Haemoglobin Hammersmith precludes monitoring with conventional pulse oximetry

Scott A. Lang FRCPC,* Paul C. Chang FRCPC,*
Victor A. Laxdal PhD FCACB,*
Titus H.J. Huisman PhD DSc†

We report a case of a 15-yr-old North American Indian female with haemoglobin Hammersmith, scheduled for elective tonsillectomy, whose arterial oxygen saturation could not be reliably monitored perioperatively because of technical limitations of conventional dual wavelength pulse oximetry. The patient was chronically icteric. She had an atrial septal defect with a small L → R shunt demonstrated by echocardiography. On arrival in the operating room pulse oximetry (Nellcor-Model N100) demonstrated a saturation of 45% whilst breathing room air. Her oxygen saturation increased to 60% whilst breathing 100% oxygen via a face mask. An arterial blood gas performed whilst breathing 100% oxygen revealed a PaO_2 of 418 mmHg. Tonsillectomy was completed uneventfully under general anaesthesia. The pulse oximeter did not provide any clinically useful information throughout the case. In conclusion, conventional dual wavelength pulse oximeters cannot give an accurate estimate of oxygenation in patients with haemoglobin Hammersmith. Assessment of oxygenation in these patients requires alternative monitoring techniques.

Nous rapportons le cas d'une autochtone nord-américaine de 15 ans, porteuse d'hémoglobine Hammersmith, programmée pour une amygdalectomie et dont la saturation en oxygène ne peut être mesurée avec fiabilité à cause des limitations de la technique habituelle de l'oxymétrie pulsée à deux longueurs d'ondes. La patiente est une ictérique chronique. L'échographie a révélé une communication interauriculaire avec un léger shunt d-g. A sont arrivée en salle d'opération, l'oxymétre (Nellcor-Model N100) affiche une saturation à 45% en air. La saturation sous oxygène à 100% par masque facial augmente à 60%. Un gaz artériel réalisé sous oxygène à 100% montre une PaO_2 de 418 mmHg. L'amygdalectomie est complétée sans incident sous anesthésie générale. L'oxymétrie pulsée ne procure pas d'autres renseignements cliniques pertinents. Pour conclure, l'oxymétrie pulsée à double longueur d'ondes ne peut évaluer avec précision l'oxygénation en présence d'hémoglobine d'Hammersmith. L'évaluation de l'oxygénation dans ces cas nécessite des techniques de monitorage différentes.

Key words
BLOOD: haemoglobin Hammersmith;
MEASUREMENT TECHNIQUES: oximeters, pulse;
MONITORING: oxygen.

From the *Departments of Anaesthesia and Pathology, Royal University Hospital, Saskatoon, Saskatchewan, Canada S7N 0X0, and †Department of Biochemistry and Molecular Biology, Medical College of Georgia, Augusta, GA, 30912-2100, USA.

Address correspondence to: Dr. S.A. Lang, Department of Anaesthesia, Royal University Hospital, Saskatoon, Saskatchewan, Canada S7N 0X0.

Accepted for publication 12th June, 1994.

Currently there are more than 600 haemoglobins described with primary structural abnormalities.[1] The functional properties of several of these haemoglobins are altered. Clinicians are keenly aware of the clinical implications of altered haemoglobin function,[2,3] but are less familiar with associated alterations of physical properties (e.g., absorption spectra) secondary to these primary structural abnormalities. Haemoglobin Hammersmith (Hb Hamm) is a rare unstable haemoglobin with low oxygen affinity.[1,2,4–6] An amino acid substitution at position 42 of the β chain of haemoglobin (phenylalanine → serine) causes a lesion that results in severe haemolytic anaemia requiring frequent blood transfusions to sustain life.[6] Haemolytic episodes can be precipitated by systemic infections including tonsillitis.[6]

We describe a case of a 15-yr-old North American Indian female with known haemoglobin Hammersmith who could not be monitored with conventional pulse oximetry during anaesthesia for tonsillectomy because the dual wavelength pulse oximeter used (Nellcor-Model N100) could not identify haemoglobin Hammersmith.

Case report

A 43.4 kg 15-yr-old North American Indian female with

known Hb Hammersmith[6] was scheduled for an elective tonsillectomy to try to decrease the frequency of severe haemolytic episodes requiring transfusion. She had had a splenectomy at age two. She had been treated with Pneumovax innoculations and was receiving penicillin prophylaxis (penicillin V 250 mg *po od*). She was chronically icteric and had prominent maxillary hyperplasia. Chest auscultation revealed normal respiratory sounds and a Grade II/VI midsystolic murmur consistent with her known atrial septal defect – ASD (Echo-Doppler revealed a secundum ASD with a small L→R shunt).

Her preoperative ECG was normal. Her haemoglobin concentration was 88 $g \cdot L^{-1}$ on admission. She received a transfusion of 250 ml washed red blood cells the day before surgery which increased her haemoglobin concentration to 94 $g \cdot L^{-1}$. She was cross-matched preoperatively for two units of blood. She received cefuroxime 1.5 g *iv* and penicillin V 300 mg *po* 90 min before surgery.

On arrival in the operating room pulse oximetry (Nellcor Model N100 – known to be functioning normally) showed a saturation of 45% on room air. The saturation increased to 60% while breathing 100% oxygen with a face mask. An arterial blood gas sample obtained while she was breathing 100% oxygen by face mask revealed a PaO_2 of 418 mmHg. We felt this indicated that the low saturation reading was unlikely to be due to a right to left shunt through her atrial septal defect. An arterial line was considered, but was judged to be unnecessary.

An intravenous catheter was inserted in her right hand after securing additional monitors (ECG, automatic blood pressure, precordial stethoscope, nerve stimulator, temperature probe and end-tidal capnography). Anaesthesia was induced with propofol (100 mg) and fentanyl (75 μg) and tracheal intubation was facilitated with d-tubocurarine (4.5 mg) and succinylcholine (120 mg). Anaesthesia was maintained with 100% oxygen, isoflurane (end-tidal concentration 1.5%) and muscle relaxation was maintained with atracurium (20 mg) following return of her adductor pollicis muscle twitch. Nellcor pulse oximetry was 60% throughout the case and end-tidal capnography was stable at 25 mmHg. Blood pressure was stable (120–130/70 mmHg) as was heart rate ($70–80 \cdot min^{-1}$). Tonsillectomy was completed uneventfully. Muscle relaxation was reversed with neostigmine (3 mg) and glycopyrrolate (0.3 mg). The trachea was extubated when the patient was awake and she was transferred to the Recovery Room breathing supplemental oxygen by face mask. The patient recovered uneventfully but was transfused with another two units of washed red blood cells before discharge because her haemoglobin concentration had decreased to 80 $g \cdot L^{-1}$ and because of her geographically remote home.

Discussion

Pulse oximetry functions by positioning any pulsating arterial bed between a two wavelength light source and a detector.[7] The light is generated by light emitting diodes at wavelengths corresponding to red light (660 nm) and near infra-red light (940 nm). A photodiode is used to measure the transmitted light. Total absorbance is composed of both a nonpulsatile (DC) component and a pulsatile (AC) component. The pulsatile component is assumed to be due entirely to arterial pulsations. A normalization process allows the pulse oximeter to distinguish between background absorbance and pulsatile "arterial" absorbance. This allows the pulse oximeter to measure arterial oxygen haemoglobin saturation *in vivo* independent of changes in background absorbance. The normalized ratio of absorbance at 660 nm and 940 nm is represented by

$$R = \frac{AC660/DC660}{AC940/DC940};$$

R can be shown to be mathematically related to arterial oxygen saturation. However, manufacturers calibrate pulse oximeters empirically, in a large group of healthy volunteers, by correlating the "normalized" absorbance signals at 660 nm and 940 nm with arterial oxygen saturation measured by a gold standard technique (i.e., co-oximetry). For example, an R value of 1.0 is interpreted by the pulse oximeter's calibration algorithm as a saturation of 85%. These dual wavelength pulse oximeters assume that all absorbance at both measured wavelengths is due to two haemoglobin species – oxyhaemoglobin and deoxyhaemoglobin.[7–9] "Functional" haemoglobin saturation is therefore defined as:

$$\text{"Functional" } SaO_2 = SpO_2 = \frac{O_2Hb}{O_2Hb + HHb} \times 100\%$$

where SaO_2 = arterial oxygen saturation; SpO_2 = pulse oximeter oxygen saturation; O_2Hb = oxyhaemoglobin; HHb = reduced or deoxyhaemoglobin.

In contrast, co-oximeters are capable of measuring the concentration of several haemoglobin species by utilizing absorbance measurements at multiple wavelengths *in vitro*.[9,10] A multi-wavelength oximeter measures "fractional" haemoglobin saturation defined as:

$$\text{"Fractional" } SaO_2 = \frac{O_2Hb}{O_2Hb + HHb + COHb + MetHb + x} \times 100\%$$

where COHb = carboxyhaemoglobin; Met Hb = methaemoglobin; X = any other haemoglobin species the oximeter is calibrated to detect.[7,10]

Dyshaemoglobins (e.g., methaemoglobin and carboxyhaemoglobin) do absorb some light at the frequencies employed in dual wavelength pulse oximeters and therefore can cause errors in the pulse oximeter reading.[7-9,11-13] For example, carboxyhaemoglobin is read by conventional oximeters as oxyhaemoglobin because oxyhaemoglobin and carboxyhaemoglobin are isobestic* at 660 nm while carboxyhaemoglobin has virtually no absorbance at 940 nm. Methaemoglobin causes a large absorbance at both wavelengths (660 and 940 nanometers) and the pulse oximeter reading gravitates toward 85% as R approaches 1.0. Therefore, SpO_2 may be virtually independent of the actual arterial oxygen saturation.[12,13] There are many excellent reviews on pulse oximetry dealing with these issues.[7-9,11-13]

There are two recent case reports of patients with haemoglobin Köln (another unstable haemoglobin) in which the pulse oximeter readings (Nellcor-N100 and Ohmeda Biox) were unusually low in the presence of PaO_2's well over 100 mmHg[14,15] – a situation similar to ours. Elevated levels of methaemoglobin and carboxyhaemoglobin (Corning 2500 co-oximeter) were reported. However, the presence of methaemoglobin and carboxyhaemoglobin were interpreted by the authors to provide an incomplete answer for the low saturation readings exhibited by the pulse oximeters. Katoh *et al.*[14] have provided evidence that the absorption spectrum of haemoglobin Köln is altered and Gottschalk *et al.*[15] suggest that an altered absorption spectrum may be the primary reason for the observed reductions in oxygen saturation measured by pulse oximetry in patients with haemoglobin Köln.

It is known from previous investigations[6] that our patient's haemoglobin existed as approximately 30–40% Hb Hammersmith and 60–70% normal haemoglobin. Haemoglobin Hammersmith's absorption spectrum, when oxidized (as it virtually always is because of its unstable nature), would be expected to be isobestic with deoxyhaemoglobin at approximately 660 nanometers. We speculate that our Nellcor pulse oximeter was measuring Hb Hammersmith as deoxy or reduced haemoglobin and thus read 60% (all of her normal haemoglobin was fully oxygenated). This can be represented as:

$$\text{Nellcor "Functional" } SpO_2 = \frac{O_2Hb}{O_2Hb + HHb + HbHamm} \times 100\%$$

where O_2Hb = oxygenated "normal (A)" haemoglobin; HHb = deoxyhaemoglobin "A" and HbHamm = Hb Hammersmith (which is read by the pulse oximeter as deoxyhaemoglobin).

In conclusion, conventional dual wavelength pulse oximeters cannot give an accurate picture of oxygenation in patients with Hb Hammersmith or with comparable unstable haemoglobins. Assessment of oxygenation in these patients may require alternative monitoring[16] (e.g., arterial blood gas analysis, continuous transcutaneous $PTCO_2$, special co-oximeters, continuous intravascular PaO_2 or $P\bar{v}_{O_2}$, end-tidal O_2 concentration etc.). However, we feel that knowledge of the limitations of conventional pulse oximetry, attention to detail, and increased vigilance, are all that are necessary to conduct a safe anaesthetic for a brief uncomplicated surgical procedure for rare situations like the one described in this case report.

*The isobestic point is the point at which two solutes (i.e., haemoglobin species) have identical absorbances.

Acknowledgements

We wish to thank the secretaries of the Department of Anaesthesia, Royal University Hospital, Saskatoon, Saskatchewan for their help in preparing this manuscript.

References

1 *Carver MFH, Huisman THJ.* Policies of the International Hemoglobin Information Center. Hemoglobin 1993; 17: 89–177.
2 *Liebhaber SA, Manno CS.* Update on hemoglobinopathies. Disease-a-Month 1983; 28: 1–74.
3 *Roizen MF.* Anesthetic implications of concurrent diseases. *In*: Miller RD (Ed.). Anesthesia, 3rd ed. New York: Churchill Livingstone, 1990; 860–3.
4 *Shinton NK, Thursby-Pelham DC, Williams HP.* Congenital Heinz-body haemolytic anaemia due to Haemoglobin Hammersmith. Postgrad Med J 1969; 45: 629–32.
5 *May A, Huehns ER.* The oxygen affinity of Haemoglobin Hammersmith. Br J Haematol 1975; 30: 185–95.
6 *Cunningham TA, Baker F, Kobrinsky NL, et al.* The unstable Hb Hammersmith or $\alpha_2\beta_2$42(CDI)Phe→Ser observed in an Indian child; identification by HPLC and by sequence analysis of amplified DNA. Hemoglobin 1992; 16: 19–25.
7 *Tremper KK, Barker SJ.* Pulse oximetry. Anesthesiology 1989; 70: 98–108.
8 *Mendelson Y.* Pulse oximetry: theory and applications for noninvasive monitoring. Clin Chem 1992; 38: 1601–7.
9 *Tremper KK, Barker SJ.* Pulse oximetry. Anesthesiology 1989; 70: 98–108.
10 *Mahoney JJ, Vreman HJ, Stevenson DK, Van Kessel AL.* Measurement of carboxyhemoglobin and total hemoglobin by five specialized spectrophotometers (CO-oximeters) in comparison with Reference Methods. Clin Chem 1993; 39: 1693–700.
11 *Severinghaus JW, Kelleher JF.* Recent developments in pulse oximetry. Anesthesiology 1992; 76: 1018–38.

12 *Ralston AC, Webb RK, Runciman WB.* Potential errors in pulse oximetry. III: Effects of interference, dyes, dyshaemoglobins and other pigments. Anaesthesia 1991; 46: 291–5.
13 *Chisholm DG, Stuart H.* Congenital methaemoglobinaemia detected by preoperative pulse oximetry. Can J Anaesth 1994; 41: 519–22.
14 *Katoh R, Miyake T, Arai T.* Unexpectedly low pulse oximeter readings in a boy with unstable hemoglobin Köln. Anesthesiology 1994; 80: 472–4.
15 *Gottschalk A, Silverberg M.* An unexpected finding with pulse oximetry in a patient with hemoglobin Köln. Anesthesiology 1994; 80: 474–6.
16 *Tremper KK, Barker SJ.* Monitoring of oxygen. *In*: Lake CL (Ed.). Clinical Monitoring. Philadelphia: WB Saunders Co., 1990; 283–313.