Behaviour of lab parameters and neonatal weight loss in relation to neonatal breathing movements and cord clamping time

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Summary

Background: To date, delaying cord clamping two to three minutes after birth is considered effective for newborn well-being. This time does not consider the newborn's breathing movements, which may also condition neonate well-being. *Aim:* To investigate the behaviour of neonatal weight loss and of some umbilical vein lab parameters, in relation to timing of newborn breathing and cord clamping. *Materials and Methods*: Time from birth to cord clamping and time from birth to first cry of the newborn were collected in 87 full-term healthy women. First cry is a sign of effective breathing. Birth weight loss at the first, second, and third day from birth and lab parameters were assessed in relation to: time from birth to cord clamping, time from birth to first cry, and cord clamping before or after the first cry. *Results:* Partial pressure of carbon dioxide (pCO_2) decreased if cord clamping was performed after first cry and increased if first cry occurred after cord clamping, independently from the time elapsed from birth to first cry ($p = 0.012$). Calcium (Ca^{2+}) concentration decreased if cord clamping was performed after the first cry and increased if first cry of the baby after birth was delayed ($p = 0.021$). Each second of delay from birth to cord clamping resulted in an increase in Cl^- concentration ($p < 0.001$). Each second of delay in cord clamping resulted in a reduction in the percentage of weight loss at the first day ($p = 0.024$), at the second day ($p = 0.007$), and at the third day ($p = 0.028$) after birth. *Conclusions:* Neonate breathing after birth should induce umbilical vein flow from placenta to lungs, conditioning the reduction of birth weight loss after birth and umbilical lab parameters modifications.

Key words: Delayed cord clamping; Neonatal breathing; Neonatal circulation.

Introduction

Delayed cord clamping has proven useful for newborn infants in the perinatal period and in the first year of life [1]. Delayed cord clamping provides neonates with an adequate blood volume and iron reserve [1]. Moreover, evidence from the literature suggests better adaptation for preterm babies and higher red blood cell flow to vital organs during the first few days of life for all babies [2-4]; additionally, behavioural benefits of delayed cord clamping may be helpful for fostering early breastfeeding [2].

Two pivotal concepts should be drawn from the aforementioned evidence. Firstly: one should wait a reasonable time to clamp cord to allow the transfusion of an adequate blood volume from cord and placenta to the neonate. Secondly: one should consider at least two minutes as the adequate time for clamping cord, as considered in randomized trials [5, 6]. The aforementioned concepts are however not congruent. Indeed, flow is a function of volume and time, and is a continuous variable. Therefore, the volume of blood transfused is in continuous relation with the time elapsed from birth to cord clamping. Mathematically, when the time from birth to cord clamping is infinite (if one does not clamp the cord), the flow from placenta and cord to neonate is infinite, since the blood volume in cord and placenta is not null.

Some authors [1] consider it useful to delay cord clamping by two to three minutes because cord pulse stops within the same minutes, suggesting that placental flow has stopped. The authors do not agree with this concept: cord flow is directed from the left fetal heart to the placenta through the umbilical arteries, and from the placenta to right fetal heart through the umbilical vein. With breathing movements, the newborn infant induces a depression in the chest and shifts the direction of blood flow to the lungs from the placenta, through the umbilical vein, and right heart atrium and ventricle [7]. Moreover, intrauterine pressure after birth is higher than before delivery [8-10]. As explained by Laplace's rule, the pressure within a sphere is inversely related to the sphere radius. Therefore, when the infant has been delivered, the uterine volume and, therefore, the uterine radius are reduced, leading to a rise in intrauterine pressure. The higher intrauterine pressure encounters blood pressure in the fetal umbilical arteries and favours flow through the uterine vein to the neonate lungs, for as long as the placenta is still within the uterine cavity. Therefore, there may be a time lapse in which umbilical arterial flow has stopped while umbilical vein flow is still present, with the effect of transferring the whole blood volume content in cord and placenta from the cord and placenta to the newborn infant.

As a logical consequence, one should consider the time from birth to cord clamping as a continuous variable that, along with time elapsed from birth to first breathing movements, may influence neonate well-being in a continuous way.

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The following study will quantitatively investigate the behaviour of neonatal weight loss and of some umbilical vein lab parameters in relation to timing of newborn breathing and cord clamping.

Materials and Methods

A sample of 87 full-term healthy women who delivered vaginally was enrolled from March 2011 to November 2011 at the G.B. Grassi hospital of Ostia (Italy). Immediately after delivery, time from birth and cord clamping was collected by stopwatch and expressed in seconds. The time from birth to the first cry was collected in the same way. Crying is considered an objective sign of at least an appropriate breathing movement. The midwife was free to decide the time of cord clamping after birth and did not know the aim of the study. Therefore the study is observational and does not modify the current practice of the facility. Immediately after cord clamping, a blood sample from the umbilical vein was collected to instantly assess the following lab parameters: partial pressure of oxygen (pO_2), partial pressure of carbon dioxide (pCO_2), pH, bases excess (BE), sodium (Na^+), potassium (K^+), calcium (Ca^{2+}), chlorine (Cl^-), hematocrit. An analyser was used for specific assessment of such parameters. Capillary bilirubin and glucose levels were assessed on the first day after delivery, as routine screening tests of newborn infants. Birth weight was collected at birth and on days one, two, and three after birth. Weight loss on the same days was expressed using a percentage scale. Each of those variables was considered as dependent variables in regression models. The independent variables considered in each multivariable regression model were: time from birth to cord clamping (seconds), time from birth to first cry (seconds), cry after cord clamping (yes/no).

Moreover, to check the interdependence among dependent variables, a three-component, rotated, factor analysis was built, in order to aggregate the associated variables. By checking the interdependence among the dependent variables, it is possible to determine which dependent variables are linked and, therefore, which ones vary together, according to trends found in regression models.

SPSS 16.0 package was used for statistical calculations and $p < 0.05$ was set as minimum significance.

Results

Mean time from birth to cord clamping was 95.6 seconds (± 66.6). Mean time from birth to first cry was 38 seconds (± 29.4). Fourteen (16.1%) patients underwent cord clamping before the baby's first cry, and 73 (83.9%) patients underwent cord clamping after first cry. Table 1 reports the mean values with standard deviations of lab parameters assessed in umbilical vein samples and the mean values with standard deviations of the first, second, and third day of weight loss.

Regression models found significant relationships for pCO_2, Ca^{2+}, Cl^-, and for weight loss at first, second, and third day after birth (Table 2). pCO_2 decreased if cord clamping was done after first cry and increased if first cry occurred after cord clamping, independently from time elapsed from birth to first cry (partial regression coefficients (B) = -5.951, 95% confidence intervals (CI) -10.580 - -1.323) ($p = 0.012$). Moreover, each second of delay from birth to cord clamping increased pCO_2 (B = 0.039, CI 95% 0.013 - 0.065) ($p = 0.003$). Ca^{2+} concentration decreased if cord clamping was performed after the first cry and increased if first cry of the baby after birth was delayed (B = -1.081, 95% CI -1.996 - -0.165) ($p = 0.021$). Each second of delay from birth to cord clamping resulted in an increase in Ca^{2+} concentration (B = -0.01, 95% CI -0.005, - -0.015) ($p < 0.001$) and an increase in Cl^- concentration (B = -0.022, 95% CI 0.011 - 0.033) ($p < 0.001$).

Table 1. — *Descriptive statistics including mean values with standard deviations of continuous variables.*

	Means	Standard deviations
pH	7.31	± 0.08
$p0_2$	34.4 mmHg	± 13.6 mmHg
$pC0_2$	39.7 mmHg	± 7.6 mmHg
Bases excess	-5 mmol/l	± 1.9 mmol/l
Na^+	134 mmol/l	± 3.6 mmol/l
K^+	5 mmol/l	± 0.9 mmol/l
Ca^{2+}	5.08 mg/dl	± 1.54 mg/dl
Cl^-	107.5 mmol/ml	± 3.72 mmol/ml
Bilirubin	1.87 mg/dl	± 0.49 mg/dl
Glucose	90.1 mg/dl	± 20.5 mg/dl
Hematocrit	53%	± 11%
1st day percentage of weight loss	3.5%	± 1.68%
2nd day percentage of weight loss	5.7%	± 2.03%
3rd day percentage of weight loss	5%	± 3.48%

Table 2. — *Regression analyses and factor analysis. Time in seconds between birth and cord clamping between birth and first cry of the baby and the effects on lab tests and neonatal weight loss.*

	Cry after cord clamping	Time from birth to first cry	Time from birth to cord clamping	Variables interdependence
ph	N.S.	N.S.	N.S.	3
$p0_2$	N.S.	N.S.	N.S.	3
$pC0_2$	-5.951 $p = 0.012$	N.S.	0.039 $p = 0.003$	2, 3
Bases excess	N.S.	N.S.	N.S.	2, 3
Na^+	N.S.	N.S.	N.S.	2, 3
K^+	N.S.	N.S.	N.S.	2, 3
Ca^{2+}	-1.081 $p = 0.021$	N.S.	0.01 $p < 0.001$	2, 3
Cl^-	N.S.	N.S.	0.022 $p < 0.001$	2, 3
Bilirubin	N.S.	N.S.	N.S.	3
Glucose	N.S.	N.S.	N.S.	3
Hematocrit	N.S.	N.S.	N.S.	3
1st day percentage of weight loss	N.S.	N.S	-0.216 $p = 0.024$	1
2nd day percentage of weight loss	N.S.	N.S.	-0.328 $p = 0.007$	1
3rd day percentage of weight loss	N.S.	N.S.	-0.441 $p = 0.028$	1

Each second of delay in cord clamping resulted in a reduction in the percentage of weight loss at the first day (B = 0.216, 95% confidence interval (CI) -0.403 - -0.029; p = 0.024), at the second day (B = -0.328, 95% CI -0.564 - -0.092; p = 0.007), and at the third day (B = -0.441, 95% CI -0.832 - -0.050; p = 0.028) after birth.

The three-component rotated factor analysis highlights interdependence among variables (Bartlett's test of sphericity: $p < 0.001$). The interdependence is strong with weight loss variables (marked with 1 on Table 2, right-hand column). Interdependence is less strong for pCO_2, BE, Na^+, K^+, Ca^{2+}, Cl^- (marked with two in Table 2, right-hand column). Additionally, pO_2, pH, pCO_2, BE, Na^+, bilirubin, and hematocrit depict a scanty interdependence (marked with three in Table 2, right-hand column).

Discussion

This study aimed to assess if time lapse from birth to cord clamping can independently influence neonate well-being, as measured by neonatal weight loss, and if it is related to breathing.

Interestingly, pCO_2 rises if the sample is taken before a breathing movement and when cord clamping is delayed. A pCO_2 behaviour similar to the one reported has been reported by Wiberg *et al.* [11]. These authors found an increase in pCO_2 levels both in the artery and vein most markedly at 45 minutes after birth. Interestingly, De Paco *et al.* [12] did not find an increase in pCO_2 at two minutes from birth, but pO_2 increased after more than two minutes from birth. Taken together, those data suggest that pCO_2 in the umbilical vein is strongly related to breathing movements, which usually occur some seconds after birth. Therefore, when the umbilical vein cord clamp is performed two minutes after birth, a healthy neonate will have already taken a breath in at least the majority of the cases. A logical conclusion drawn from this pCO_2 behaviour, is that lung function is needed for the ventilation of CO_2 in newborn infants after birth, and that the placenta is not needed to ensure respiratory function during the few minutes after birth, because pO_2 increases in umbilical blood vein if cord clamping is delayed [12].

Ca^{2+} behaviour would suggest that pCO_2 modifications in the umbilical cord vein are linked with umbilical vein flow. Ca^{2+} concentration in peripheral venous blood increases due to blood stasis [13]. Ca^{2+} increases in the umbilical vein may be linked to blood stasis as well: if the neonate cries (denoting breathing), the Ca^{2+} concentrations decrease. Therefore, breathing movements induce blood flow through the umbilical vein, and are able to induce CO_2 ventilation through the lungs.

Cl^- concentration changes follow the Ca^{2+} and the pCO_2 modifications. This is demonstrated by the second cluster of interdependence found by factor analysis (the one marked with two in the right-hand column of Table 2). Such interdependence could be explained by anionic gap behaviour in the very special condition of the umbilical vein of the newborn infant some seconds after birth. It was reported by Wiberg *et al.* [11] that lactate increases 45 and 90 seconds after birth in the umbilical vein. Even if the increase of lactic acid was not assessed in the present study, it does indeed occur. Usually, the rise in lactates does alter the anionic gap in an adult, reducing the Cl^- concentration, and is buffered by bicarbonates [14], producing CO_2 and H_2O. In the umbilical vein, however, due to blood stasis, the authors found that Ca^{2+} increases, thereby explaining the rise in Cl^- in order to maintain electrical neutrality. Therefore the excess of anions could be neutralized by the rise in Ca^{2+} concentrations.

Another weak interdependence (marked as 3 in the right-hand column of Table 2) was found among pO_2, pH, pCO_2, BE, Na^+, bilirubin, and hematocrit. Nelle *et al.* [15] reported that delayed cord clamping leads to a rise in hematocrit value. This behaviour may influence some metabolic and respiratory parameters in a pathophysiological relationship, as depicted by the interdependence found in the present study. Interestingly, the blood volume of neonates is higher in the case of delayed cord clamping, rising by about 32% when cord clamp is delayed by at least three minutes [15]. The interdependence relationships found by the present authors and results from Nelle *et al.* [15, 16] lead to consider that delaying cord clamping supplies both blood cells and water to the newborn infant. This idea impacts neonatal well-being, since neonatal weight loss at first day after birth is reduced. Consequently, this supply of water impacts weight loss at second and third days after birth too, as proven by the strongest interdependence (one on the right-hand column of Table 2).

Caution should be used in interpreting the percentage of reduction of weight loss from partial regression coefficients (B). As suggested by large intervals of confidence for each coefficient of regression, the percentage of weight loss varies very much for each newborn, and it may be explained by other variables not considered in the multivariable regression models (such as, breastfeeding or milk formula supplements). Therefore the authors judged that the reduction of the weight loss percentage predicted by timing of cord clamping may be overestimated.

In summary, the authors depict the following evolution of cord flow after birth. Umbilical arteries restore the placental bed until cord pulsation stops. Then, placental and cord blood volume halts until the first breathing movements occur, accumulating CO_2, lactate, O_2, and Ca^{2+}. This could be due to oxygenation in the placenta and to the anaerobic metabolism of red blood cells in the cord, producing lactic acid, buffered by bicarbonates. Vein stasis leads to increased Ca^{2+} ions that neutralize anions. With breathing, a quantity of blood volume stored in the placental vascular bed and umbilical vein is shifted to lungs, supplying blood cells, iron, and water to the newborn infant. Each second of delaying cord clamping supplies the neonate with blood volume for perfusing lungs and removing CO_2. The supply of water prevents newborn weight loss in the days after birth.

An intriguing speculation suggests that blood flow through the umbilical vein may exist until blood volume in the placenta is detectable (five days after birth, according to Nelle *et al.* results [16]). This blood volume could be helpful for avoiding neonatal weight loss, substantiating the lotus birth practice [17]. The topic will require appropriate investigations that quantify the blood volume transfusion through the umbilical vein in relation to neonatal breathing movements and time elapsed from birth.

Conclusion

Delaying cord clamping reduces newborn weight loss during the first days after birth. The hypothesis that umbilical vein flow after birth would not stop with artery pulse seems to be supported by data variations of lab parameters in relationship with breathing. Therefore, it is useful to clamp cord after the initial newborn breathing movements, and breathing movements are needed for perfusing lung vascular bed.

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