the aircraft on their own without experiencing dyspnea.

General recommendations for air travellers with underlying chronic diseases include placing sufficient medication for the length of the travel in their carry-on luggage, adhering to dietary guidelines (such as avoiding high-sodium in-flight meals, alcohol and caffeinated beverages), carrying copies of their medical records (including their latest electrocardiogram, information on any implantable cardiac device and an updated medication list including any allergies), contacting the airline in advance if in-flight supplemental oxygen is required and wearing compression stockings for flights of more than 5000 km or longer than 8 hours.[15] Known contraindications for air travel for patients with cardiac disease include myocardial infarction or coronary artery bypass in the previous 2 weeks, unstable angina, poorly compensated heart failure, uncontrolled ventricular or supraventricular arrhythmias and NYHA functional class IV.[15] A requirement for pacemakers and defibrillators is no contraindication in itself, and there is no interference between modern implantable devices and aircraft systems. The US Federal Aviation Administration required in 2001 that larger aircrafts should carry at least one automatic external defibrillator and that at least one flight attendant should be trained in its use;[16] extrapolated data suggest that these precautions prevent up to 93 in-flight deaths from ventricular fibrillation worldwide each year.[15]

Our study suggests that air travel can be safe and well tolerated in patients with PH. In addition to the recommendations for air travel for patients with PH, evidence-based guidelines for other chronic diseases should also be adapted to some extent. If paO_2 at rest is less than 75 mm Hg, a HAST should be performed. If a HAST is not available, patients with PH should undergo a cardiopulmonary exercise test (6-minute walk, spiroergometry according to their capacity). With additional right-heart echocardiography one can assess the response of the right heart to acute hypoxaemia by estimating systolic pulmonary pressure, especially an

increase in pulmonary pressure, and parameters of right heart function (i.e., TAPSE, TEI, S´) during ventilation of hypoxic air.[8]

Despite the fact that this method is not validated by the time, it enables an assessment for possible reaction to acute pulmonary vasoconstriction and may help to decide if patient could be allowed to fly. It is recommended that patients with PH should only fly in a stable and compensated condition, and should use supplemental oxygen during the flight to minimize hypoxic vasoconstriction. However, this does not apply to patients with congenital heart diseases with severe right to left shunt, in whom supplemental oxygen has no additional effect.

A limitation of our retrospective, descriptive analysis is a potential selection bias. It is possible that patients who had positive experiences regarding their flight travels would have been more likely to return the questionnaire. In addition, patients who died during or shortly after their air travel would by necessity have been excluded from this analysis.

Further limitation is, that the hemodynamic status of the patient at the time of the air travel is unknown, because of the survey based retrospective analysis character of this work, so that we cannot compare the outcome with the hemodynamic severity of the disease. The classification in WHO functional class groups was made by transferring self-assessment of the patients' physical capacity at the time of the flight into the classification.

CONCLUSION

In conclusion, a surprisingly large proportion of patients with PH travel by air despite the additional risk, and air travel can be safe and well tolerated in these patients in WHO functional class II and III in a stable clinical condition. Compared with alternative methods of transport, air travel might be advantageous to some extent in patients with PH, as it has the potential of dramatically reducing the duration of travel. Those patients with relevant hypoxaemia at sea level should use supplemental oxygen during air travel. Patients who have an unstable physical condition, suffer from acute infections or recently changed their PH-specific medication should avoid travelling by air. This applies also for patients in WHO functional class IV. Hence, a physician evaluation is ultimately required prior to travel for every patient.

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