

Implication of Delayed Cord Clamping for Reducing Anaemia in Term Infants

IRAM MOBUSHER, TAYYABA MAJEED, FATIMA WAHEED, KAMWAL SHAR

Department of Gynaecology, Mayo Hospital, Lahore

Correspondence to: Dr. Iram Mobusher, Department of Gynaecology, Mayo Hospital, Lahore

ABSTRACT

Objective: This study was carried out to assess whether delayed cord clamping is effective in improving the haematological status of term infants born to anemic mothers and whether this is associated with complications in infants and mothers.

Methods: we randomly assign women delivering vaginally term babies in Lady Willingdon Hospital Lahore to immediate cord clamping (ICC, n=100) or delayed cord clamping (DCC, n=100) and follow their infants until the age of 3months. We compared infant hemoglobin change from cord value. Secondary outcomes were related to infant and maternal safety.

Results: infant hemoglobin level at 3months declined in both groups but more in group of immediate cord clamping. Mean infant Hb at 3months in ICC group was and in DCC group was. Difference of Mean infant Hb in ICC group was and in DCC group was. No adverse events were seen in infants and mother.

Conclusion: DCC improved the haematological status of term infants born to anemic mothers. It is a simple, safe and cost free intervention to reduce early infant anemia risk.

Key words: Umbilical cord clamping, infant anemia, term birth.

INTRODUCTION

Iron deficiency anemia is a serious health problem that affects the physical and cognitive development of children.¹ It is one of the most critical factors contributing to neonatal and infant mortality in developing countries.^{2,3} Therefore it is important to develop cost effective interventions to improve hematological status of the millions of children affected by this condition worldwide.¹ One of the most important trials which studied primary anemia prevention in Tanzania observed a 20% incidence of severe anemia even in infants who had received prophylactic antimalarials and iron supplements.⁴ In view of this there is interest in evaluating cheap and effective interventions to reduce the risk of infant anemia and increase red cell mass in term infants by delayed cord clamping.⁵ In hospital deliveries, immediate cord clamping (ICC) is the routine standard of care. It is estimated that neonatal blood volume may increase by 32% if cord clamping is delayed until umbilical cord has completely stopped pulsating.⁶ For a 3kg infant this amounts to an additional 45mg of iron added to iron stores. Theoretically this amount of iron would be sufficient to meet the requirement of an infant of more than three months.⁷ Due to poverty and malnutrition our women are very anemic. A

previous trial indicated that the effect of delayed cord clamping was significantly greater for infants born to mothers with low ferritin at delivery, breast fed infants not receiving iron fortified milk or formula and infants born with birth weight between 2500g and 3000g.⁸ We performed a randomized controlled trial to see the implications of delayed cord clamping for reducing anemia in term infants up to age of 3months and its complications in infant.

OBJECTIVE

To study the effect of delayed cord clamping on Hb level of term infant up to the age of three months.

To study its complication in infants (Hyperbilirubinemia, Polycythemia) and mother (excessive blood loss after delivery)

MATERIAL AND METHODS

This randomized controlled trial was conducted in the Department of Obstetrics and Gynaecology, Unit 1, Lady Willingdon Hospital Lahore between 1st Jan 2010 and 30th June 2010. It was a partially blinded randomized controlled trial. Paediatrician and laboratory staff was blinded. Although study staff did not inform mothers of their assignment, the nature of intervention made it impossible to

blind them. Full term (37-41 weeks gestation) pregnant women delivering vaginally in Lady Willingdon Hospital were candidates for inclusion in the study. Prespecified exclusion criteria were¹ twin pregnancy,² previous history of PPH,³ gestational diabetes,⁴ pre-eclampsia,⁵ congenital abnormality,⁶ gestational age below 37weeks⁷ placental separation before delivery,⁸ caesarean section,⁹ tight umbilical cord necessitating early cutting. Criteria 1-6 were applied before randomization. Criteria 7-9 were assessed after randomization. Randomization was done on admission to the labour ward, when the women were in the first stage of labour. Women meeting the inclusion criteria and who consented to enroll were entered in trial in sequential manner. They were randomized into two groups each having 100 patients by using random number tables. Group A was subjected to immediate cord clamping within 20sec of delivery and Group B was subjected to delayed cord clamping at three minutes` interval after delivery. A structured questionnaire was used to gather obstetrical and medical details and a venous blood sample was taken from mother for Hb measurement from laboratory in the first stage of labour. After vaginal birth all infants `were placed approximately 10cm below vaginal introitus, dried and wrapped in a warm towel. The infants remained in this position until cord was clamped. Intramuscular syntocinon was administered to mother after clamping the cord. After cutting the cord, sample of blood was collected from cut end of cord of newborn for Hb(g/dl), packed cell volume and S/bilirubin measurement. Birth weight and sex of baby noted.

In the first 24 hours `after delivery child was observed for jaundice and clinical signs of hyper viscosity syndrome (plethora, apathy, tachypnoea=respiratory rate>60/min, poor sucking and hypoglycemia=blood glucose level<45mg/dl) by paediatrician. A venous blood sample was taken from baby twenty four hours after birth for Packed cell volume and serum bilirubin measurement. A maternal blood sample was drawn for heamoglobin measurement 24 hrs after delivery to compare it with Hb level in first stage of labour. Samples were sent to laboratory for analysis Mother-infant pairs were called for follow up at three months of age. At that time a venous blood sample of baby was taken and was sent to laboratory for Hb measurement. All data were entered on proforma and analyzed using SPSS version11.

RESULTS

Table # 1: Maternal baseline characteristics

Variable	Group A (ICC)	Group B (DCC)
Age (years)-median range	20.5 (15.5-41.9)	22.9 (15.6-46.0)
BMI (Kg/m2)	22.1	23.1
Primigravidae	43%	39%
Last interpartum interval (months)	14	12
Socioeconomic status	poor	Poor
No. of antenatal visits	2	2
Iron supplementation in pregnancy	56%	51%
Hb (g/dl)	9.8	9.9
Proportion maternal anemia		

Data were mean unless indicated otherwise.

Table # 2: Maternal haematological outcome on first day postpartum

Variable	Group A (ICC)	Group (DCC)
Maternal Hb (g/dl)	9.6	9.7
Hb (g/dl) decrease compared to baseline	0.2	0.2

Table#3 Infant baseline characteristics

Variable	Group A (ICC)	Group B (DCC)
Clamping time	20seconds	3minutes
Gestational age (weeks)	39	39
Birth weight (g)	3102	3129
Females (%age)	51	52
Apgar score After 1 min- median (range)	9(7-10) 10(9-10)	9(8-10) 10(9-10)
Apgar score After 5 min- median (range)		
Cord Hb(g/dl)	14.1	14.9
Cord PCV	0.47	0.50
Cord S/Bilirubin (mg/dl)	1.5	1.6

Data were mean unless indicated otherwise.

Table # 4: Infant haematological outcome on first day postpartum

Variable	Group A (ICC)	Group B (DCC)
PCV	0.54	0.63
PCV increase compared with cord blood	0.07	0.13
S/Bilirubin (mg/dl)	2.4	2.6
S/Billi increase compared with cord	0.9	1.0
Proportion above phototherapy threshold	0%	0%

Data were mean unless indicated otherwise.

Table # 5: Infant haematological status at 3months

Variable	Group A (ICC)	Group B
Hb (g/dl)	10.4	11.9
Hb change from baseline (g/dl)	3.7	3.0
Proportion anemia (cut-off value 10.3g/dl)		

Data were mean unless indicated otherwise.

DISCUSSION

In traditional African home deliveries the umbilical cord is cut after placental descent into the vagina⁹, but in hospital deliveries and in resource-poor settings immediate cord clamping is the routine standard of care. It is estimated that total foetoplacental blood volume is roughly is 120ml/kg of foetal weight. After immediate cord clamping the distribution of blood reflected in the foetus:placenta ratio is approximately 2:1. Allowing placental transfusion to occur for at least 3minutes results in a larger foetal blood volume with 15ml/kg of blood remaining in the placenta.^{10,11} Compared with immediate clamping, a clamping delay of 3minutes provides an additional blood volume of 20-35ml/kg of body weight.¹² Delayed clamping of the umbilical cord increases the infant's iron endowment at birth and haemoglobin concentration.⁸

In my study, at baseline the groups had similar demographic and biomedical characteristics. Mean maternal haemoglobin of Group A was 9.8 g/dl and of Group B was 9.9g/dl. Mean of haemoglobin of cord blood of Group A was 14.1g/dl and of Group B was 14.9g/dl. Similar results were obtained in a

study from Karachi¹³. Mean of infant haemoglobin at three months of Group A was 10.4g/dl and of Group B was 11.9g/dl. Similar results were obtained in another study¹⁴. By three months the decrease in hemoglobin compared with cord blood values was small in the delayed cord clamping group as compared to immediate cord clamping. Difference in infant hemoglobin of Group A from baseline was 3.7g/dl and of Group B was 3.0 g/dl. Similar results were obtained in a study from Zambia.¹⁵ The results of my study showed that anemia is more prevalent in Group A of immediate cord clamping as compared to Group B of delayed cord clamping. Trial from Guatemala and India^{1,22} also showed the beneficial effect of delayed cord clamping on infant hemoglobin. A trial Mexico (80 did not find a difference in Hb, although the iron status at 6months was significantly higher in DCC group. This lack of difference in Hb is most likely due to the fact that iron deficiency was relatively uncommon in the Mexican study. Hemoglobin is normally not affected until iron stores are depleted.

Delayed cord clamping has been shown to be more beneficial in babies of anemic mothers^{22,23} as proven in my study also.

Neonatal hyperbilirubinemia and polycythemia are potential consequences of placental transfusion. The difference in bilirubin level after 24hours in two groups was insignificant. It didn't reach the level requiring phototherapy or exchange transfusion. It shows that delayed cord clamping does not lead to significant hyperbilirubinemia requiring phototherapy or exchange transfusion. Similar results were obtained in a study from Karachi.¹³

Mean increase in PCV on the first day postpartum was significantly higher in newborn from DCC group. But none of the infants showed clinical signs of hyper viscosity syndrome. Safety of delayed cord clamping in appropriate for gestational age term infants has been demonstrated in several trials.^{1,12,16,17,18,19,20} However, there is paucity of information on DCC in small for gestational age (SGA) infants. SGA infants from industrialized countries often manifest an increased incidence of polycythemia caused by chronic hypoxemia in utero leading to increased erythropoiesis. These infants are considered to be at greater risk of symptoms and clinical consequences of altered viscosity.²¹ However, base line risk for polycythemia-hyper viscosity syndrome in SGA infants from developing

countries might be lower and needs to be investigated.

Difference in maternal hemoglobin 24hrs after delivery between two groups was insignificant. This shows that delayed cord clamping does not lead to excessive maternal blood loss after delivery. Two other trials(8,14) evaluated the effect of cord clamping on maternal blood loss. But major limitations of these trials were diversity in measuring blood loss (visual estimation vs. measuring jar).

CONCLUSION

Delayed cord clamping is a simple, safe and cost free delivery procedure that augments red cell mass in term infants born to anemic mothers. It offers a sustainable strategy to reduce early infant anemia risk when other interventions are not yet feasible. It should be included in integrated programmes aimed at reducing anemia in young children in Pakistan like developing countries.

REFERENCES

1. Grajeda R, Perez-Escamilla R, Dewey KG. Delayed clamping of the umbilical cord improves hematological status of Guatemalan infants of 2 mo of age. *Am J Clin Nutr.* 1997 Feb; 65 (2): 425-31.
2. Brabin BJ, Premji Z & Verhoeff F (2001) An analysis of anemia and child mortality. *Journal of Nutrition* 131, 636S–645S
3. Brabin BJ, Prinsen-Geerligs P, Verhoeff F & Kazembe P (2003b) Anaemia prevention for reduction of mortality in mothers and children. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 97, 36–38.
4. Menendez C, Kahigwa E, Hirt R et al. (1997) Randomised placebo-controlled trial of iron supplementation and malaria chemoprophylaxis for prevention of severe anaemia and malaria in Tanzanian infants. *Lancet* 350, 844–850.
5. Van Rheenen PF, Gruschke S, Brabin BJ. Delayed Umbilical cord clamping for reducing anemia in low birth weight infants: implications for developing countries. *Ann Trop Paediatr.* 2006 Sep; 26 (3): 157-67.
6. Ned Tijdschr Geneesk. Delayed cord clamping in the interest of newborn. 2008 Jun 21; 152(25): 1419-25.
7. Oski FA (1993) Iron deficiency in infancy and childhood. *New England Journal of Medicine* 329, 190–193.
8. Chaparro CM, Neufeld LM, Tena Alavez G, Eguia-Liz Cedillo R, Dewey KG. Effect of timing of umbilical cord clamping on iron status in Mexican infants: a randomized controlled trial. *Lancet.* 2006 Jun 17; 367(9527): 1997-2004.
9. Lefeber Y & Voorhoeve H (1997) Practices and beliefs of traditional birth attendants: lessons for obstetrics in the north? *Tropical Medicine and International Health* 2, 1175–1179.
10. Yao AC & Lind J (1969) Effect of gravity on placental transfusion. *Lancet* 294, 505–508.
11. Linderkamp O (1982) Placental transfusion: determinants and effects. *Clinics in Perinatology* 9, 559–592.
12. Linderkamp O, Nelle M, Kraus M & Zilow EP (1992) The effect of early and late cord-clamping on blood viscosity and other hemorheological parameters in full-term neonates. *Acta Paediatrica* 81, 745–750.
13. Jaleel R, Deeba F, Khan A. Timing of umbilical cord clamping and neonatal haemoglobin status. *J Pak Med Assoc.* 2009 Jul; 59(7): 468-70
14. Ceriani Cernadas JM, Carroli G, Pellegrini L, Ferreira M, Ricci C, Casas O, Lardizabal J, Morasso Mdel C. The effect of early and delayed umbilical cord clamping on ferritin levels in term infants at six months of life: a randomized controlled trial. *Arch Argent Pediatr.* 2010 Jun; 108(3):201-8.
15. Van Rheenen P, de Moor L, Eschbach S, de Grooth H, Brabin B. Delayed cord clamping and hemoglobin levels in infancy: a randomized controlled trial in term babies. *Trop Med Int Health.* 2007 May; 12(5): 103-16.
16. Nelle M, Zilow EP, Kraus M, Bastert G & Linderkamp O (1993) The effect of Leboyer delivery on blood viscosity and other hemorheologic parameters in term neonates. *American Journal of Obstetrics and Gynecology* 169, 189–193.
17. Nelle M, Zilow EP, Bastert G & Linderkamp O (1995) Effect of Leboyer childbirth on cardiac output, cerebral and gastrointestinal blood flow velocities in full-term neonates. *American Journal of Perinatology* 12, 212–216.
18. Nelle M, Kraus M, Bastert G & Linderkamp O (1996) Effects of Leboyer childbirth on left-and right systolic time intervals in healthy term neonates. *Journal of Perinatal Medicine* 24, 513–520.
19. Brabin BJ, Kalanda BF, Verhoeff FH, Chimsuku LH & Broadhead RL (2004) Risk

- factors for fetal anaemia in a malarious area of Malawi. *Annals of Tropical Paediatrics* 24, 311–321.
20. Emhamed M, van Rheenen P & Brabin BJ (2004) The early effects of delayed cord clamping in term infants born to Libyan mothers. *Tropical Doctor* 34, 218–222.
 21. Anderson M & Hay W (1999) Intrauterine growth restriction and the small-for-gestational-age infant. In: *Neonatology. Pathophysiology and Management of the Newborn*, 5th edn (eds G Avery, M Fletcher & M McDonalds) Lippincott Williams and Wilkins, Philadelphia, PA, pp. 411–444.
 22. Gupta R & Ramji S (2002) Effect of delayed cord clamping on iron stores in infants born to anemic mothers: a randomized controlled trial. *Indian Pediatrics* 39, 130–135.
 23. van Rheenen P & Brabin BJ (2004) Late umbilical cord clamping as an intervention for reducing iron deficiency anaemia in term infants in developing and industrialised countries: a systematic review. *Annals of Tropical Paediatrics* 24, 3–16.