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Spurious Hypoxaemia in a Patient with Leukaemia and Extreme Leucocytosis

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ABSTRACT

Rapid consumption of oxygen by leucocytes can result in erroneous diagnosis of severe hypoxaemia in patients with extreme leucocytosis. We report a case of chronic myeloid leukaemia, extreme leucocytosis and arterial hypoxaemia which was out of proportion to the clinical and radiological evidence of lung disease. The pseudohypoxaemia was confirmed by pulse oximeter and became less significant after successful reduction of leucocyte counts following leucophoresis and chemotherapy. Serial arterial blood gas analysis also demonstrated a slower initial rate of decay of PaO_2 as the leucocyte count decreased with treatment.

Keywords: pseudohypoxaemia, leukaemia, pulse oximeter, arterial blood gas

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INTRODUCTION

Extreme leucocytosis secondary to leukaemia can cause spurious lowering of the arterial oxygen tension when this is determined by arterial blood gas analysis[1-4]. This is due to the in vitro consumption of oxygen by the extremely high number of leucocytes in leukaemic patients. Awareness of this phenomenon is important in the evaluation and management of this group of patients to avoid errors in the interpretation of arterial blood gas and inappropriate intervention. The determination of oxygen saturation by the pulse oximeter provides a rapid noninvasive alternative to the assessment of the true oxygenation status of patients who have leukaemia and extreme leucocytosis[3,5].

We report a case of chronic myeloid leukaemia, extreme leucocytosis and arterial hypoxaemia which was out of proportion to the clinical and radiological evidence of lung disease. The pseudohypoxaemia was confirmed by pulse oximeter and became less significant after successful reduction of leucocyte counts following leucophoresis and chemotherapy.

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REPORT

A 31-year-old gentleman was admitted after an episode of syncope with brief loss of consciousness witnessed by his wife. Further questioning revealed that he has had shortness of breath on exertion, fatigue and weight loss of 8 kg in the three months prior to current admission.

On examination, he was not cyanosed but appeared pale and cachectic. His temperature was 36.5ºC, pulse rate was 102/min, respiratory rate was 18/min and blood pressure was 110/70 mmHg. His chest was clear and heart sounds were normal. Palpation of the abdomen found massive splenomegaly down to the left iliac fossa. Full blood count showed haemoglobin 6.7 g/dL, white cell count (WCC) 846.90 X 10^9/L (6% metas, 13% myelos, 2% promyelocytes, 13% blasts), platelets 444 X 10^9/L, prothrombin time 14.9 seconds, partial thromboplastin time 30.8 seconds, Na 140 mmol/L, K 3.3 mmol/L, urea 4.4 mmol/L, creatinine 82 mmol/L. Chest radiograph was unremarkable. Arterial blood gas on 2L/min oxygen via nasal prongs showed pH 7.41, PaO_2 37.2 mmHg, $PaCO_2$ 37.5 mmHg, base excess -0.4 mm Hg, standard bicarbonate 23.4 mmol/L, calculated oxygen saturation (SaO_2) 71.8%. Pulse oximeter (SpO_2) at that time showed a saturation of 96%. Pseudohypoxaemia was recognised and a pulse oximeter was used to monitor the patient's oxygenation status. Subsequently, a diagnosis of chronic myeloid leukaemia with blast transformation was made. The patient was started on chemotherapy and leucopheresis.

An arterial blood sample was taken from an arterial catheter in the patient's right radial artery after the first cycle of leucophoresis at which point the WCC was 453.90 X 10^9/L (myelos 9%, promyelocytes 6%, blast 21%). The sample was then analysed with the blood gas analyser (Chiron Diagnostics 865, Ciba Corning Diagnostics Corp, USA) at time 0 (immediately), two min and five min. Blood sample was not iced. The lag between the time when blood sample was drawn from the arterial catheter and time zero was about one minute. That was the time required

to bring the blood sample from the patient to the blood gas analyser, inject the blood into the analyser and obtain a reading. During the drawing of the arterial blood, the oxygen saturation was read of the pulse oximeter (Oxisensor II D-25, Nellcor Puritan Bennett Inc. Pleasanton, CA, USA) attached to the patient's finger (SpO_2). The same procedure was repeated three days later. The patient had then received a few more cycles of leucopheresis, hydroxyurea and the WCC had come down to 152.30 X 10^9/L. The WCC, SpO_2, serial PaO_2 and calculated SaO_2 after the first and third cycle of leucophoresis were as shown in Table I. The patient's WCC remained high at 453.90 X 10^9/L after the first cycle of leucophoresis. At this point, the oxygen saturation (SaO_2) derived from blood gas (87.3%) was much lower than that measured by the pulse oximeter (SpO_2) (96%). There was also a more rapid initial drop in the PaO_2 and SaO_2. When the same experiment was repeated at a WCC of 152.30 X 10^9/L, we found that there was better correlation between the SpO_2 (96%) measured by pulse oximeter and the SaO_2 derived from blood gases (95.6%) and a slower initial rate of decline in the PaO_2 and SaO_2.

Table I. Comparison of total white count, pulse oximetry, serial PaO_2 and SaO_2 from arterial blood gases after first and third leucopheresis.

Date	WCC	SpO_2*	ABG (PaO_2/SaO2†) 0 min	1 min	5 min
After first cycle of leucopheresis	453.90 X 10^9/L	96%	54.3/87.3	43.6/–	40.3/72.0
After third cycle of leucopheresis	152.30 X 10^9/L	96%	74.1/95.6	69.7/94.9	61.6/93.2

* Oxygen saturation measured by pulse oximeter
† Oxygen saturation derived from arterial blood gas

DISCUSSION

Hess et al demonstrated in 1979 that the PaO_2 of blood stored in syringe and kept at room temperature fell at a faster rate in patient with leukocytosis and thrombocytosis than in control subjects and that the fall was great enough to result in an incorrect diagnosis of hypoxaemia[1]. They also found that the type and maturity of the proliferating cell appeared to be important in the rate of fall in PaO_2. Subsequently, various terms including "leucocyte larceny" and "oxygen steal" had been used to describe this phenomenon of spurious lowering of arterial oxygen tension in patient with leukaemia due to oxygen consumption by leucocytes[2]. Between the times when an arterial blood sample is obtained and blood gas is analysed, the markedly increased number of leukaemic white cells with high metabolic rate rapidly metabolise dissolved plasma oxygen resulting in a dramatic drop in PaO_2 and calculated oxygen saturation[1-3]. Observations of normal oxygen saturation with pulse oximetry, correction of hypoxaemia when potassium cyanide was added to the specimen and normoxia with continuous blood gas analysis further lend support to this mechanism[2-4,6].

Reticulocytes, platelets and white blood cells are among the constituents of blood that may affect the PaO_2. Oxygen consumption by mature red blood cells and plasma is negligible. Leucocytes and platelets account for most of the oxygen consumed in shed blood. It has been postulated that more primitive leukaemic white blood cells have higher metabolic rates and may cause a larger fall in PaO_2 than normal white cells. However, the explanation for high oxygen consumption by human leukaemic lymphocytes and granulocytes remains controversial[3].

With the advent of pulse oximeter, which shines narrow bandwidth light on the nail bed and measures the *in vivo* percentage of functional haemoglobin combined with oxygen, the problem of pseudohypoxaemia in leukaemic patients with extreme leucocytosis can be circumvented. We observed in our patient a pronounced discrepancy between the SaO_2 derived from blood gas and the SpO_2 measured by pulse oximeter when his leucocyte count was as high as 453.90 X 10^9 /L. Following successful reduction in his leukocyte count to 152.30 X 10^9 /L with leucophoresis and hydroxyurea chemotherapy, there was better correlation between the SpO_2 (96%) and the SaO_2 derived from blood gas (95.6%). SpO_2 measured by pulse oximeter has remained the same despite the drastic drop in the PaO_2 and SaO_2 with the increased WCC. Pulse oximeter hence provides a consistent measurement of the true oxygenation status of patient with leukaemia and extreme leucocytosis.

A few studies had also looked at the use of metabolic inhibitors like ice and potassium cyanide to inhibit the rapid oxygen consumption by leucocytes and eliminate the errors created by pseudohypoxaemia. Hess et al demonstrated that the problem of pseudohypoxaemia can be averted if the arterial blood sample was immersed in ice immediately. In contrast, others had observed that immediate cooling of samples was insufficient to eliminate this process[3,6,7]. Small studies performed have shown continuous blood gas analysis to be useful, but its reliability and cost effectiveness need confirmation by larger controlled prospective studies[4].

Fox et al studied the rate of decay of oxygen tension (PO_2) and the effect of changing leucocyte counts on the time-related decrease in oxygen tension in venous blood[2]. They demonstrated an initial rapid decay in PO_2 and that this rapid decay decreased as the leucocyte counts decreased with treatment. In our patient, we

have observed the same correlation between the rate of decline of PaO_2 and the leucocyte count in arterial blood measurement. At a white cell count of 453.90 X 10^9/L, the PaO_2 measured immediately (54.3 mmHg) was much lower than the immediate PaO_2 measured at a white cell count of 152.30 X 10^9 /L (74.1 mmHg) despite the pulse oximeter recording the same oxygen saturation (SpO_2) of 96% on the two occasions. The initial rate of decay of PaO_2 was also slower with the reduction of the white cell count following leucophoresis and chemotherapy. We have also observed a decline in the rate of decay of PaO_2 as the oxygen content decreased. It has been postulated that the leucocyte oxygen consumption is a function of oxygen content. Initially, when oxygen content is high, the decay is occurring on the flat part of the oxyhaemoglobin dissociation curve. This results in a relative larger change in PaO_2 for a given change in oxygen content. Later, the oxygen content is lower and therefore the decay takes place on the steep part of the curve where there is a smaller change in PaO_2 for a given change in oxygen content[2].

Patients with leukaemia may have respiratory distress and hypoxaemia secondary to pulmonary complications. Arterial blood gas determination is a useful way of assessing the oxygenation status in this group of patients. However, spurious hypoxaemia due to oxygen consumption by leucocytes in patients with extreme leucocytosis can create difficulty in the interpretation of blood gas result. Failure to recognise this phenomenon could lead to serious unnecessary interventions. In a case report by Charoenratanakul et al, a leukaemic patient was intubated because of pseudohypoxaemia[5]. Pseudohypoxaemia should hence be suspected in any leukaemic patients with extreme leucocytosis and arterial blood gas measurement that is out of proportion to the clinical and CXR evidence of lung disease. In this context, pulse oximeter is a useful method of establishing the spurious nature of the hypoxaemia.

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