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EFFICACY OF INTRAVENOUS IMMUNOGLOBULINS IN RH INCOMPATIBLE NEONATES

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ABSTRACT

Objectives: *To compare the efficacy of intravenous immunoglobulins in reducing the need for exchange transfusion in Rh incompatible neonates.*

Materials and Methods: *This Randomized Controlled Trial was conducted from 1st September 2021 to 31st August 2022 at Department of Pediatric Medicine, Khyber Teaching Hospital, Peshawar. A total of 92 Rh incompatible neonates having bilirubin more than 8mg/dl were included in the study. Randomization was performed through lottery method. All neonates received conventional intensive phototherapy given by air shield and Ohmeda lamps with white light having an intensity of 22 µW/cm/nm plus blue light of 32 µW/cm/nm. Extra fluids (10 mL per kg) was administered during the phototherapy session. Subjects in group A received conventional intensive phototherapy and IVIG single dose(1 gm/kg). In group B saline was given instead of IVIG. A change in bilirubin of 1mg was considered effective after 4 hours of starting treatment.*

Results: *Mean age of Group A was 15.369± 4.98 days in Group A while 17.782± 3.31 days in Group B. Mean gestational age at birth was 37.608±1.58 weeks in Group A and 38.173±1.71 weeks in Group B. Mean parity was 3.534±0.28 in Group A and 3.387±0.36 in Group B. Mean hospital stay in group A was 3.2±1.5days while 5.7±1.2 days in group B. In group A, efficacy was seen in 38 (82.6%) patients as compare to 26 (56.5%) patients in group B, resulting in significant reduction of exchange transfusions, duration of phototherapy session and hospital stay (P=0.006).*

Conclusion: *It is concluded that a IVIG administration in patients having significant hyperbilirubinemia of Rh incompatible neonates caused reduction in requirement for exchange transfusion ,decreased hospital and time duration of phototherapy treatment thus an effective and safe treatment.*

Key words: *Rh incompatible neonates, Intravenous immunoglobulin, phototherapy*

INTRODUCTION

Hemolysis of blood in the fetus and newborn is a condition in which there is immunologic hemolysis of fetal / neonatal red blood cells. It occurs usually with transplacental passage of maternal antibodies[1]. Antibodies such as anti A and anti B which develop after getting transfused with blood or pregnancy. This ultimately results in hemolysis of blood causing anemia or hyperbilirubinemia.[2] Hemolysis due to anti D is the significant reason behind perinatal morbidity and mortality. This Rh hemolytic disease is reduced by giving Rh IG antenataly and shortly after the birth. In western world ABO incompatibility is the main factor causing HDFN.[3] Other alloantibodies are also responsible for greater proportion of these cases. Tranfusion in these type of cases play an important role which necessitates timely diagnosis and close follow up. Maternal D alloimmunization has reduced from incidence of 14 to 1-2%.[4] Rh D alloimmunization reduced to 0.1% with antenatal immunoprophylaxis. ABO incompatibility is currently known to be

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the single main etiology of HDFN. In most of the developing countries , anti D antibodies still remains the common antibodies noticed in gravid women[5]. In a study by Safinaz A, et al shows the frequency of exchange transfusion of 15% in intravenous immunoglobulin treatment group as compare to 41% in control group, while mean duration of hospitalization was 27.9±18.7 hours as compare to 103.5±30.8 hours while mean duration of intensive phototherapy was 9.96±6.3 hours as compare to 35.5±27.3 hours in Rh incompatible neonates.[6]

The rationale of the study is that results of my study will pave the way for further research in this topic in our local population as no such study has been done before in our local population. Moreover, use of IVIG in Rh-incompatibility is usually neglected as it is costly. This study will help in recommending IVIG routinely where there are no affordability issues to prevent prolonged hospital stay and exchange transfusion. To get local data on this subject, it is planned to compare the efficacy of intravenous immune globulin to reduce exchange transfusions rate and compare the mean duration of phototherapy and hospitalization in Rh incompatible neonates.

To compare the efficacy of intravenous immunoglobulins in reducing the need for exchange transfusion in Rh incompatible neonates.

MATERIALS AND METHODS

This Randomized Controlled Trial was conducted from 1st September 2021 to 31st August 2022 at Department of Pediatric Medicine, Khyber Teaching Hospital, Peshawar. A total of 92 Rh incompatible neonates having bilirubin more than 8mg/dl were included in the study. Randomization was performed through lottery method. All neonates received conventional intensive phototherapy given by air shield and Ohmeda lamps with white light having an intensity of 22 µW/cm/nm plus blue light of 32 µW/cm/nm. During phototherapy, extra fluids of 10 mL per kg was given. Subjects in group A are given conventional intensive phototherapy and IVIG single dose(1 gm per kg). In group B saline was given. Data was recorded for efficacy.

RESULT

Mean age of Group A was 15.369± 4.98 days and 17.782± 3.31 days in Group B. Mean gestational age at birth was 37.608±1.58 weeks in Group A and 38.173±1.71 weeks in Group B. Mean parity was 3.534±0.28 in Group A and 3.387±0.36 in Group B as shown in Table-I. Most of the patients were male in both groups, group A (69.6%) and in group B (80.4%) as shown in Table-II. Mean hospital stay in group A was 3.2±1.5days while 5.7±1.2 days in group B. In group A, efficacy was seen in 38 (82.6%) patients as compare to 26 (56.5%) patients in group B, resulting in significant reduction of exchange transfusions, duration of phototherapy session and hospital stay (P=0.006) (Table-III).

DISCUSSION

The management of isoimmune hemolysis is intensive phototherapy in combination with exchange transfusion despite of phototherapy, still cause bilirubin encephalopathy. Treatment of neonates with IVIG has been recommended as an alternative management option having HDFN. Woman who has not received immunopropylaxis(IP) and RhD negative has a risk of 16% to become immunized in every pregnant lady resulting in RhD positive neonate[7]. The potentially immunizing events occur during pregnancy and delivery by vaginal route or by Caesarean section. Successful postnatal IP having reached 98–99% as a result of anti-D immunization[8,9]. The potentially immunizing events that occurs during the pregnancy has not been eliminated in non-sensitised RhD negative women. The reason is unrecognised bleeding, which occurs during the third trimester of pregnancy and results in silent immunization[10,11]. Routine antenatal prophylaxis in pregnant ladies in the last trimester, leads to further reduction of the risk of immunization from 1 to 0.21%[12]. Similar results are noted in a meta-analysis of multiple studies which showed absolute reduction of risk from 0.9 to 0.32%[13].

The intended study include full term neonates with Rh incompatibility. This study support the evidence based recommendations of the American Academy of Pediatrics.[14-15] This study results also shows that treatment with administration of IVIG showing fewer newborns/neonates which need exchange transfusion in comparison to those who are given phototherapy session alone. The IVIG antagonizes reticuloendothelial receptor sites thus reducing hemolytic process. The prevention of destruction of red blood cells of neonate in the ex-

travascular compartment by maternal antibodies is acquired transplacentally.[16] The competitive action of isoantibodies and IVIG has led us to the conclusion that for effectivenss of IVIG which must be started right after when isoimmune hemolytic anemia is confirmed.[17] The administration of IVIG to prevent exchange transfusion treatment in hemolytic disease of newborn was reported in many clinical trials and the results were conflicting. New born having ABO or Rh hemolytic disease were administered with single dose IVIG resulted in reduced need for exchange transfusion.[18] Standard low-dose of IVIG (0.5gm/kg) had the same effectiveness as high dose (1gm/kg) in terms of reducing the time duration of phototherapy sessions and hospital stay[19]. Multiple doses of IVIG when administered caused less exchange transfusion treatments in ABO incompatibility and Rh HDFN[20]. The intended study shows that with administration of IVIG cause a marked reduction in the time duration of intensive phototherapy session which is consistent with all the other trails conducted.[21,22]. Hence showing the benificial of IVIG in the management of hemolysis in new born. Damage to retina, skin changes , diarrhea and bronze baby syndrome are significantly reduced by minimizing phototherapy exposure.[23] IVIG administered in dosage of 0.51gm/kg for two days to eight Rh isoimmunized babies. Need for exchange transfusion was significatly reduced. Further time duration of phototherapy was comparable in both groups.[24]

Table 1: Demographics

Demographics	Mean±SD (Group-A) n=46	Mean±SD (Group-B) n=46
Age (years)	15.369± 4.98	17.782± 3.31
Gestational age at birth (weeks)	37.608±1.58	38.173±1.71
Parity	3.534±0.28	3.387±0.36

Table 2: Frequency and %age of patients according to both genders

Gender	n=46	n=46
	Group A	Group B
Male	32 (69.6%)	37 (80.4%)
Female	14 (30.4%)	9 (19.6%)
Total	46 (100%)	46 (100%)

Table 3: Comparison of efficacy

Efficacy	n=46	n=46	P Value
	Group A	Group B	
Yes	38 (82.6%)	26 (56.5%)	0.006
No	8 (17.4%)	20 (43.5%)	
Total	46 (100%)	46 (100%)	

CONCLUSION

It is concluded that a IVIG administration in patients having significant hyperbilirubinemia of Rh incompatible neonates caused reduction in requirement for exchange transfusion ,decreased hospital and time duration of phototherapy treatment thus an effective and safe treatment.

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