Effect of gravity and delayed cord clamping on the volume of placental transfusion.

The ideal timing for umbilical cord clamping has been controversial. After birth the first intervention with the baby is cord clamping. When clamping is delayed for more than one minute it is known as “delayed cord clamping”. Not only it is well tolerated by infants and mothers but results beneficial. Delayed cord clamping allows for passage of blood from the placenta to the infant. This passage of blood is known as Placental Transfusion.

It has been estimated that the volume of placental transfusion may be as large as 100 milliliters. This placental transfusion provides with a large amount of iron. Several studies performed in various countries including three large randomized controlled trials and one metanalisis have demonstrated that delayed cord clamping in term newborns increases the hematocrit and decreases the risk of iron deficiency in infancy.

Nowadays delayed cord clamping is currently recommended by ILCOR and other organizations. The recommended delay ranges between 45 seconds and 2 minutes, and even longer periods.

The volume of placental transfusion is influenced by the time from birth to umbilical cord clamping, the frequency and intensity of uterine contractions, and the use of early oxytocin. It may be larger in vaginal births than in cesarean deliveries. Some studies performed in the fifties and sixties, suggested that gravity has a strong impact in the volume of transfusion.

On the assumption that gravity influences the volume of placental transfusion, it is frequently recommended that the infant should be held at or below the level of the vagina. To hold a baby in this position for over one minute interferes with immediate contact with the mother, is difficult to accomplish, and therefore, it may affect the compliance with the recommendation of delaying cord clamping.

Most newborns could be placed immediately after birth on the mother’s abdomen or chest before clamping the umbilical cord, and, depending on the mother’s position (if she is lying down, semi-sitting or sitting), the infant would be 20 to 40 cm above the vaginal level. There is insufficient evidence about the influence of the level at which the infant is held on the volume of placental transfusion.

Hypothesis: When umbilical cord clamping is delayed for two minutes, the volume of placental transfusion in infants placed on the maternal abdomen or chest would not be inferior to that of those held at the level of the introitus.

Interventions:

Informed consent will be obtained during pregnancy or during labor, but before the beginning of the second stage of labor.

After obtaining informed parental consent patients will be randomized to the introitus or to the abdomen group.

In both groups: The newborn will be immediately placed on a scale, previously set at the level of the maternal introitus to record his/her weight.
Group 1: Clamping at level of introitus: The infant will be held by the neonatologist at introitus level, immediately after the initial weight.

Group 2: Clamping on Maternal Abdomen: The newborn will be placed on the abdomen or chest of the mother immediately after the first weight measurement.

In both groups: A plastic clamp will be put at approximately 1cm from the cutaneous insertion of the umbilical cord at 120 seconds after birth and then a new weight will be obtained after clamping.

**Primary outcome:** To compare the increment of the infant's birth weight before delayed cord clamping (2 minutes after birth) as an indirect measure of the volume of placental transfusion in a group of healthy and fullterm newborns, placed at the level of the introitus versus another group placed on the abdomen or chest of the mother.

**Justification for the Primary outcome**

The difference between the weight obtained immediately after birth and the weight after delayed clamping the umbilical cord has been shown to be a proxy for placental transfusion. 5,6,13

It is known that 1.05 grams of blood equals 1 milliliter. 14

**Secondary outcomes:** to compare the bilirubins and Hematocrits between groups, obtained simultaneously with metabolic screening at 36/48 hs. Evaluate the incidence of polycythemia and need for phototherapy. Relationship between the weight increment and birth weight. Evaluate the influence of the position adopted by the mother during delivery. Relate the use of early oxytocin on the increment in weight. Control for other co-variables using regression models.

Definitions:

Policytemia was evaluated with 2 definitions: Htoc >65 and Htoc > 70.

Need for phototherapy was upon the clinician’s decision.

Birth weight: The weight obtained after clamping of the cord was taken as the birth weight.

Positions of the mother at birth were defined as semi sitting/ sitting if an angle of more than 30° with the horizontal surface of the bed was estimated, and horizontal if the estimated angle was between 0 and 30°.

Prophylactic oxytocin use was defined as the intramuscular or intravenous administration of 10 IU of oxytocin to the mother within the first minute after birth.
METHODS

Multicenter, non inferiority, randomized controlled trial, not blind. Informed consent will be obtained during pregnancy or admittance and previous to birth.

Term newborns by vaginal delivery and without complications will be included. Study subjects will be assigned to two groups, both with delayed clamping, according to a sequence of random numbers generated by computer. The assignment will be done through opaque, sealed, easy opening envelopes, opening the envelope at the moment the mother enters the delivery room. Both parents and obstetric group will be then informed about which group the infant will be assigned to.

Venous hematocrit and bilirubin will be obtained at 36 to 48 hours simultaneously with routine neonatal screening.

Maternal history, perinatal, delivery and infant data will be recorded in the CRF and evaluated.

Participants:

Inclusion Criteria:

Term newborns.
Vigorous
Vaginal delivery.
Informed consent signed
Investigator present in the delivery area

Exclusion Criteria:

History of Placenta previa,
History of postpartum hemorrhage.
Multiple gestation.
IUGR.
Major congenital malformations diagnosed previous to delivery.
Maternal diseases such as: eclampsia, Rh incompatibility, congestive heart failure.
Request by the parents of saving cord blood for banking

Elimination criteria:

Need for immediate assistance of the newborn,
Birth weight less than 2500 g,
Tight nuchal cord.

Short umbilical cord preventing the possibility to place the infant in the assigned position.

Major congenital malformations not diagnosed during prenatal period,

Delivery finished by Forceps or Cesarean section

**Sample size**

A difference in weight of 90 g and a standard deviation of 60 g were assumed.

170 infants per group are needed for 80% power and a significance level of 5%.

**Statistical analysis plan**

In this non-inferiority clinical trial, all the recollected variables will be summarized: categorical variables with frequencies and percentages and quantitative variables with descriptive statistics (minimum, maximum, mean, standard deviation, median and range).

The response variable is the weight increment, calculated as the difference between the weight obtained after umbilical cord clamping at 2 minutes and the weight obtained immediately after birth. To test non-inferiority, a pre-specified margin of 18g will be compared with the upper limit of the 95% confidence interval for mean difference in weight gain between the introitus group and the abdomen group. Based on a recent study with mean weight gain of 90g, we consider that the abdomen group will be non-inferior for a difference within a margin of 20% (18g). If necessary, intention to treat analysis and per-protocol analysis will be presented. Chi-squared test and student’s t-test will be used to compare treatments for all the response variables.

Multivariate models will be used to control for covariates, such as, gestational age, sex, birth weight, etc.

All data will be analyzed with SPSS software and a significance level of 5% will be used for all the tests.

**Power and sample size**

Using the confidence interval approach, we estimated that at least 170 patients per group will be needed to have an 80% power to test the non-inferiority considering a mean weight gain of 90g, a standard deviation of 60g, a non-inferiority margin of 18g (20%) and a significance level of 5%.

**Randomization**

A computer generated randomization table will be used. Sequentially numbered opaque envelopes will be used for patient allocation. Blocks of variable size will be used.

**Data safety monitoring committee**

We will analyze data when we recruit 100 patients, to monitor safety and security.
Board review

This protocol was reviewed and approved by the independent “Comité de Etica de Investigación CEMIC Centro de Educación Médica e Investigaciones clínicas "Norberto Quirno" Approval Number: 694 and by the IRBs of the 3 participating Hospitals

References


