Original Article

Frequency of Kernicterus in Rh Incompatibility after Receiving Effective Phototherapy and Intravenous Immunoglobulin Therapy

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ABSTRACT

Objective: To compare Frequency of Kernicterus in Rh incompatibility after receiving effective phototherapy and Intravenous immunoglobulin therapy.

Study Design: Randomized Controlled Trial study

Place and Duration of Study: This study was conducted at the Special Care Baby Unit, Department of Pediatrics Medicine, HMC, Peshawar from January, 2021 to June, 2021.

Materials and Methods: A total of 152 neonates with jaundiced due to Rh incompatibility and fulfilling the inclusion criteria were included in the study and were randomly assigned to two groups A and B. Phototherapy and Immunoglobulin therapy was used for group A and B respectively. The patients were observed for response to therapy. .Data was analyzed by SPSS version 23.

Results: Majority of the individuals were male that is 71.1% in group B while females were more (65.8%) in group A. mean age of neonates in group A (phototherapy) were 13.67±6.46 days and group B (IVIG) were 14.18±5.94 days respectively. Mean duration of jaundice in group A was 3.76±1.24 days compared to group B 3.78±1.11 days. Mean gestational age was observed as 35.63±2.33 and 36.53±1.99 weeks at birth.

Kernicterus was more prevalent in group A (69.7%). Gestational age was found to be significantly ($p<0.05$) associated with kernicterus. Intravenous immunoglobulin treatment was found more effective ($p<0.05$) therapy.

Conclusion: Immunoglobulin therapy is more effective in reducing the number of Kernicterus in neonates with hemolytic diseases of the newborn.

Key Words: Neonatal Jaundice, Kernicterus, Phototherapy, Immunoglobulins

Citation of article: Ali S, Khan MA, Munir A, Afridi MA, Siddiqi WA, Ali K. Frequency of Kernicterus in Rh Incompatibility after Receiving Effective Phototherapy and Intravenous Immunoglobulin Therapy. Med Forum 2023;34(2):11-14.

INTRODUCTION

Neonatal jaundice is one of the common conditions of the admission in neonates. Kernicterus is one of the neurodevelopmental complications of neonatal jaundice in these patients especially having severe hyperbilirubinemia (>20 mg/dl)[1-3].

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Received: June, 2022
Accepted: November, 2022
Printed: February, 2023

There are several other factors which can add on to development of kernicterus in these neonates including low gestational age, sepsis, cephalohematoma and hemolysis[4,5]. Bilirubin caused neurodevelopment complication is quite common in low resource countries as compared to high income one due to either limited resources and facilities availability or inability to deliver these facilities in time[6]. Acute bilirubin encepaholopathy is caused by acute rise in the serum bilirubin and is characterized by inability to take feed, lethargy, increase or decrease tone, cry becomes high pitched and patients may acquire opisthotonus posture and seizures and even death if not treated timely[7,8]. If patient having kernicterus (bilirubin encephalopathy) survive initially experience convulsions but later on if a patient who survive to bilirubin encephalopathy survive and experience convulsion other causes should be ruled out. A typical kernicteric facies is the combination of setting sun eyes collier sign and facial dystonia.

The frequency of bilirubin encephalopathy is high especially in patients with Rh incompatibility. Studies have shown that phototherapy have decreased the incidence of kernicterus upto 10%[9] while kernicterus

have been observed 0 in patients with immunoglobulin therapy[10].

Intravenous immunoglobulin therapy has been found one of the effective therapeutic tools in the treatment of Rh incompatibility causes hemolytic disease of newborn. Due to limited regional studies availability on this topic the study was considered for confirming the efficacy of immunoglobulin.

MATERIALS AND METHODS

This randomized controlled trial was conducted at Nursery Unit, department of pediatrics Medical teaching instituted Hayatabad Medical complex, Peshawar from January to June 2021. A total of 152 neonates with neonatal jaundice were included in the study fulfilling the inclusion criteria. Patients were randomly allocated to Group A and B receiving phototherapy or immunoglobulin respectively. Non-probability consecutive technique was used for sample collection. Neonates having jaundice for five days, Rh incompatible, gestational age of 32 to 39 weeks and both gender were included in the study. Low birth weight neonate (<2500 grans), with history of drug ingestion, and having other causes of jaundice than Rh incompatibility were excluded from the study.

A total number of 152 Rh incompatible jaundiced neonates admitted to nursery unit of the department with their guardian's consent and permission of Institutional Ethical Board were included in the study. The patients demographic data including name, age, gender, duration of jaundice, family history of kernicterus, gestational age and weight at birth and informed consent ensuring confidentiality and no risk to patient was explained to the patients and attendants. The patients were randomly assigned to group A and B on lottery method. Both group A and B had 76 patients who received phototherapy and immunoglobulin therapy respectively. Effective and double phototherapy was given to group A till the serum bilirubin decreased to safe limits below phototherapy level. Group B neonates were given Intravenous immunoglobulin 500 mg /Kg of the body weight of the neonate in infusion form over 2-4 hours of duration. A total of three doses were given each 12 hours apart. Exchange transfusion was in the treatment consideration where the jaundice was clinically (jaundiced up to soles) and/or biochemically (≥20 mg/dl) found in the exchange range. Breast feeding and hydration was adequately maintained. The data was analyzed by SPSS (Statistical Package for social science) version 23. For qualitative variables including gender, kernicterus history in family and gestational age frequency and percentages were calculated. For quantitative variables like age, duration of jaundice, gestational age at birth and weight Mean and standard deviation was calculated. Chi square test was applied to compare kernicterus in both groups and p value of ≤0.05 was taken as statistically significant. Stratification was done for age, gender, duration of jaundice, family history of kernicterus and gestational age at birth. Post stratification chi square test was used for both groups and p value of ≤0.05 was considered significant statistically.

RESULTS

Majority of the individuals were male that is 71.1% in group B while females were more (65.8%) in group A. mean age of neonates in group A (phototherapy) were 13.67±6.46 days and group B (IVIG) were 14.18±5.94 days respectively. Mean duration of jaundice in group A was 3.76±1.24 days compared to group B 3.78±1.11 days. Mean gestational age was observed as 35.63±2.33 and 36.53±1.99 weeks at birth.

Kernicterus was more prevalent in group A (69.7%). Gestational age was found to be significantly ($p<0.05$) associated with kernicterus. Intravenous immunoglobulin treatment was found more effective ($p<0.05$) therapy.

Prevalence of kernicterus is given in table 1. Stratification of kernicterus according to gender, age and gestational age is has been given in tables 2,3 and 4 respectively. Efficacy of treatment has been documented in table 5.

Table No.1: Prevalence of Kernicterus (n=152)

Variables		Frequency (%)/Mean±SD	
		Group A	Group B
Kernicterus	Yes	53 (69.7)	41 (53.9)
	No	23 (30.3)	35 (46.1)

Table No.2: Stratification of Kernicterus among Gender (n=152)

Variables		Frequency (%) Kernicterus		P-value
		Yes	No	
Gender	Male	61	43	0.28
	Female	33	15	

Table No.3: Stratification of Kernicterus among Age (n=152)

Variables		Frequency (%) Kernicterus		P-value
		Yes	No	
Age	0-14 days	56	38	0.40
	15-28 days	30	28	

Table No.4: Stratification of Kernicterus among Gestational Age at Birth (n=152)

Variables	Frequency (%) Kernicterus		P-value
	Yes	No	
Gestational age	35.74±2.22	36.62±2.09	**0.01**

Table No.5: Efficacy of Treatment

Variables		Frequency (%)		P-value
		Kernicterus		
		Yes	No	
Treatment	Group A	53	23	**0.03**
	Group B	41	35	

DISCUSSION

Severe unconjugated bilirubinemia causes permanent damage to brain tissue and results in either death or lifelong morbidity of the affected individuals[11-13]. Intravenous immunoglobulins have been found effective in the treatment of this notorious condition caused by blood group incompatibilities.

In our study we found though the mean gestational age was non-significant among the both groups yet gestational age was significantly associated with the prevalence of kernicterus in all neonates. Studies around the globe have documented no significant difference of the efficacy of IVIG in all gestational age neonates Khan et al[14] has given almost the same result of statistical insignificance between the two groups in terms of the gestational age. Maryam S et al[15] and Gamze D et al[16] respectively in their studies concluded that there was no significant statistical difference between the two groups in the treatment of jaundiced neonates.

We also found no significant statistical difference in the two groups in terms of gender and weight of the neonates in our study. Almost the same results were shown by Manar A et al[17] in there study on intravenous immunoglobulin as adjacent treatment with phototherapy in isoimmune hemolytic disease of the newborn. They documented non-significant statistical difference between the two groups in regard to their birth weight and gender.

In the current study there was no statistically significant difference between group A and group B in gender distribution, weight and family history. These findings are in line with the results of Shaimaa WIFE et al[18], who concluded that there were no difference inthe distribution of gender, birth weight, infant group, and family history.The results of the current study were also in agreement with Zwiers Cet al[19], who showed no significant difference as regards weight, and gender.

In our study we found better efficacy and result in neonates group who were treated with immunoglobulin as compared to the group treated with the effective phototherapy. Almost the same results have been documented by previous study who compared the efficacy of the two groups i.e. phototherapy and intravenous immunoglobulin by Nasseri F et al in Rh and ABO isoimmunization[20].

CONCLUSION

Intravenous immunoglobulin therapy is more effective than phototherapy in neonates with isoimmune hemolytic jaundice especially Rh and ABO isoimmune hemolytic anemia.

We recommend larger scale studies encouraging use of intravenous immunoglobulin in the management of jaundiced neonates with isoimmune hemolytic disease of the newborn. In severe cases a combination of both intravenous immunoglobulin and effective phototherapy may be more fruitful.

Author's Contribution:

Concept & Design of Study:	Saima Ali
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Revisiting Critically:	Saima Ali, Muhammad Aqeel Khan
Final Approval of version:	Saima Ali

Conflict of Interest: The study has no conflict of interest to declare by any author.

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