Blood-Injection-Injury (B-I-I) Specific Phobia Affects the Outcome of Hypoxic Challenge Testing

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BACKGROUND: Blood-injection-injury (B-I-I) phobia is capable of producing inaccurate hypoxic challenge testing results due to anxiety-induced hyperventilation.

CASE REPORT: A 69-yr-old woman with a history of hypersensitivity pneumonitis, restrictive spirometry, exercise desaturation requiring supplementary oxygen on mobilizing, reduced DLco, and B-I-I phobia was referred for hypoxic challenge testing (HCT) to assess in-flight oxygen requirements. HCT was performed by breathing a 15% F_IO_2 gas mixture, simulating the available oxygen in ambient air onboard aircraft pressurized to an equivalent altitude of 8000 ft. S_pO_2 fell to a nadir value of 81% during HCT, although it rapidly increased to 89% during the first of two attempts at blood gas sampling. A resultant blood gas sample showed an acceptable Po_2 outside the criteria for recommending in-flight oxygen and a reduced Pco_2. Entering the nadir S_pO_2 value into the Severinghaus equation gives an estimated arterial Po_2 of 6 kPa (45 mmHg), which was felt to be more representative of resting values during HCT, and in-flight oxygen was recommended.

DISCUSSION: While hyperventilation is an expected response to hypoxia, transient rises in S_pO_2 coinciding with threat of injury are likely to be attributable to emotional stress-induced hyperventilation, characteristic of B-I-I specific phobia and expected during the anticipation of exteroceptive threat, even in normal subjects. In summary, should excessive hyperventilation be detected during HCT and coincide with transient increases in S_pO_2, HCT should be repeated using S_pO_2 only as a guide to the level of hypoxemia, and S_pO_2 maintained using supplementary oxygen in accordance with alternative methods described in guidelines.

KEYWORDS: hypoxia, anxiety, oxygen, hypoxic challenge testing.

Spurling KJ, McGoldrick VP. *Blood-injection-injury (B-I-I) specific phobia affects the outcome of hypoxic challenge testing*. Aerosp Med Hum Perform. 2017; 88(5):503–506.

Passengers on board commercial aircraft are protected from the hypobaric atmosphere at altitude by the provision of an artificial pressure environment, i.e., a pressurized cabin, so that the occupants are not exposed to a significantly reduced barometric pressure.[10] The cabin altitude should not exceed an equivalent altitude of 8000 ft (2438 m) during normal operations, and this hypobaric atmosphere results in a reduction in available atmospheric oxygen when compared to sea level. In healthy passengers, arterial oxygen tension (P_aO_2) at 8000 ft (2438 m) typically falls to between 8 and 10 kPa (60–75 mmHg), with S_pO_2 between 89–94%. Increasing hypoxemia stimulates an increase in ventilation through action on the chemoreceptors of the carotid and aortic bodies in order to maintain arterial Po_2 and protect from excessive hypoxia, a response that differs between individuals, but normally occurs when arterial oxygen tension falls below a value between 7.3–8 kPa (55–60 mmHg).[11] When ventilation is increased to a level above metabolic requirements, it results in alveolar hyperventilation, with a fall in alveolar Pco_2 (P_ACO_2) and a subsequent fall in P_aCO_2.[9] This mechanism is protective against mild hypoxia in that it exchanges a reduction in P_ACO_2 for an increase in P_AO_2, with P_AO_2 rising by 1 mmHg for every 1 mmHg reduction in P_ACO_2.[11]

Hypoxia is not the sole cause of hyperventilation; it is also commonly seen in response to fear and anxiety. When psychological influences change breathing patterns in the absence of changes in metabolic activity, a state of hypocapnia can quickly result even for subjects without an anxiety disorder.[7] Anxiety is

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This manuscript was received for review in July 2016. It was accepted for publication in January 2017.

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DOI: https://doi.org/10.3357/AMHP.4730.2017

to be expected in most individuals during the anticipation of exteroceptive threat (such as the threat of a painful electric shock),[12] and even low levels of emotional stress, which may not be perceived as such by the individual, commonly give rise to hyperventilation.[4] The margin between normal ventilation and hyperventilation is small, and a partial pressure of CO_2 measured at the end of a normal tidal breath ($P_{ET}CO_2$) can be halved with only a 10% increase in ventilation.[6] Hypocapnia from hyperventilation causes vasoconstriction of the arterioles of the brain and in the skin, the former leading to a reduction in cerebral blood flow (CBF).[9] An arterial P_{CO_2} value of 20–25 mmHg (2.7–3.3 kPa) can reduce CBF by up to 50% in a healthy brain,[14] which can lead to altered sensations and perception, and a heightened fear reaction in some patients. This serves to compound the effects of any initial threat response and subsequent hyperventilation.[8,12]

CASE REPORT

A 69-yr-old woman presented to the respiratory clinic with increased resting dyspnea and a reduced exercise capacity. Lung function testing showed a mildly restrictive spirometry pattern with reduced alveolar volume (V_A) and carbon monoxide diffusion capacity (DLco) from the single breath method, with a subsequent biopsy confirming a diagnosis of hypersensitivity pneumonitis. Her baseline pulse oximetry (S_pO_2) value is consistently 96% on room air, although a 6-min walk test showed a fall in S_pO_2 to 85%, and consequently she requires ambulatory oxygen at a continuous flow rate of 4 $L \cdot min^{-1}$ in order to maintain $S_pO_2 > 90\%$ when moving. At her most recent visit to the respiratory clinic, she expressed a wish to travel by air in the near future. For a number of reasons, those with respiratory disease may be unable to compensate for the reduction in available oxygen in the commercial aircraft cabin,[1] so the physician referred the patient for a preflight oxygen assessment in accordance with guidelines issued by the British Thoracic Society.[2] These guidelines describe a procedure known as the hypoxic challenge test (HCT) or high-altitude simulation test (HAST), during which the patient breathes a gas mixture containing 15% oxygen, which simulates the level of available oxygen in ambient air in the aircraft cabin at cruising altitude.[1,2] The response to hypoxia during the HCT is assessed using direct measurement of arterial or capillary oxygen tension, or alternatively oxygen saturation by pulse oximetry should blood gas analysis be unavailable or unreliable. Guidelines issued by the British Thoracic Society recommend that arterial P_{O_2} remain >6.6 kPa (50 mmHg) during HCT (and therefore in flight), and the results of the test dictate whether supplementary oxygen will be required onboard the aircraft in order to prevent excessive in-flight hypoxemia.[2] These guidelines recommend assessment for prospective air passengers with a spectrum of respiratory diseases, including those with a pre-existing requirement for oxygen therapy such as the individual described here. During the preparations for the HCT the patient revealed that she suffers from a blood-injection-injury (B-I-I) specific phobia. This is one of five subtypes of specific phobia, which is defined by the American Psychiatric Association (DSM-5) as "an anxiety disorder subtype that represents unreasonable or irrational fear related to a specific object or situation," which in this case is exposure to needles or invasive medical procedures.[3] While B-I-I phobic individuals often demonstrate hyperventilation and a vasovagal fainting or near-fainting response,[3] this patient stated that she had never experienced anything more than anxiety and nausea during any kind of procedure involving injections or blood. Despite some reservations over the prospect of injury from earlobe puncture and a fear of the sight of blood from capillary blood gas sampling, she expressed a wish to proceed with the test in order to take her proposed flight safely.

The HCT was performed by the patient breathing a gas mixture containing 15% oxygen delivered to the patient via a mask worn over the mouth and nose, and supplied from a hypoxic gas generator (Hypoxico Everest Summit II, Sequal Technologies, Ball Ground, GA). The fraction of inspired oxygen was verified by a calibrated oxygen analyzer (Maxtec OM25-RME, Maxtec, Salt Lake City, UT) to ensure accurate simulation of the cabin environment and to avoid excessive hypoxia, while oxygen saturation was continually monitored by finger pulse oximetry (Nellcor N550, Tyco Healthcare, Nellcor Puritan Bennett Division, Boulder, CO). The introduction of the hypoxic gas was followed by a steady fall in S_pO_2 over a period of approximately 8 min. As S_pO_2 passed the threshold of 85%, the patient was prepared for an arterialized capillary blood gas sample from an earlobe site as per the HCT protocol. S_pO_2 at the time the patient was prepared for the sample was 81%, although she began to describe symptoms of anxiety at the prospect of earlobe puncture, and within 1 min S_pO_2 had risen to 89%. The results of the blood gas sample at this point are shown in **Table I**. It shows a P_{CO_2} below the normal range, increased pH, and an acceptable HCT P_{O_2} value of 7.09 kPa (53 mmHg).

Although an expected response to arterial oxygen tension <7.3 kPa is a compensatory increase in pulmonary ventilation, it was suspected that the recorded P_{O_2} was artificially high due to anxiety-induced hyperventilation and the patient was allowed to rest prior to another attempt at blood gas sampling. While continuing to breathe the hypoxic gas, with the threat of injury removed, S_pO_2 again fell to 82% and the equipment for the capillary blood gas sample was prepared for a further attempt. At this point the patient described a return to her anxious state and S_pO_2 again increased to 88%, even though no blood was taken on the second occasion. **Fig. 1** shows a plot of serial S_pO_2 measurements throughout the entire test, with stress events and the timing of the capillary blood gas sample marked.

Table I. Results of the Blood Gas Sampling.

PARAMETER	MEASURED VALUE	NORMAL RANGE
pH	7.558	7.350–7.450
P_{CO_2} (kPa)	4.31	4.60–6.00
P_{O_2} (kPa)	7.09	12.60–14.00
$cHCO_3$- (mmol · L^{-1})	28.7	22.0–28.0
SO_2 (%)	88.7	---

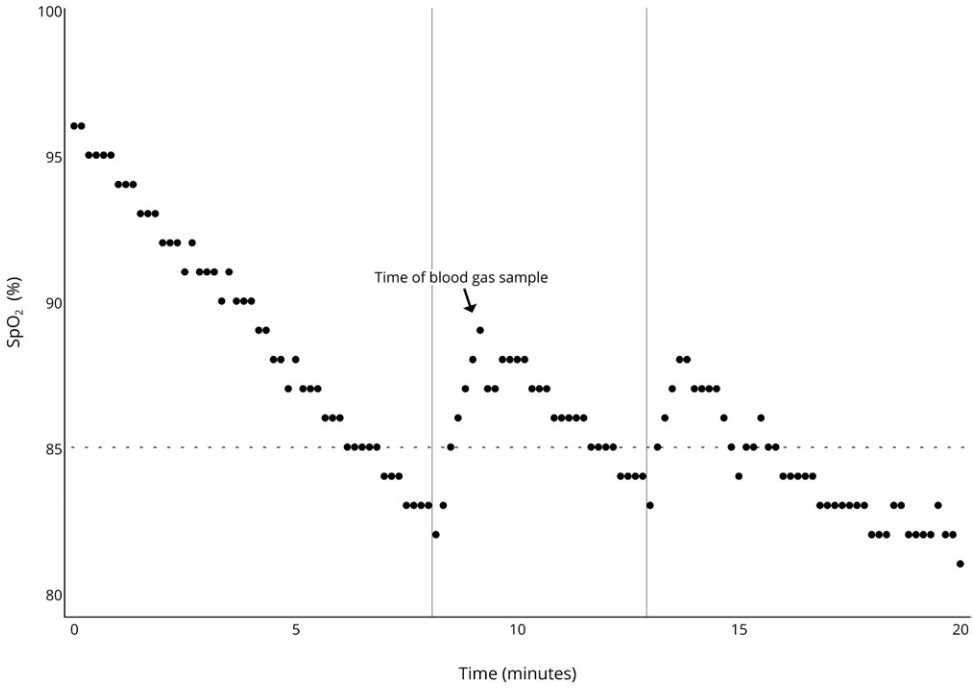

Fig. 1. Graphical representation of continually monitored S_pO_2 during the hypoxic challenge test. Stress events (vertical lines) and capillary blood gas sampling (arrow) are marked.

DISCUSSION

Blood gas sampling in conjunction with S_pO_2 is the recommended method to determine oxygenation during hypoxic challenge testing,[2] but the decision was taken in this case to disregard a Po_2 value that appeared abnormally high in the context of the patient's S_pO_2 values when she was undisturbed. With the patient's history of B-I-I specific phobia taken into account, this apparently abnormally high Po_2 value was assumed to be a result of the patient hyperventilating on being exposed to the sight of sharps and the prospect of injury. Anxiety-induced hyperventilation is a documented confounding factor for several types of diagnostic procedures, namely those that rely on stable blood gas values and cerebral blood flow,[7] although hyperventilation is also a normal response to arterial oxygen tension <7.3 kPa, which could be expected in this case with a recorded capillary Po_2 of 7.09 kPa. It may, therefore, initially appear difficult to determine which of these responses are responsible for the increased Po_2 recorded during HCT. However, by taking into account the features of the anxiety response, it becomes more apparent that the hyperventilation described in this case report is unlikely to be in response to hypoxia. $P_{ET}CO_2$ has been measured in a group of similarly affected subjects while exposed to their specific stimuli, such as video films depicting surgical procedures.[13] Hyperventilation was recorded as part of their fear response and caused transitory disturbances in $P_{ET}CO_2$ that coincided with exposure, which are similar to the transitory increases in S_pO_2 that coincided with the threat of injury reported in this case.

Due to the presence of several factors, namely the history of B-I-I specific phobia, the transitory nature of the disturbances and their coinciding exactly with either the first attempt at an earlobe puncture or the fear of injury alone on the second attempt (Fig. 1), it would be reasonable to assume that it was anxiety-induced hyperventilation that caused this patient's S_pO_2 and Po_2 values to increase to levels that would have not otherwise been seen during this test. Any decision based on the patient's capillary blood gas and pulse oximetry values at the time of the earlobe puncture would have cleared the patient to fly without supplementary oxygen due to a recorded Po_2 value >6.6 kPa (50 mmHg), based on the recommendations in the British Thoracic Society guidelines.[2] However, when the threat of injury was not present, S_pO_2 fell to a nadir value of 81% while breathing 15% F_IO_2, which was felt to be far more representative of the patient's resting oxygen saturation at an equivalent altitude of 8000 ft (2438 m). Predictive equations such as the Severinghaus equation can be used to provide an estimated arterial Po_2 value from S_pO_2 in these cases and, while they are not a substitute for direct measurement, they have been shown to correlate well with arterial Po_2 values and are adequate for clinical decision making in the absence of reliable blood gas measurements.[5] Using this method to calculate arterial Po_2 from nadir S_pO_2 gives an estimated P_aO_2 of 6 kPa (45 mmHg), and so the capillary blood gas data was discarded as unreliable. Based on the S_pO_2 value and estimated Po_2 at the nadir S_pO_2 point, the patient was advised to request in-flight oxygen based on the fact that 2 $L \cdot min^{-1}$ supplementary oxygen was later shown to raise S_pO_2 to a value >90% during HCT. The consensus opinion is to err on the side of recommending supplementary oxygen should there be any doubt over adequate oxygenation in flight.[2]

In summary, patients with B-I-I specific phobia who are likely to hyperventilate on exposure to their specific stimuli will produce confounding results while undergoing any tests relying on the accuracy of blood gas or S_pO_2 data while anxious. Any resulting values from a blood gas sample would therefore show artificially increased Po_2 and S_pO_2 values. This case report shows that it is possible for a B-I-I specific phobia to cause a patient to hyperventilate to an extent that makes the results of hypoxic challenge testing unreliable when blood gas sampling is involved. Despite an acceptable recorded Po_2 during HCT, in-flight oxygen was recommended for this patient as the blood gas data was felt to be unreliable and unrepresentative of the patient's true hypoxemia at rest at 8000 ft (2438 m) equivalent altitude. Taking into account the S_pO_2 profile of the test (Fig. 1), anxiety-induced hyperventilation had clearly distorted the blood gas data and provided a false-normal result for the HCT,

potentially leaving the patient vulnerable to excessive hypoxemia in flight. While blood gas sampling is the recommended method for this type of assessment, a physician in possession of a falsely high Po_2 and S_pO_2 could easily clear a patient as fit to fly without supplementary oxygen. It may, therefore, follow that a patient is cleared to fly following this test, when in reality they may be vulnerable to in-flight hypobaric hypoxia once onboard an aircraft. Although this is only one single observation in a subject with abnormal baseline lung function, other work has shown that anxiety-induced hyperventilation is a common confounding factor for diagnostic testing,[7] so it is reasonable to assume that any patient with a history of B-I-I specific phobia may produce falsely acceptable values during HCT. Using S_pO_2 alone for HCT assessment is an acceptable method of measuring hypoxia, as described in the British Thoracic Society guidelines as a valid alternative to blood gas sampling should it be unavailable.

Based on the observations from this case report, it would be advisable to scrutinize the continuous display of S_pO_2 during HCT for unusual increases. While this is usually done in order to prevent excessive hypoxia by maintaining awareness of falls in S_pO_2, a significant sudden rise in S_pO_2 on exposure to the sight of blood, sharps, or a threat of injury could be an indication of emotional stress-induced hyperventilation. One may then consider abandoning, or even not attempting blood gas measurements if the S_pO_2 value shows instability in patients with a history of B-I-I specific phobia. If transient disturbances occur in the S_pO_2 trace and appear to be in response to threat of injury, HCT should be repeated using S_pO_2 only as a guide to the patient's level of hypoxemia. Additional calculations using S_pO_2 data to estimate a Po_2 value are not essential, but may be a useful subsequent addition for clarity when reporting the HCT results. While hypoxic challenging remains a rarely used test, these observations are useful in other more routine investigations, such as oxygen therapy assessments, which could also be significantly affected by anxiety-induced hyperventilation.

ACKNOWLEDGMENTS

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