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The Difference of Hematocrit in Term and Preterm Vaginal Births in Different Timing of Delayed Cord Clampin

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ABSTRACT

Objective: To compare fetal hematocrit in different timing of delayed cord clamping and fetomaternal outcome at 48 hours after vaginal births.

Materials and Methods: 200 term and preterm vaginal births were recruited by inclusion criteria and randomized to 1 and 2 minutes delayed cord clamping followed vaginal births. Fetal hematocrit, hemoglobin, microbilirubin were collected at 48 hours after birth. Primary outcome was the difference in fetal hematocrit among groups. Secondary outcomes were adverse fetomaternal outcomes.

Results: 200 term and preterm singleton pregnancies met the criteria; 100 cases were randomized to each groups to perform 1 minute versus 2 minutes of delayed cord clamping. Baseline characteristics were similar. Fetal blood was obtained at 48 hours after birth. Fetal hematocrit, hemoglobin and microbilirubin statistical significantly increased in 2 minutes delayed cord clamping group. (53.44% vs. 52.39 % (p = 0.041) 16.33 g/dL vs. 14.74 g/dL (p = 0.001) and 11.04 mg/dL vs. 10.17 mg/dL (p = 0.011)). Neonatal jaundice and phototherapy requirement were higher in 2 minutes cord clamping (1% vs. 9% (p = 0.009), 1% vs. 8% (p = 0.017) and 2% vs. 10% (p = 0.017). The study showed no incidence of fetal anemia, polycythemia and exchange transfusion in both groups. No significant difference in APGAR score, maternal blood loss, postpartum hemorrhage and third stage of labor length.

Conclusion: Significantly increased hematocrit, hemoglobin and microbilirubin in 2 minutes of cord clamping obtained at 48 hour of life. Thus, this group complicated with neonatal jaundice leads to phototherapy.

Keywords: delayed cord clamping, maternal outcomes, neonatal jaundice

Introduction

The anemia prevalence is 47.4% and affects 293 million children globally. Especially in South-East Asia, the prevalence is 65.5%[1]. In Thailand, the prevalence of anemia in young infants in small survey areas was as high as 32 and 62%, despite fairly proper growth[2]. Iron-deficiency anemia in infancy is concerned because it has been consistently shown to negatively influence performance in tests of psychomotor development despite complete hematologic replenishment[3].

Physiological studies have shown that there is a transfer from the placenta of 80 ml of blood at 1 minute, reaching 100 ml at 3 minutes after birth[4,5]. These additional volumes of blood can supply extra iron amounting to 40–50 mg/kg of body weight. When this extra iron is added to the approximately 75 mg/kg of body iron of term newborn, it may help prevent iron deficiency during the first year of life[6]. Delayed cord clamping, compared with early clamping, resulted in improved iron status and reduced prevalence of iron deficiency at 4 months of age, and reduced prevalence of neonatal anemia, without demonstrable adverse effects. As iron deficiency in infants even without anemia has been associated with impaired development[7]. This simple, free and safe delivery procedure might offer to reduce early infant anemia risk[8]. A delay of at least 30 seconds up to 2 minutes or more increases hematocrit and hemoglobin status in the neonatal period and reduces the frequency of iron-deficiency anemia at 4–6 months of age[9].

The 2013 Cochrane review studied the effect of timing of umbilical cord clamping of term infants on maternal and neonatal outcomes. The review showed hemoglobin concentration in infants at 24 to 48 hours was increased in the late clamping group. The difference in hemoglobin was not seen at subsequent assessments. However, improvement in iron stores was significant (with infants in the early cord clamping over twice as likely (risk ratio 2.65 with 95% confidence interval 1.04, 6.75) to be iron deficient at three to six months compared with infants whose clamping was delayed[10]. In preterm infants' mean blood volume in delayed clamping group were also significantly greater than early clamping[11].

As noted in the latest Committee opinion in timing of cord clamping[12], the optimal time for cord clamping is still debated and suggested to delay at least 60 seconds. The 2008 WHO recommendations for the prevention and treatment of postpartum hemorrhage suggested late cord clamping from 1 to 3 minutes for all births while initiating simultaneous essential newborn care[13].

In Thailand, early cord clamping is still the common methods. This study would encourage the health care provider to delayed clamping for further fetal benefit. This study tried to determine the most optimal time for the practice and also the most benefit for newborns. The primary object is to compare fetal hematocrit at 48 hours of age among different time of cord clamping and its fetomaternal outcomes.

Materials and Methods

This study was approved by the Ethics Committee of Chonburi Hospital and performed in Obstetrics & Gynecology Department at Chonburi hospital by randomized controlled trial from 1st March 2014 to 30th August 2014. After informed consent and clearly explained the procedures, participants were encouraged to discuss or answered the questions by the residents or obstetric staffs. Participants were recruited by inclusion criteria (1. singleton pregnancy 2. gestational age 34 to 42 weeks which confirmed by certained LMP and ultrasonography performed before 26 weeks of gestation 3. vaginal delivery). Then some would be excluded if the participants were unwilling to participate. Other exclusion criteria were maternal comorbidities (underlying diseases, preclampsia or eclampsia, antepartum hemorrhage, chorioamnionitis, abruptio placenta, placenta previa, unknown serology), fetal distress or need instant resuscitation, meconium stained amniotic fluid, malpresentation. Preterm and term singleton were randomized into two groups to perform 1 and 2 minutes of delayed cord clamping by block of four randomization and the randomized numbers were written on the sealed envelopes in the labor room then delivered by residents or staffs. We used the standard digital clock to countdown the time for 1 and 2 minutes by attended nurse. The period was started since the delivery of head. The babies were placed at 10 centimeters below maternal introitus and initiated newborn care simultaneously. Cord-controlled traction was performed and intravenous 10 units of Oxytocin were administrated as in active management of third stage of labor in WHO Recommendations[13]. After the procedures, maternal vital signs were monitored, estimated blood loss with scaled plastic bags and third stage were documented. Maternal complication was observed such as hypovolemic shock, postpartum hemorrhage and prolonged third stage of

labor. At 48 hours after delivery, fetal venous blood was obtained at fetal heel by 2 capillary tubes for hematocrit, hemoglobin and microbilirubin at the same time they would routinely measure Thyroid function test by attended nurse. Neonatal anemia defined as hematocrit more than 2 SD below mean for age (< 45% in term infants)[14]. Polycythemia defined as hematocrit > 65%[7]. Hyperbilirubinemia, need of phototherapy or blood transfusion based on nomogram for evaluation of screening total serum bilirubin concentration[15]. The sample size was calculated relied on Emhamed et al[16]. The difference in mean fetal hematocrit is 3.6%. The power was supposed to be 80% and confidence level was 95%. As a result, 44 neonates were determined in each group. To prevent unexpected drop out samples, we recruited more participants than we already estimated by formula.

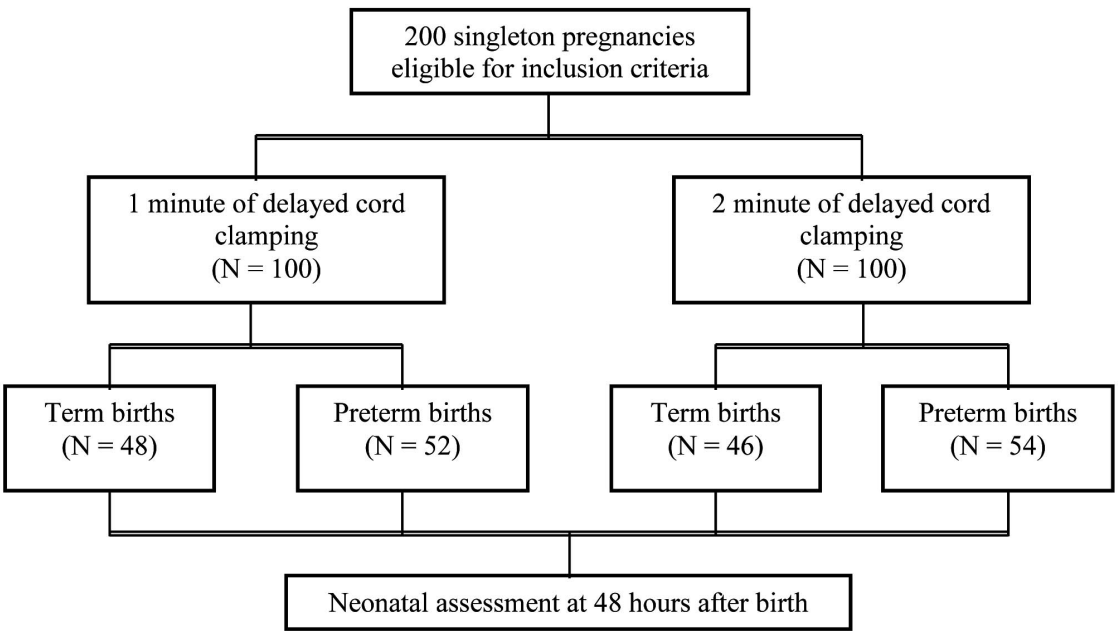

Fig. 1. The recruitment of participants.

Statistical analysis

The data was obtained from our filling forms finished by residents or staffs and printed summary of labor. The study used SPSS program (Version 16.0) for analysis. Overall, this study used intention to treat analysis. Continuous variables were analyzed with independent t-test and categorical data was analyzed with the Pearson's chi-squared test. The results were reported in means, standard deviations, percentages and $p < 0.05$ was considered statistically significant.

Results

200 participants met the criteria. They were randomized into two groups. 100 singleton pregnancies were performed 1 minute of delayed cord clamping (48 Term births and 52 preterm births). Another half was performed 2 minutes of cord clamping (46 Term births and 54 preterm births). Maternal baseline characteristics showed no significant difference in age, gestational age, parity, nationality, frequency of antenatal visits, hematocrit, hemoglobin, weight on admission and antepartum iron supplement. Length of third stage, estimated blood loss and postpartum hemorrhage were not significantly different among groups as shown in Table 1.

Table 1. Maternal demographic data.

	1 minute of DCC (N = 100)	2 minutes of DCC (N = 100)	P
Age (yr)	26.30 (4.58)	24.11 (5.46)	0.26
Gestational age (wk)	37 (3)	37(2)	0.33
Term	52 (52)	54 (54)	
Preterm	48 (48)	46 (46)	
Parity			0.88
Nulliparous	41 (41)	40 (40)	
Multiparous	59 (59)	60 (60)	
Nationality			0.53
Thai	88 (88)	85 (85)	
Non - Thai	12 (12)	15 (15)	
Frequency of ANC (times)	7.95 (2.43)	8.07 (3.08)	0.21
Hematocrit (%)	35.38 (3.61)	35.63(3.10)	0.32
Hemoglobin (g/dL)	11.71 (1.09)	11.99 (1.12)	0.25
Weight on admission (kg)	68.03 (1.05)	68.19 (1.15)	0.58
Length of 3rd stage (min)	9.04 (5.24)	9.39 (4.37)	0.23
Postpartum hemorrhage	1 (1)	0 (0)	0.31
EBL (ml)	233 (125)	234 (107)	0.65
Iron supplement	100 (100)	100 (100)	-

$p < 0.05$ considered significant, N = Number of newborn, DCC = Delayed cord clamping.
Data is presented as Mean (SD) or Percentage.

Neonatal demographic data such as birth weight, APGAR, Sex showed no significantly different between two groups as in Table 2.

Table 2. Neonatal demographic data.

	1 minute of DCC (N = 100)	2 minutes of DCC (N = 100)	P
Birth weight (grams)	2875.49 (584.50)	2754.09 (506.38)	0.158
APGAR score < 7 at 5 minutes	0 (0)	0 (0)	
Sex			0.744
Male	44 (44)	38 (38)	
Female	56 (56)	62 (62)	

$p < 0.05$ considered significant, N = Number of newborn, DCC = Delayed cord clamping. Data is presented as Mean (SD) or Percentage

Overall, neonatal hematocrit and hemoglobin at 48 hours of life in 1 minute group were 52.39%, 14.74 g/dL and in 2 minutes group were 53.44%, 16.33 g/dL which is statistically significant increased in the latter group (p = 0.041, p = 0.001 respectively). Microbilirubin was significantly increased in 2 minutes group (11.04 mg/dL vs. 10.17 mg/dL, p = 0.011). As a result, jaundice, phototherapy and admission to sick unit were also significantly increased in this group (p = 0.009, p = 0.017 and p = 0.017 consequently). No significant difference in length of hospital stay. No anemia, polycythemia and blood transfusion need found in both groups. (Table 3.)

Table 3. Neonatal outcome at 48 hours after vaginal births.

	1 minute of DCC (N = 100)	**2 minutes of DCC (N = 100)**	**P**
Hematocrit (%)	52.39 (1.56)	53.44 (2.56)	0.041
Hemoglobin (g/dL)	14.74 (2.06)	16.33 (2.04)	0.001
Microbilirubin (mg/dL)	10.17 (1.82)	11.04 (2.85)	0.011
Anemia	0 (0)	0 (0)	-
Polycythemia	0 (0)	0 (0)	-
Jaundice	1 (1)	9 (9)	0.009
Phototherapy	1 (1)	8 (8)	0.017
Blood Exchange	0 (0)	0 (0)	-
Admitted to SNB	2 (2)	10 (10)	0.017
Length of hospital stay (day)	2.03 (0.30)	2.18 (0.64)	0.100

p < 0.05 considered significant, N = Number of newborn, DCC = Delayed cord clamping,
SNB = sick newborn unit. Data is presented as Mean (SD) or Percentage

The subgroup analysis of term births showed significantly increase of hematocrit and hemoglobin in 2 minutes group (53.73% vs. 52.31%; p = 0.011 and 16.20 g/dL vs. 14.28 g/dL, p = 0.031). No significant difference between groups in jaundice, phototherapy, sick unit admission and length of hospital stay as shown in Table 4.

Table 4. Subgroup analysis of term vaginal births.

	1 minute of DCC (N = 48)	**2 minutes of DCC (N = 46)**	**P**
Hematocrit (%)	52.31(1.34)	53.73(2.61)	0.011
Hemoglobin (g/dL)	14.28 (2.16)	16.20 (2.04)	0.031
Microbilirubin (mg/dL)	10.44 (1.84)	10.88 (2.08)	0.457
Anemia	0 (0)	0 (0)	-
Polycythemia	0 (0)	0 (0)	-
Jaundice	1 (1)	0 (0)	0.405

Table 4. Subgroup analysis of term vaginal births.

	1 minute of DCC (N = 48)	2 minutes of DCC (N = 46)	P
Phototherapy	1 (1.06)	0 (0)	0.405
Blood Exchange	0 (0)	0 (0)	-
Admitted to SNB	1 (1.06)	0 (0)	0.237
Length of hospital stay (day)	2.06 (0.43)	2 (0)	0.405

P < 0.05 considered significant, N = Number of newborn, DCC = Delayed cord clamping,
SNB = sick newborn unit. Data is presented as Mean (SD) or Percentage

Subgroup analysis of preterm births showed significantly increased of hematocrit and hemoglobin in 2 minutes group (53.19% vs. 51.47%; p=0.032 and 16.45 g/dL vs. 15.31 g/dL; p=0.017). Contrast to subgroup analysis in term births, microbilirubin was significantly increased in 2 minutes group (12.44 mg/dL vs. 9.86 mg/dL, p=0.011). Jaundice, phototherapy, admission to sick unit and length of hospital stay were significantly increased in 2 minutes group as shown in Table 5.

Table 5. Subgroup analysis of term vaginal births.

	1 minute of DCC (N = 52)	2 minutes of DCC (N = 54)	P
Hematocrit (%)	51.47 (1.76)	53.19 (2.52)	0.032
Hemoglobin (g/dL)	15.31 (1.64)	16.45 (2.05)	0.017
Microbilirubin (mg/dL)	9.86 (1.78)	12.44 (2.85)	0.011
Anemia	0 (0)	0 (0)	-
Polycythemia	0 (0)	0 (0)	-
Jaundice	0 (0)	9 (9.54)	0.009
Phototherapy	0 (0)	8 (8.48)	0.016
Blood Exchange	0 (0)	0 (0)	-
Admitted to SNB	1 (0.94)	10 (10.6)	0.016
Length of hospital stay (day)	2	2.33 (0.84)	0.040

P < 0.05 considered significant, N = Number of newborn, DCC = Delayed cord clamping,
SNB = sick newborn unit. Data is presented as Mean (SD) or Percentage

Discussion

According to very few previous studies about different timing of delayed cord clamping and few data in study of preterm and term altogether in one study, There were scarcely found the comparable evidence. The results of this study showed that 2 minutes of delayed cord clamping significantly increased in hematocrit compared with 1 minute (53.44% vs. 52.39%). The results from this study seem similar to some previous studies on effect of delayed cord clamping: Emhamed 2004 (52.9% vs. 49.3%)[16], Ceriani Cernadas 2006 (56.4% vs. 51.1%)[17], Thawinkarn 2008 (56.2% vs. 49.7%)[18], Mitra 2009 (49.4% vs. 46.7%)[19] respectively.

From this study, fetal hemoglobin measured at 48 hours showed significantly increasing in 2 minutes group (16.33 g/dL vs. 14.74 g/dL) correlated with Emhamed 2004 (18.5 g/dL vs. 17.1 g/dL)[16], Thawinkarn 2008 (18.7 g/dL vs. 16.8 g/dL)[18], Mitra 2009 (16.3 g/dL vs. 15.6 g/dL)[19].

No fetal anemia found in this study might result from both group are performed delayed cord clamping, small sample size or long term follow up should be considered.

Overall, significantly increased in bilirubin, jaundice, phototherapy and admission to sick unit were found in 2 minutes group in this study. Aim at subgroup analysis of preterm births, the indicators mentioned before were also significantly increased. We already reviewed all newborn documents during admission and found no diagnosed neonatal jaundice from preterm birth, also, normal jaundice work-up laboratory results. We may presume that jaundice leaded from delayed cord clamping as from previous studies.

Fetal distress (indicated from APGAR less than 7 in 5 minutes) and overall length of hospital stay showed no statistically difference except significantly increased length of hospitalization in preterm who was performed 2 minutes of cord clamping due to jaundice and need of phototherapy. This result implied that fetal benefit from increasing of hematocrit and hemoglobin in 2 minutes group might not be superior to 1 minute group because these significant changes accompanied with their complications. Moreover, length of hospital stay was prolonged in 2 minutes group for jaundice investigation and phototherapy. This unfavorable results made 1 minute of delayed clamping more superior.

For maternal outcomes, this study showed no difference in maternal blood loss, postpartum hemorrhage and length of third stage. One case found in 1 minute-group could be explained from retained placenta caused by history of curettage 3 years ago. She was performed placenta removal and estimated blood loss 900 ml.

Our study was limited to blind due to the different length of the procedures and it will not change the results though. This study was initiated to encourage practitioners for delayed cord clamping which our study already shown the increasing in hemoglobin and hematocrit even in 1 minute of delay. 1 to 2 minutes were not consumed much time. It is effective and worth to perform in our country with high prevalence of anemia.

Conclusion

Although the significant increase of hematocrit in 2 minutes delayed cord clamping, the risk of adverse fetal outcome should be considered. No significant difference on maternal outcomes. Long term fetal outcome should be further studied for fetal benefit and the most optimal time for delayed cord clamping.

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ความแตกต่างของความเข้มข้นเลือดในทารกคลอดทางช่องคลอดก่อนและครบกำหนดด้วยการหนีบสายสะดือช้าต่างกัน

สมปรารถนา มังกรแก้ว, ธีระ ศิวดุลย์

***วัสดุและวิธีการ**: เปรียบเทียบความแตกต่างความเข้มข้นเลือดของทารกคลอดทางช่องคลอดหลังการหนีบสายสะดือช้า 1 และ 2 นาที และผลต่อมารดาและทารกที่เวลา 48 ชั่วโมงหลังคลอด*

***วัสดุและวิธีการ**: หญิงตั้งครรภ์เดี่ยวก่อนและครบกำหนด คลอดทางช่องคลอดในโรงพยาบาลชลบุรี เข้าได้กับการวิจัย 200 คน แบ่งโดยการสุ่มได้กลุ่มละ 100 คน คลอดโดยหนีบสายสะดือช้า 1 และ 2 นาที เจาะเลือดทารกหลังคลอด 48 ชั่วโมง ดูความแตกต่างความเข้มข้นเลือดของสองกลุ่ม ติดตามผลแทรกซ้อนต่อทารกและมารดา*

***ผลการศึกษา**: หญิงตั้งครรภ์ในสองกลุ่ม ไม่มีความแตกต่างทางข้อมูลทั่วไป พบว่าค่าความเข้มข้นของเลือดฮีโมโกลบิน และไมโครบิลลิรูบินของทารกที่ 48 ชั่วโมง ในกลุ่มหนีบสายสะดือช้า 2 นาที มากกว่าอย่างมีนัยสำคัญทางสถิติ คือ 53.44% กับ 52.39 % (p = 0.041) 16.33 g/dL กับ 14.74 g/dL (p = 0.001) และ 11.04 mg/dL กับ 10.17 mg/dL (p = 0.011) ตามลำดับ พบภาวะเหลือง ใช้การส่องไฟรักษา และรับเข้าแผนกทารกป่วยในกลุ่มหนีบสายสะดือช้า 2 นาทีมากกว่า คือ 1% กับ 9% (p = 0.009) 1% กับ 8% (p = 0.017) และ 2% กับ 10% (p = 0.017) ตามลำดับ ไม่พบความแตกต่างทางสถิติในคะแนนแอปการ์ ปริมาณเลือดที่เสียในมารดา การตกเลือดหลังคลอด และระยะการคลอดที่สาม ไม่พบภาวะซีด ความเข้มข้นเลือดสูงและการแลกเปลี่ยนเลือดในทารก*

***สรุป**: การหนีบสายสะดือช้า 2 นาทีเพิ่มความเข้มข้นเลือด ค่าฮีโมโกลบิน และไมโครบิลิรูบินอย่างมีนัยสำคัญทางสถิติ ส่งผลให้เกิดภาวะแทรกซ้อนมากกว่า คือ เหลือง และต้องรักษาโดยการส่องไฟ*