Original Paper

Iron Status in Early versus Delayed Cord Clamping Groups of Preterm Neonates Delivered in a Tertiary Level Hospital

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Abstract

Introduction: During pregnancy, most of the iron endowment occurs in third trimester; so preterm infant are deprived of iron which leads to anaemia of prematurity. The problems associated with anaemia in preterm babies as well as its treatment (blood transfusion) are multiple and involve significant risks. Anaemia hinders normal growth and contributes to postnatal malnutrition in most low birth weight preterm neonates who are hospitalised for a long time. Delayed cord clamping in preterm infants results in an 8% to 24% increase in blood volume.This extra amount of blood may increase haemoglobin as well as iron content in preterm neonates.

Objective: To observe the effect of timing of cord clamping on iron status of preterm neonates.

Methods: It is a prospective randomized control trial. Total 40 preterm neonates of gestational age of less than 37 weeks were included in this study, they were allocated in Early Cord Clamping (ECC) group and Delayed Cord Clamping (DCC) group by random sampling technique. To estimate iron status in both groups at neonatal period, blood was collected to measure Hb, MCV, TIBC, serum iron, ferritin at 24 hrs of age and at 28 days of age.

Results: This study shows that there is significant high Hb, iron and ferritin levels in delayed cord clamping group of preterm neonates. The results of Hb, serum iron and ferritin levels at 24hrs of age in ECC group were 16.53(±2.13)g/dl, 52.20(±38.78)µg/dl and 127.63(±57.45)µg/L, these parameters in DCC group were 18.65(±2.08)g/dl, 84.35(±35.03)µg/l and 188.88(±107.58)µg/L respectively. These results were significant with the p value of <0.05. These results were also significant at 28 days of life. But regarding Mean Corpuscular Volume (MCV) and Total Iron Binding Capacity (TIBC) parameters, they were not significant either in day 1 or in day 28.

Conclusion: Delayed cord clamping improves iron status in preterm neonates status in early versus delayed cord clamping groups of preterm neonates delivered in certain referral hospital.

Key-words: Early cord clamping, delayed cord clamping, preterm neonates, serum iron.

Introduction

Iron is essential in several aspects of brain development including myelination, dendritogenesis and neurotransmitter function[1]. Preterm neonates are at particular risk of iron deficiency because of less iron endowment at third trimester, frequent blood extraction for laboratory testing and increased iron requirement during rapid growth[2]. Iron deficiency with or without anaemia has been associated with altered affective responding,impaired motor development and cognitive delays[3]. Berden et al and Lozoff et al.(2006) found that anaemia of infancy, even when treated with iron resulted in lower IQs, less favourable neurodevelopmental outcomes and more behavioural problems upto 19 years of age[4]. Current obstetric practice is to clamp the umbilical cord of the very low birth weight infant immediately after delivery. The possible reasons are concern about polycythaemia, hyperbilirubinaemia, perceived need to initiate skin to skin contact as soon as possible and

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to provide active management of the third stage of labour. However delay in cord clamping of about 30 to 45 sec of delivery in preterm infants results in an 8% to 24% increase in blood volume (2-16ml/kg) after caesarean birth and 10 to 26ml/kg after vaginal birth)[5]. Immediate cord clamping may deprive VLBW (Very Low Birth Weight) infant of essential blood volume and create a state of potential circulatory compromise resulting in hypotention and poor perfusion of tissue. Delayed Cord Clamping (DCC) benefits with higher blood pressure, higher haematocrit, more oxygen transport, higher red cell flow, fewer days on oxygen and ventilation, fewer transfusion, lower rates of Intra-Ventricular Haemorrage (IVH).

A two minutes delay in cord clamping increases the child's iron reserve by 27-47 mg of iron, which is equivalent to 1-2 months of an infant iron requirement. This can help to prevent iron deficiency before 6 months of age. Most centres discourage DCC due to polycythaemia and hyperbilirubinaemia; but several studies show that these side effects are insignificant[6]. Because of the increase in red cell volume, preterm infants are more prone to develop hyper-bilirubinaemia but this can be managed by phototherapy[8]. In the contrary, Early Cord Clamping (ECC) puts the newborn at increased risk of hypovolumic change and iron loss, as well as of several blood disorders and type 2 diabetes as a consequence of loss of hematopoietic stem cells[1]. Study conducted by Mercer et al DCC showed increase in blood glucose levels in 24-32 weeks old babies. Considering all these benefits, recent WHO protocol is to clamp the umbilical cord within 1-3 minutes of birth. This study was carried out to see whether this delayed cord clamping practice helps to prevent iron deficiency in preterm neonates.

Methodology

Neonates delivered at less than 37 weeks of gestation either per vaginally or by caesarean section were randomly allocated in ECC (≤ 1minute) or DCC (≥ 3minutes) group. Sampling technique was systematic random sampling. Randomized control study was conducted in the Department of Obstetrics & Gynecology of Bangabandu Sheikh Mujib Medical University (BSMMU) from December 2012 to October 2013. Neonates were observed in the Dept of Neonatology of BSSMU.

Intervention

In the starting, first woman in labour was included either in ECC or DCC group by opening a sealed envelope. The newborns were held at the level about 20 cm below the vulva for about 30 sec and then babies were placed on mother's abdomen which is the standard protocol of Department of Gynecology and Obstetrics, BSMMU. Babies born by caesarean section were placed beside mother by assistant before clamping the cord. The time from complete expulsion of the baby from the introitus to the first clamp of umbilical cord was measured with a stop watch by the investigator. In ECC group first clamp was given at about 1 minute and in DCC group cord was clamped at around 3 minutes. Exclusion criteria were serious congenital malformation, neonates of mother having severe anaemia(Hb <7gm/dl),severe perinatal asphyxia cases(Apgar score 3). Infant's venous blood (6cc) was collected for estimation of blood Hb, serum ferritin, serum iron and TIBC at 24hrs of age. Total 45 babies were observed. Follow up was done after 4 weeks; again blood sample was taken for estimation of Hb, serum iron,ferritin and TIBC. All the neonates were on breast milk except the one whose mother died and was on artificial milk.

Results and Observation

Table-I shows sex distribution of preterm neonates. In ECC group 45 % were male and 55% were female. Male were predominant in DCC group, they constituted 60% and female 40% of cases. Difference in sex distribution was not significant (p>0.05).

Table-I: Sex distribution of preterm neonates in both groups (n=20).

Sex	ECC Group	DCC Group	p value
Male	9(45%)	12(60%)	0.31
Female	11(55%)	8(40%)	

Table-II shows proportions of normal vaginal delivery and caesarean section which were 55% and 45% respectively in ECC group while in DCC group number of normal vaginal delivery and caesarean section were equal. Differences in mode of delivery were not statistically significant (p>0.05).

Table-II: Mode of delivery among preterm neonates (n=20).

Mode of Delivery	ECC Group	DCC Group	p value
Normal vaginal	11(55%)	10(50%)	0.75
Caesarean Section	9(45%)	10(50%)	

Table-III shows that mean Hb levels at day 1 and day 28 of preterm neonates in DCC group were significantly higher than that of ECC group. Results of day 1 were highly significant when compared to 28 days' results. P values were 0.003 and 0.03 respectively.

Table-III: Hb levels among preterm neonates at day 1 and day 28 in both groups (n=20).

	ECC Group (Mean±SD)	DCC Group (Mean±SD)	p value
Hbgm/dl day 1	16.53±2.13	18.65±2.08	0.003
Hbgm/dl day 28	10.74±1.50	11.75±1.47	0.03

Table-IV shows mean value of MCV at day 1 and day 28 among preterm neonates in two groups. The differences in levels between the groups were not statistically significant (p>0.05).

Table-IV: MCV at day 1 and day 28 among preterm neonates in both groups (n=20).

	ECC Group (Mean±SD)	DCC Group (Mean±SD)	p value
MCV fl day 1	99.55±9.08	102.20±5.90	0.28
MCV fl day 28	87.00±8.20	94.10±9.59	0.16

Table-V shows mean serum iron levels at day 1 and day 28 among preterm neonates in both groups. The results were statistically significant were compared between two groups and between day 1 and day 28 also. P values were 0.02 and 0.04 respectively.

Table-V: Serum iron at day 1 and day 28 among preterm neonates in both groups (n=20).

	ECC Group (Mean±SD)	DCC Group (Mean±SD)	p value
Iron µg/dl day 1	52.20±38.78	84.35±35.03	0.02
Iron µg/dl day 28	70.10±25.88	88.50±29.70	0.04

Table-VI shows serum TIBC levels at day 1 and day 28 among preterm neonates in two groups. Differences of mean value between the two groups were not statistically significant neither at day 1 nor at day 28 (p>0.05).

Table-VI: Serum TIBC at day 1 and day 28 among preterm neonates in both groups (n=20).

	ECC Group Mean ±SD	DCC Group Mean ±SD	p value
TIBC µg/dl day 1	238.10±59.06	277.150±89.01	0.11
TIBC µg/dl day 28	217.650±61.77	252.600±69.34	0.10

Table-VII shows mean values of Serum ferritin levels at day 1 and day 28 among preterm neonates. The differences of mean ferritin levels between the two groups were statistically significant (p=0.04).

Table-VII: Serum Ferritin at day 1 and day 28 among preterm neonates in both groups (n=20).

	ECC Group Mean ±SD	DCC Group Mean ±SD	P value
Ferritin µgm/L day 1	127.63±57.45	184.88±107.58	0.04
Ferritin µgm/L day 28	83.742±35.56	119.303±66.50	0.04

Discussion

The comparative risks and benefits of early rather than delayed cord clamping have been a subject of much debate. This study has been carried out to see the effect of timing of cord clamping on iron status in preterm newborns in a developing country like Bangladesh, where iron deficiency is prevailing. Total 40 preterm neonates, 20 in ECC group and 20 in DCC group were analyzed to see the Hb & iron status. Males have physiologically more Hb; here male female difference i.e. sex distribution was not statistically significant.Vaginal delivery allows more blood flow than caesarean section[9]. In our study difference in results between caesarean and vaginal delivery was also not significant. Differences of Hb, serum iron and ferritin levels in preterm neonates between ECC and DCC groups were statistically significant,there p values are 0.003. 0.02 and 0.04 respectively. These values were also significant in follow up visits at 4 weeks of age.

C A Ultee et al also found significant rise in Hb parameter in DCC group; but they found no change in ferritin levels. Study also conducted by Judith et all found higher haematocrit levels in pretrem neonates of <32 weeks. They also made inference that DCC protect VLBW infants from intraventricular haemorrage (IVH)and late onset neonatal sepsis (LOS). This persistent high levels of Hb after birth in DCC group when compared to ECC group in neonates were observed by Gina Eichenbaum and Joanna S.Zasloff; Ceriani cernadas et al; Allistair G.S. and Saroj Saigal. To see the iron status we also observed MCV, TIBC levels in this study population but timing of cord clamping did not affect these values. The study showed delay in cord clamping for

around 3 minutes improved hemoglobin level as well as iron values in preterm neonates after birth and these effects persisted upto 4 weeks of postnatal age. Limitation of the study was small sample size and single center based intervention.

Conclusion

Delayed cord clamping improves iron status and haemoglobin level in preterm newborn. This higher level was maintained throughout the neonatal period in DCC group. Long time follow up is needed to conclude that DCC reduces the incidence of anaemia of prematurity.

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