Original Article

ROLE OF INTRAVENOUS IMMUNOGLOBULIN IN ISO-IMMUNE JAUNDICE IN NEONATE

Faten AL-Awaysheh[1], Mona Kuwar[2], Raeda AL-Ghananim[3], Nisreen AL-Hamiedeen[4], Omyma Al-Jarrah[5]

ABSTRACT

Objective: To show that intravenous immunoglobulin is safe and effective alternative treatment in newborn with iso-immune hemolytic jaundice.

Methodology: This study was carried out in neonatal unit in King Hussein Medical Center (KHMC) and Queen Alia Hospital during two years period of all cases who presented with jaundice either RH or ABO iso-immune jaundice in the first day of life. All patients received phototherapy and intravenous immunoglobulin.

Results: There were 91 patients with iso-immune jaundice admitted to the neonatal unit in their first day of life. Eighty five patients out of 91 (93.4%) were due to ABO incompatibility. Six patients out of 91 (6.6%) were due to RH incompatibility. Direct coombs test was positive in all cases of RH incompatibility and in 16 cases of ABO incompatibility. Intravenous immunoglobulin (0.5g/kg) was given to all patients over four hours every 24 hours for three doses. Exchange transfusion was done for one patient only (1%). Blood transfusion was given for 22 patients out of 91 (24%). Hospital stay was around 3-4 days in majority of cases.

Conclusion: Intravenous immunoglobulin in newborn with ABO or RH hemolytic jaundice is effective in reducing hemolysis, serum bilirubin level and the need for exchange transfusion.

KEY WORD: Intravenous immunoglobulin, RH, ABO, Jaundice.

Pak J Med Sci July - September 2010 Vol. 26 No. 3 538-541

How to cite this article:

Al-Awaysheh F, Kuwar M, AL-Ghananim R, AL-Hamiedeen N, Al-Jarrah O. Role of intravenous immunoglobulin in iso-immune jaundice in neonate. Pak J Med Sci 2010;26(3):538-541

1. Faten AL-Awaysheh, MD, Neonatologist.
2. Mona Kuwar, MD, Senior Pediatric Specialist.
3. Raeda AL-Ghananim, MD,
4. Nisreen AL-Hamiedeen, MD,
5. Omyma Al-Jarrah,

3-4: Pediatric Specialist.

1-5: All authors are attached to Royal Medical Services, Amman, Jordan.

Correspondence:

Dr. Nisreen Al-Hamiedeen, MD,
Specialist Pediatric Doctor at Royal Medical Services,
King Hussain Medical Center,
P.O Box 15015, Postal Code 11134
Amman - Jordan.
E-mail: nisreen17@yahoo.com

* Received for Publication: September 3, 2009

* Accepted: April 10, 2010

INTRODUCTION

Iso-immune hemolytic jaundice means production and transplacental passage of specific maternal immunoglobulin G (IgG) antibodies directed against fetal antigen, resulting in immune destruction of fetal RBCs, and leads to anemia and hyper-bilirubinemia. The usual antigen involved prenatally is RH (D) antigen, and postnatally is the A and B antigens.[1]

The standard management of hemolytic disease of newborn due to RH iso-immunization includes phototherapy and exchange transfusion for infants with severe anemia and/or severe or rapidly increasing hyper-bilirubinemia, but this is not always successful.[2]

High-dose intravenous immunoglobulin (500-1000 mg) over 2-4 hours has been used to reduce bilirubin levels in infants with iso-immune jaundice. The mechanism is unknown, but theoretically the immunoglobulin acts by occupying the Fc receptors of the reticuloendothelial cells, thereby preventing them from taking up and lysing antibody-coated RBCs.[1,3,4]

METHODOLOGY

The study was carried out in the neonatal unit in King Hussein Medical Center (KHMC) and Queen Alia Hospital during two years period between first of January 2007 till end of December 2008.

Ninety one patients were admitted to the neonatal unit due to jaundice on their first day of life. All cases were RH or ABO iso-immune jaundice and full term. Premature babies were excluded from the study.

Complete blood count (CBC), retic count, blood film, liver function test and bilirubin level total and direct, blood group of the mother and the baby, direct combs test and blood culture were taken and recorded for all cases. Duration of the hospital stay was documented. All cases received phototherapy and intravenous immunoglobulin in the dose of 0.5gm/kg over four hours every 24 hour for three doses.

RESULTS

During the study period, a total number of ninety one neonates presented with iso-immune jaundice in first day of life. Level of total serum bilirubin for admission was according to American Academy of Pediatrics guidelines in Fig-I. Table-I shows the causes of iso-immune jaundice. We noticed in our study that most cases are due to ABO incompatibility nearly 94% of cases. About 48.4% of these cases had A+ blood group and their mothers had O + while 45% had B+ blood group and their mothers had O+. On the other hand only 6.6% of cases were due to RH incompatibility. We found that direct coombs test was positive in all cases of RH incompatibility and only in 16 cases out of 85 patients with ABO incompatibility.

Table-I: Causes of Jaundice (n = 91)

Cause	*No.*	*%*	*+ DCT*
ABO incompatibility	85	93.4	16
Mother o+, baby A+	44	48.4	
Mother o+, baby B+	41	45	
RH incompatibility	6	6.6	6

Table-II illustrates the course during hospitalization of the cases included in this study. All cases received phototherapy and intravenous immunoglobulin 0.5gm/kg/dose every 24 hours for three doses. Exchange transfusion was done for one case only out of ninety one, and it was noticed that this case presented late at the age of ten hours.

The average hospital stay was 3-4 days for most cases (95.7%). Some cases (4.3%) needed 10-15 days at hospital due to element of neonatal sepsis where three cases had gram negative sepsis and one case had gram positive sepsis. A significant increase in number of blood transfusion was noticed in our study (22 cases out of ninety one).

DISCUSSION

Exchange transfusion and phototherapy have traditionally been used to treat jaundice and avoid the associated neurological complica-

Table-II: Course during hospitalization.

Course	*No. of Patients*	*%*
Phototherapy	91	100
IVIG	91	100
Exchange transfusion	1	1
Hospital stay (3-4 days)	87	95.7
Hospital stay (10-15 days)	4	4.3
Blood transfusion	22	24
Positive blood culture gram negative	3	3.3
Positive blood culture gram positive	1	1

tions. Exchange transfusion is not without risk and intravenous immunoglobulin has been suggested as an alternative therapy for iso-immune hemolytic jaundice to reduce the need for exchange transfusion.[4]

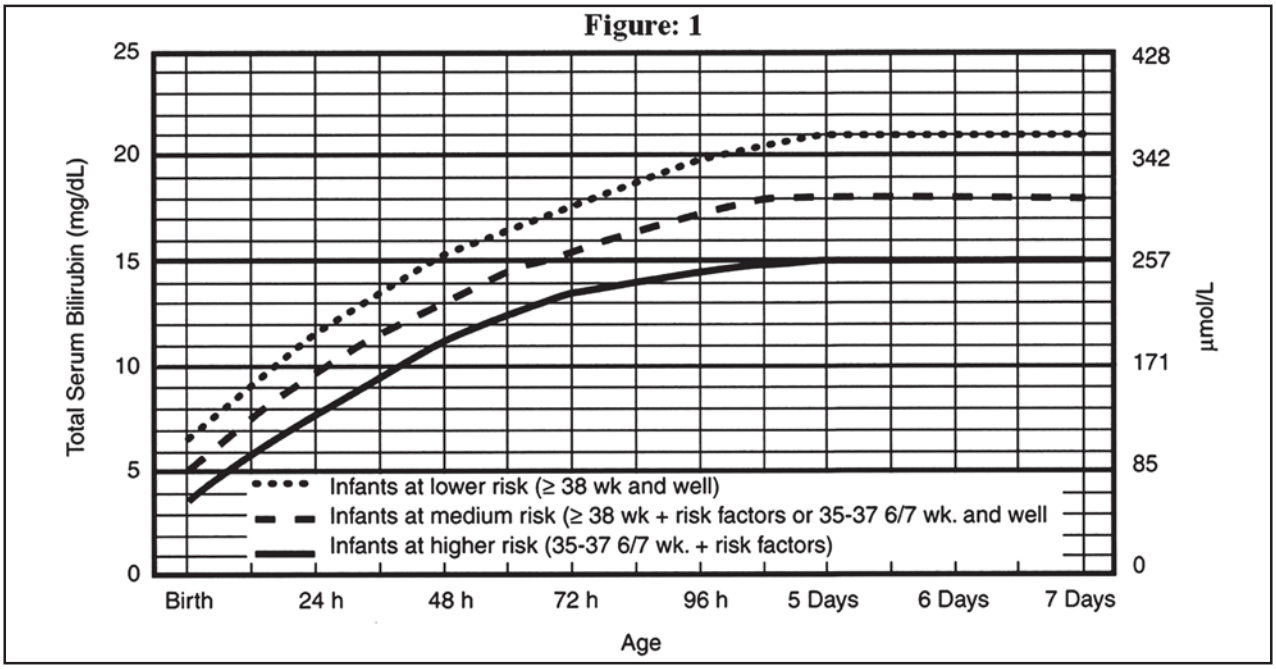
The use of anti-D prophylaxis in Rhesus negative women has led to a marked decrease in rhesus sensitization and hemolytic disease of the newborn. However, sensitization can occur despite anti-D immunoglobulin, particularly if it is given too late or in insufficient dose. So it is still common to encounter jaundice due to hemolytic causes.[5-8]

Intravenous immunoglobulin (IVIG) has emerged as an important component of treatment in iso-immune hemolytic jaundice. Use of IVIG has been found to be associated with reduced need for exchange transfusion which has many risks. Most studies on the safety of exchange transfusion report exchange transfusion-associated mortality as that occurring within six hours of the procedure.[4] Death is more common in sick or premature infants and is rare when it's performed on healthy term infants. It has many complications and published morbidity rates have been relatively low varying from 2.8-5.2% per procedure.[3]

The rationale of using IVIG is that in iso-immune hemolysis red blood cells are probably destroyed by an antibody-dependent cytotoxic mechanism mediated by Fc bearing cells of the neonatal reticuloendothelial system. The mechanism of IVIG action is non-specific blockade of Fc receptors. Carboxyhemoglobin levels are a sensitive index of hemolysis and many studies show a decline in its level after treatment with IVIG and thus indicated that immunoglobulin could decrease hemolysis.[4] IVIG may have a role in specific circumstances such as parental refusal for exchange transfusion or where appropriate blood components for exchange transfusion are not available.

The American Academy of Pediatrics recommends the use of IVIG in neonates with hemolytic jaundice in a dose of 0.5-1 gm/kg.[2] We used the lowest dose of 0.5 gm/kg as stud-

Figure: 1



- Use total bilirubin. Do not subtract direct reacting or conjugated bilirubin.
- Risk factors = isoimmune hemolytic disease, G6PD deficiency, asphyxia, significant lethargy, temperature instability, sepsis, acidosis, or albumin < 3.0g/dL (if measured)
- For well infants 35-37 6/7 wk can adjust TSB levels for intervention around the medium risk line. It is an option to intervene at lower TSB levels for infants closer to 35 wks and at higher TSB levels for those closer to 37 6/7 wk.
- It is an option to provide conventional phototherapy in hospital or at home at TSB levels 2-3 mg/dL (35-50mmol/L) below those shown but home phototherapy should not be used in any infant with risk factors.

ies that compare different doses of IVIG showed comparable effects of both doses on duration of phototherapy, duration of hospitalization and the need for exchange transfusion.[2] In our study, there was a decrease in percent of exchange transfusion (only one case out of 91) and a decrease in duration of hospital stay like most of the published studies.[2,3,9-15]

One study showed no significant difference between IVIG and double source phototherapy in ABO hemolytic disease.[11] A study from Turkey showed that the duration of phototherapy and hospitalization was shorter in patients who received IVIG.[10] An increase in number of blood transfusion was noticed in our patients just comparable to other studies.[2- 4,11,12]

Adverse effects of IVIG including allergy, transmission of diseases, sepsis, hemolysis, acute renal failure, hypoglycemia and hypocalcemia[4] were not encountered in our study. None of the published studies assessed long term outcomes such as incidence of hearing loss, kernicturus and cerebral palsy. The advantages of IVIG over exchange transfusion are obvious. It is less invasive therapy and its administration is less complicated.

CONCLUSION

Intravenous immunoglobulin in newborn with ABO or RH hemolytic jaundice is effective in reducing hemolysis, serum bilirubin level and the need for exchange transfusion.

REFERENCES

1. Cloherty JP, Eichenwald E, Stark A. Iso-immune hemolytic disease of the newborn. Manual of Neonatal Care, Sixth edition, 2009, 209.
2. Greenough A. Intravenous immunoglobulin in neonatal Rhesus hemolytic Disease. Indian Pediatrics 2008;45:649-665.
3. Gottstein R, Cooke RWI. Systemic review of intravenous immunoglobulin in hemolytic disease of the newborn. Arch Dis Child Fetal Neonatal Ed 2003;88:F6-10.
4. Copelan EA, Strohm PL, Kennedy MS, Tutschka PJ. Hemolysis following intravenous immunoglobulin therapy. Transfusion 1986;26:10-12.
5. Alcock GS, Liley H. Immunoglobulin infusion for isoimmune hemolytic jaundice in neonate. Cochrane database of systematic reviews 2002 issue 3.
6. Girish G, Chawla D, Agarwal R, Paul UK, Deorari K. Efficacy of two doses regimen of intravenous immunoglobulin in rhesus hemolytic disease of newborn. A randomized controlled trial. Indian Pediatrics 2008:653-659.
7. Rubo J, Albrecht K, Lasch P, Laufkotter E, Leititis J, Marsan D, et al. High dose intravenous immunoglobulin therapy for hyperbilirubinemia caused by RH hemolytic disease. J Pediatr 1992;121:93-97.
8. Dagoglu T, Ovali F, Samanci N, Bengisu E. High dose intravenous immunoglobulin therapy for rhesus hemolytic disease. J Int Med Res 1995;23:264-271.
9. American Academy of Pediatrics Subcommittee on hyperbilirubinemia. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. Pediatrics 2004;114:297-316.
10. Merchant RH, Pradeep S. Intravenous immunoglobulin therapy for hyperbilirubinemia caused by Rhesus hemolytic disease. Indian Pediatrics 1994;31;1269-1271.
11. Alpay F, Sarili SU, Okutan V, Erderm G, Ozcan O, Gokcan E. High dose intravenous immunoglobulin therapy in neonatal immune hemolytic jaundice. Acta Pediatrics 2007;216-219.
12. Mukhopadhyay k, Mark S, Narang A, Dutta S. Intravenous immunoglobulin in rhesus hemolytic disease. Indian Pediatrics 2003;70(9):697-699.
13. Fatemeh N, Gholan AM, Homa B. Intravenous immunoglobulin in ABO and Rhesus hemolytic disease of newborn. Saudi Med J 2006;27:1827-1830.
14. Felc Z. Hemolytic disease of the newborn caused by Rhesus isoimmune (anti-c). Eastern Mediterranean Health J 2001;7:1056-1060.
15. Gupta G. High dose intravenous immunoglobulin in hemolytic disease of neonates. Archives of Diseases in Childhood-Fetal and Neonatal Edition 2003;88:444-445.