Iranian J Publ Health, Vol. 32, No. 4, pp.64-67, 2003

Retinopathy of Prematurity and Blood Transfusion Protocols

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Abstract

To determine the role of blood transfusion protocols on retinopathy of prematurity (ROP), a prospective cohort study on 57 premature infants under 1501 grams birth weight was performed. Fourteen day-old infants were divided into two groups randomly. Infants in group 1 (n=27) received packed red blood cell transfusion only if specific medical signs were met and their hematocrit level was under 30%. Infants in group 2 (n=30) received blood transfusion to maintain their hematocrit level > 40% regardless of their signs. All infants had an eye examination by indirect ophthalmoscopy from 28 to 40 days of life for detecting ROP. We did not find any significant difference in ROP incidence between both groups.

Keywords: *Retinopathy of prematurity (ROP), Blood transfusion, Premature neonate*

Introduction

Retinopathy of prematurity (ROP) is a serious complication of retinal vascular development in premature, very low birth weight infants(1-3) The incidence of ROP increases with decreasing gestational age, so that up to 90% under 26 weeks gestational age infants suffer from some degrees of ROP(4). As with technical improvement more premature infants survive, the overall incidence of ROP has not changed recently (5). In industrialized countries, ROP accounts for between 6-20% of childhood blindness (6-8). However, in countries with an infant mortality rate of 10-60 per 1000 live births, ROP is now emerging as a major cause of childhood blindness (7, 8). The incidence of ROP has not been studied in a large trial in Iran but in Hazrat Rassoul Hospital which has a neonatal intensive care unit, the incidence of ROP was about 16.6%. Retinal neovascularization in premature infants is suggested to result from production of Vascular Endothelial Growth Factor (VEGF), which is an oxygen-regulated factor in response to hyperoxia or anoxia (9-11). Conflicting reports regarding the relative role of anemia or blood transfusion on ROP have been published (12-16). Anemia could exacerbate retinal hypoxia, so blood transfusion for correction of anemia may play a role in reducing the incidence of ROP (17, 18). In contrast frequent blood transfusions and a high hematocrit level may increase the oxidative stress on the immature retina (19-21). Because of the controversy regarding the relative role of the hematocrit level on the incidence of ROP, a prospective, randomized trial was performed in a high risk infant unit.

Methods and Materials

Beginning in June 2000 and ending in May 2002, all infants with birth weight under 1501 g who were admitted to the Neonatal Intensive

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Care Unit of Hazrat Rassoul Akram Hospital before 14 days of life were considered for enrollment into the study. Infants were excluded if they had lethal congenital anomalies, anomalies of the eye or died before 14 days of life. All parents of infants signed an informative consent. Eligible infants were enrolled in 14 days of life. Infants were randomized into one of the two groups. A total of 61 infants were enrolled, of which 4 died before eye examination. Infants in group 1 (anemia; n=27) received packed red blood cell transfusion from 14 days of life until discharge from hospital only if specific medical signs were met and their hematocrit level was under 30%. Medical signs were: 1) significant apnea and bradycardia requiring bag and mask ventilation while receiving therapeutic levels of methylxanthines; 2) weight gain < 10 g daily over a 5 day period while receiving > 80 Kcal/kg/d enterally or parenterally; 3) requiring more than 40% oxygen for maintaining O2Saturation of >87%. Blood transfusions were not given solely for replacing blood drawn for routine sampling. Infants in group 2 (transfusion group; n=30) received packed red blood cell transfusions to maintain their hematocrit level >40% from 14 days of age until their discharge from hospital regardless of their signs. Packed red blood cells at a volume of 10- 15 mL/kg were given over 2 to 3 hours to both groups when necessary. Serum hematocrit was measured every three days or if signs of anemia were noted. Supplemental oxygen was given to all infants in the NICU to maintain an oxygen saturation of 87-95%. There was not an approved protocol to give erythropoeitin to premature infants in our institute in that time. All eye examinations by indirect opthalmoscopy were performed from 28 to 40 days of life inpatients or outpatients by expert ophthalmologists. The examiners were blind to the groups of infants. ROP was graded using the international classification system and follow-up examinations were performed if indicated. Ophthalmic follow-up was provided until retinal vascularization was complete in either eyes or threshold retinopathy developed. Statistical analysis of data was performed using *x* analysis or a Fisher's exact test to determine the significance of difference between the two groups.

Results

Fifty-seven infants were randomized into two groups. Twenty-seven infants were assigned to group 1and 30 to group 2.There were no statistical differences in birth weight, gestational age, sex, inborn patients or death in both groups Table 1. The mean birth weight was 1137+162.3 g in group 1 and 1098+133.3 g in group 2 (*P*=.32). The mean gestational age of infants was 28.7+1.9 weeks in group 1 and 28.4+1.6 weeks in group 2 (*P*=.57). Seventeen infants were born in Rassoul Akram hospital (29.8%) and inborn patients were 29.6% in group 1 and 30% in group 2 (*P*=.97). From 57 infants examined for ROP, 10 showed some degrees of retinal vascular involvement (17.5%), from which 5 infants were in group 1 (18.5%) and 5 in group 2 (16.7%) which showed no difference between groups (*P*=.854). There were 2 deaths in group 1 (7.4%) and 3 in group 2 (10%) during the study period (*P*=.735). Table 2 shows the mean hematocrit value, mean hemoglobin value, and mean number of red blood cell transfusions for the groups. The mean hematocrit value was 28.8+3.8 in group1 and 37.1+2.3 in group 2 (*P*=.0001). The mean number of transfusions were 2.8+1.9 in group 1 and 4.6+ 2.5 in group 2 (*P*=.003).

Table 1: Demographic characteristics of premature infants in NICU of Rassoul Akram Hospital

	Group 1 (n=27)	**Group 2 (n=30)**	***P* value**
Birth weight (g) (mean+SD)	1137+162.3	1098+133.3	.32
Gestational age (week) (mean+SD)	28.7+1.9	28.4+1.6	.57
Born at study center	8/27 (29.6%)	9/30 (30%)	.97
Gender			
Male	12/27 (44%)	14/30 (47%)	.86
Female	15/27 (56%)	16/30 (53%)	
Death	2/27 (7.4%)	3/30 (10%)	.73
ROP			
With ROP	5/27 (18.5%)	5/30 (16.7%)	.85
Without ROP	22/27 (81.5%)	25/30 (83.3%)	

Table 2: Transfusion Status of premature infants in NICU of Rassoul Akram Hospital

	Group 1 (n=27)	**Group 2 (n=30)**	**P value**
Mean Hematocrit,% (SD)	28.8+3.8	37.1+2.3	.0001
Mean Hemoglobin, g/dL (SD)	10.1+1.8	13.2+.58	.0000
Mean Transfusion number, n (SD)	2.8+1.9	4.6+2.5	.003

Discussion

Although the survival rate of very low birth weight infants has increased dramatically in recent years, some of the complications of prematurity have not resolved. ROP is a potentially blinding disorder which is the second etiology of blindness in the U.S (21). The incidence of ROP has not changed in most developed countries (2-5), but is increasing in developing countries (6-9). In Iran the incidence of the disease is not fully published, but in Rassoul Akram Hospital which is a tertiary care center, about 16.5% of infants fewer than 1501 g suffer from some degrees of ROP (unpublished results). Whether or not blood transfusion has any role in decreasing the incidence of ROP is a matter of debate (13, 14). As there are different policies in red cell transfusion to premature infants, we have designed a prospective randomized trial to determine the effects of red blood cell transfusion protocols on the relative risk of ROP. There was no difference in the incidence of ROP in group of infants receiving red blood cell transfusions for maintaining a high hematocrit (about 40%) and those who received transfusions only after showing anemic symptoms and a low hematocrit (about 30%). As there are some limitations in ordering irradiated blood in Iran, we used non-irradiated blood. No transfusion-related events were noted and graft-versus host disease which is a grave reaction in premature infants was not observed. Long term follow-up of these children would be necessary to determine any difference in their growth and development. In summary, we did not find any relation between transfusion policies and risk of ROP. Although additional investigations are needed to confirm this observation, there is no need to change the current transfusion policies.

Acknowledgments

We should give our best respects to our fellow ophthalmologists in Rassoul Akram Hospital, who completed the infants' eye examinations.

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