Annotation

OXYGEN PARAMETERS IN THE PRESENCE OF HEMOGLOBIN H

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Keywords α-thalassemia, dyshemoglobins, effective hemoglobin, half-saturation tension, oxygen binding affinity, oxygen binding capacity, oxygen saturation, oxygen status algorithm

The study by Papassotiriou 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 O_2 with high affinity with a P_{50} 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 Papassotiriou et al.

It is necessary to determine the concentration of HbH in order to calculate and interpret the oxygen parameters correctly. Papassotiriou 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 P_{O_2} 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 O_2 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

Received 3 January 1997; accepted 3 January 1997.

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0888-0018/97 $12.00 + .00

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

1. The arterial oxygen tension (P_{O_2}) presents no problems in relation to HbH.

2. The hemoglobin oxygen binding capacity corresponds to the concentration of effective hemoglobin (C_{EHB}) and is calculated as the concentration of total hemoglobin minus the concentration of dyshemoglobins, which include methemoglobin, sulfhemoglobin, and carboxyhemoglobin. Hemoglobin H must necessarily be included among the dyshemoglobins because it binds O_2 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 P_{50}, 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: $S_{O_2} = C_{O_2HB}/C_{EHB}$ [3]. 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 O_2Hb when calculating the oxygen saturation: $S_{O_2} = (C_{O_2HB} - C_{HBH})/C_{EHB}$. In this way P_{50} becomes a measure of the affinity of the effective hemoglobin or HbA.

4. The oxygen extraction tension (P_x) is defined as the oxygen tension after reduction of the concentration of total oxygen by 2.3 mmol/L. When the oxygen binding curve is determined experimentally, P_x can be read off the curve at the appropriate oxygen concentration.

5. The concentration of extractable oxygen (C_x) is determined as the difference between the concentration of total oxygen in the arterial blood and the concentration at a P_{O_2} 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, P_{CO_2}, and P_{O_2}, combined with a multiwavelength spectrophotometer, measuring the concentrations of the hemoglobin pigments: oxyhemoglobin, deoxyhemoglobin, methemoglobin, and carboxyhemoglobin. On the basis of these measurements the concentration of effective hemoglobin, P_{50}, and P_x or C_x may be calculated.

Papassotiriou 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_2EHB} = ("C_{O_2HB}" − C_{HBH})/("C_{EHB}" − C_{HBH}), where "C_{O_2HB}" and "C_{EHB}" are the provisionally calculated data.

2. The measured concentration of total hemoglobin (CtHb) is then replaced by C_{THB} minus C_{HBH}.

The oxygen status algorithm then automatically calculates the correct effective hemoglobin concentration, half-saturation tension, and oxygen extraction tension. The recalculated oxyhemoglobin concentration (C_{O_2HB}) and total oxygen concentration (C_{tO_2}) do not include O_2 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.

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