Original Article

Indian Journal of Trauma and Emergency Pediatrics
Volume 9 Number 1, January - March 2017
DOI: http://dx.doi.org/10.21088/ijtep.2348.9987.9117.2

Effect of Timing of Umbilical Cord Clamping on Neurodevelopmental Outcomes At 6-8 Weeks of Life in Healthy Term Neonates

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Abstract

Objective: To investigate the effects of delayed umbilical cord clamping, compared with early clamping, on infant's neurodevelopmental outcomes at 6-8 weeks of age in healthy term neonates. *Design:* A hospital based prospective, observational study. *Setting:* Lady Harding Medical College and Smt. Sucheta Kriplani Hospital, Delhi. *Participants:* 238 full term singleton infants born through normal vaginal delivery. *Intervention:* Infants were divided in two groups delayed umbilical cord clamping (≥60 seconds after delivery) or early umbilical cord clamping (<60 seconds after delivery) from the data collected. *Outcome Measures:* To study the effects of delayed umbilical cord clamping, compared with early clamping on neurodevelopmental outcomes at 6-8 weeks of age in healthy term neonates. *Results:* At 6- 8 weeks of age, there were no significant differences between the neurodevelopmental outcome of babies in the delayed and early umbilical cord clamping groups. *Conclusions:* Delayed cord clamping did not result in any difference in neurodevelopmental outcome compared with early umbilical cord clamping.

Keywords: Umbilical Cord Clamping; Neuro-Development.

Introduction

The optimal timing of cord clamping has been a controversial issue for decades. Clamping and cutting of the umbilical cord at birth is by far the oldest and most prevalent intervention in humans. In spite of that, there are no clear cut guidelines on the clamping of umbilical cord after childbirth.

Delayed clamping of the umbilical cord is very much a physiological and inexpensive way of enhancing the hematologic status of infants, preventing anaemia over first 3-6 months of age and enhancing iron stores and ferritin levels for as long as 6 months [1]. It delivers 20-40 ml of blood and 30-35 mg of iron to the newborn.

Policies for the timing of cord clamping vary, immediate cord clamping is generally carried out in the first 60 sec after birth. Whereas, delayed umbilical cord clamping usually involves clamping the umbilical cord greater than 60 sec after the birth or when cord pulsation has ceased. Some texts also describe delayed umbilical cord clamping as umbilical cord clamping as 30-180 sec or after cessation of cord pulsation [2,3].

The disadvantages of early clamping include infant anemia, acidemia, and increased risk of hypovolemia and iron loss. It has been hypothesized that this anemia in infancy is culprit for poor neurodevelopmental outcome in late childhood [1,4].

Hence, delaying the clamping of umbilical cord is especially crucial for resource poor settings by preventing anemia and poor neurodevelopmental outcome [4,5].

This practice is likely to have an important impact on majority of newborns, regardless of their birth settings. However, both maternal and neonatal risks and benefits associated with different timings of umbilical cord clamping require further research.

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Received on 05.11.2016, **Accepted on** 26.11.2016

Methods

Study Design

We conducted a hospital based prospective, observational study in which timing of cord clamping was noted in real time birth settings and later classified them in early and delayed group.

Participants

All mothers with full term gestation, who were admitted in our main labor room, were explained about the nature of study and after their written informed consent they were included in the study cohort.

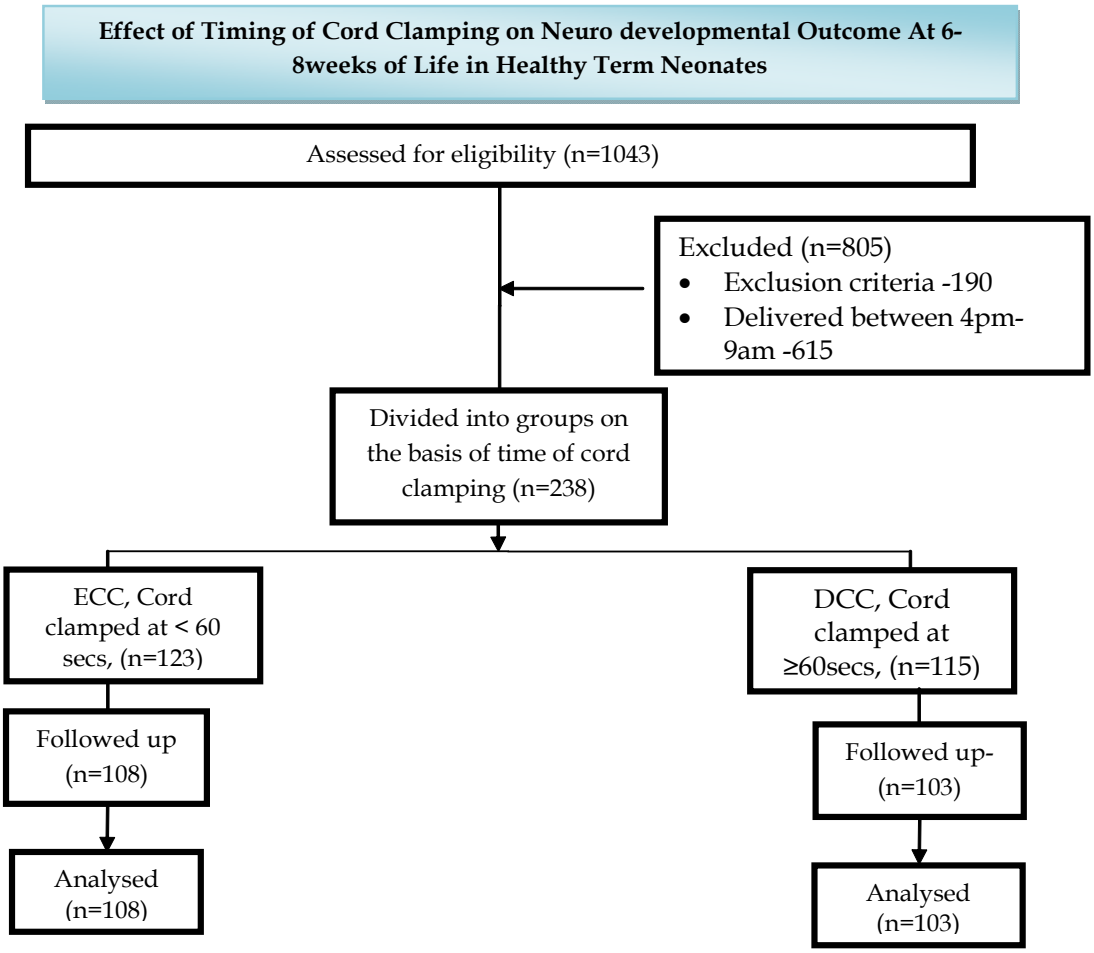
The study was carried out from August 2014 to January 2015. A total of 6540 mothers delivered at our hospital during this period. Term deliveries during this time period were 5392 (82.44 %). Out of all term deliveries, 3854 mothers delivered vaginally. Mothers with Hb≥11 gm/dl were 1043 of all vaginal deliveries.

Term newborns requiring resuscitation, multiple pregnancies, rhesus sensitization, cord factors-cord prolapse, cord abnormalities, true knot, infants born to mothers with abruptio placenta, infants born to mother by caesarean section, infants of mothers with haemoglobin < 11 mg/dl, major congenital malformations detected antenatally or at birth were excluded from the study.

All pregnant women satisfying the inclusion and exclusion criteria were enrolled. The progress of labor was monitored by the health care provider involved in the care of the mother. Based on logistic issues enrolment time was pre-fixed from 9 am to 4 pm. The timing of clamping of cord was observed by an independent observer not involved in the care of mother or the baby. Early cord clamping was defined as <60 secs and delayed cord clamping- >60 secs.

This observation of timing of cord clamping was done using a digital stop watch (kadio-1069) from the time of complete expulsion of the baby till the cord was clamped by the obstetric health care provider. Information relevant to the baseline and other parameters was entered in a predesigned

Flow Chart of Study



pretested case proforma.

All neonates were discharged home when the mother was confident to take care of baby and the baby was on exclusive breast feeds. All the mothers were instructed to seek health care if any of the explained danger signs were obtained in the baby. All the mothers were asked to bring the baby for follow up and vaccination at 6-8 weeks of age. On their visit, neurodevelopmental assessment was done for all babies (DASII score).

Statistical Analysis

For group comparisons of continuous variables, we used Student's *t* test for variables with normal distribution. For variables with skewed distribution, we used Mann-Whitney U test for group comparisons. Categorical data were analyzed by chi-square test.

Results

A total of 1043 neonates were assessed for eligibility, out of which 238 neonates were enrolled based on inclusion and exclusion criteria. Of 238 neonates enrolled, in 123 babies the cord was clamped before 60 seconds which constituted the early cord clamping group, in another 115 babies the cord was clamped at or after 60 seconds of life which constituted the delayed cord clamping group.

Of 238 neonates at 6-8 weeks, 211 came for follow up and 27(11.38%) were lost to follow up. The lost-to-follow up rate was 15 (12.19%) in early cord clamping group and 12 (10.43%) in delayed cord clamping group. There were no significant differences between the delayed cord clamping and early clamping groups with respect to maternal characteristics or neonatal baseline data (Table 1).

Table 2 and Figure 1 shows the distribution of median Apgar score in two groups. There is no significant difference between the two groups (p=0.161 & 0.444).

Difference in neuro-developmental outcome assessed in each group by DASII scoring was statistically insignificant (p<.05). Distribution of mean DASII score was 92.23±4.09% in Early cord clamping (ECC) group and 93.34±3.17% in Delayed cord clamping (DCC) group. Difference in two groups was not significant (p=0.078) (Table 3 and Figure 2).

Table 1: Distribution of demographic variables in study subjects of ECC and DCC

Variable	ECC (n=123)	DCC (n=115)	p value
Birth weight (mean ± SD) (grams)	2895.56±374.56	2901.22±384.11	.908
Gestational age (median ± SD) (weeks)	38.5±1.31	39±1.22	0.994
Maternal Hb. (mean ± SD) (gm/dl)	12.03±0.78	12.11±0.87	0.464
Mode of delivery			
NVD (%)	37 (29.83%)	27 (23.68%)	0.488
Assisted (%)	87 (70.17%)	87 (76.32%)	
Apgar score			
1 min (median ± SD	8±0.26	8±0.35	0.059
5 min (median ± SD)	9±0.44	9±.452	0.840
Gender			
Male (%)	69(55.65%)	54 (47.37%)	0.202
Female (%)	55 (44.35%)	60 (52.63%)	

Table 2: Distribution of median for APGAR score among two study groups

APGAR Score	ECC (n=70)	IQ Range	DCC (n=115)	IQ Range	P value
At 1 min (median ± IQR)	8	0	8	0	0.161
At 5 min (median ± IQR)	9	0	9	1	0.444

Table 3: Distribution of mean DASII score in two study groups

Group	ECC (n=60)	Range	DCC (n=103)	Range	p value
DASII score (% ± SD)	92.23±4.09	81.55-100	93.34±3.71	84.08-102.78	0.078

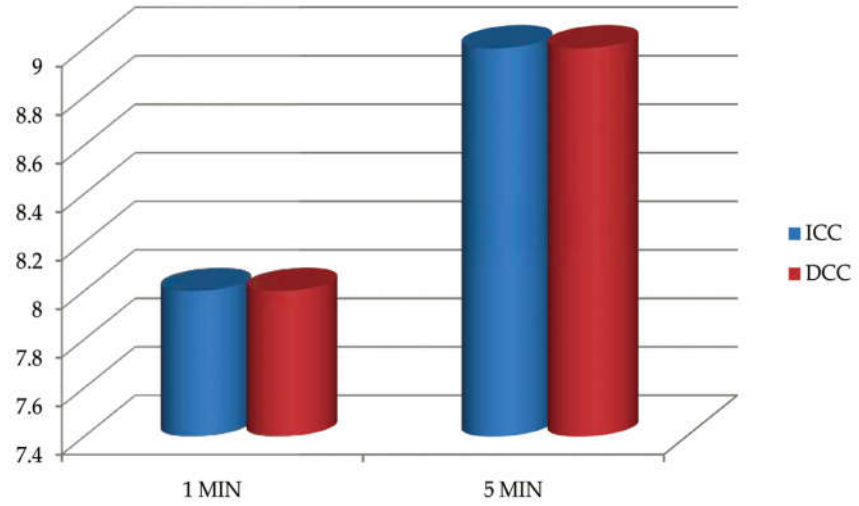


Fig. 1: Distribution of median APGAR score

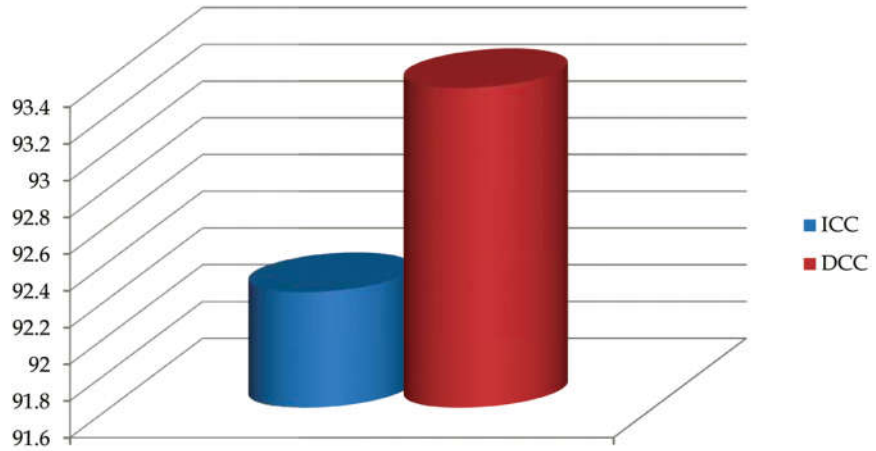


Fig. 2: Distribution of mean DASII score in newborns at 6-8 weeks

Discussion

Currently, the literature, along with different professional bodies including World Health Organization 2012, Society of Obstetricians and Gynecologists of Canada 2009, the American College of Obstetricians and Gynecologists 2012 and the NRP 2010 recommend delayed cord clamping after 60 seconds to maximum of 180 seconds [6,9-13). The advantage of delayed cord clamping also include higher haemoglobin levels, additional iron stores, less fall in haemoglobin (by about 1gm/dl) at 3 months and less anemia later in infancy [4,7,8,14-19]. Increased iron stores as a consequence of DCC might reduce the occurrence of anemia, which is known to be in inverse relation to neurodevelopment [22-32].

In this observational study, we tried to see the effect of timing of umbilical cord clamping on neuro-developmental parameters in newborns at an early age of 6 to 8 weeks in contrast to earlier studies which were performed at term or later time frame of 4 to 6 months.

Difference in neuro-developmental outcome assessed in each group by DASII scoring was statistically insignificant ($p<.05$), indicating that neither early nor delayed umbilical cord clamping has any adverse effect on neuro-development. DASII (Developmental Assessment Score for Indian Infants) score was used for neurodevelopmental assessment, as it is used to measure motor and mental development at follow up for Indian infants. Mean DASII composite score in two groups had shown difference, but it was statistically insignificant.

No earlier study has compared these two groups on the basis of neurodevelopmental outcomes at such an early age. Majority studies till date in term newborns, have been performed at later time frame of 3-6 months of age, with inference that a delay in clamping of cord by >60 secs will significantly effect serum ferritin status (increased in delayed cord

clamping group)[17,20,21]. In our study, age at which we studied the outcomes of cord clamping was crucial one, just before nadir when anaemia of infancy occurs as iron affects neuro-developmental outcomes.

The present study has concluded that delaying clamping of the umbilical cord prevents neuro-developmental delay at the age of 6-8 weeks in term neonates. A possible explanation is that delayed umbilical cord clamping prevented an exaggerated fall in haemoglobin and haematocrit just before the nadir of physiological anemia of infancy in babies.

The current study, although observational in nature further affirms the fact that delaying the timing of clamping the umbilical cord is beneficial and the same should be advocated.

Further research is needed to determine the optimum time required to provide maximum benefit of placental transfusion, along with minimal disadvantages to both mother and newborn.

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