CASE REPORT

Pulse oximetry error in a patient with a Santa Ana haemoglobinopathy

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SUMMARY

A young man with a rare unstable haemoglobinopathy presented with a high fever, worsening shortness of breath and abdominal pain. At triage his pulse oximetry (SpO₂) suggested that his blood oxygen saturation was 84% at room air. However, an arterial blood gas (ABG) oxygen saturation reading (SaO₂) was 100%. The significant disparity between the two measurements demonstrates that using pulse oximetry in some unstable haemoglobinopathies may significantly underestimate the actual reading. This error is most probably due to the structural differences in the variant haemoglobin causing light to be absorbed at a different wavelength beyond the normal range of the oximeter. Haemoglobinopathies affect about 7% of the world's population and is often asymptomatic; so, there may be many more undiagnosed cases. Therefore, clinicians may confirm low SpO₂ readings with an ABG and, where there is significant disparity with no obvious extrinsic cause, they should consider haemoglobinopathies.

BACKGROUND

The present case has been written to reinforce the existing literature about unstable haemoglobinopathies and seeks to bring them to the attention of healthcare professionals when they come across aberrantly low SpO₂ readings. Santa Ana haemoglobinopathy is an extremely rare variant of this disease and so this case report would add to the very limited peer-reviewed literature on this specific condition.

The case also highlights an example of measurement error that may occur in the acute setting. It demonstrates that pulse oximetry error may be spotted quickly with an arterial blood gas (ABG) to check the reading. Healthcare professionals are capable of spotting more common causes of extrinsic errors in pulse oximetry but when more obvious culprits have been ruled out, the less obvious intrinsic causes should also be considered.

CASE PRESENTATION

The patient is a young man of Indian descent who self-presented to an Urgent Care Centre with a 3-day history of high fever, lethargy, severe shortness of breath on minimal exercise and abdominal pain. His medical history included chronic anaemia secondary to Santa Ana haemoglobinopathy and splenomegaly. Two days before presentation, his general practitioner had started a course of clarithromycin for a suspected chest infection. Two months previously he was admitted for an atypical chest infection from which he felt he had never

fully recovered. He described that his urine had always been very dark and his sclera were constantly coloured yellow to a varying degree.

INVESTIGATIONS

His observations at triage were abnormal with a temperature of 39.0°C, pulse rate of 122, blood pressure of 128/90 and pulse oximetry saturations (SpO₂) of 84% at room air (Model 506N3, Criticare Systems, USA) with a respiratory rate of 20. His peak flow was 460 L/min, and Glasgow Coma Score was 15/15. From the end of the bed, he appeared to be comfortable and there were no signs of respiratory distress, no audible cough or wheeze. He did not have the moribund appearance typical for an individual with an SpO₂ of 84%. His pulse oximetry saturations increased to 91% on 2 L/min of oxygen. On examination, there was jaundiced sclera with pale conjunctivae. Cardiorespiratory and neurological examinations were unremarkable, but there was tenderness in the left upper quadrant and his spleen was palpable to his umbilicus.

An ABG at room air revealed a pH 7.50, HCO₃ 26.7 mmol/L, base excess 3.5 mmol/L, PO₂ 10.6 kPa, PCO₂ 4.58 kPa, SaO₂ 100%, lactate 1.0 mmol/L, glucose 5.0 mmol/L. A desktop full blood count (pocH-100i, Symex, USA) reported Hb 81 g/L, mean corpuscular volume 117.4 fL, mean corpuscular haemoglobin concentration 285 g/L, RBC $2.42 \times 10^{12}/L$, WCC $9.0 \times 10^9/L$, platelets $86 \times 10^9/L$.

An ECG demonstrated sinus tachycardia.

The blood film report noted (figure 1) macrocytosis, tear drops, polychromasia, basophilic stippling, numerous nucleated red cells, genuine thrombocytopenia, neutrophils not hypersegmented.

His blood group was B Rh positive.

DIFFERENTIAL DIAGNOSIS

Initially, given the clinical picture and the initial blood findings, the following differential diagnoses could be considered:

- haemolytic crisis,
- atypical chest infection,
- ruptured spleen,
- tuberculosis.

The laboratory bloods were comparable to similar cases of a haemolytic crisis found in the literature. An ultrasound of the patient's abdomen reported splenomegaly with no suggestion of rupture. A haemolytic crisis triggered by an infection was suspected; so, he was admitted for treatment and further investigation.

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Figure 1 Blood film using May-Grünwald-Giemsa staining from a patient with Santa Ana haemoglobinopathy showing polychromasia. A nucleated red cell and basophilic stippling of red cells are denoted with arrows.

TREATMENT

The literature on the treatment of unstable haemoglobinopathies is not expansive. Supportive treatment is considered the mainstay in the acute setting. Infection and some notable medications, especially 'oxidative' drugs, are widely cited to provoke haemolytic crises. Therefore, immediate cessation and avoidance of these medications are advised. Gallstones are common, so many patients undergo a cholecystectomy but there is debate surrounding the merits of a splenectomy. Post splenectomy, some patients find their anaemia is corrected but Beutler highlights cases where thromboembolic complications, including fatalities, have occurred. Supplementation with 1 mg/day of folic acid has been reported in the literature although the specific benefit has not been established.¹

Although there was only a modest rise in C-Reactive protein to 29 mg/L, an infectious cause was suspected to be the trigger. No obvious source of infection was evident from the imaging although the admitting consultant reported some fine bi-basal crepitations. He was managed with intravenous coamoxiclav, paracetamol and was transfused 2 units of red cells with the post-transfusion Hb increasing to 130 g/L.

OUTCOME AND FOLLOW-UP

He improved clinically although his blood parameters remained largely unchanged during the course of his 5-day admission. The exception was the lactate dehydrogenase, which rose from 982 IU/L at admission to 1377 IU/L at the time of discharge (reference range 135–225 IU/L). It is noteworthy that multiple samples for biochemistry were deemed unsuitable for analysis by the laboratories due to the excessive level of haemolysis. His bilirubin remained around 100 µmol/L for the duration of his admission.

He was discharged after 5 days with oral coamoxiclav to complete a 1-week course. He has since reported to be in good health with no further concerns.

DISCUSSION

Pulse oximetry is sometimes referred to as the fifth vital sign.² It is used as part of the standardised National Early Warning Score

system for assessment and monitoring of the acutely unwell patient. The causes of error in oximetry are best explained in the context of the way the device functions. The principle is based on the difference between the 'colour' of oxygenated haemoglobin (oxyhaemoglobin) which is essentially more 'red' than deoxygenated haemoglobin (deoxyhaemoglobin). As their colour is different, their corresponding position on the light spectrum differs and thus by measuring the amount of light absorption at the two spectra the ratio of the two haemoglobins present in a vascular bed was calculated.^{1–5}

The inner workings of an oximeter

An oximeter flashes two light emitting diodes around 400–480 times a second alternating between the two light frequencies; oxyhaemoglobin at 940 nm and deoxyhaemoglobin at 660 nm. It then uses a photo diode to measure the light that either passed through (transmittance oximetry) or being reflected back from (reflectance oximetry) the vascular bed. Transmittance probes are typically placed on a finger, earlobe or often the toe in neonates. These are the most common types in clinical practice. Reflectance probes may be used on a flat body surface like the chest or forehead and are most suited where rapid changes in saturations need to be detected like an intensive care setting. The ratio of the two haemoglobins is calculated by the device and then compared against an inbuilt result table. These tables are typically created by the device manufacturer from tests performed on cohorts of 'normal' patients. As it is not appropriate to deliberately de-saturate a trial subject, the tables are developed from cohorts with normal levels of oxygen saturation and relatively normal levels of variant haemoglobin. This is the one reason that the literature in this area suggests why saturations <70% are quoted to be less accurate.⁶ Measurements are taken continuously for around 2–16 s and then an average value is calculated. This time is user programmable in some high-end devices.⁷ The result is then displayed as the percentage of haemoglobin that is oxygenated along with the heart rate. Many devices also have a visual display which demonstrates the signal strength of the pulsatile flow of blood across the vascular bed.

Sources of error in oximetry

Errors in oximetry are introduced when the normal functioning of the device as described is compromised. The causes of error have been examined in the literature for over 25 years and the findings are summarised subsequently.

Physical causes: nail polish, acrylic nails, clubbing, movement and skin pigment

Pretto *et al* describe variable results across numerous papers on nail polish. They surmise that dark colours of nail varnish may cause a small decrease in saturation readings. Lighter colours are not likely to cause any issue.⁴ Acrylic nails may affect readings between –1% and +3%.⁸ Digital clubbing was reported to cause up to 8% lower readings, especially at reduced oxygen saturations level.⁴

Movement artefact is a term used to describe the signal 'dropout' and in an oximeter typically when the patient moves their hands. Rather than providing an incorrect reading, the oximeter display may read an error message or go blank. This is probably because moving causes the normally near-stationary venous blood and tissue fluids to shift rapidly. This may make the non-arterial readings indistinguishable from the arterial pulse. This can be especially problematic during patient transport, shivering, tremor or exercise.^{4 6} Skin pigmentation is not reported to affect the accuracy of pulse oximetry at normal

levels. But oxygen saturations <90% in those with very dark skin may lead to a small overestimation of about 2%.⁴

Blood-related causes: any cause of low vascular bed perfusion, carbon monoxide, haemoglobinopathies and intravenous dyes

Oximeters rely on the presence of pulsatile arterial blood flow for their calculations. Therefore, any factor that disturbs the arterial flow can affect the oximeter's function. Subsequently any cause of low perfusion may affect the oximeter's ability to generate a reading at all rather than generating an inaccurate one. Causes of low perfusion may typically be hypovolaemia or low cardiac output. Significant arrhythmias rather than minor ones could also lead to low perfusion and subsequent signal dropouts.⁷ Local vasoconstriction caused by cold temperatures may also affect perfusion. Carbon monoxide binds to haemoglobin with a considerably greater affinity than oxygen to create carboxyhaemoglobin. It is increased by smoking but most clinically important after inhalation of carbon monoxide. Increased levels of carboxyhaemoglobin will falsely overestimate the oxygen saturation. Differences in the structure of variant haemoglobin compared to normal haemoglobin may cause a variation of its position on the light spectrum which is not read correctly by the oximeter. This is discussed in greater detail in the next section. Intravenous dyes can cause an interference to the normal light absorption and some dyes cause rapid and drastically low oximeter readings. Methylene blue, which is used to treat drug-induced and congenital methaemoglobinemia, may cause a drop in SpO₂ to around 65% but only lasts 60–120 s. However, they are normally injected under specialist situations by those who should be expecting this reaction and aware of its transient nature.^{9–11}

In a comprehensive paper by Veyckemans *et al* hyperbilirubinaemia was deemed not to affect the accuracy of pulse oximetry. The 99% confidence levels between the control (−0.89%, 1.08%) and icteric groups (−0.81%, 1.03%) was not significantly different.¹² Ralston *et al*⁹ reviewed the same issue and drew the conclusion that it may cause a 'discrepancy' between SpO₂ and SaO₂ no 'significant error'.

Sources of error unlikely to be of any clinical significance

There has not always been full agreement in the literature about the causes of error in oximetry. However, what should be gleaned from the review articles is that some factors do not affect the accuracy to a 'clinically significant degree'. That degree at which the error becomes clinically significant is subjective and may depend on the situation in which oximetry is being used. An intensive care setting may consider a 2% error as clinically significant. This list reports sources of error that may only affect oximetry to a modest degree and a list of suggestions to reduce them.

- ▶ light colours of nail polish and acrylic nails,
- ▶ skin pigmentation,
- ▶ coloured skin disinfectants,
- ▶ normal ambient light conditions,
- ▶ minor changes in blood temperature and pH,
- ▶ hyperbilirubinaemia,
- ▶ anaemia,
- ▶ mild arrhythmia.

Solutions to help reduce error

- ▶ turn the oximeter probe 90° so light passes underneath the finger nail,
- ▶ removal of nail varnish and acrylic nails,

- ▶ change location or type of probe,
- ▶ correct training and routine maintenance checks,
- ▶ vasodilator cream to increase perfusion of the vascular bed.

Oximeter error in haemoglobinopathies

Haemoglobinopathies have also been widely documented to produce aberrantly low SpO₂ reading. Haemoglobinopathies affect about 7% of the world population and may hamper the haemoglobin molecule's ability to carry oxygen efficiently. Verhovsek *et al*¹³ cite that more than 1000 variant haemoglobins are currently documented but most of these are not associated with abnormal SpO₂ readings. They are broadly categorised into thalassaemias, disorders with abnormal haemoglobin and unstable haemoglobinopathies.^{13–14} The unstable haemoglobinopathy disease is caused by a substitution or deletion of an amino acid in the haemoglobin molecule. More than 200 types have been identified and are reported to have an autosomal-dominant pattern of inheritance.¹⁵ Santa Ana haemoglobinopathy is an extremely rare variant of unstable haemoglobinopathy. This particular defect of the β-chain causes the haemoglobin molecule to be unusually susceptible to degrade in response to heat.^{13–16–17} This causes the formation of precipitations within the red cell that attach themselves to the membrane.¹⁶ Figure 1 shows the blood film on which a nucleated red cell, multiple basophilic stippling of cells and a general picture of polychromasia may be seen. These findings have been reported in other cases of unstable haemoglobinopathies.^{1–16} The literature explains that the structural differences of the variant haemoglobin may mean that light is absorbed at a different wavelength beyond that of the pulse oximeter. Therefore, it cannot correctly measure the percentage of oxygenated haemoglobin and thus underestimate the figure.^{1–13–14}

This presentation is typical of the situation where a patient with a haemoglobinopathy has an aberrantly low SpO₂ of 84% but subsequent arterial oxygen saturations (SaO₂) readings are normal at 100%.^{15–17} Hannallah and Budde report a similar case of a 45-year-old male with Santa Ana haemoglobinopathy who was undergoing an esophageal–duodenoscopy.¹⁶ They highlight that the only clinical manifestation of his condition was falsely low SpO₂ of 85% at room air. Their dilemma concerned how to monitor their patient's cardiopulmonary status as his SpO₂ was not accurate. As the procedure was only 5 min long and uncomplicated, they were happy with close monitoring of the patients using auscultation and inspection of the chest excursions. They recommended that longer procedures should consider the placement of an arterial line with frequent blood gas analysis.

In conclusion, pulse oximetry allows a fast and accurate assessment of a patient's arterial oxygenation, but it should not replace thorough cardiorespiratory examination. Extrinsic causes of SpO₂ measurement error should be identified and

Learning points

- ▶ Pulse oximetry saturation (SpO₂) is widely considered as the 'fifth vital sign'.
- ▶ Extrinsic factors like nail polish can produce aberrant low SpO₂ readings.
- ▶ Low SpO₂ readings should be confirmed with an arterial sample.
- ▶ Where a genuine disparity exists between SpO₂ and SaO₂ then consider an intrinsic cause like an unstable haemoglobinopathy.

minimised by the user. If low pulse oximetry readings are found, an ABG may be used to determine whether SpO₂ and SaO₂ are discordant. In which case, consideration of an intrinsic cause for the disparity like a haemoglobinopathy should be given. This might spare the patient unnecessary and time-consuming cardiorespiratory investigations that may prolong the duration of their admission.¹⁴

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Contributors AIR reviewed the patient in the Urgent Care Centre, performed the literature review, collated and analysed the results, wrote and referenced the case report. AmR reviewed the patient during their admission from a haematology perspective and assisted AIR in writing the case report.

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