Hypoxia Tolerance Studies in Aircrew with Sickle Cell Trait: A Case Report

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Abstract

A case of an experienced pilot in whom sickle cell trait was detected during routine medical examination, is reported. He was subjected to aeromedical evaluation by exposure to simulated flight conditions of hypoxia in an altitude chamber. Sickling could not be demonstrated during prolonged repeated exposures upto altitudes of 4,570 m (15,000 ft) even when combined with moderate exercise. Clinical hypoxia induced by disconnecting oxygen supply at 9,140 m (30,000 ft) also did not produce any evidence of sickling. The pilot was assessed to be fit for full flying duties. Since the extremely low oxygen tensions required to precipitate sickling in sickle cell trait carriers are exceptionally rare in modern aviation, the need for reconsideration of the present aircrew licensing policy is stressed.

Introduction

Sickle cell trait, a heterozygous disorder involving the abnormal haemoglobin S, shows high incidence in tropical Africa, Greece, Southern Turkey, Jamaica, the United States and Southern India[13, 16]. Although sickle cell trait may be classified as a haemoglobinopathy, it is an inherited abnormality and not a disease. It is almost impossible to make a clinical distinction between a person with normal haemoglobin and one with sickle cell trait. The individuals with this trait do not show any evidence of anaemia. The number of red cells the haemoglobin level of the blood and the volume of the packed cells[18] and even the length of red cell survival[17, 25] are entirely normal. A few abnormalities such as haematuria[1, 18], hyposthenuria,[2] priapism[18] and a septic necrosis of the head of Femur[23] have been reported. However, these are extremely rare and no definite correlation between the incidence of these conditions and sickle cell trait has so far been established. For all practical purposes, an individual with the trait can expect to lead a normal life unless exposed to extreme conditions of hypoxia. This a report of studies conducted on a Zambian Air Force pilot referred to IAM, Bangalore by the first author while he was on deputation to that country.

Case Study

HMS, a 24 years old fighter pilot of Zambia Air Force had completed 338 hours of flying including 196 jet hours when sickling test carried out as part of a routine medical examination was found to be positive in him. His medical documents showed that this test had been reported as negative on two earlier occasions. He had been flying uneventfully for the past four years. Initially, he had been flying an unpressurized piston engined aircraft with a ceiling of 4,875 m (16,000 ft) at the usual cruising altitude of 3,050 to 3,660 m (10,000 to 12,000 ft) without the use of oxygen in routine flights. Later he flew unpressurized jet fighters having a maximum ceiling of about 12,190 m (40,000 ft), oxygen being available through a demand diluter type of regulator during flight. The usual cruising altitude was about 5,180 m (17,000 ft) with each sortie lasting about 50 minutes. The pilot was in the habit of donning his oxygen mask loosely on the face or even removing it off and on during flight because of sweating caused by the inadequate air conditioning system. During one cross country sortie he had flown at 7,315 m (24,000 ft) with the oxygen mask disengaged for about 15 minutes without any ill effects. Throughout this period of his service he neither showed any clinical abnormality nor had any complaints. Routine laboratory investigations of blood and urine were within normal limits. Electro-

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phoretic examination of his haemoglobin confirmed that his haemoglobin was of AS genotype. He was diagnosed as a case of sickle cell trait and was declared unfit for flying duties as per the existing aircrew licensing policy. The authorities, however, agreed to review his case after a thorough aeromedical evaluation at the Institute of Aviation Medicine, Indian Air Force, Bangalore (India).

Investigations

The pilot was subjected to a thorough general physical and systemic examination. The clinical investigations included electro-cardiography, electroencephalography and radiological examination of the chest. Haematological investigations like complete haemogram, RBC fragility, reticulocyte count, ESR, WBC count and examination of peripheral blood film as well as biochemical estimations of cholesterol, urea, uric acid, sodium, potassium and bicarbonate were carried out. Time to sickle, *i.e.*, the time taken by the red cells to sickle in sealed wet preparations incubated at 37°C without the addition of any reducing agent, was determined. Qualitative and quantitative analysis of haemoglobin was done by paper electrophoresis using barbital buffer at pH 8.6. Urine was examined. A standard glucose tolerance test was done. He was also subjected to Tilt Table studies. His +Gz tolerance was determined in a human centrifuge using peripheral light loss as the end point. At the end of the eight consecutive centrifuge runs his venous blood was collected and examined for evidence of sickling or changes in RBC fragility.

In an altitude chamber the subject was instrumented for monitoring various physiological parameters like heart rate, respiration and electrocardiogram. He was instructed to report any untoward symptoms as and when they occurred. He was taken to gradually increasing altitudes on different days. Thus, he was exposed to 2,285 m (7,500 ft), 3,050 m (10,000 ft) and 3,760 m (12,500 ft) for two hours each and to 4,570 m (15,000 ft) for one hour while sitting at rest breathing ambient air. Capillary blood samples were collected at 15 minutes intervals. He was then given a standard exercise at these altitudes and blood samples were collected immediately after the exercise and 15 minutes later. All these samples were examined for evidence of sickling instantaneously and at regular intervals with the help of a microscope set up inside the altitude chamber. Sealed wet preparations were incubated at 37°C to determine the time to sickle at the end of each altitude exposure. Urine was examined after each exposure for evidence of microscopic haematuria.

On a subsequent day, the subject was taken upto 9,140 m (30,000 ft) while breathing oxygen through a demand diluter type of oxygen regulator. On levelling off at this altitude, his oxygen supply was manually disconnected and he was given a set of tasks to elicit his psychomotor response. After about two minutes, when his performance had notably deteriorated, capillary blood samples were collected and oxygen supply resumed. At the end of the exposure, venous blood was collected for haematological and biochemical investigations and urine was examined for evidence of haematuria.

The pilot was also subjected to a rapid decompression from 2,440 to 6,705 m (8,000 to 22,000 ft) in five seconds and blood samples examined for the presence of sickle forms.

Results

The pilot did not reveal any clinical abnormality. ECG, EEG and skiagram of chest were normal. The haematological and biochemical investigations were within normal limits (Table–I, II).

TABLE I Basal Haematological Investigations

Hb : 15.0 gm%	TRBC : 4.5 Mil/cmm Reticulocytes : 0.8%	PCV : 46%
Hb Genotype 'AS'	TWBC : 8200/Cmm	MCV : 102.2 cu microns
Hb A 53.0%	Neutrophils 74% Lymphocytes 16%	MCH : 33.3 microgram
Hb A2 : 3.6%	Eosionophils 3% Monocytes 7%	MCHC : 32.6%
Hb S : 43.4%	Basophils Nil ESR 2 mm fall in	Peripheral Blood
Sickling — Positive	1st hour (Wintrobe)	Film – Normal.

TABLE II

Basal Biochemical Investigations

Serum Cholesterol	:	143mg/100 ml	Serum Sodium	:	139 m Eq/L
Blood Urea	:	22mg/100 ml	Serum Potassium	:	5.3 m Eq/L
Blood Uric Acid	:	3mg/100 ml	CO2 Combining Power/Plasma Bicarbonate	:	25 m Eq/L 56 Vol/100 ml Plasma

Haemoglobin electrophoretogram showed the 'AS' pattern with Hb A 53%, Hb S 43.4% and Hb A2 3.6%. Glucose tolerance and response to 45° and 90° tilts on the Tilt Table were within normal limits. His +Gz tolerance for peripheral sight loss was +3.5 g which increased to +5.2 g with anti 'g' suit. There was no evidence of sickling or changes in RBC fragility at the end of the centrifuge runs.

The subject was fully asymptomatic throughout the various altitude exposures and his physiological parameters were within normal limits. During these exposures the peripheral blood did not show any abnormality of the erythrocytes before or after exercise. The time to sickle also did not change from its basal value of 24 hours. No significant haematological or biochemical changes were noted after the acute exposure to hypoxia at 9,140 m (30,000 ft) (Table III).

TABLE III

Haemotological Values before and after Exposure to Hypoxia at 9,140 m (30,000 ft)

	Before	After
Hb (gm%)	15.0	15.0
ESR mm fall in I hr (Wintrobe)	2	2
TRBC (Mill/cmm)	4.5	4.6
PCV (%)	46.0	44.0
MCV (cu microns)	102.2	95.6
MCH (micro-micrograms)	33.3	32.5
MCHC (%)	32.6	34.0
Reticulocytes (%)	0.8	0.7
Red Cell fragility :		
0–5% lysis	0.4% Nacl	0.4% Nacl
50% lysis	0.34% Nacl	0.34% Nacl
95–100% lysis	0.2% Nacl	0.2% Nacl
Peripheral Blood picture	Normal	Normal
Time to sickle	24 hours	24 hours

Exposure to rapid decompression also did not produce any changes in the blood picture. There was no evidence of macroscopic or microscopic haematuria at any stage during these studies.

Discussion

A person may become hypoxic by flying or residing at high altitude and in mishaps during anaesthesia. Splenic infarctions have repeatedly been reported amongst some passengers with this trait during high altitude flight in unpressurized aircraft due to sickling of red blood cells (3, 4, 10, 24, 26, 27). Jones et al[13] have reported fatal sickling crisis in four Negroes with sickle cell trait due to hypoxia caused by voilent exercise at a moderately high altitude of 1,220 m (4,000 ft). However, no sickling crisis were reported among the African competitors with the trait competing in the Mexican Olympic games held at an altitude of 2,135 m (7,000 ft).[9] Evidence, often cited for sickle cell trait individuals getting splenic infracts or sudden death while flying at high altitudes has come under criticism by various authors [7, 15, 20]. It is possible that before the discovery of haemoglobin C in 1951, symptomatology in what was in fact haemoglobin SC disease, was described to the sickle cell trait. There is no recorded incident of infarctive crisis among the many thousands of sickle cell trait carriers who must be flying in pressurized aeroplane all over the world. Also, there is no record of any mishap associated with sickling in a member of the aircrew so far in the literature.

It has been shown that, for the erythrocytes of a person with Hb AS to produce appreciable sickling, the required fall in oxygen tension is of the values as low as 10 – 15 mm Hg.[14] Studies have shown that during the first few minutes of an acute exposure to hypoxia at altitudes of less than 9,000 m (29,527 ft), the arterial oxygen saturation does not fall to levels capable of producing blood oxygen tensions as low as 10 – 15 mm Hg.[21] The altitude

at which significant sickling is produced following a sufficient reduction of oxygen has not been scientifically established so far.[12] Further, there is no evidence to show that the relatively small reduction in oxygen which occurs within the cabin of a pressurized aircraft during normal operations is sufficient to cause serious effects.

In vitro and in vivo studies on sickle cell trait individuals during simulated flight environments are not widely reported. Loyke[10] had exposed heparinized samples of blood containing Hb AS to altitudes and demonstrated the appearance of oat-shaped cells at 1,980 m (6,500 ft) and multipointed sickle cells at 3,050 m (10,000 ft) which increased in number to 40% at 12,190 m (40,000 ft). These abnormal cells reduced in number with return to sea level. 100% sickling was noticeably absent even after the exposure to 12,190 m (40,000 ft) for 30 minutes, the equivalent oxygen tension being about 30 mm Hg. Henderson and Thronell,[11] however had found no sickling occurring in sickling positive subjects upto 4,570 m (15,000 ft). Findlay[8] demonstrated in vivo sickling in three sickle cell trait carriers flying at 4,570 m (15,000 ft).

The present case brings to light the fact that there might be many undetected carriers of sickle cell trait on active flying duties in many parts of the world. The sickling test used as a routine screening method is known to have some inherent fallacies. Once these individuals are identified as carriers of Hb S, the medical authorities are faced with the problem of their medical evaluation and assessment of fitness for flying. A firm internationally acceptable licensing policy is still not available and the existing policy of rejecting all such individuals from further flying duties is controversial. Examples of splenic infraction occurring in individuals with sickle cell trait on exposure to high altitude flying in support of the hazards of this triat have also been criticised. The flight history of the pilot, studied by us, prior to the detection of the trait is clear in that he had been repeatedly exposed to altitudes around 4,570 m (15,000 ft) without any ill effects. During various exposures in the altitude chamber also he tolerated a prolonged stay at 4,570 m (15,000 ft) even when the test was coupled with moderate exercise. He did not show any evidence of sickling even after clinical hypoxia was induced in him at an altitude of 9,140 m (30,000 ft). He showed a normal response to situation of rapid decompression and repeated +Gz stress. The fact that his Hb S level was as high as 43.15 %, the usual range in sickle cell trait being 20 to 40%, reinforces these observations and suggests that individuals with lower amounts of Hb S are likely more likely to withstand such exposures in flight conditions without any ill effects. The results of our study are in conformity with the view expressed by Lewis[18] that individuals with this trait should not enter a career involving airplane flying. However, those already trained, but subsequently found to have the sickle cell trait, should be allowed to continue flying under medical supervision. An ICAO information paper[12] suggests that while assessing medical fitness for aviation duties, previous exposure to high altitude including flight experience or exposure to hypoxia by other means (e.g. decompression chamber) indicating tolerance to a hypobaric environment without clinical symptoms of sickling should be specially noted. Recently, two pilots in Ghana in whom sickle cell trait was detected after 670 and 635 hours of their flying experience respectively were classified as medically fit for further flying duties after thorough medical evaluation by Djabanor[5] and Djabanor et al.[6] The pilot in question was therefore considered medically fit for full flying duties with the stipulation that the standard operational procedure of breathing supplementary oxygen whenever the cabin altitude exceed 3,050 m (10,000 ft) must be strictly enforced in his case as an added safety measure.

Conclusion

Our detailed studies on an experienced Zambian pilot in whom sickle cell trait was detected during a routine medical examination, have shown that when he was exposed to simulated flight conditions including several acute exposures to hypoxia he did not show any evidence of sickling crisis. He was assessed to be fit for full flying duties with stipulation to use supplemental oxygen at altitudes above 10,000 ft as an added safety measure. Available evidence suggests that sickle cell trait individuals already trained for aircrew duties need not be rejected outright from continuing with flying duties after adequate evaluation. However, eventualities where trained aircrew would have to be so relegated should be very few with adequate screening tests before their acceptance for a flying career.

The problem of sickle cell trait has a special significance in India. High incidence of Hb S has been established among the Veddoids of Nilgiri Hills and the Mahars of Central India. Individuals from these ethnic groups showing presence of Hb S have already been identified in the Indian Armed Forces. The possible chances of their being engaged in aviation duties presently and in future cannot be ruled out, because there is as yet, in India, no routine screening of the candidates for abnormal haemoglobins. On the face of it, problems related to this trait have not come to our notice. This does not mean that likely hazards of this trait in flying need no attention particularly in the case of flying aircrew who hail from ethnic groups mentioned above. Whether or not individuals with sickle cell trait be accepted for flying in the beginning itself is a policy matter. It is the view of the authors, that unless a country's Air Force suffers from man power shortage for flying duties because of the prevalence of this trait, there is no need to reject individuals with this abnormality at the stage of entry.

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