shttp://jmscr.igmpublication.org/home/
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v9i4.04

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Original Article

Efficacy of early IV Immunoglobulin in management of neonatal hyperbilirubinemia due to Rh incompatibility and ABO incompatibility: A hospital based study

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Abstract

Introduction: *Blood group incompatibility induced haemolytic jaundice can cause significant morbidity and mortality in the neonates. This present study is to show the usefulness of IVIG in the management of neonatal jaundice.*

Objective: *To assess the efficacy of early intravenous immunoglobulin in reducing the duration of phototherapy and the need for exchange transfusion in Rh and ABO incompatibility.*

Methodology: *In this randomised control trial 50 patients diagnosed with haemolytic disease of new-born were grouped into group A and B. All neonates were treated with standard protocol for phototherapy and exchange transfusion. Only group A patients received intravenous immunoglobulin in a dose of 0.5gm/kg of body weight and phototherapy. Exchange transfusion was done to the patients of both groups if the bilirubin reached exchange level in AAP chart.*

Result: *Improvement in bilirubin level was significant in group A 80 % vs group B 48 % (p-value <0.O5, S). Similarly phototherapy duration was reduced in the group A 76% vs group B 20 % (p<0.05, S). Exchange transfusion was reduced in group A 12% vs group B 48%.*

Conclusion: *Addition of intravenous immunoglobulin for treatment of haemolytic disease of new born significantly reduces bilirubin levels, duration of phototherapy and need for exchange transfusion.*

Keywords: *Bilirubin, Immunoglobulin.*

Introduction

Blood group incompatibility induced hemolytic jaundice sometime causes significant morbidity and mortality in the newborn period[1]. Hemolysis from ABO incompatibility is one of the most common cause of iso-immune hemolytic disease during neonatal period. Infants with blood group type A or B, carried by blood group type O mother, have a positive antibody because of maternal anti-A or anti-B transfer into the fetal circulation. Ten percent of these infants will present with hemolytic disease. Most of the infants present with unconjugated hyperbilirubinemia in the first 24 h of life and it is

rarely a cause in patients who are discharged from nursery and readmitted with severe hyperbilirubinemia[1].Appropriate intervention is important to prevent long term neurologic sequelae such as kernicterus in every infant with ABO hemolytic disease[1].

Early administration of intravenous immunoglobulin (IV IG) after diagnosis of neonatal immune hemolytic disease decreases the need for phototherapy and exchange transfusions. The decreased bilirubin levels in infants treated with intravenous immunoglobulin is attributed to reduction in hemolysis secondary to blockade of reticuloendothelial Fc receptors and therefore preventing the extravascular destruction of neonatal red blood cells by transplacentally acquired maternal antibodies[2]. American Academy of Pediatrics, recommends IV IG (0.5–1 g/kg) as an additional treatment of Rh and ABO hemolytic disease[1].

The use of Anti-D immunoglobulin and more effective phototherapy has decreased the need for exchange transfusion to be performed, however it is still required, especially where there is aggressive haemolysis. If there is a past history of Hemolytic disease of newborn, that should be taken into account when choosing the most appropriate treatment[3].

Aims and Objective

Efficacy of IV immunoglobulin in neonatal hyperbilirubenemia due to ABO and Rh incompatibility.

Materials and Methods

This was a prospective, single centred, randomised controlled trial study conducted in neonatal intensive care unit of a tertiary care centre, SMCH over period of 6 months from February 2020 to July 2020 .The study protocol was approved by the Institutional Ethical Committee. A written and verbal informed consent was obtained from the parents before inclusion in the study. Total neonates included into this study were 50. They were divided into group A (25) test and group B (25) control. The group A patients received intravenous immunoglobulin in a dose of 0.5 gm/kg of body weight and phototherapy according to the AAP (American academy of paediatrics) normagram for phototherapy. The group B received only phototherapy. Exchange transfusion was given to the patients of both groups if the bilirubin reached exchanged level in AAP normogram for exchange transfusion.

Inclusion Criteria

Inclusion criteria included neonates of both sex, term and less than 10 days old with hemolytic disease of newbornwith hyperbilirubenemia due to ABO or Rh incompatibility.

Exclusion Criteria

Neonates with NNJ (neonatal jaundice) more than 2 weeks and due to causes other than ABO and Rh incompatibility. Those babies in who needed exchange transfusion at presentation were excluded.

Result

In the present study, majority of babiesi.e 84% were less than 5 days old. Majority of the babiesi.e 54% were born at 39-40 GA and 40% had birth weight 2.5 - 3 kg. The predominant blood group among the neonates were ABO incompatibility (54%) followed by Rh incompatibility (22%) and both (24%) respectively. In group A, 13 (52%) were female and 12 (48%) were male while 15 (60%) female and 10(40%) male patients in group B. Considering the weight , maximum weight were between 2.5 -3.0kg (40%). (Table-1).

Table 1: Details of neonates studied.

Details of neonates	*Group A Cases (%)*	*Group B Control (%)*
Age:		
1-5 days	20(80)	22(88)
5-10days	5(20)	3(12)
Total	25(100)	25(100)
Sex:		
Male	12(48)	10(40)
Female	13(52)	15(60)
Total	25(100)	25(100)
Weeks of Gestation:		
37-38Weeks	10(40)	13(52)
39-40Weeks	15(60)	12(48)
Total	25(100)	25(100)
Birth weight(kg):		
2.50-3.00	11(44)	9(36)
3.01-3.50	9(36)	7(28)
3.51-4.00	5(20)	9(36)
Total	25(100)	25(100)
Blood group:		
ABO	12(48)	15(60)
Rh type	6(24)	5(20)
Both	7(28)	5(20)
Total	25(100)	25(100)

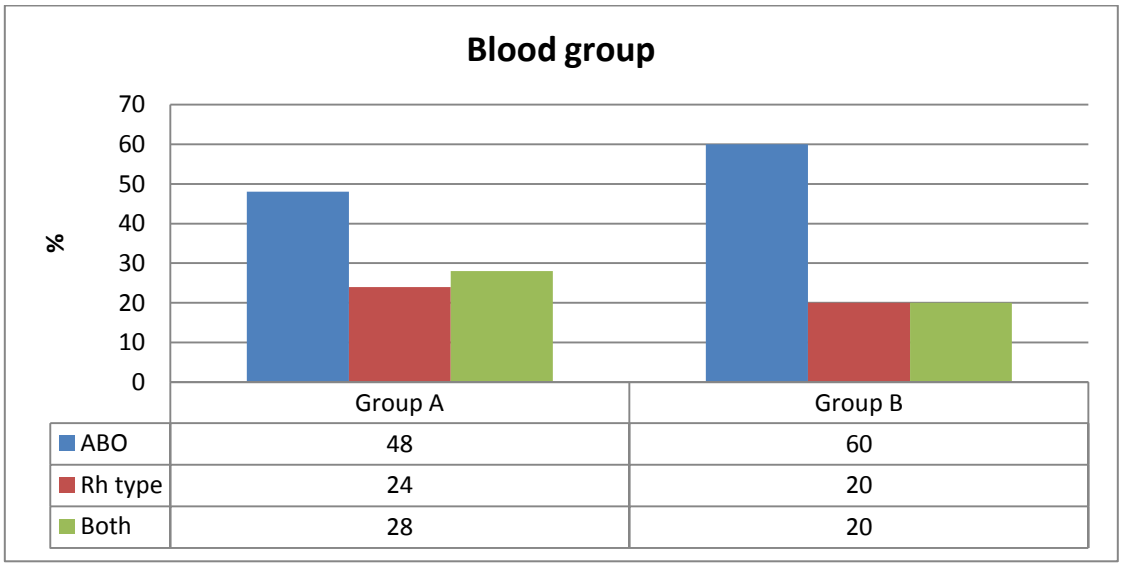

Figure 1: blood grouping of the subjects

Table 2: Change in bilirubin level (%)

	Group A (%)	Group B (%)	
Decrease in bilirubin	20(80)	12(48)	P <0.05
Increase in bilirubin	5(20)	13(52)	
Total	25(100)	25(100)	

Decrease in bilirubin was more pronounced (80%) in group A as compared to group B (Table 2).Which was significant ,p value <0.05.

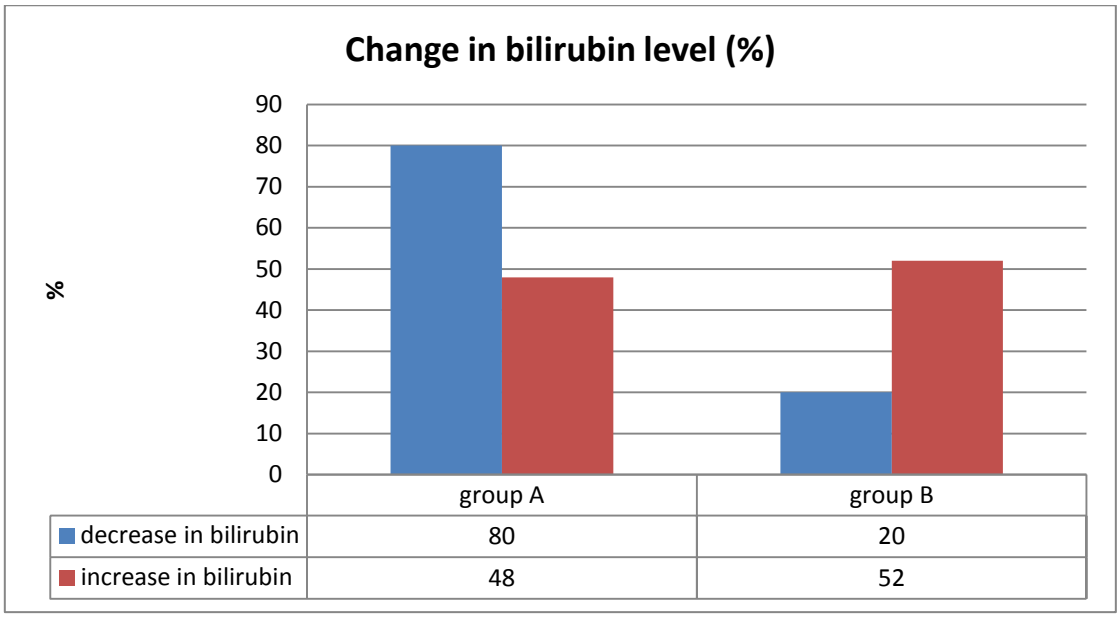

Figure 2: Change in bilirubin level (%)

Table 3: Duration of phototherapy (%)

Days	Group A (%)	Group B (%)	
≤ 3 days	19 (76)	5 (20)	
>3 days	6 (24)	20 (80)	p<0.05
Total	25 (100)	25(100)	

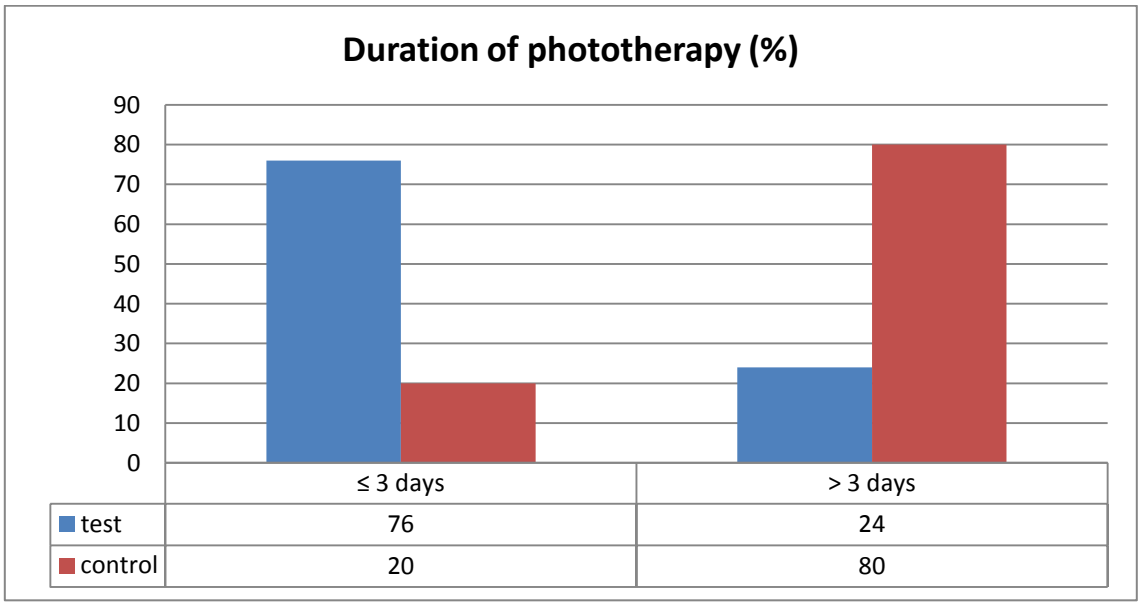

Figure 3: Duration of phototherapy (%)

Group A patients who received immunoglobulin required less days of phototherapy and duration of hospital stay was thus reduced as compared to group B in which stay was more than 3 days (table 3). Chi-square test p value <0.05, which is significant.

Total bilirubin was measured 4-6 hourly after intitiation of phototherapy till bilirubin decreased and then repeated in 8-12hours. For the easy understanding of difference in both the group mean total bilirubin was compared on admission and after 72hrs of hospital admission. There was significant decrease in group A at 72 hours, unpaired t test p <0.05 S.

Table 4: Mean level of total bilirubin on 0 hr and 72 hours of hospitalization

Time from admission	Group A	Group B	p value
0hrs	16.64 ± 1.37	16.96 ± 1.98	0.546
72hrs	12.04 ± 4.23	16.08 ± 2.45	0.006

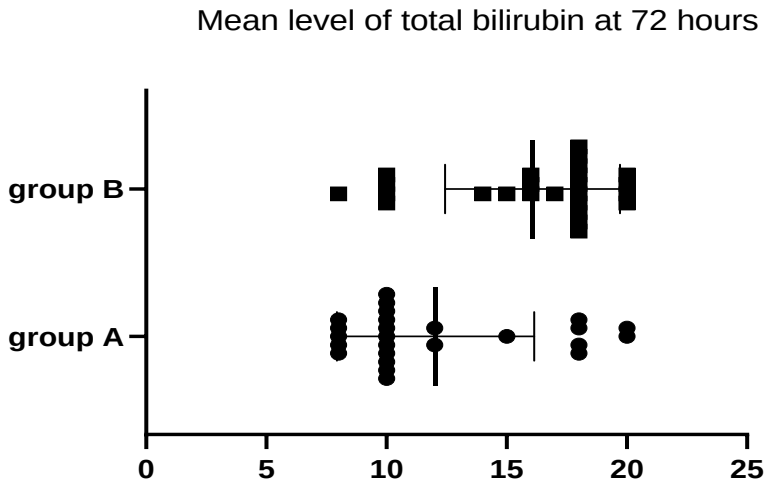

Fig: 4: Mean level of total bilirubin at 72 hours of hospitalization

Table 5: Exchange transfusion in both groups.

Exchange needed	Group A (%)	Group B (%)	
YES	3(12)	12(48)	p<0.05
NO	22(88)	13(52)	
Total	25(100)	25(100)	

In group A patients who received immunoglobulin treatment, only 12% needed exchange transfusion while on the other hand group B patients who were not treated with immunoglobulin needed more exchange transfusion 48 % (Table 4). Chi-square test p value <0.05, which is significant.

Figure 5: Exchange transfusion in both groups.

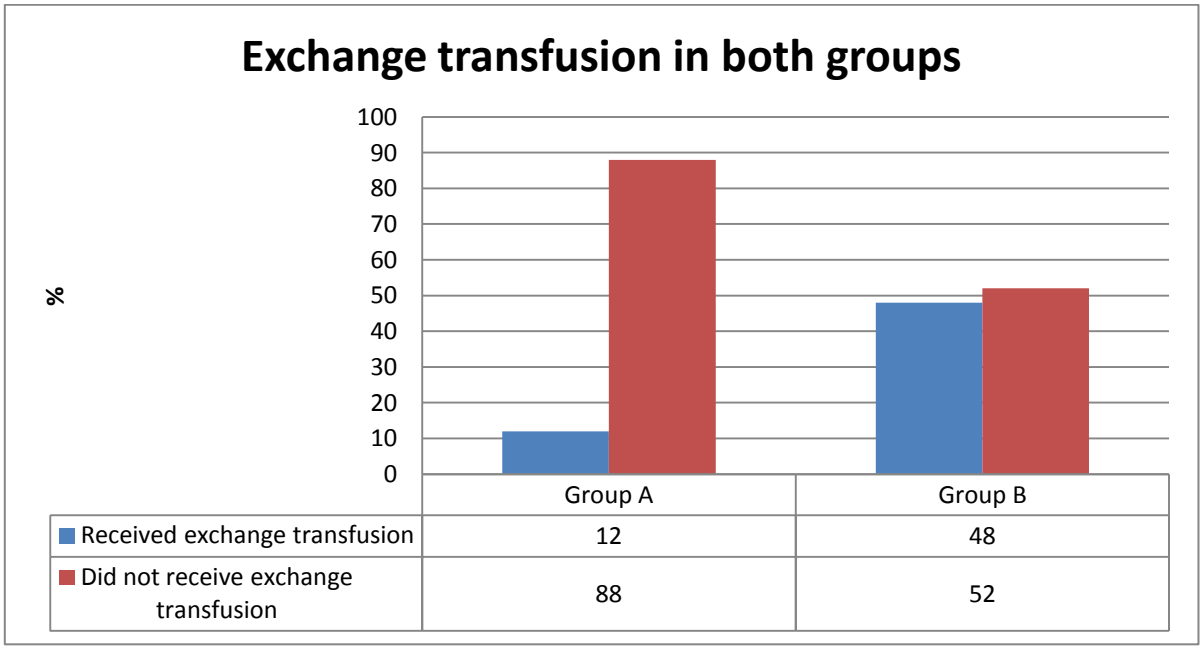

Table 6: Mean days of hospital stay

Group A	Group B
3.76 ± 1.28	4.8 ± 1.0

p = 0.0023, S.

Hospital stay was decrease in test group A compared to control group B.

Discussion

Early reduction of bilirubin levels will reduce the phototherapy session, requirement for the exchange transfusion and also stay duration in the hospital. All of these factors have significant effect on the morbidity and mortality of the neonates.[9-11]

Exchange transfusion carries a many risk like anaphylactic reactions, transmission of infections and risk of sepsis in patient. However these complications can be overcome with the introduction of immunoglobulin as it is evident from our study that immunoglobulin given in hemolytic disease of newborn reduced the need for exchange transfusion and as only 12% needed exchange transfusion. Present study showed that immunoglobulin reduced the hospital stay which is similar to the data of study by F Alpay et al, that duration of hospitalization in terms of hours were significantly shorter in IVIG group ($p < 0.05$)[12] .

Alpay et al. showed that, high dose of IVIG (1 g/kg) reduces hemolysis, serum bilirubin levels and risk of exchange transfusion in rhesus and ABO hemolytic disease on the other hand[12]; Girish et al. demonstrated that, low dose of IVIG (0.5 g/kg) was also found to be as efficacious as high dose IV IG in reducing the duration of phototherapy[13]. In the present study low dose IV IG was used and similar reduction in duration of phototherapy was found on test group.

Mukhopadhyay K et al. also Concluded Intravenous immunoglobulins is effective in decreasing the maximum bilirubin levels and the need for repeated exchange transfusions in Rh hemolytic disease of newborn[14].

Apart from these results, Smits-Wintjen concluded that prophylactic treatment with IVIG in rhesus hemolytic disease did not reduce the need for exchange transfusion or adverse neonatal outcomes[15]. While the present study shows decrease need of exchange transfusion on using IV IG.

Use of phototherapy, blood transfusion requirements will ultimately cause increased in mortality and morbidity.Considering all the issues in direct comparison with the expense on immunoglobulin appears important. Cost of immunoglobulin will be equal to or less than the expense of prolonged hospitalization.

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