Original Research Article

Prognostic value of peripheral blood eosinophil count on first day of infancy in the incidence of neonatal hyperbilirubinemia

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ABSTRACT

Background: Neonatal jaundice is one of the most common problems in the neonatal period. Eosinophilia is common in preterm and term newborns, and it is considered when the absolute count of eosinophil is ≥ 500 cell/mm^3. It is thought that there was some relationship between hyperbilirubinemia and increasing of blood eosinophil count in newborns hospitalized by jaundice. The aim of this study was to determine the prognostic value of peripheral blood eosinophil count on first day of infancy in the incidence of neonatal hyperbilirubinemia.

Methods: 150 newborns with gestational ages of 35-40 weeks, born in Ardabil city hospital, were engaged in this study. After obtaining the parents' consent, getting patients biography and their physical examination, we got a blood sample from umbilical cord of newborns to measure differential count of white blood cells. The neonates were observed up to 28 day followed. Then, second blood test conducted for the purpose of measuring serum level of bilirubin. Data were analyzed by statistical methods in SPSS version 19.

Results: Various group of age, sex, blood type and gestational age showed no significant difference in their eosinophil rate. Total serum bilirubin doesn't had a significant relationship with gestational age, sex, type of delivery and major or minor blood groups of neonates.

Conclusions: Results showed that there was no significant relationship between the amount of eosinophil in newborn umbilical cord and total serum bilirubin. So, we could say that newborns eosinophil count isn't a good criteria for predicating the appearance of neonate hyperbilirubinemia.

Keywords: Jaundice, Bilirubin, Eosinophil, Neonatal period, Umbilical cord

INTRODUCTION

Eosinophils are a type of blood granulocyte that their number different according to age, sex, race, and ethnicity but typically form only 2-4% of normal blood leukocytes. Eosinophil function in newborns is not clear but they had typically role in allergic and parasitic reactions, phagocytosis of immune complexes, and modulation of inflammatory responses. Neonatal eosinophilia is considered when the absolute count of eosinophils is ≥ 500 cell/mm^3 and divided in three groups such as: mild (1500-3000), moderate (3000-5000) and sever ≥ 5000 cell/mm^3. Eosinophilia is a common finding in preterm and term infants and may not require treatment.[1-4]

The importance of increasing eosinophils is in granules containing their toxin because release of these toxins in the long term deal to irreversible effects and side effects and limiting the physiological activity of other organs such as nerves, muscles, heart, digestion, breathing, endocrine and others. In addition, in time of suddenly release of these toxins, the disruption of other systems can be very deadly.[5] There are various assumptions about eosinophilia in infants included: Maternal related stress as a result of reducing levels of circulating adrenal

steroids such as cortisol, autoimmune diseases, congenital, genetic diseases, allergic reactions to the antigens of the body through upper airways and oral pathways, invasive procedures such as venipuncture and endotracheal intubation, various infections (parasitic, bacterial, viral, fungal), using antibiotic, injection of blood products, eosinophilic leukemia, hyporosinophilic syndrome, chronic lung disease, feeding of L-tryptophan supplements by the mother during pregnancy.[1-5] Neonatal jaundice is the yellowish skin and sclera in neonates which caused by hyperbilirubinemia.

Hyperbilirubinemia is one of the most prevalent findings in the first days of birth, which is benign and was seen physiologically in about 60% of term and 80% of preterm neonates. Neonatal hyperbilirubinemia is occur when the total bilirubin level reach to greater than 5 mg/dl.[6] In normal conditions, the amount of indirect bilirubin in the umbilical cord blood serum is 1-3 mg / dl and then increase by speed less than 5 mg / dl in 24 hours. Therefore, jaundice appears on the second and third days after birth and usually, on the third to fourth days, it increases slightly and in the fifth to seventh days of birth reduced to less than 2 mg / dl. The jaundice associated with these changes is called physiologic jaundice and its cause due to the breakdown of red blood cells with the transient limitation of bilirubin conjugation by the neonate's liver. Physiological jaundice in term and preterm newborns is diagnosed by getting history, clinical findings and laboratory data. Other factors for pathological jaundice included: familial history of hemolytic disease, hepatosplenomegaly, vomiting, lethargy, poor nutrition, apnea, bradycardia, clear stool, dark and positive urine based on bilirubin and signs of encephalopathy caused by hyperbilirubinemia.[7-10]

Risk factors for hyperbilirubinemia are: Incompatibility of maternal and fetal blood group, maternal diabetes, premature infants, race, medications, height, polycythemia, male gender, trisomy 21, cephalohaematoma, breast feeding, weight loss, delay in meconium excretion and history of jaundice in the family and in most cases, jaundice occurs without any particular causes.

The causes of this disorder are classified into three groups: excessive bilirubin production, decreased conjugated bilirubin or decreased bilirubin excretion due to biliary obstruction. Accordingly, hyperbilirubinemia is physiologically associated with breast feeding or is considered pathologically.[11-12]

METHODS

This descriptive analytical study was done on 150 newborns with gestational age greater than 35 weeks who were admitted to the hospital of Ardabil due to jaundice from Jan 2016 to the end of June 2017. CBC Diff, Blood group (ABO & Rh) tests has been done for infants. Then infants was followed up during a 24 hour in hospital and

in the case of jaundice, the second experiment was performed for measure total and direct bilirubin. After discharge of the newborn from the hospital, the neonate was followed up to 28 days and in the case of jaundice, the second experiment was conducted for direct and total bilirubin due to ethics and missing veins in the baby, most of infants at 2-7 days of age and during routine screening of hypothyroidism the second experiment was done for total and direct bilirubin. Data from umbilical cord blood test in the first day of birth at the beginning of the study and other test results in the second and follow up to the age of 28 days, all of data analyzed by statistical methods in SPSS version 19. Infants with gestational age less than 35 weeks were excluded from the study if they were not satisfied with the condition and the underlying eosinophilic illness in their parents (especially the mother).

RESULTS

72 (48%) of newborns were boys and 78 (52%) were girls. Of them, 79 (53%) were born by cesarean delivery and 116 (77%) infants had weight 2500-4000 gr and 52 (34.7%) had a blood type A and 135 (90%) had positive Rh (Table 1).

Table 1: Demographic data of study newborns.

Variables		n	%
Sex	Girl	78	52
	Boy	72	48
Type of delivery	Cesarean	79	52.7
	Vaginal	71	47.3
Blood type	a	52	34.7
	b	39	26
	ab	52	34.7
	o	7	4.7
Blood Rh	+	135	90
	-	15	10
Weights of newborns	<2500	8	6
	2500-4000	116	77
	>4000	26	17
Gestational age	35-37	70	46.7
	38-41	80	53.3

Of all newborns, 26 cases were hospitalized due to jaundice, of which 23 (88.5%) were under phototherapy and 3 (11.5%) underwent transfusion. The majority of newborns attending in second bilirubin test at the age of 3 day (n=49, 32%).

According to the result of laboratory tests, the rate of eosinophil in newborns was in range 1-11% or in range 58-2530 cell/mm^3 (Table 2).

The mean of total bilirubin in newborns was 10.6±4.5 mg/dl (range: 4-23.8) and direct bilirubin was 0.5±0.3 mg/dl (range: 0.2-1.9).

Table 2: Differential count of neonatal umbilical cord blood cells indexes.

Statistical indexes	WBC	Neutrophil (%)	Lymphocyte (%)	Monocyte (%)	Eosinophil (%)	Hemoglobin (mg/dl)	Platelet
Mean	13040	48.91	42.07	5.06	3.96	16.45	232660
SD	4342.77	11.83	11.70	2.35	2.27	1.43	102372.38
4.5 mg/dl (range min)	5800	17	21	1	1	9	85000
max	23000	72	80	12	11	18.7	532000

Table 3: Rate of eosinophil by age, delivery type, gestational age and blood type.

Variables		Mean±SD	P value
Sex	Boy	3.8±2.1	0.6
	Girl	4.5±2.4	
Type of delivery	Cesarean	4.1±2.2	0.2
	Vaginal	3.7±2.2	
Blood type	a	3.7±1.8	0.8
	b	4±2.7	
	ab	4±2	
	o	4.1±2.3	
Blood Rh	+	4±2.3	0.1
	-	3.2±1.8	
Gestational age	35-37	4.1±2.1	0.2
	38-41	3.6±2.8	

Table 4: Rate of total bilirubin by age, delivery type, gestational age and blood type.

Bilirubin total (mg/dl)		Mean±SD	P value
Sex	Boy	11.1±4.8	0.2
	Girl	10.3±4	
Type of delivery	Cesarean	10.7±4.2	0.7
	Vaginal	10.8±4.8	
Blood type	a	10.9±4.3	0.5
	b	10.9±4.8	
	ab	12.2±4.4	
	o	12.2±4	
Blood Rh	+	10.4±4.4	0.09
	-	12.5±4.6	
Gestational age	35-37	10.8±4.3	0.9
	38-41	10.5±4.3	

Table 5: Relationship between eosinophil and bilirubin total

Eosinophil (%)	n	Mean	SD	P value
1	18	11.356	4.89	
2	29	10.748	4.89	
3	31	10.465	3.96	
4	18	9.761	3.18	
5	15	10.873	5.02	
6	18	9.372	3.84	**0.6**
7	7	11.914	2.95	
8	9	12.500	6.37	
9	2	8.850	5.30	
10	2	8.500	0.00	
11	1	23.000	0	
Total	150	10.67	4.48	

There was no significant difference in the rate of eosinophil between age, sex, gestational age and blood type (Table 3).

There was no significant difference in the rate of bilirubin total between age, sex, gestational age and blood type (Table 4).

There was no significant relation between eosinophil rate and total bilirubin in neonatal period (1-28 days) (Table 5).

DISCUSSION

In this study, eosinophilia in umbilical cord blood of newborns was a common finding in the study group but in newborns who were born with cesarean delivery and had gestational age ≥40 weeks, there was a higher incidence, but there was no difference in the eosinophilic prevalence in different weight and according to the newborn's blood type. All infants born with eosinophilia were followed up during the neonate period and did not find any problems until 28 days old, and even the incidence of jaundice in infants with moderate to severe eosinophilia in their umbilical cord blood was not significantly different with other infants. Therefore, it seems that eosinophilia is a common finding in infants and may be not even require to treatment. Also, the prevalence of jaundice in boys and infants with more than 3 day birth was more but there was no difference in the prevalence of jaundice in hospitalized infants based on gender, age, weight and blood type. Hyperbilirubinemia can also be observed physiologically in all newborns, especially during the first week due to serum bilirubin levels, may be no need for special action and could say to parents that during time the jaundice will be reduced. The mean of neonatal bilirubin and eosinophil cord blood were not significantly different in terms of gestational age, gender, delivery type, major and minor blood groups. Also, the range of changes in the percentage of cord blood eosinophil count is between 1% -11% which was similar the rate of bilirubin in different percentages and there was no significant correlation between cord blood eosinophil count and neonatal bilirubin in 1-28 days of infancy. In a study by Aydin et al in Turkey, the serum level of eosinophil could be affected by the serum bilirubin level and phototherapy and in neonates with sever hyperbilirubinemia which treated with phototherapy, the serum levels of eosinophil were increased.[13]

In this study, the relationship between cord blood eosinophil and serum total bilirubin during neonatal period was studied in 150 term neonates with gestational age ≥35 weeks and there was no significant relationship. In a study in 2004, Sandra et al showed that the prevalence and severity of eosinophilia was significantly correlated with Prematurity and influenced by factors such as infection, blood transfusion and necrotizing enterocolitis.[14]

In the study of Hye and et al in South Korea, differential counting of blood cells in newborns with a range of 0.7-7% in the level of eosinophil cord blood.[15]

In this study, in range of changes in cord blood eosinophilia was between 1-11%. These changes can be due to race, geography and lifestyle of pregnant mothers and maternal diseases during pregnancy that the relationship between the count of eosinophil count of umbilical cord blood with the geographical areas and underlying diseases of the mother and the infant should be done in a study with big sample size.

CONCLUSION

The results showed that there was no significant relationship between the number of neonatal umbilical cord blood eosinophils and serum total bilirubin levels in infants. Therefore, eosinophilia on the first day of infancy is not a good measure to predict the incidence of hyperbilirubinemia during infancy. It is recommended that all infants of mothers with different gestational age and underlying illness should also be included in the study. Also it is recommended that the underlying illnesses of the parents, their residence place and lifestyle be assessed in the future.

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