Commercial Air Travel and In-Flight Pulmonary Hypertension

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Background: It has recently been shown that commercial air travel triggers hypoxic pulmonary vasoconstriction and modestly increases pulmonary artery pressure in healthy passengers. There is large interindividual variation in hypoxic pulmonary vasoreactivity, and some passengers may be at risk of developing flight-induced pulmonary hypertension, with potentially dangerous consequences. This study sought to determine whether it is possible for a susceptible passenger to develop pulmonary hypertension in response to a routine commercial flight. ***Case Report:*** Using in-flight echocardiography, a passenger was studied during a 6-h commercial flight from London to Dubai. The passenger was generally well and frequently traveled by air, but had been diagnosed with Chuvash polycythemia, a genetic condition that is associated with increased hypoxic pulmonary vasoreactivity. Hematocrit had been normalized with regular venesection. During the flight, arterial oxygen saturation fell to a minimum of 96% and systolic pulmonary artery pressure (sPAP) rapidly increased into the pulmonary hypertensive range. The in-flight increase in sPAP was 50%, reaching a peak of 45 mmHg. ***Discussion:*** This study has established that an asymptomatic but susceptible passenger can rapidly develop in-flight pulmonary hypertension even during a medium-haul flight. Prospective passengers at risk from such responses, including those who have cardiopulmonary disease or increased hypoxic pulmonary vasoreactivity, could benefit from preflight evaluation with a hypoxia altitude simulation test combined with simultaneous echocardiography (HAST-echo). The use of in-flight supplementary oxygen should be considered for susceptible individuals, including all patients diagnosed with Chuvash polycythemia.

Keywords: aircraft cabin hypoxia, hypoxic pulmonary vasoconstriction, Chuvash polycythemia, hypoxia altitude simulation test, hypoxic challenge test.

USING IN-FLIGHT echocardiography, we recently established that the mild hypoxia of a commercial aircraft cabin modestly increases pulmonary artery pressure in healthy passengers (11). The underlying phenomenon of hypoxic pulmonary vasoconstriction varies greatly between individuals, and highly sensitive passengers could be susceptible to large adverse responses during air travel. The clinical syndrome of acute cor pulmonale has been reported in airline passengers (6,14) and pulmonary hypertensive responses could contribute to in-flight cardiac emergencies, which are the most common cause of flight diversions and in-flight deaths (3). However, flight-induced pulmonary hypertension has not previously been demonstrated.

Chuvash polycythemia is a congenital erythrocytosis that is known to cause increased hypoxic pulmonary vasoreactivity (9,10). This rare autosomal recessive disorder was originally described in the Chuvash population of Russia, but has since been reported around the world (10). Affected individuals are homozygous for a specific mutation in the hypoxia-inducible factor intracellular oxygen sensing pathway, which results in activation of hypoxia-inducible factor target genes such as erythropoietin (10). Patients usually present with symptoms of polycythemia in early adulthood or are diagnosed on family screening, and are typically asymptomatic following treatment with venesection. Chuvash polycythemia predisposes to pulmonary hypertension and is associated with early mortality (1,9,10), and patients have been shown to have increased pulmonary vascular sensitivity to hypoxia in the laboratory setting (9). Chuvash polycythemia is not included in existing aeromedical guidelines and affected patients currently travel by air without restriction. Through measurements conducted in a passenger with Chuvash polycythemia, this study aimed to determine whether a susceptible individual can develop pulmonary hypertension during a commercial flight.

CASE REPORT

A 30-yr-old man with Chuvash polycythemia was studied during a 6-h commercial flight on a Boeing 777-300 aircraft from London to Dubai. He had been diagnosed with polycythemia at the age of 8 yr and subsequent genetic analysis had identified the causative Chuvash mutation. His treatment consisted of venesection every 3 mo, which had maintained a normal hematocrit for many years. He had no other medical problems and was asymptomatic and generally well. He had once experienced an episode of dyspnea during a long-haul flight, but had since flown extensively without incident. His height was 1.76 m and weight was 50 kg. At the time of the study, his hematocrit was normal, but he had profound iron deficiency due to the regular venesection. Results of baseline venous blood analyses were: hemoglobin 14.1 $g \cdot dl^{-1}$

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(normal range 13.0-17.0 $g \cdot dl^{-1}$), hematocrit 0.51 $L \cdot L^{-1}$ (0.40-0.50 $L \cdot L^{-1}$), mean cell volume 56.5 fl (83-105 fl), serum iron 3.6 $\mu mol \cdot L^{-1}$ (14-31 $\mu mol \cdot L^{-1}$), serum ferritin 2.3 $\mu g \cdot L^{-1}$ (20-300 $\mu g \cdot L^{-1}$), and serum transferrin 3.5 $g \cdot L^{-1}$ (1.8-3.6 $g \cdot L^{-1}$). The study was approved by the airline and the Oxford Tropical Research Ethics Committee, and the passenger gave written informed consent.

Pulmonary artery pressure was assessed using echocardiography. These measurements were made using a standard Doppler technique that is widely used in clinical practice and research (8,9,12), and has been previously described for in-flight measurements in healthy passengers (11). Briefly, the maximum systolic pressure gradient across the tricuspid valve was determined using Doppler with the patient reclining in a left lateral position (Vivid *i* portable machine, GE Medical Systems, Hatfield, UK), and systolic pulmonary artery pressure (sPAP) was determined using an estimated right atrial pressure of 5 mmHg. Measurements were made immediately preflight, hourly in flight, immediately postflight, and then daily for 2 d. Supplementary oxygen was available should symptoms develop or sPAP exceed 50 mmHg. Each set of measurements also included arterial oxygen saturation (S_pO_2), blood pressure, heart rate, and an echocardiographic assessment of cardiac output (11). Aircraft cabin pressure was recorded as equivalent cabin altitude throughout the flight.

The passenger remained asymptomatic throughout the study. Baseline sPAP was 30 mmHg, confirming the absence of pulmonary hypertension, for which the sPAP threshold is defined as 36 mmHg (5). Cruising cabin altitude was relatively low (**Fig. 1**), only exceeding 5400 ft (1645 m) for the last hour and cabin hypoxia was, therefore, relatively mild. S_pO_2 fell from 100% preflight to a minimum of 96% in flight, and sPAP dramatically increased into the pulmonary hypertensive range (Fig. 1). The peak sPAP was 45 mmHg, corresponding to a mean pulmonary artery pressure of approximately 30 mmHg (2). The peak increase in sPAP was 50%, considerably greater than the 20% increase observed in the previous study of healthy passengers (11).

Heart rate, cardiac output, and blood pressure remained stable throughout the study. Minute ventilation was measured by Wright's respirometer (nSpire Health Ltd, Hertford, UK) prior to takeoff and hourly in flight, and increased from 11.7 $L \cdot min^{-1}$ to a mean of 14.1 $L \cdot min^{-1}$ (SD 0.8) in flight. End-tidal partial pressure of carbon dioxide was measured by Normocap Oxy gas analyzer (Datex Engstrom, Finland) immediately prior to takeoff and descent, and decreased from 34 mmHg to 31 mmHg in flight. These respiratory measurements were consistent with the increased acute hypoxic ventilatory response previously observed in patients with Chuvash polycythemia (9).

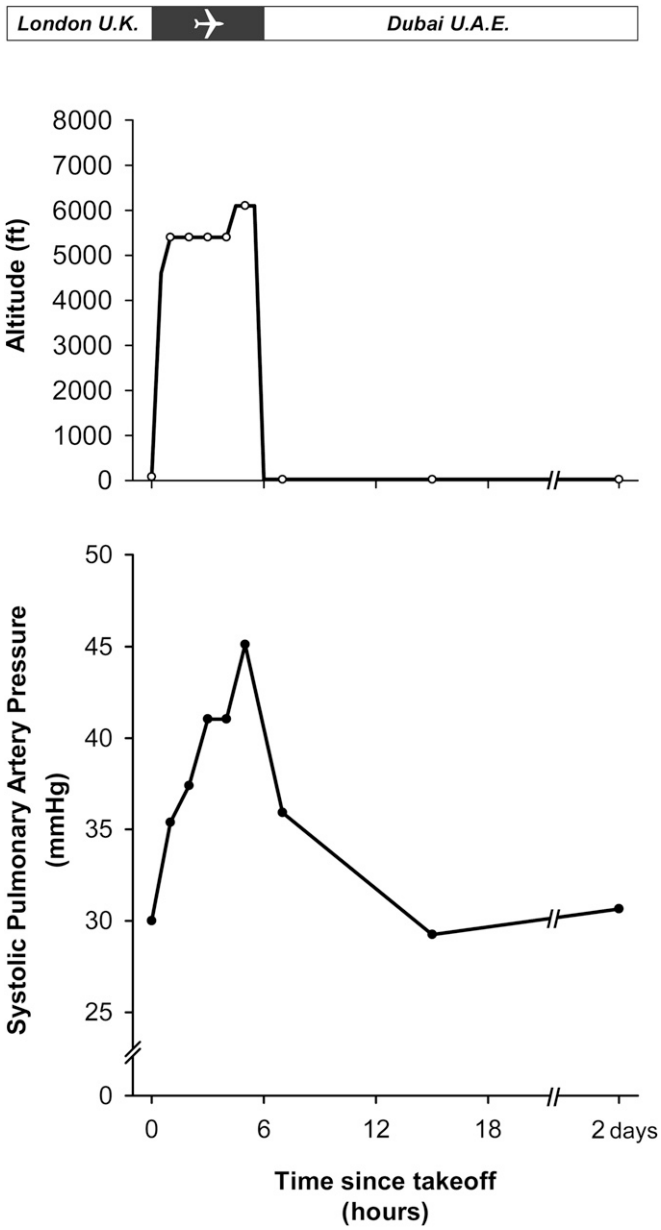

Fig. 1. Altitude (top) and systolic pulmonary artery pressure (bottom) in a passenger with Chuvash polycythemia during a commercial airline flight. For the duration of the flight, the altitude presented is the equivalent cabin altitude. Symbols indicate measurement time points.

DISCUSSION

This case report has established that commercial air travel can cause in-flight pulmonary hypertension. The sharp rise in sPAP observed in this study nearly breached our trigger for commencing oxygen therapy, yet air passengers are commonly exposed to greater cabin hypoxia over much longer sectors of up to 19 h. Similar responses are likely to occur in other passengers with Chuvash polycythemia (9) or with related genetic mutations that cause a similar pulmonary phenotype (4). This passenger's iron deficiency may also have contributed to his excessive response—reduced iron availability increases hypoxic pulmonary vasoreactivity (8,12) and was recently associated with higher pulmonary artery pressures in a study of 120 patients with Chuvash polycythemia (7). As a result of our findings, this passenger has been advised to use supplementary oxygen when traveling by air, at least for longer flights.

Although based on a single case, this study has broad implications that extend beyond patients with rare genetic diseases, including the many patients with heart and lung problems who wish to fly. Flight-induced pulmonary hypertension such as that seen in this study could exacerbate or precipitate cardiopulmonary disease and contribute to in-flight morbidity and even mortality. The risks are presumably greater in those with naturally higher pulmonary vascular sensitivity and those in whom pulmonary artery pressures are already elevated. Passengers with pre-existing pulmonary hypertension, for example, can often tolerate air travel well, but a significant minority experience adverse effects requiring medical intervention (13).

In the aeromedical assessment of vulnerable prospective passengers, these risks could be evaluated by combining echocardiography with a standard hypoxia altitude simulation test (HAST), in which in-flight responses are predicted by breathing a mildly hypoxic gas mixture (11). HAST-echo may allow prediction of in-flight changes in pulmonary hemodynamics, guiding decisions regarding prescription of in-flight supplementary oxygen and, ultimately, fitness to fly. Further research is required to investigate the possible benefits of this approach and to confirm that the normobaric HAST and the hypobaric hypoxia of air travel induce similar pulmonary vascular responses.

Critically ill patients undergoing aeromedical transportation may be at particular risk from pulmonary hypertensive responses, and this study's findings suggest that even very mild hypoxia should be avoided in this setting. In addition to passengers and patients, this study has occupational health implications for the aviation industry. Employment as aircrew or cabin crew may be unsafe for individuals who are prone to flight-induced pulmonary hypertension, even in the absence of symptoms. Pre-employment screening with HAST-echo may be advisable where exaggerated hypoxic pulmonary vasoreactivity can be anticipated, such as in those diagnosed with Chuvash polycythemia or with a previous history of high altitude pulmonary edema. We conclude that hypoxic pulmonary hypertension can rapidly develop even during a medium-haul flight. Until further evidence is forthcoming, preflight evaluation with HAST-echo and the provision of in-flight supplementary oxygen should be considered for susceptible individuals, including all prospective passengers diagnosed with Chuvash polycythemia.

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