INDIVIDUAL CORRELATION OF OXYGEN DELIVERY WITH HAEMOGLOBIN LEVEL IN 20-YEAR-OLD WOMAN WITH HB 1.8 WITH INCOMPATIBLE CROSS-MATCH RESULTS: CASE REPORT STUDY

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ABSTRACT

Background: Clinical assessment of the delivery of tissue oxygenation is very challenging for clinicians to study. Anaemia reflects a decrease in oxygen carrying capacity in the blood which is very at risk of *oxygen delivery* (DO_2) insufficiency and cellular hypoxemia, to assess tissue hypoxia in addition to being a reliable tool, the clinician must also adjust to the patient's clinical and hemodynamic. Blood transfusions are generally used to correct anaemia precisely and efficiently, but in certain circumstances that make it impossible for clinicians to perform blood transfusions, at that time we have to think of other methods of therapy in patients.
Case presentation: 20-year-old woman came with anaemia, with a haemoglobin (Hb) level of 6.0 g/dl, a stable clinical condition and hemodynamic within normal limits, a blood transfusion was planned but the results of the Comb test was incompatible, so it was an absolute contraindication for transfusion. The patient experienced clinical changes that indicated the occurrence of tissue hypoxia when the Hb level was 2.0gr/dl. The clinician decided to maximize DO2, and reduce oxygen demand/consumption (VO_2), so that there is a balance. The patient was treated with steroids, suspected autoimmune haemolytic anaemia (AIHA). On the eighth day of clinical treatment the patient improved, hemodynamically stable, and Hb increased.
Conclusion: Clinical valuation of the distribution of tissue oxygenation is very important for AIHA patient.

Keywords: Autoimmune haemolytic anaemia, oxygen demand, oxygen delivery, treatment.

INTRODUCTION

One of the main functions of the lungs is to promote gas exchange between the circulatory system and the external environment. Gas exchange occurs between alveolar air and pulmonary capillary blood. For effective gas exchange, the alveoli must be ventilated and perfused.[1] Ventilation refers to the flow of air into and out of the alveoli, while perfusion refers to the flow of blood into the capillaries of the alveoli whereas perfusion refers to the flow of blood into the alveolar capillaries. The blood flow through the lungs is equal to the amount of cardiac output with factors controlling cardiac output especially peripheral factors controlling pulmonary blood flow. Individual alveoli have varying degrees of ventilation and perfusion in different areas of the lung.[2,3] Factors that affect the ventilation and perfusion process include the state of the lungs, circulation, and blood flow.[1]

Circulation and blood flow in the individual are affected by haemoglobin (Hb) as the oxygen carrier of red blood cells and is fully saturated when it binds four oxygen molecules. Children, young adults, adults, men or women, even women of reproductive age, especially during pregnancy, have Hb levels in their bodies that vary due to their respective physiological characteristics.[4–6] Each oxygen molecule released by Hb into tissues, binds to the remaining oxygen molecules with greater affinity. Haemoglobin analysis is one of the simplest and most economical laboratory parameters so it is quite often used in studies. Another method used to see the state of low, normal or high haemoglobin levels can be studied through a clinical physical examination of the patient, among others, identifying pale skin or mucous membranes as a clinical sign of a decreased Hb level. Anatomical segments such as the conjunctiva, palms, nail beds, lips, and tongue have been used to identify a rough outline of haemoglobin levels. Each individual has a haemoglobin tolerance depending on the clinical condition.[7]

Hemoglobin tolerance greatly affects the oxygen exchange and delivery of each individual, and the amount of oxygen delivered to the tissues is usually at least four times the actual use of body tissues. In other words, the ratio of oxygen delivery (DO2) to oxygen demand/consumption (VO2) is usually maintained at 4:1.[6,8] Things that affect the size of DO2 include cardiac output including heart rate and stroke volume, arterial oxygen saturation, the concentration of oxygen, and hemoglobin.[9]

DO2 capacity can be decreased in a number of conditions including decreased haemoglobin concentration or decreased haemoglobin oxygen saturation. For example, anaemia is lower than the average healthy red blood cell count.[8,10] When anaemia occurs over a long period of time, and blood volume is maintained, there are four main compensatory mechanisms by the body, including an increase in cardiac output, redistribution of cardiac output primarily to the brain and heart, increased oxygen extraction resulting in decreased mixed venous oxygen saturation and changes in oxygen-haemoglobin affinity.[10–12]

The compensatory mechanism occurs in chronic anaemia, chronic anaemia, among others, can occur in haemolytic anaemia patients. One of the haemolytic anaemias is autoimmune haemolytic anaemia (AIHA) which usually occurs in incompatible cross-matches.[13] AIHA is characterized by the production of autoantibodies against red blood cell antigens. Overcome anemia in AIHA according to the patient's clinical condition. Transfusion decisions in AIHA patients can also be considered if the patient is in a critical condition. Other treatments include increasing DO2 and decreasing VO2 with drugs such as steroids and certain conditions such as bed rest and supplemental oxygen administration to optimize plasma dissolved oxygen.[14,15] The aim of this case report is to describe a unique case of a patient with AIHA who was optimally managed.

CASE ILUSTRATION

A 20-year-old woman with a history of anaemia, comes with compos mentis consciousness, is not short of breath, hemodynamically stable, on physical examination, the patient looks anaemic and weak. Investigations showed Hb 6.0 g/dl and then a cross-match test was performed for blood transfusion, but the result was positive major incompatible, and it was not recommended for blood transfusion. On the second day of treatment, the patient's Hb dropped to 5.0 g/dl with hemodynamic remained the same as before, on the 3rd day of treatment, Hb changed to 3.0 g/dl, with clinically the patient experienced a decrease in consciousness with the Glasgow Coma

Scale (GCS) E2V3M4 SpO2 95% room air. The fourth day of treatment Hb 2.0 with GCS E3V3M4 SpO2 96% with a nonrebreathing oxygen face mask (NRM) 10L/minute, the lowest Hb on day 5 was 1.8 gr/dl with GCS E3V3M4, then high dose methylprednisolone was given. The patient was not transfused because there was an incompatibility which is a major contraindication to blood transfusion, Hb showed improvement on the 7th day of treatment, full consciousness returned on the 9th day of treatment with a Hb level of 7 gr/dl. Patient follow-up can be seen in Table 1.

DISCUSSION

Oxygen is necessary for human beings to survive through aerobic breathing, and it can be said to be the most commonly used drug in anesthesia and intensive care medicine. At the mitochondrial level, oxygen acts as the terminal electron acceptor at the end of the electron transport chain, where oxidative phosphorylation leads to the synthesis of adenosine triphosphate, which is a coenzyme that provides energy for all active metabolic processes.[6] Traditionally, in anesthesia and intensive care medicine, DO2 includes cardiac output and arterial oxygen content i.e. active external delivery processes responsible for ensuring oxygen delivery to cells. However, this series of processes can be easily seen from the perspective of cells that absorb oxygen to meet their own needs. Global DO2 describes the amount of oxygen delivered to the tissues per minute and is the product of cardiac output and arterial oxygen. While VO2 is the amount of oxygen consumed by the tissues per minute and can be calculated either through direct or indirect respiratory gas analysis, using Fick's principle, by measuring the oxygen content of mixed venous blood, it is depicted in Figure 1.[16] In this patient DO2 is very necessary, This is because the condition of low haemoglobin which if too long will cause tissue hypoxia.

Changes in cardiac output, arterial oxygen saturation, and haemoglobin concentration will affect oxygen delivery. Classically described conditions describing tissue hypoxia include "Stagnation hypoxia" (decreased carbon dioxide or reduction in local blood flow), "hypoxic hypoxia" (arterial hypoxemia), and "anemic hypoxia" (decreased hemoglobin). Recently, "cytopathic hypoxia" (E.g. secondary to sepsis and inflammation) and "tissue toxic hypoxia" (e.g. cyanide poisoning). In these cases, cells are relatively or absolutely unable to use oxygen, and increasing DO2 has little effect on correcting hypoxia.[6,12,17] Any cause of microcirculation dysfunction will have an impact DO2 including in these patients i.e. severe anaemia, physiological explanation of the oxyhaemoglobin dissociation curve in Figure 2.

The VO2 level depends on the metabolic requirements of the cell and can be manipulated. For example, the use of hypothermia therapy to reduce the need for brain metabolism after cardiac arrest has been shown to improve neurological outcomes.[6] Common factors affecting VO_2 are documented in Table 2.

Anaemia is a condition where the Hb level drops from normal. Haemolytic anaemia (AH) is anaemia characterized by the disproportionate destruction of erythrocytes. Pathophysiological they fall into two basic categories: 1) Intrinsic AH, in which red blood cells (RBC) are intrinsically damaged (for example, sickle cell disease, thalassemia, pyruvate kinase deficiency, hereditary spherocytosis, etc.) externally destroys healthy red blood cells (for example, drug poisoning, transfusion of incompatible blood groups, Escherichia coli poisoning, malaria, leukaemia, etc.). Clinical signs arise from a progressive decrease in the oxygen-carrying capacity of the blood due to a

decrease in the total circulating haemoglobin (tHb). They range from mild fatigue and shortness of breath to fever, chest pain, and life-threatening complications. The severity of HA is grouped according to the concentration of tHb. The normal range for a healthy human male is 14 - 18 g/dL, with women about 2 g/dL lower. Moderate anaemia is from 8 - 10 g/dL, and severe is less than 8 g/dL (5, 34). A tHb level below 7 g/dL is an indication for blood transfusion (unless there are additional comorbidities).[18,19]

This patient has a tHb level below 7 g/dl who should receive a blood transfusion, but the major incompatibility condition in the patient is suspected to have an autoimmune type of haemolytic anaemia or also known as autoimmune haemolytic anaemia (AIHA). AIHA is a relatively rare disease caused by autoantibodies against the red blood cells themselves. It can be idiopathic or secondary. According to the temperature range of autoantibodies, it is divided into warm, cold (cold hemagglutinin disease and paroxysmal cold hemoglobinuria) or mixed type. AIHA may develop gradually or suddenly attack with life-threatening anemia. AIHA treatment is not yet evidence-based. The first-line treatment for warm AIHA is corticosteroids, which are effective in 70-85% of patients and should be gradually reduced for 6-12 months. For refractory/relapsed cases, the current second-line treatment sequence is splenectomy (approximately 2 of 3 cases are effective, but the cure rate is estimated to be as high as 20%), rituximab (approximately 80-90% of cases are effective), followed by immunosuppressive drugs (azathioprine, cyclophosphamide, cyclosporine, mycophenolate mofetil). Adjunctive therapy is intravenous immunoglobulin, danazol, plasma exchange, and high-dose alemtuzumab, and cyclophosphamide as a last resort.[20,21]

If indeed this patient is required to have a blood transfusion, several considerations that must be considered include, before blood transfusion the examination carried out is the detection of pretransfusion antibodies, which involves mixing the patient's plasma with two or three samples of HR reagents that represent all clinically important HR antigens. If a negative result is obtained, the patient can be safely transfused with ABO and Rh compatible blood, as the patient does not have clinically significant HR antibodies. On the other hand, if a positive test is found with one or more screening cells, further investigation is indicated to evaluate the identity of the antibody. Three main clinical situations that can cause difficulties in providing crossmatch compatible blood, (1) Alloantibodies due to previous transfusion or pregnancy, (2) Autoantibodies reacting with common red cell antigens in autoimmune haemolytic anaemia (AIHA), and some forms of haemolytic anaemia. drug-induced immunity and (3) ABO differences. In particular, transfusion of patients with AIHA involves the detection of concurrent alloantibodies in the patient's plasma.[22,23]

Alloantibody detection in AIHA patients is only to help if the patient is in a critical condition that requires blood transfusions. However, other treatments such as high-dose corticosteroid administration as given to this patient have good effects, with the mechanism being a direct effect on the red blood cell membrane indicating that the insertion of oxygenated cholesterol derivatives into the erythrocyte membrane causes membrane expansion. In an isotonic situation, there is no change in the rate of haemolysis. In a hypotonic setting, an increase in the ratio of cell surface zone to volume allows the buildup of a greater volume of water within the cell before the point of osmotic lysis (critical haemolytic volume) is reached. When applied to HR

from patients with AIHA, the compound successfully shifted the osmotic fragility curve. Another mechanism is that mineralocorticoid action leads to an increase in the quantity of sodium that is actively extruded from the cell or a decrease in the amount of sodium that inertly leaks into the cell and suppresses the activity of the autoimmune-induced destruction of RBCs. Corticosteroids can play a role in suppressing IgG so that it does not play a role in further haemolytic processes.[20]

Moreover, in these patients when anaemia develops over a long period time, the oxyhaemoglobin dissociation curve shifts to the right, where haemoglobin has a decreased affinity for molecular oxygen and releases oxygen to tissues at a higher partial pressure. Since this process occurs only after an increase of 2,3 DPG, this process only occurs in chronic anaemia and not when the patient is undergoing isovolemic hemodilution.[6,10,12] In many of the above processes these patients are treated for an increase in their Hb using various methods so that, DO2 in the patient will increase to avoid the occurrence of tissue hypoxia which makes the patient's condition lose consciousness. Patients after being given optimal management, can go home with Hb that has not reached normal but has been able to improve hemodynamic conditions and patient awareness.

CONCLUSION

Cases of severe haemolytic anaemia with major incompatibility can be suspected with the diagnosis of AIHA, management is supportive in helping increase DO2 and decrease VO2. The use of transfusions can be avoided except in critical conditions where the use of other drugs is not adequate to help restore the patients hemodynamic.

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