

Pre-operative screening for sickle cell trait in adult day surgery; is it necessary?

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1. Introduction

Routine pre-operative screening for sickle haemoglobin (HbS) in individuals considered at risk for a sickle haemoglobinopathy is common practice. This has arisen out of the perceived risks in these individuals when undergoing anaesthesia and surgery. Anaesthesia in patients with sickle cell anaemia is potentially hazardous. These patients have a chronic haemolytic anaemia and are symptomatic of their disease in childhood. But it would be unusual for an adult to present for day surgery without this condition having previously been identified. In pre-operative screening of adults, therefore, the purpose seems to be to identify those with the sickle trait, or milder genotypes of sickle cell disease, such as HbSC or HbS β -thalassaemia, who have not been diagnosed earlier on clinical grounds. The question of whether patients should be routinely screened pre-operatively for the carrier state, sickle trait, is a controversial one [1]. In this review, we discuss the clinical and anaesthetic implications of sickle trait, and the limitations of screening protocols and other issues involved in routine screening.

2. Sickle cell trait

Sickle cell trait refers to the heterozygous state for the HbS gene. It is one end of the spectrum of sickle

haemoglobinopathies which includes the homozygous state HbSS (sickle cell anaemia) and the co-inheritance of HbS with other haemoglobin variants (e.g. HbSC disease, HbS β -thalassaemia). The HbS gene codes for the formation of an abnormal haemoglobin in which valine is substituted for glutamic acid in the 6th position of the β -globin chain giving rise to the relatively insoluble HbS. In conditions of oxygen deprivation, HbS forms crystals which distort the shape of the red cell membrane causing the cells to assume an inflexible sickle shape. These cells may then become stuck within capillary beds generating a vicious cycle of circulatory stasis, acidosis, further hypoxaemia and ultimate tissue infarction [2]. The extent of sickling and the ease with which it is precipitated depends on the percentage of deoxygenated HbS. Hypoxaemia is therefore the biggest risk factor. The individual with sickle trait has 20–45% HbS in the blood. The critical PO₂ at which irreversible sickling occurs is 2.7 kPa. Thus conditions of extreme hypoxaemia are required to precipitate sickling in a patient with the trait. For instance, in an individual with sickle trait who has 40% HbS in his red cells, sickling will begin at 40% oxygen saturation. This is in contrast to the patient with HbSS with 85–95% HbS in his red cells, where the critical PO₂ is 5.5 kPa and some sickling will always occur even with 100% oxygen saturation, and all cells are sickled at 50% oxygen saturation [3].

Acidosis and conditions which promote circulatory stasis such as hypothermia, dehydration and hypotension can also aggravate sickling. Individuals who have co-inherited other abnormal haemoglobins such as those with HbSC and HbS β -thalassaemia disease also have a greater tendency to sickle than traits [2].

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3. Clinical implications of sickle trait

Sickle trait is a benign haemoglobinopathy that is not associated with anaemia. Individuals with sickle trait are generally asymptomatic. However, they are reported to be at increased risk of the following. A higher risk of splenic infarction at high altitudes of > 10,000 feet and in unpressurized aircraft; commercial flights where cabin pressures equivalent to \approx 8000 feet are maintained do not pose any problems. A higher risk of sudden unexplained death with exertion has been reported amongst black military recruits with sickle trait compared to those without. Renal complications such as haematuria, bacteriuria and pyelonephritis in pregnancy are also more common. Sickle trait has been associated with a higher risk of pulmonary embolism [4].

4. Historical background/epidemiology of sickle trait

The HbS gene is most prevalent in equatorial Africa where it has its origins (Table 1). Population migration and interbreeding resulted in genetic drift out of Africa. Clusters of high gene frequency occur elsewhere in the world e.g. in Arabia, India, Israel, Turkey, Greece and southern Italy. This can be attributed to the ancient trade routes connecting the Niger River basin with the Mediterranean Sea, and the power struggles which ensued within Mediterranean domains and subsequent assimilation of the gene into conquering nations. The gene arrived in the Western world with the slave trade initially, and in the last century, with voluntary immigration [5]. Today, ease of international mobility, and intermix of different ethnic groups have resulted in a

Table 1
Gene frequency of HbS in different populations [17]

Country	Frequency
Africa	
Nigeria	0.133
Angola	0.202
Bantu	0.0006
Senegal	0.142
Europe	
Greece	0.012
Portugal	0.0005
Asia	
Saudi Arabia	0.081
Punjab	0.011
Gujerat	0.12
Bangladesh	0.002
Madhya Pradesh	0.086
West Indies (Black)	0.058
USA (Blacks only)	0.042

NB, carrier rate is approximately twice gene frequency.

widening of the gene pool to an extent that the identification of physical or racial characteristics can no longer be the only criteria used to identify those likely to carry the gene, whether in the heterozygous or homozygous form. Patients with sickle cell disease range from individuals with blond hair and blue eyes to those with olive skin and straight dark hair to those with dark skin and curly black hair [5]. In the USA, white patients with sickle cell disease have been identified who have no phenotypically distinguishable characteristic or identifiable African ancestry [6]. Neonatal screening programmes have also yielded interesting results. Cord blood screening of white babies in California revealed a 0.7% incidence of sickle trait. In urban centres in the USA, 10% of patients with various sickling disorders identified themselves as non-black.

5. Screening protocols

The recommendations of the General Haematology Task Force of the British Society for Haematology are that pre-anaesthetic screening for HbS should be offered to all patients of African or Afro-Caribbean descent in order to identify individuals with the trait as well as the clinical sickling syndromes [7]. In addition, routine screening of peoples originating from the Middle East, southern Italy, Greece, Turkey, Cyprus and India is also recommended. In the light of recent knowledge, it would appear that the identification of at risk groups is less clear. What should the selection criteria for screening be if individuals with the sickle gene are no longer easily identifiable on the basis of racial or physical characteristics or by country of origin or ancestry?

Screening is recommended for several reasons; to inform affected individuals of health risks, to warn of potential risk to the fetus antenatally, to be able to initiate early effective treatment for sickle cell anaemia in the neonatal period and to facilitate genetic counselling of affected parents. Screening for a condition induces great anxiety. The terms sickle positive, sickle negative and trait are often misunderstood. Therefore, any effective screening programme requires follow-up counselling. This seldom happens in anaesthetic practice. It is not uncommon for patients to remain unaware of their test result. Undoubtedly, this contributes to repeated and unnecessary screening when the patient next presents for surgery.

6. Screening tests: limitations

The sickle solubility test (e.g. Sickledex) is used to screen for the presence of HbS by its precipitation in the presence of a reducing agent. It cannot distinguish

between the trait and disease. Furthermore, in the patient being investigated for anaemia, the solubility test can give a false negative result. False negatives will also arise in babies in the first few months of life. False positives may arise in dysproteinaemic states [7].

Haemoglobin electrophoresis is the definitive screening test. Its value in an emergency is limited because the result is unavailable immediately. A facility for rapid haemoglobin electrophoresis exists but is not cost-effective for the majority of hospitals.

7. The risks of anaesthesia in sickle trait

Concerns about anaesthetic related morbidity and mortality in sickle trait have often been based on anecdotal case reports alleging causality simply by association. In the 1970s, a few of these reports highlighted the risks and focused attention on the peri-operative management of this group of patients [2,8,9]. It led to recommendations such as the need for pre-oxygenation to minimize potential hypoxia during induction, use of 50% oxygen mixtures, continuous oxygen therapy until full recovery, maintaining adequate hydration with intravenous fluids, keeping the patient warm and avoiding the use of tourniquets to create a bloodless surgical field.

A case of cardiac arrest and subsequent maternal death was reported to have occurred during Caesarean section under general anaesthesia [10]. It was postulated that aortocaval compression had occurred, and its relief at delivery allowed the sudden return of hypoxic, acidotic and sickled blood to the heart. The finding of sickled red cells at postmortem is often presented as evidence that sickling was responsible for the complication. However, sickling at or near death is an inevitable event and sickle cells will always be found at post-mortem.

Two reports in the literature alleging significant morbidity associated with sickle trait consist of a case of superior sagittal sinus thrombosis [9] and a case of presumed splenic infarction [8] that occurred during recovery from anaesthesia. In both cases, the patients were of Negro origin, and experienced conditions of hypoxia, dehydration and hypotension to an extent which might have been harmful even to patients without the trait. Both cases occurred before the advent of pulse oximetry.

In contrast, two studies have looked objectively at the risks of anaesthesia associated with sickle trait and found no real correlation. Searle reviewed five series of general anaesthetics in sickle trait patients [2]. There were four deaths out of a total of 513 cases. Anaesthesia was attributed as the main cause of death in only one of these cases. This was the case of a 12-year-old Negro boy who died as a result of longitudinal sinus

thrombosis thought to have been triggered by a difficult open ether induction. Had the presence of sickle trait been known, the choice of anaesthetic and outcome might have been different. In the three remaining cases, death was attributed to co-existing conditions unrelated to sickle trait e.g. carcinoma of the stomach, an inoperable necrotic haemorrhagic pelvic neoplasm and pulmonary embolism.

In the second study, 56 black patients with sickle trait were matched for procedure, type of anaesthetic, age and sex with black patients with normal haemoglobin [11]. There were no significant differences found in the rate or type of complications, and no difference in the length of post-operative stay. The complications observed did not relate to the anaesthetic or haemoglobin makeup but appeared to reflect the type and severity of the procedure.

8. The risks of tourniquets

The use of a tourniquet to provide a bloodless field during surgery results in circulatory stasis, acidosis and hypoxaemia, conditions known to induce sickling.

These concerns were highlighted in an early case report which warned against tourniquet use [12]. These theoretical concerns were not substantiated in a study of sickle trait patients undergoing orthopaedic procedures involving the use of tourniquets. No significant acid-base disturbances were found, nor was there any evidence of sickling or post-operative complication related to tourniquet use [13]. It was suggested that the use of tourniquets in patients with sickle trait was safe provided that the limb was exsanguinated beforehand.

9. Implications for anaesthetic management

There have been no reports of sickling complications associated with anaesthesia in sickle cell trait patients in the past 15 years. The place of ether has long been relegated to history. Anaesthetic practice has changed since the original reports of anaesthetic related complications of sickle cell trait.

Modern drugs and volatile agents possess better induction and maintenance characteristics and a rapid recovery profile. Improved monitoring techniques such as pulse oximetry and capnography, and in recent years, the AAGBI's recommendations for standards of monitoring during anaesthesia and recovery [14], have all contributed to the safety of general anaesthesia in current practice. With pulse oximetry, hypoxia should not go unrecognised even in the dark skinned.

Shorter periods of starvation and fluid deprivation are now actively encouraged, and the use of intravenous fluid rehydration is not so unusual. Modern

theatres are equipped with a temperature-controlled environment and the use of effective warming systems (e.g. Bair Hugger) make accidental hypothermia less likely.

The development of recovery facilities and increased anaesthetic involvement in post-operative management have all led to improved post-operative outcome. In recent years, the introduction of acute pain services have contributed towards safe and effective post-operative analgesia.

Therefore, in the context of modern anaesthetic practice, the conditions which could induce sickling such as hypoxaemia, acidosis, dehydration, circulatory stasis and hypothermia should not occur. It could be argued that a universal standard of safe practice applicable to all patients irrespective of the presence or absence of a haemoglobinopathy should exist. The knowledge of the presence of sickle trait would therefore become irrelevant.

10. Implications for day case surgery

In this context, relatively minor surgery of short duration involving minimal physiological disturbance is performed in fit and healthy patients. A careful history and pre-operative assessment ensures optimal patient selection. Pre-operative investigations should be kept to a minimum. In this context, is the performance of a sickle test relevant to management?

The conditions which could induce sickling should not occur in the course of a well conducted anaesthetic, nor in the recovery period. Appropriate monitoring including pulse oximetry is routine at induction, intra-operatively and in recovery. Hypoxaemia, when it occurs, is usually unexpected and unpredictable. The causes are many and diverse, and include equipment failure and patient-related complications e.g. anaphylaxis, laryngospasm and bronchospasm. In some cases, hypoxaemia may be anticipated e.g. in the very obese, in heavy smokers and in patients with chronic lung disease. In all cases, the treatment of hypoxaemia is directed at the cause and measures taken to minimise the risk of hypoxaemia in those at risk. Sickle cell trait per se is not a cause of hypoxaemia.

In the post-operative period, hypoxaemia has been shown not to be a significant problem following minor surgery [15,16]. Operations which result in severe post-operative pain and risk of significant haemorrhage are excluded as day cases. Day case patients are ambulant immediately before and very soon after surgery which is of short duration. The risk of deep vein thrombosis is minimal.

Day case surgery has to be convenient, efficient and economic. Pre-operative investigations should be performed only where indicated and where the result alters

management and improves safety. Otherwise, the adherence to strict screening protocols will inevitably lead to unnecessary cancellations and disruptions to lists and wastage of limited resources.

11. Conclusion

Sickle cell trait is not a disease. It is a benign condition with few, if any, implications on health. It does not have significant implications either surgically or anaesthetically particularly in the context of day case surgery. Is it necessary to screen for sickle trait pre-operatively?

One can argue that the purpose of screening is to detect those individuals with HbSC disease who remain asymptomatic and without detectable anaemia into adulthood. Such individuals, even if identified, would not be managed any differently. As an analogy, we cannot guarantee to identify all patients with asymptomatic ischaemic heart disease, and do not perform routine pre-operative ECGs on patients before day surgery. Fitness for day case surgery is mainly based upon our clinical assessment. Language barriers in ethnic groups can present difficulties. However, better patient education, antenatal and neonatal screening programmes make the individual who remains unaware of a sickle haemoglobinopathy uncommon.

Screening protocols have to be justified on medical, ethical and economic grounds. Current guidelines, where they exist, range from recommendations on screening all black patients pre-operatively, to screening all patients of non-Northern European extraction. The sickling disorders are not confined to black patients but can be found in white patients who are phenotypically indistinguishable from the rest of the population. What criteria should be applied in order to justify screening in a particular racial group?

It is interesting to note that the practice of screening for HbS pre-operatively has not been routine or considered necessary for several years now outside of the UK e.g. in the USA. A careful pre-operative assessment and full blood count evaluation will identify those with sickle cell anaemia, and the rest would not be managed any differently. This practice of applying a universally safe standard of practice to all patients has much to commend it. After all, as anaesthetists we do not willingly allow our patients to become dangerously hypoxic, acidotic, hypothermic, dehydrated or hypotensive.

We suggest that routine screening for HbS is not indicated prior to day surgery and that formal testing should be confined to patients with clinical or haematological problems where it is relevant to their overall management. Standards of practice have to be based on good scientific evidence and not anecdote. Can we

justify screening for a benign condition which does not alter management? There is no value of screening as defensive medicine. Does failure to test imply negligence? Or is testing any defense for sub-standard anaesthesia?

References

- [1] Eichorn JH. Pre-operative screening for sickle cell trait. *J Am Med Assoc* 1988; **259**: 907.
- [2] Searle JF. Anaesthesia in sickle cell states: a review. *Anaesthesia* 1973; **28**: 48–58.
- [3] Mason RA. Haemoglobinopathies. *Anaesthesia Databook: A Clinical Practice Compendium*. Harlow: Longman, 1994.
- [4] Sears DA. *Sickle Cell Trait. Sickle Cell Disease: Basic Principles and Clinical Practice*. New York: Raven Press, 1994.
- [5] Powars DR. Sickle cell disease in non-black persons. *J Am Med Assoc* 1994; **271**(23): 1885.
- [6] Rogers ZR, Powars DR, Kinney TR, Williams WD, Schroeder WA. Non-black patients with sickle cell disease have African beta-S gene cluster haplotypes. *J Am Med Assoc* 1989; **261**(20): 2991–2994.
- [7] General Haematology Task Force. *Clin Lab Haematol* 1988; **10**: 87–94.
- [8] Howells TH, Huntsman RG, Boys JE, Mahmood A. Anaesthesia and sickle cell haemoglobin. With a case report. *Br J Anaesth* 1972; **44**: 975–987.
- [9] Dalal FY, Schmidt GB, Bennett EJ. Sickle cell trait. A report of a post-operative neurological complication. *Br J Anaesth* 1974; **46**: 387–388.
- [10] The Anaesthesia Advisory Committee to the Chief Coroner of Ontario. Intra-operative death during caesarean section in a patient with sickle cell trait. *Can J Anaesth* 1987; **34**: 67–70.
- [11] Atlas SA. The sickle cell trait and surgical complications. A matched-pair patient analysis. *J Am Med Assoc* 1974; **229**: 1078–1080.
- [12] Willinsky JS, Lepow R. Sickle cell trait and use of the pneumatic tourniquet. A case report. *J Am Podiatry Assoc* 1984; **74**: 38–41.
- [13] Adu-Gyamfi Y, Sankarankutty M, Marwa S. Use of a tourniquet in patients with sickle cell disease. *Can J Anaesth* 1993; **40**: 24–27.
- [14] *Recommendations for Standards of Monitoring During Anaesthesia and Recovery*. The Association of Anaesthetists of Great Britain and Ireland, 1988.
- [15] Fogg K, Saunders PR. The role of oxygen therapy in the recovery phase of day surgery. *Ambul Surg* 1996 (accepted for publication).
- [16] Rosenberg J, Kehlet H. Postoperative mental confusion — association with postoperative hypoxaemia. *Surgery* 1993; **114**: 76–81.
- [17] Raychoudhury AK, Nei M. *Human Polymorphic Genes World Distribution*. New York: Oxford University Press, 1988.