OXYGEN PARAMETERS IN THE PRESENCE OF HEMOGLOBIN H

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The study by Papasotiriou et al. [1] on tissue oxygenation in patients with hemoglobinopathy H raises some questions concerning measurement and calculation of the oxygen status of the arterial blood. Hemoglobin H (HbH) is a tetramer of β chains occurring in α-thalassemia. It binds O₂ with high affinity with a P₅₀ as low as 0.23 kPa (<1.7 mmHg). It shows neither a Bohr pH effect nor heme-heme interaction (i.e., Hill slope = 1). "These properties deprive HbH of any active role in delivering oxygen to the tissue," according to Papasotiriou et al.

It is necessary to determine the concentration of HbH in order to calculate and interpret the oxygen parameters correctly. Papasotiriou et al. measured HbH by cation-exchange high-pressure liquid chromatography. They also determined the hemoglobin oxygen binding curve with an Aminco Hem-O-Scan, which simultaneously scans P₅₀ in the gas phase and the absorbances at two wavelengths in a thin film of blood in equilibrium with the gas phase. The biphasic shape of the curve allows approximate quantification of HbH, which is saturated with O₂ before binding to HbA begins.

The oxygen status of the arterial blood comprises three independent variables: (1) arterial oxygen tension, (2) hemoglobin oxygen binding capacity, and (3) hemoglobin oxygen binding affinity. The degree of compensation among these three is indicated by either (4) the oxygen extraction tension or (5) the concentration of extractable oxygen [2]. Definitions

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and determination of these quantities in the presence of HbH are described in the following:

1. The arterial oxygen tension (PaO₂) presents no problems in relation to HbH.

2. The hemoglobin oxygen binding capacity corresponds to the concentration of effective hemoglobin (O₂Hb) and is calculated as the concentration of total hemoglobin minus the concentration of dyshemoglobins, which include methemoglobin, sulfohemoglobin, and carboxyhemoglobin. Hemoglobin H must necessarily be included among the dyshemoglobins because it binds O₂ so strongly that it is fully saturated with oxygen under all physiological conditions.

3. The hemoglobin oxygen binding affinity is always expressed in terms of the P₅₀, half-saturation tension, where saturation refers to effective hemoglobin. Hemoglobin oxygen saturation is defined as the concentration of oxyhemoglobin divided by the concentration of effective hemoglobin: $S_{O₂} = [O₂Hb] / [O₂Hb] + [Hb]$. However, the definition ought to be concentration of reversibly bound oxygen divided by concentration of effective hemoglobin. In other words, the concentration of HbH should be subtracted from the concentration of O₂Hb when calculating the oxygen saturation: $S_{O₂} = ([O₂Hb] - [Hb]) / [O₂Hb]$. In this way, P₅₀ becomes a measure of the affinity of the effective hemoglobin or HbA.

4. The oxygen extraction tension (P₅₀) is defined as the oxygen tension after reduction of the concentration of total oxygen by 2.5 mmol/L. When the oxygen binding curve is determined experimentally, P₅₀ can be read off the curve at the appropriate oxygen concentration.

5. The concentration of extractable oxygen (C₅₀) is determined as the difference between the concentration of total oxygen in the arterial blood and the concentration at a P₅₀ of 5.0 kPa read off the oxygen binding curve.

The oxygen status of the arterial blood is routinely determined with a pH-blood gas analyzer, measuring pH, PaO₂, and PaCO₂, combined with a multichannel spectrophotometer, measuring the concentrations of the hemoglobin pigments: oxyhemoglobin, deoxyhemoglobin, methemoglobin, and carboxyhemoglobin. On the basis of these measurements the concentration of effective hemoglobin, P₅₀, and P₅₀ or C₅₀ may be calculated.

Pappasotiriou et al. draw attention to difficulties with such calculations in the presence of HbH and they specifically mention the oxygen status algorithm [4]. Nevertheless, the calculations can be made as we shall briefly describe. We assume that the measured data are transferred on line from the analyzer to the oxygen status algorithm computer program, or alternatively keyed in manually, and a provisional calculation is automatically performed. It is then necessary to make two corrections manually:
1. The measured "oxygen saturation" is first recalculated to the saturation of effective hemoglobin: \(S_{O_2,\text{eff}} = (\frac{G_H - G_Hb}{G_H - G_Hb})\), where \(G_H\) and \(G_Hb\) are the provisionally calculated data.

2. The measured concentration of total hemoglobin (GHB) is then replaced by GHB minus GHH.

The oxygen status algorithm then automatically calculates the correct effective hemoglobin concentration, half-saturation tension, and oxygen extraction tension. The recalculated oxyhemoglobin concentration \((G_H,\text{eff})\) and total oxygen concentration \((G_O_2)\) do not include O2 bound to HbH. We are prepared to incorporate the option of keying in HbH in future versions of the oxygen status algorithm if a real need exists.

When the arterial oxygen status is calculated as described, the study by Papassotiriou et al. shows that the predominant problem for patients with HbH is the marked reduction in effective hemoglobin, whereas changes in oxygen binding affinity of the effective hemoglobin are of minor importance.

REFERENCES