Hypercapnic Respiratory Acidosis During An In-Flight Oxygen Assessment

Kristofer J. Spurling; Ian K. Moonsie; Joseph L. Perks

BACKGROUND: Patients with respiratory disease are at risk of excessive hypoxemia in the hypobaric commercial aircraft cabin environment, and the consensus is that this is easily corrected with supplementary oxygen. However, despite the risks of hypercapnia with increasing inspired oxygen in some patients being well established, this issue is not currently addressed in medical guidelines for air travel.

CASE REPORT: A 76-yr-old woman with chronic type 2 respiratory failure underwent hypoxic challenge testing (HCT) to assess in-flight oxygen requirements. She is stable on home ventilation, and baseline arterial blood gases showed mild hypoxemia (P_aO_2 9.12 kPa), normal P_aCO_2 (5.64 kPa) and pH (7.36) with 98% S_pO_2. HCT was performed delivering 15% F_IO_2 via a mask, and the patient desaturated to $<$ 85%. HCT blood gases revealed significant hypoxemia ($P_aO_2 < 6.6$ kPa), indicating in-flight oxygen. Continuous oxygen at 2 L · min^{-1} via nasal cannula corrected the hypoxia, although P_aCO_2 increased to 6.9 kPa with reduction in pH to the threshold of severe respiratory acidosis (pH 7.25). The patient was advised against flying due to hypoxemia during HCT and the precipitous drop in pH on oxygen.

DISCUSSION: It is possible to hyperoxygenate patients with type 2 respiratory failure in flight with the minimum level of supplementary oxygen available on many aircraft. In these cases P_aCO_2 and pH should be scrutinized during HCT before recommending in-flight oxygen. No current guidelines discuss the risk of hypercapnia from in-flight oxygen; it is therefore recommended that this be addressed in future revisions of medical air travel guidelines, should further research indicate it.

KEYWORDS: acidosis, hypoxia, hypercapnia, oxygen.

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Some patients with respiratory disease are at risk of excessive hypoxemia in the hypobaric commercial aircraft cabin environment. This is due to the maximum permissible cabin altitude on commercial flights being equivalent to 8,000 ft (2438 m), resulting in a reduction in available atmospheric oxygen equivalent to breathing 15.1% oxygen at sea-level.[2] This would cause a healthy individual's oxygen saturation to fall to approximately 90%, although they would be able to compensate for this level of hypoxemia with a normal physiological response.[3] This may not be the case in those with respiratory disease as these individuals may already have a reduced baseline P_aO_2 or be unable to sufficiently compensate for the reduction in available oxygen. In this case the reduced PO_2 in ambient air in the aircraft cabin will bring them to the steep part of the oxyhemoglobin dissociation curve with a resultant low saturation, which could cause distress and/or exacerbation of their illness.[1] The consensus is that this issue may be easily corrected by using supplementary oxygen while onboard the flight,[1–3] and where there is doubt, it appears prudent to err on the side of recommending oxygen.[2]

In order to assess the individual passenger's in-flight oxygen requirements the current guidelines describe a hypoxic challenge test (HCT), also known as a hypoxia altitude simulation test (HAST), which is performed by asking the patient to breathe a gas mixture containing 15% oxygen, thereby replicating the amount of available oxygen in ambient air in the aircraft cabin.[1,2] The response to hypoxia during the HCT is assessed after 20 min using direct measurement of arterial or capillary

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oxygen tension, or pulse oximetry should blood gas measurement be unavailable.[2] The resultant values dictate whether supplementary oxygen will be required onboard the flight and at which flow rate it should be delivered. In the majority of patients it is a case of increasing the fraction of inspired oxygen (F_IO_2) in flight using supplementary oxygen at continuous flow rates of 2 L · min^{-1} or 4 L · min^{-1} in order to maintain arterial/capillary $Po_2 > 6.6$ kPa or > 7.3 kPa and/or $S_pO_2 > 85\%$, depending on the guidelines followed and methods available.[1,2]

The risks associated with increasing F_IO_2 in some groups of patients have been well described in numerous literature reviews and guidelines.[5,9,10] It can lead to hyperoxic-induced hypercapnia, which may occur due to a complex set of mechanisms which are still the current focus of research.[10] Hypoxia causes local vasoconstriction in pulmonary capillaries (hypoxic pulmonary vasoconstriction, or HPV) in an attempt to balance ventilation and perfusion; reoxygenation causes vasodilatation and an increase in physiological dead space, exacerbating any ventilation/perfusion mismatches. Hyperoxic respiratory depression and a reduction in lung function from absorption atelectasis as a result of higher F_IO_2 may reduce ventilation, and the Haldane effect (the binding of oxygen and hemoglobin resulting in an increase in unbound CO_2) may all contribute to hypercapnia.[10] The net result in some patients is an increase in arterial Pco_2 when supplementary oxygen is introduced, with a consequential fall in pH in advance of the slower compensatory metabolic alkalosis response.[10] In fact the highest levels of hypercapnia and respiratory acidosis have been found in patients that have received supplementary oxygen, and many of these patients experience a resolution of this hypercapnia following a reduction in their inspired oxygen.[9,10] It is for this reason that, whereas in previous times oxygen was seen as a nonspecific, nonharmful treatment for respiratory disease symptoms, guidelines now exist to ensure that patients with type 2 respiratory failure are not hyperoxygenated with long-term oxygen therapy, avoiding a potentially dangerous rise in P_aco_2.[6,10] As these guidelines recommend scrutinizing P_aco_2 in addition to Po_2 with flow rates as low as 1 L · min^{-1} (or 24% F_IO_2), it would be reasonable to assume that it is possible to hyperoxygenate the same patients as commercial aircraft passengers with supplementary oxygen. This would be more likely in cases where the airline can only supply a minimum continuous fixed flow of 2 L · min^{-1} with no means of reducing the flow rate, with some long-haul flights only able to supply 4 L · min^{-1}.[2,4] The current medical air-travel guidelines do not address Pco_2 or pH when administering supplementary oxygen during HCT, or when recommending a flow rate for the flight.[1,2]

CASE REPORT

This case report concerns a 76-yr-old female with a history of chronic type 2 respiratory failure secondary to restrictive lung disease. She contracted pulmonary tuberculosis as a young woman and as a result developed pulmonary fibrosis with loss of volume in the left hemithorax as verified with subsequent radiological imaging. She had presented with non-ST segment elevation myocardial infarction 14 mo prior to this consultation but is now stable with no subsequent cardiac events. She is overweight with a body mass index of 27.5 kg · m^{-2}, and recent pulmonary function testing showed a severely restrictive pattern; $FEV_1 = 0.62$ L (-4.44 z), FVC = 0.78 L (-3.98 z), with a normal FEV_1/FVC% ratio = 79% (0.19 z). Transfer factor values (Dlco and Kco) are unavailable due to insufficient lung volume for single breath assessment. This patient was relatively well until 5 yr ago, when she required invasive ventilation for respiratory failure shortly after a long haul flight to visit her daughter abroad. Despite a subsequently normal convalescent P_aco_2, she has deteriorated on numerous occasions and required hospital admissions in several countries with acute type 2 respiratory failure. Two of these episodes occurred shortly after long haul flights, the second of which followed the use of in-flight oxygen. All of these subsequent admissions required the application of noninvasive ventilation (NIV) to correct acute hypercapnic respiratory acidosis. She does not currently require home oxygen therapy due to a resting oxygen saturation of 98%, and she had demonstrated a small degree of CO_2 retention on previous occasions when assessed for home oxygen therapy during a hospital admission. She has been successfully established on domiciliary nocturnal NIV for the past 4 mo; she is fully compliant with her treatment, using the ventilator every night for a minimum of 5 h and has reported no recent health issues. During a recent routine outpatient consultation in the respiratory clinic the patient discussed plans to undertake another long-haul journey by air, so taking into account her recent history the examining physician referred her for hypoxic challenge testing in accordance with guidelines issued by the British Thoracic Society, which recommends preflight assessment for patients in the following categories:

I. Pre-existing requirement for oxygen, CPAP, or ventilator support;
II. Severe (vital capacity < 1 L) restrictive disease (including chest wall and respiratory muscle disease), especially with hypoxemia and/or hypercapnia.[2]

The results of an arterial blood gas sample taken prior to HCT showed mild but acceptable hypoxemia with normal Pco_2 and acid-base values, which indicates that the patient's respiratory failure is corrected with domiciliary nocturnal NIV (all blood gas data is shown in **Table I**, taken from a radial artery and analyzed using Radiometer ABL90 FLEX, Radiometer, Copenhagen, Denmark). At this point oxygen saturation was 98%, indicated by finger pulse oximetry (Nellcor N-550, Nellcor Puritan Bennett Inc, Boulder, CO) following a period of rest and breathing room air. Hemoglobin was calculated by the blood gas analyzer at 109 g · L^{-1} which, while indicating mild anemia, gave us no cause for concern over the validity of S_pO_2 as an indicator of oxygenation over the range encountered during HCT.

The HCT was performed by asking the patient to breathe a gas mixture containing 15% oxygen. In this case the gas mixture was delivered to the patient by way of a mask worn

Table I. Arterial Blood Gas and Pulse Oximetry Values from HCT.

BASELINE		15% F_IO_2		15% F_IO_2 + 2 L · min^{-1} O_2	
P_aO_2 (kPa)	***9.12***	***P_aO_2 (kPa)***	***5.2***	***P_aO_2 (kPa)***	***9.25***
P_aCO_2 (kPa)	5.64	P_aCO_2 (kPa)	5.4	***P_aCO_2 (kPa)***	***6.9***
pH	7.36	pH	7.36	***pH***	***7.25***
$cHCO_3^-$ (mmol · L^{-1})	23.9	$cHCO_3^-$ (mmol · L^{-1})	22.3	$cHCO_3^-$ (mmol · L^{-1})	23.1
SpO_2	98%	***SpO_2***	***79%***	SpO_2	98%

Abnormal values highlighted in bold italic, ($cHCO_3^-$ values are calculated).

over the mouth and nose, and supplied from a hypoxic gas generator (Hypoxico Everest Summit II, Sequal Technologies, San Diego, CA). The validity and performance of this equipment when used for this purpose is described elsewhere.[11] The fraction of inspired oxygen was continually verified by a calibrated oxygen analyzer (Maxtec OM25-RME, Maxtec, Salt Lake City, UT), with the output ranging between 14.9% and 15.1% throughout the entire test. The patient's pulse oximetry reading remained initially stable but fell to < 85% after 10 min of the HCT procedure, which is one of the criteria for terminating this part of the test and providing supplementary oxygen. S_pO_2 was indicated at 79% at the time the blood gas sample was obtained. These blood gas values showed significant hypoxemia, and in-flight oxygen is therefore indicated due to P_aO_2 falling to a value of less than 6.6 kPa.[2] Although there are no gas transfer values available, pulmonary gas exchange is likely to be reduced in this patient due to both significant loss of lung volume and pulmonary fibrosis, and a strong relationship between poor in-flight oxygenation and low DLCO has been demonstrated.[8] Overall it appears that a combination of the patient's restrictive lung function, obesity, and impaired gas exchange has prevented her from mounting an appropriate physiological response to hypoxia due to a reduction in respiratory function and reserve. For the second stage of the HCT, continuous supplementary oxygen was administered to the patient at a flow rate of 2 L · min^{-1} via nasal cannula for 20 min in addition to the hypoxic gas mixture. This successfully corrected the patient's hypoxia as shown by both the P_aO_2 (9.25 kPa) and finger pulse oximetry (98%), although it was also noted that P_aCO_2 had increased significantly from both the baseline and HCT values to 6.9 kPa, with a consequential reduction in pH from a normal value to the threshold of severe respiratory acidosis (pH 7.25).

DISCUSSION

When referring to current air travel medical guidelines, this patient's P_aO_2 and pulse oximetry values were satisfactory while using 2 L · min^{-1} continuous supplementary oxygen during HCT.[1,2] However these guidelines do not address P_aCO_2 or pH when administering oxygen, and after taking these values into account it is clear that in her current state of health, this patient would not be fit to undertake a standard commercial flight either with or without oxygen. She was therefore advised not to undertake the flight due to both her significant hypoxemia during the first stage of HCT and the precipitous drop in her pH after a short time on oxygen, considering her proposed flight was to be a minimum of 8 h in duration. It is clear that a patient with this history would have benefited from assessment using a graded approach with lower flow rates or different delivery methods (such as pulse dose delivery). However, oxygen could only be delivered at a minimum fixed continuous flow rate of 2 L · min^{-1} on this patient's proposed flight, and the airline's Conditions/Contract of Carriage forbade her from taking any oxygen equipment onto the aircraft that could have provided lower flow rates. It is worth noting again here that supplementary oxygen is limited to fixed flow rates of 2 L · min^{-1} and 4 L · min^{-1} on some aircraft (although on some long-haul flights it is limited to a fixed continuous flow rate of 4 L · min^{-1}), and that current guidelines recommend the use of these flow rates in flight.[1,2,4]

Although not replicating the cabin environment exactly, the HCT procedure has been reported to predict accurately the physiological response to the hypoxic environment both in hypobaric chambers and during flight under various conditions.[7,8] Therefore based on the results of the HCT we can confidently assume that although 2 L · min^{-1} oxygen was sufficient to maintain adequate oxygenation at a simulated cabin altitude, the sequelae to this patient undertaking air travel with supplementary oxygen would likely have been hypercapnia and consequent severe respiratory acidosis, considering the anecdotal evidence that a previous similar journey with oxygen was followed by admission to a critical care unit requiring NIV on landing. A blood pH value below 7.3 is associated with depression in neurological and cardiorespiratory function and multiorgan failure, and guidelines recommend that patients with pH < 7.25 should be managed in an intensive care unit.[5,10] Reduction in pH also results in a rightward shift in the oxyhemoglobin dissociation curve and a reduced saturation at a given oxygen tension.[10] This potentially further endangers the patient while in the hypobaric hypoxic environment of the aircraft cabin, especially if supplementary oxygen is subsequently removed in flight. Although it is impossible for us to predict the exact outcome, the consequences of the patient taking the proposed flight with supplementary oxygen may well have been an in-flight medical emergency, and it is worth noting at this point that in some cases progressively rising P_aCO_2 and a falling pH such as seen here are eventually fatal.[9]

In conclusion, this case study reports the onset of acute severe respiratory acidosis in a normally stable type 2 respiratory failure patient during hypoxic challenge testing only 20 min after being given the minimum level of supplementary oxygen available on many commercial aircraft. It would therefore be prudent to recommend that pCO_2 and pH are closely scrutinized during HCT prior to recommending in-flight oxygen for the reasons outlined in this case report, even though none of the current published recommendations discuss this risk to the passenger. Concentrating solely on P_aO_2 and S_pO_2 during HCT provides false reassurance that while a supply of

oxygen will maintain oxygenation in flight, the patient may have developed significant hypercapnia and acidosis; this issue has already been identified and extensively addressed by guidelines when administering oxygen therapy at sea-level. Although the HCT has been shown to simulate accurately the hypoxia experienced in the commercial aircraft cabin, further research into the effects of supplementary oxygen on patients with type 2 respiratory failure in a true aircraft cabin environment may provide more comprehensive data. This is due to additional factors such as expansion of trapped gas reducing respiratory reserve, physical exertion, and emotional stress all having the potential to exacerbate respiratory symptoms and compound the effects of hypobaric hypoxia.[2,8] Given the prevalence of patients with type 2 respiratory failure, future revisions of air travel guidelines should address the risk of acute hypercapnic respiratory acidosis when recommending in-flight oxygen to this group of patients. Further research is also needed into the validity of alternative oxygen delivery systems such as 'pulse dose' delivery during the hypoxic challenge test or during flight, or even the use of noninvasive ventilation in these scenarios in order to better cater for this group of patients during preflight assessment and in the aircraft cabin.

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