INTRODUCTION

Blood group incompatibilities are most frequent and severe conditions causing hyperbilirubinaemia in the neonatal period.1 Phototherapy and in severe cases, exchange transfusion are used to prevent kernicterus and reduce perinatal mortality. Exchange transfusion is not free of severe complications such as thrombocytopenia, anemia, pulmonary hemorrhage, hemodynamic instability, sepsis and necrotizing enterocolitis (NEC).2

Intravenous immunoglobulin (IVIG) can also be used for newborns with significant hyperbilirubinaemia and it reduces the need for exchange transfusion.3 IVIG is a concentrated, purified solution of immunoglobulins derived from pooled plasma of the donor population. IVIG is indicated for severe iso-immune thrombocytopenia and iso-immune haemolytic jaundice in neonates with a dose of 500 – 1000 mg/kg infused over 2 to 6 hours.4 IVIG administration has been successfully employed to block circulating maternal antibodies and to reduce the need for exchange transfusion in iso-immune haemolytic jaundice.5 Although studies performed showed a significant reduction in the need for exchange transfusion in those treated with IVIG, the applicability of the results is limited because the number of studies and infants included was small. IVIG may also cause important adverse reactions,6 one of which is described hereby.

CASE REPORT

A female newborn was admitted to our neonatal unit because of jaundice on the tenth hours after being born. The baby was born by uncomplicated vaginal delivery to a healthy 31-year-old mother who was fourth gravida and second para. Her body weight was 2,600 grams and her gestational age was 40 weeks. Her Apgar score were 8 and 9 for the first and fifth minute respectively. The mother's past history was unremarkable. The first sibling were treated with phototherapy due to neonatal hyperbilirubinaemia. At the time of admission, the patient's physical examination was normal except yellowish colour of skin.

The laboratory data indicated a haemoglobin value of 20 mg/dL, a reticulocyte count of 14.9% and moderate anisocytosis and severe polychromasia in the peripheral blood smear. The seroanalysis showed a total bilirubin of 8 mg/dL at 10 hours of life, a direct bilirubin of 0.6 mg/dL, blood urea nitrogen (BUN) value of 25 mg/dL, creatinine level of 0.5 mg/dL, sodium level of 137 mEq/L, potassium level at 4.1 mEq/L, chloride level of 102 mEq/L and a strong positive result (+++) on the direct Coombs test. Blood group was A+. The mother's blood group was O+. Double phototherapy was initiated; however, 4 hours later total bilirubin level rose to 10 mg/dL.

After obtaining approval from the parents, administration of two courses of IVIG dose: 1 g/kg/dose/day at a slow rate (over 3 hours) was started. Breastfeeding was satisfactorily initiated. After second dose of IVIG, the patient developed vomiting followed by abdominal tenderness and distention. X-ray abdomen showed diffuse pneumatosis intestinalis (Figure 1). After

ABSTRACT

ABO iso-immunization is the most frequent haemolytic disease of the newborn. Treatment depends on the total serum bilirubin level, which may increase very rapidly in the first 48 hours of life in cases of haemolytic disease of the newborn. Phototherapy and, in severe cases, exchange transfusion are used to prevent hyperbilirubinaemic encephalopathy. Intravenous immunoglobulins (IVIG) are used to reduce exchange transfusion. Herein, we present a female newborn who was admitted to the NICU because of ABO immune haemolytic disease. After two courses of 1 g/kg of IVIG infusion, she developed necrotizing enterocolitis (NEC). Administration of IVIG to newborns with significant hyperbilirubinaemia due to ABO haemolytic disease should be cautiously administered and followed for complications.

diagnosis of NEC, feeding was stopped and intravenous antibiotics and total parenteral nutrition was started. The patient’s condition worsened and was suspected to be due to an intestinal perforation. Abdominal percutaneous drainage was performed. After 5 days, drainage was stopped and oral feeding was started and intravenous antibiotic therapy completed for 14 days with an adequate clinical response.

DISCUSSION

Intravenous immunoglobulin can be used for newborns with significant hyperbilirubinaemia. Adverse events that were reported after the use of IVIG include pyrogenic reactions, volume overload (with transient tachycardia or hypertension), hypoglycemia, and hypotension that disappeared after stopping the infusion. Hemolysis can be an uncommon complication as well as acute renal failure and NEC. NEC is the most common and severe gastrointestinal disease in newborns. The aetiology and pathophysiology of NEC remain unclear; however, both intestinal immaturity and bacterial overgrowth are prerequisites for its development. Moreover, pre-maturity and low birth weight are risk factors consistently associated with the development of NEC. In mature newborns perinatal asphyxia, presence of umbilical catheters, antecedent respiratory distress, polycythemia, and maternal pre-eclampsia are the risk factors for NEC.

NEC episodes have been previously described after intravenous IVIG infusion in patients with iso-immune thrombocytopenia. Moreover, it has also been reported in full term neonates with haemolytic disease of the newborn (HDN), and after exchange transfusion for this condition, thus implicating that HDN in itself is a risk factor for NEC in term infants. In this case, the patient was term and she has got ABO iso-immune haemolytic disease. There was no other risk factor for NEC. But it started abruptly with clinical symptoms of NEC immediately after receiving IVIG.

The pathophysiologic process and clinical presentation of NEC in late-preterm infants or term newborns is different from standard NEC in more immature preterm infants because it is especially attributable to intestinal hypoxia-ischaemia (as a result of thrombosis) instead of infection. Hyperviscosity of the IVIG solutions may increase the risk for intestinal thrombosis. Because IVIG is administered during the first day of life, its prothrombotic effect may also increase the physiologic hypercoagulability of the fetus and newborn after birth. There was a possible combination of various factors such as HDN, intense phototherapy, IVIG infusion and the appearance of NEC symptoms shortly thereafter in this patient.

Alcock and Liley concluded that the role of IVIG remains uncertain, although its use reduces the need for exchange transfusion. IVIG may play a role in special circumstances, such as parental refusal or unavailability of blood components for exchange transfusion. In contrast, Gottstein and Cooke showed that IVIG is an effective treatment for neonatal haemolytic disease because it reduces the need for exchange transfusion, duration of phototherapy, and length of hospital stay. Adverse events were mild and usually clinically irrelevant.

Figueras-Aloy et al. reported that the administration of high-dose IVIG for severe iso-immune haemolytic jaundice was associated with a higher incidence of NEC in late-preterm and term infants, female gender, low birth weight, and need for resuscitation maneuvers at the time of delivery, in the presence of caesarean delivery and low Apgar score at 5 minutes. They also referred that the infusion should be administered slowly (at least during 4 hours) to reduce the effects of hyperviscosity. This patient was female, but there was no other risk factors and infusion rate was 3 hours. The authors believe that a multicentre, randomized controlled trial is needed to examine the safety and efficacy of high-dose IVIG treatment to assess the incidence of adverse events, short-term results, and long-term neurodevelopmental outcomes.

REFERENCES


