

Neonatal anemia, several possible reasons

Introduction

Anemia is defined as the reduction of red blood cells, hemoglobin and/or hematocrit. The values considered normal for haemoglobin and hematocrit depend on gestational age and days of life.

In this review, we will focus on objective anemia in the first days of life.

In general, in the first week of life the normal values of haemoglobin and hematocrit at the central level should be greater than 15gr/dl and 45% respectively.¹ If we take into account gestational age, in term newborns the normal value of haemoglobin on the first day of life corresponds to values between 14–20gr/dl, whereas in prematurely born the value can oscillate between 13.5–19gr/dl.^{1–3}

The causes of neonatal anemia can be: blood loss, destruction of red blood cells and lack of production.²

- Causes of blood loss include antenatal (fetal-fetal transfusion, fetal-maternal transfusion);⁴ intrapartum (obstetric accidents, placental vascular malformations or umbilical cord vessels); postpartum (internal bleeding, excessive extractions).
- Among those caused by the destruction of red blood cells we highlight: hemolysis due to incompatibility of blood group and Rh, spherocytosis or other hemoglobinopathies, infections or toxins.
- Finally, the lack of production may be secondary to physiological hypoplastic anemia (produced in the newborn at term between 6–12 weeks of life and in the premature newborn between 4–10 weeks of life); congenital or secondary aplastic anemia (infectious processes, haematological...).

The time of onset of anemia can provide guidance on its etiology. The anemia that appears on the first day of life can lead to anemia due to incompatibility of blood group and Rh or haemorrhagic anemia. That which appears between the second day and the month of life may be due to physiological anemia, haemorrhagic anemia, spherocytosis or non-spherocytic haemolytic anemia. On the other hand, that which appears from the month of life up to the third month can lead to physiological anemia, due to lack of folate, congenital hypoplastic anemia or anemia of prematurity.^{1,2}

To make a correct diagnostic approximation in cases of low numbers of hemoglobin and hematocrit in a newborn we must rely on the anamnesis and obstetric history (placental alterations, cord ligation time, drugs, visible bleeding), family history (blood group and Rh, anemia, jaundice, biliary lithiasis, splenectomy) and complementary tests that will confirm the type of anemia.^{1,2,5}

Among the tests to request we highlight the hemogram and reticulocytes, which in the first 3 days of life, should be between 4–6% of the total value of red blood cells. They are elevated in anemia due to chronic or hemolytic losses and decreased in infections and production defects. Bilirubin is elevated in cases of hemolysis. In all cases, especially in suspected hemolysis, it is important to determine the blood group and Rh along with the direct Coombs.

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Other tests to be performed to determine the aetiology of anemia are: morphology of red blood cells in peripheral blood, determination of fetal haemoglobin value in maternal blood, coagulation study, serological test (Toxoplasma, rubella, cytomegalovirus, herpes, parvovirus and syphilis). Imaging tests such as ultrasound (abdominal and transfontanellar) in the newborn are necessary to rule out internal bleeding.

Clinical case presentation

We describe three clinical cases of neonatal anemia in the first days of life.

Case 1 anemia due to blood loss

Newborn who was admitted because of neonatal maladaptation from the first gestation of a healthy mother. Controlled pregnancy without complications. Born at the gestational age of 40 weeks with birth weight of 3200gr. Instrumented eutocic vaginal birth. Normal fetal cardiac registration. No resuscitation required at birth, Apgar 9/10, pH cord 7.25. Faced with skin paleness and mild respiratory distress, hospitalization was decided. In analytical control hemoglobin of 10.5g/dL was observed, with reticulocytes of 6% and without elevation of bilirubin, nor infection parameters. No incompatibility of blood group or Rh, with direct negative Coombs and normal ultrasounds. Hemodynamic stability at all times and asymptomatic with good diet and adequate weight gain. The clinical suspicion was regenerative anemia due to possible antenatal or intrapartum blood loss, without any problems in the placenta or bleeding in the cord vessels. Fetal hemoglobin in maternal blood was 0.2%, ruling out fetal-maternal transfusion. Hemoglobin numbers were progressively increasing without further subsequent declines.

Case 2 fetus-maternal transfusion

28-year-old woman, first pregnancy, controlled pregnancy without complications. Consulted at gestational age of 40 weeks +5 days due to decreased fetal movements of about 4–5 hours of evolution. Sinusoidal pattern in the cardiotocographic record and absence of fetal movements, not being in active period of childbirth, so urgent caesarean section was performed, without being able to perform calotte pH.

A girl was born with a poor general appearance, no respiratory effort, undetectable heart rate and marked generalized cutaneous-mucosal paleness. Ventilation was initiated with intermittent positive pressure for less than 30 seconds, but at a heart frequency of less than 60bpm the patient was intubated and ventilated with an auto inflatable bag. Urgently, umbilical vein was channeled and intravenous fluids (physiological serum) perfusion at 15 ml/kg and IV adrenaline was initiated.

After a first bolus of physiological serum and two doses of adrenaline, a heartbeat >100bpm was obtained, but with great hemodynamic instability that required doses of adrenaline and continuous fluids to maintain a heart rate >100 bpm. Apgar 0/3/3. Cord pH 7.20, with excess bases - 8.1. Blood analysis at 30 minutes of age showed a hematocrit of 11.7% and hemoglobin of 3.6g/dL, with negative infection parameters and metabolic acidosis (pH 7.0, pCO₂ 26 mmHg, HCO₃ 7.5mmol/L and excess bases of -23mmol/L). In the case of severe anaemia, red blood cell concentrate was transfused at 20 ml/kg on up to two occasions. The patient was kept on mechanical ventilation in a controlled assisted modality, IV antibiotic therapy with ampicillin and cefotaxime, IV fluids and inotropic medication (adrenaline, dopamine, dobutamine) in continuous perfusion at maximum doses. Chest x-ray showed no pneumothorax or other malformative anomalies, correct position of the endotracheal tube and umbilical venous catheter.

It was maintained in passive hypothermia (because initially it did not meet exclusion criteria) but despite all the medical efforts the hemodynamic instability was in progression, with progressive gasometric worsening to severe metabolic acidosis, producing death with multiorgan failure at 5hours of life. The necropsy showed no malformations or internal bleeding, and could not determine causes of death other than severe anemia. Peripheral blood morphology was normal. Given the absence of active bleeding after birth in the neonate and the absence of lesions suggestive of haemorrhage in the necropsy, fetomaternal transfusion was suspected and confirmed by determining fetal haemoglobin in maternal blood of 2.4%. Kleihauer's equation calculated the transfer of 150ml of fetal blood to the mother.

Case 3 congenital aplastic anemia

Newborn of 24 hours of life, controlled pregnancy without complications. Born at the gestational age of 38 weeks, by caesarean section given the presentation of buttocks. Birth weight of 2400gr. Apgar 9/10. pH cord 7.35. In the first 24 hours of life, paleness of the skin and mucous membranes was detected with hemodynamic stability but regular sucking that conditioned feeding difficulties. The analytical control showed anemia with a hemoglobin value of 10.1gr/dl, normal bilirubin and reticulocytes of 5%, negativity of infectious parameters, blood group and Rh that was compatible with the mother, negative Coombs, normal abdominal and transfontanelar ultrasound, normal morphology in peripheral blood. All data suggested anemia

with possible subacute or chronic cause possibly secondary to antenatal blood loss or at time of birth. The value of fetal hemoglobin in maternal blood was less than 0.1%. Anemia progressed to 9.1g/dL in 48hours, with haemodynamic stability but with poor feeding and no weight gain and so transfusion of red blood cell concentrate at 15ml/kg was made. After transfusion there was progressive clinical improvement with good nutrition and progressive weight gain, recovering hemoglobin value within 24hours of transfusion up to 12.5g/dL.

After two weeks of life with progressive weight gain, of about 20gr a day, and correct feeding, again there was weight loss with feeding problems and foam depositions. In analytical control, haemoglobin of 10.5g/dl, low reticulocytes, with a reticulocytary index of less than 1, thrombopeny of 91000, neutropaenia with 900 absolute neutrophils and lactic acidosis were observed. These data led to the suspicion of areregenerative anemia. A new transfusion of red blood cell concentrate was required due to decreased haemoglobin of up to 8g/dL. Bone marrow study detected sideroblastic anemia suspecting genetic cause of this neonatal areregenerative anemia, possible Pearson's Syndrome, waiting to be confirmed genetically.

Conclusion

It is necessary to know the different causes of neonatal anemia and how to obtain the correct diagnosis.

Rare entities exist and we find them in our daily clinical practice. We must make a correct differential diagnosis in order to confirm the correct etiology and thus ensure the most appropriate treatment.

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Conflicts of interest

The authors declared there is no conflicts of interest.

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