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Original Article

The Combined Effect of Injectable Recombinant Erythropoietin and Oral Iron on the Hematopoiesis of Extremely Overweight Neonates

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Abstract

Erythropoietin is the major regulating blood flow hormone which can be effect on hematopoiesis of premature infants. The aim of this study was to examine the effectiveness of intravenous recombinant erythropoietin regimen associated with oral iron in hematopoiesis of premature infants. This is a randomized clinical trial that has been done on 80 (40 persons in each group) very low and premature infants. First group received intravenous recombinant erythropoietin (with 400 units per kg weight in day (3 days in week)) associated with iron drip and second group as control group iron administrated only. All information were entered in a checklist and analyzed by statistical methods in SPSS.16. In case group 62.5% and in control group 60% were boy. The average weight of cases was 1273.8 198.4 gr and controls were 1223.8 217.5 gr. The injection of erythropoietin could be significantly prevent the decreasing of hemoglobin and ferritin and leads to increase in reticulocytes levels in cases but not have significantly on Iron level. Results showed that injection of erythropoietin in premature infants deal to increasing reticulocyte, Hb and ferritin levels in case group and the results was similar with studies in other places.

Keywords: Erythropoietin, iron therapy, VLBW infant, hematopoiesis.

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Introduction

Prematurity-induced anemia is a type of normocytic anemia with low reticulocyte number. It usually appears two weeks after birth and reaches highest intensity during the second month. It is usually identified through a reduction in reticulocyte and an inadequate response to erythropoietin in many premature neonates who frequently need blood transfusion.

Erythropoietin is an important factor in hematopoiesis from fetal period up to neonatal period and maturity and leads to erythrocyte division and its greater longevity through inhibiting apoptosis of erythroid precursors.

Previously, erythropoietin was assumed to be merely a cytokine affecting hematopoiesis, but recently its receptors have been proven to be very diverse and of utility in the evolution of vascular endothelial cells, digestion system, and human brain. Recombinant erythropoietin is effectual in treatment, prevention, and stabilization of hemoglobin and hematocrit levels in premature neonates and prevents a need for blood transfusion. The objective of the present study was to determine the effectiveness of injectable recombinant erythropoietin with oral iron in the perfusion of premature neonates.

Materials and Methods

This study was a randomized double-blinded clinical experiment, and the research context was NICU unit of Bou-Ali and Alavi hospitals in Ardabil city. Participants were 80 hospitalized neonates who weighed below 1500 g. They were randomly divided into two groups, each including 40 individuals. The first group, i.e., experimental group, received injectable recombinant erythropoietin with a dosage of 400 IU per kilogram of weight in a day (three days a week) and oral iron, and the second group, i.e. control group, merely received oral iron. At study outset hemoglobin and serum iron levels as well as reticulocyte and serum ferritin percentages were measured for both groups, during discharge, and three months after discharge. The data were, then, analyzed in SPSS software, version 16 through performing statistical tests including t-tests, chi-squares, repeated-measures tests, and descriptive statistics. Results were presented in tables and figures. Significance level was set at less than 0.05.

Results

25 neonates (62.5%) in experimental group and 24 (60%) in control group were boy. Most of mothers were in 20-25 age groups. Results showed that all of variables is matched in two groups (Table 1).

Table 1: Demographic data of neonates in two study groups

Variables		Experimental	Control	p-value
Sex	Boy	25(62.5)	24(60)	0.8
	Girl	15(37.5)	16(40)	
Mother Age Groups				0.56
<20		8(20)	7(17.5)	
20-25		18(45)	23(57.5)	
25-30		5(12.5)	2(5)	
>30		9(22.5)	8(20)	
25.8± 8.3		24.5±5.6		
Neonates Weight		1273.8±198.4	1223.8±217.5	0.68
Apgar Score				0.26
<4		2(5)	4(10)	
4-8		23(57.5)	19(47.5)	
>8		15(37.5)	17(42.5)	

The mean of hemoglobin level was 16.5±1.28 mg/dl for control group and 16.8±1.6 mg/dl for experimental group. These levels decreased for both groups three months after discharge, and the rate of decreasing was statistically significant for both groups (figure 1). The mean of serum iron was 94.7±18.8 µg/dl for control group and 88.2±12.1 µg/dl for experimental and the rate of decreasing was statistically significant for the control group, but non-significant for experimental group after three mount late (figure 2). The mean of ferritin level was 104.5±23 in control group and 133.7±34.4 in experimental group at study outset. In control group 25 neonates (62.5%) had ferritin of 25-100 ng/ml, and in experimental group 29 neonates (72.5%) had 101-200 ng/ml ferritins. These numbers decreased three months after discharge and the decrease was statistically non-significant for the experimental group but significant for control group (figure 3). At study outset, the mean percentage of reticulocyte was 7.5±4 for control group and 9.8±3.5 for experimental group. At study outset, most neonates, 87.5% in experimental group and 60% in control group had a reticulocyte level higher than normal which decreased three months after discharge, and the rate of decreasing was statistically significant for both groups (figure 4). During discharge, 77.5% of participants in the experimental group had normal hemoglobin level, and 60% of those in the control group had a decreased level of hemoglobin. Hemoglobin level had decreased in both groups due to physiologic anemia which usually happens in neonates, but the decrease was greater for control group. The results of repeated-measured tests revealed that hemoglobin and ferritin levels as well as reticulocyte percentage had significantly changed during targeted phases but that serum iron level had minimally changed (Table 2). In the experimental group 13 neonates (32.5%) and in the control group 23 cases (57.5%) needed transfusion and received blood. The difference between the two groups was statistically significant in this regard (P=0.024).

Table 2: Change of blood results in groups in all study times

Variables	Time study	Case	Control	P-Value
Hb	Start of study	16.8	16.5	0.001
	Discharge	13.7	12.7	
	Three mount late	13.1	9.4	
Iron	Start of study	88.2	94.7	0.14
	Discharge	82.3	81.1	
	Three mount late	86.1	69.9	
Ferritin	Start of study	133.7	104.5	0.001
	Discharge	124.2	91.8	
	Three mount late	130	74.3	
Reticulocyte	Start of study	9.8	7.5	0.001
	Discharge	2.7	2.2	
	Three mount late	2.1	1.5	

Discussion

The present study revealed that 400 units of injectable recombinant erythropoietin per kilogram of weight in a day (3 days a week) significantly increased reticulocyte number and prevented an increase of ferritin and hemoglobin levels in premature neonates with low birth weight. Three months after discharge, mean serum level of ferritin was higher in erythropoietin group (130) than control (75.3), and the need for transfusion significantly decreased in erythropoietin group. Likewise, Ballin *et al.*, in a clinical experiment, found that reticulocyte count was higher in erythropoietin group (8.6%) than in control group

(4%). Similarly, Yeo *et al.,*'s study suggested that 750 units of erythropoietin per kilogram of weight of premature preterm neonate induced an increase in reticulocyte and hematocryt levels compared to the control group, but it induced no significant change in the amount of received blood in comparison to control group. In a similar vein, Halperin *et al.,*'s study disclosed that erythropoietin with a weekly dosage of 75-300 U/kg increased reticulocyte number, improved anemia, and heightened reticulocyte volume during treatment by 49%.10 Whitehall *et al.,* also reported that after treatment of preterm neonates with lso07 49.704 212.96]TJETQ369.07 49.7srt033.3e556.54 Tm[tre)5(a)4(tm)-342g

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