Original Articles

EFFECT OF TIMING OF CORD CLAMPING ON THE IRON STATUS OF INFANTS AT 3 MONTHS

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Objective: To determine the effect of timing of cord clamping on iron stores of term infants at 3 months of age. Design: Prospective randomized clinical trial. Setting: Tertiary hospital. Subjects: 107 term neonates born to mothers with uncomplicated pregnancies and with hemoglobin more than 10 g/dl. Methods: The 107 infants were randomized to either early (n=48) or late (n=59) clamping groups at the time of delivery. Outcome measures evaluated were serum ferritin and hemoglobin in the infant at 3 months age. Results: The groups were comparable for maternal age, parity, weight, supplemental iron intake in pregnancy, infant's birth weight, gestation and sex. Maternal and cord ferritin and hemoglobin values at birth were comparable. The infant ferritin at 3 months were also similar. Conclusions: Iron stores at 3 months in term infants are not influenced by timing of cord clamping at birth.

Key words: *Anemia, Ferritin, Hemoglobin, Cord clamping, Infant.*

ANEMIA is a major public health problem in India; its prevalence in children under 3 years is reported to be about 63%(1). The young infant is largely dependent on the supply of iron present at birth for hemoglobin production and growth during the first six months of life. The iron stores in a newborn infant at birth are related to maternal iron stores and transfer of blood from the placenta at delivery. The newborn infant has been documented to receive about 100 ml of blood from the placenta (equivalent to about 50 mg of elemental iron) if the clamping of cord at birth is delayed till the placenta starts descending into the vagina(2). Since several parturient women in India have low normal iron stores at delivery(3), delaying cord clamping could possibly increase the iron stores at birth and thereby help in preventing iron deficiency anemia in later infancy. There is a paucity of randomized controlled studies evaluating the effect of timing of cord clamping on later iron stores. The present study was, therefore, designed to observe the effect of timing of cord clamping on iron stores (measured by ferritin levels) of infants at 3 months of age.

Subjects and Methods

This prospective randomized clinical trial was designed to include hospital born term neonates born per vaginum to mothers with uncomplicated pregnancies *(i.e.,*

mothers without eclampsia, severe heart disease in failure, severe antepartum hemorrhage, Rh isoimmunization, *etc.)* and with hemoglobin more than 10 g/dl. Infants with birth asphyxia and major congenital malformations were excluded. The mothers were enrolled when they were admitted in labor. Of the two outcome variables (hemoglobin and serum ferritin), determined, the primary outcome variable was serum ferritin at 3 months. Serum ferritin was chosen because of its good correlation with iron stores and its ease of assessment.

Sample Size and Randomization

In order to detect a 30 ng/ml difference in serum ferritin levels with a SD of 3 ng/ml between the early and late cord clamping groups at 3 months of age with a power of 80% and a probability of 5%, a total sample size of about 100 infants was required for the study. There were 107 mother-infant pairs who fulfilled the enrolment criteria and were randomized to either early (n=48) or late clamping (n=59) groups at the time of delivery. The randomization sequence was placed in opaque sealed envelops. In early cord clamping group, the cord was clamped immediately after the birth of the infant. In the late cord clamping group, the cord was clamped after the placenta had descended into the vagina and during that time the newborn was held below but within 10 cm of the level of vaginal introitus. Care was taken to keep the infant warm till the cord was cut.

Sample Collection

Maternal venous blood (3 ml) was collected soon after delivery in plain tubes for serum ferritin estimation and in EDTA tubes for hemoglobin estimation. Similarly, 3 ml of cord blood at birth and infant venous blood at 3 months age were collected for ferritin and hemoglobin estimations. The samples for ferritin assay were centrifuged and the serum was separated into a sealed tube and was stored in deep freeze at — 20° C till evaluation was performed.

Ferritin and Hemoglobin Analysis

Hemoglobin was estimated by cyanmethemoglobin method(4). Serum ferritin was estimated by a sandwich ELISA technique using Melotest Ferritin Kits (Melotec Company, Italy). The assay utilizes a monoclonal antibody of human liver ferritin. The assay was performed as per manufacturer's instructions.

Data Collection

Baseline maternal data with regards to age, supplemental iron intake, parity, socioeconomic status and infant's data with regard to birth weight, gestation were recorded in all cases. Infants were followed up till 3 months of age. No medicinal iron was given to any of these infants till the end of the study. Intervening morbidities like respiratory infection and diarrhea during this period were carefully recorded.

Statistical Analysis

Continuous variables were evaluated by Student's 'f test and proportions by 'Chi-square' test. Log ferritin values were analyzed.

Results

The groups were comparable with regard to baseline characteristics-maternal age, parity, weight (51.1±7.4 Kg in early versus 49.1 ±6.8 Kg in late), total intake of supplemental iron in pregnancy (median 0 mg (range 0-36000) versus 0 mg (range 0-24000) in the late group). The groups were also comparable with regard to infant's birth weight; gestation and sex.

Table I provides the maternal and infant ferritin and hemoglobin values at birth and 3 months of age. The ferritin and hemoglo-

bin values were comparable (p >0.05) between the two groups in the mother, in cord blood and in the infant at 3 months.

To evaluate the determinants of low infant ferritin at 3 months (<50 ng/ml), a univariate analysis was performed. There were 56 infants at 3 months with serum ferritin <50 ng/ml and 51 with values ≥50 ng/ml. No difference was observed between the groups *(Table II)*. There were no differences between the group with regard to infectious morbidities during the first 3 months of life.

TABLE I–*Mean (SD) Maternal and Infant Hb and Ferritin.*

Variable	Early	Late
Hemoglobin (g/dl)		
Maternal	12.5 (1.7)	12.7 (1.8)
Cord	16.1 (2.2)	15.5 (2.3)
Infant (3 months)	8.9 (1.6)	8.3 (2.1)
*Ferritin (ng/ml)**		
Maternal	36.4 (3.6)	27.3 (2.8)
Cord	140.2 (3.2)	142.8 (2.6)
Infant (3 month)	55.7 (3.7)	73.6 (3.1)

None of the differences between the two groups were significant (p >0.05).
* geometric mean.

Discussion

A high incidence of anemia and low iron stores seem to be common features in Indian infants after 3 months of age irrespective of the socieconomic status as compared to Western infants(5-7). Bhargava *et al.* (3) had observed that cord ferritin was inversely proportional to maternal hemoglobin levels and even in iron replete mothers (serum ferritin >10 ng/ml), the cord ferritin was significantly lower compared to western reports. Thus, even infants of non-anemic mothers could have marginal iron stores at birth and transfer of additional blood from the placenta at birth by delayed cord clamping could possibly provide additional iron stores to these infants.

Clamping the umbilical cord during delivery only after the cessation of cord pulsations could provide the newborn infant an additional 80-100 ml of blood(28). It has been suggested that deprivation of placental blood may lead to iron deficiency (low mean hemoglobin, at 8-10 months of life(5).

TABLE II–*Determinants of Infant Iron Stores at 3 Months.*

Variable	Infant ferritin at 3 months	
	< 50 ng/ml (n=56)	≥ 50 ng/ml (n=51)
Maternal ferritin (ng/ml) [geometric means (sd)]	29.5 (3.1)	33.0 (3.3)
Cord ferritin (ng/ml) (geometric mean (sd)]	125.0 (3.1)	162.2 (2.6)
Maternal supplemental iron intake in pregnancy (mg) [median (range)]	0 (0-36000)	600 (0-36000)
No. early clamped (%)	28 (50%)	20 (39.2%)
No. exclusively breastfed (%)	36 (90%) (n=40)	43 (93.4%) (n=46)

None of the differences between the two groups were significant (p >0.05).

In the present study, no differences were observed in hemoglobin at 3 months in the early and late cord clamping groups. The serum ferritin values at 3 months were lower in the early than the late clamping groups, though not significant. However, it is possible that if followed till 6 months or beyond these differences may attain significance.

In conclusion, the adequacy of iron stores at 3 months (>50 ng/ml) (9,10), was not influenced by the timing of cord clamping. It is possible that if followed till six months or beyond, or in infants born to anemic mothers, the additional iron from placental blood transfer at birth may be of benefit to the infant, but this hypothesis needs further investigation.

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