The Optimum Time for Cord Clamping after Vaginal Delivery in Term Pregnancy

A Randomized Control Trial

Thesis

Submitted for Partial Fulfillment of Master Degree
in **Obstetrics & Gynecology**

By

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PROTOCOL OF A THESIS FOR PARTIAL FULFILMENT OF MASTER DEGREE IN OBSTETRICS & GYNECOLOGY

TITLE OF THE PROTOCOL: THE OPTIMUM TIME FOR CORD CLAMPING AFTER VAGINAL DELIVERY IN TERM PREGNANCY A RANDOMIZED CONTROL TRIAL

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What is already known on this subject? AND What does this study add?

Delayed umbilical cord clamping appears to be beneficial for term and preterm infants. It increases hemoglobin levels at birth and improves iron stores in the first several months of life, which may have a favorable effect on developmental outcomes

Knowing the benefits to most newborns, the American College of Obstetricians and Gynecologists now recommends a delay in umbilical cord clamping in vigorous term and preterm infants for at least 30–60 seconds after birth.

This study aims to define the optimal time for delayed cord clamping

1. INTRODUCTION

Given the benefits to most newborns and concordant with other professional organizations, the American College of Obstetricians and Gynecologists now recommends a delay in umbilical cord clamping in vigorous term and preterm infants for at least 30–60 seconds after birth ***(ACOG, 2017).***

Delayed umbilical cord clamping appears to be beneficial for term and preterm infants. In term infants, delayed umbilical cord clamping increases hemoglobin levels at birth and improves iron stores in the first several months of life, which may have a favorable effect on developmental outcomes ***(Rana et al., 2018).***

Before the 1950s, the term *early clamping* was defined as umbilical cord clamping within 1 minute of birth, and *late clamping* was defined as umbilical cord clamping more than 5 minutes after birth ***(Raju and Singal, 2012).*** After multiple small studies of blood volume changes after birth, it was reported that 80–100 mL of blood transfers from the placenta to the newborn in the first 3 minutes after birth and up to 90% of that blood volume

transfer was achieved within the first few breaths in healthy term infants ***(Alzaree et al., 2018).***

More recent randomized controlled trials of term and preterm infants as well as physiologic studies of blood volume, oxygenation, and arterial pressure have evaluated the effects of immediate versus *delayed umbilical cord clamping* ***(Fogarty et al., 2010).***

Delayed umbilical cord clamping appears to be beneficial for term and preterm infants. In term infants, delayed umbilical cord clamping increases hemoglobin levels at birth and improves iron stores in the first several months of life, which may have a favorable effect on developmental outcomes ***(Birth, 2017).*** These randomised studies have led a number of professional organizations to recommend delayed umbilical cord clamping in term and preterm infants. For example, the World Health Organization recommends that the umbilical cord not be clamped earlier than 1 minute after birth in term or preterm infants who do not require positive pressure ventilation. Recent Neonatal Resuscitation Program guidelines from the American Academy of Pediatrics recommend delayed umbilical cord clamping for at least 30–60 seconds for most vigorous term and preterm infants ***(Bolstridge et al., 2016).*** The Royal College of Obstetricians and Gynaecologists also recommends deferring umbilical cord clamping for healthy term and preterm infants for at least 2 minutes after birth ***(RCOG, 2015).***

2. **AIM/ OBJECTIVES**

The aim of the study is to determine the optimum time of cord clamping in women delivering vaginally.

3. **Question of Study**

What is the optimum time of cord clamping in women delivering vaginally?

4. **Hypothesis**

- The null hypothesis the mean ± SD packed cell volume is

assumed to be equal in both groups
- The alternative hypothesis the mean ± SD packed cell volume is assumed to be more in delayed clamping group.

5. METHODOLOGY:
Patients and Methods/ Subjects and Methods/ Material and Methods

Type of the study:
Randomized control trial.

Study settings:
The study will be conducted at Ain Shams University Maternity Hospital.

Sample size justification:

The required sample size has been calculated using the IBM© SPSS© Sample Power© software version 3 (IBM© Corp., Armonk, NY, USA).

The primary outcome measure is neonatal hemoglobin immediately after delivery.

A previous study reported that the mean ± SD haemoglobin level associated with early versus delayed cord clamping was 17.1 ± 1.9 g/dl or 18.5 ± 2.1 g/dl, respectively ***(Emhamed et al., 2004)***. In that series, the mean ± SD packed cell volume associated with early versus delayed cord clamping was 49.3 ± 5.7 % versus 52.9 ± 6.3 %, respectively.

Consequently, it is estimated that a sample size of 85 patients in each study group would achieve a power of 90% (type II error, 0.1) to detect statistical significance for a difference of 3.6% between the two groups as regards the packed cell volume. The mean ± SD packed cell volume is assumed to equal 49.3 ± 5.7 % in both groups under the null hypothesis, and to equal 49.3 ± 5.7 % versus 52.9 ± 6.3 % in the early clamping group or delayed clamping group, respectively, under the alternative hypothesis.

This sample size of 85 patients per group would achieve a higher power of 97% (type II error, 0.03) to detect statistical significance for a difference of 1.4 g/dl between the three groups as regards the hemoglobin level after 24 hours. The mean ± SD hemoglobin level is assumed to equal 17.1 ± 1.9 g/dl in both groups under the null hypothesis, and to equal 17.1 ± 1.9 g/dl versus 18.5 ± 2.1 g/dl in the early clamping group or delayed clamping group, respectively, under the alternative hypothesis.

These calculations used a two-sided unpaired t test with a confidence level of 99% (type I error, 0.01).

Statistical analysis

Data will be collected, tabulated, then analyzed using IBM© SPSS© Statistics version 22 (IBM© Corp., Armonk, NY).

Normally distributed numerical data will be presented as mean ± SD, and skewed data as median and interquartile range. Qualitative data will be presented as number and percentage. Comparison of normally distributed numerical data will be done using the unpaired Student t test. Skewed data will be compared using the Mann-Whitney U test. Categorical data will be compared using the chi-squared test or Fisher's exact test, when appropriate. A two-sided p-value <0.05 will be considered statistically significant.

Eligibility criteria

Inclusion criteria:

- Vaginal deliveries
- Term fetus
- Expected average fetal weight (3-3.5kg)
- Vigorous babies with no signs of fetal distress.

Exclusion criteria:

- Known or suspected maternofetal allimmunisation.
- Rh –ve mothers.
- Any pregnancy complicated by alloimmunization.

Method:

- All eligible women admitted to the hospital during the study period will be invited to participate in the study; those who give informed consent will consecutively be enrolled.
- The position of the newborn during delayed umbilical cord clamping generally has been at or below the level of the placenta, based on the assumption that gravity facilitates the placental transfusion.
- During delayed umbilical cord clamping, early care of the newborn should be initiated, including drying and stimulating for first breath or cry, and maintaining normal temperature by covering the infant with dry linen. Secretions should be cleared only if they are copious or appear to be obstructing the airway
- The Apgar timer may be useful to monitor elapsed time and facilitate an interval of at least 30–60 seconds between birth and cord clamp.
- Delayed umbilical cord clamping should not interfere with active management of the third stage of labor, including the use of uterotonic agents after delivery of the newborn to minimize maternal bleeding.
- If the placental circulation is not intact, such as in the case of abnormal placentation, placental abruption, or umbilical cord avulsion, immediate cord clamping is appropriate. Similarly, maternal hemodynamic instability or the need for immediate resuscitation of the newborn on the warmer would be an indication for immediate umbilical cord clamping.
- Baby will be placed on a sensitive weight scale *Rossmax WE300 elecronic babv scale* together with immediate calculating the time in seconds
- Cord clamping will be done when the cord is pulseless.
- Hemoglobin will be measured after delivery and again after 6 months using heal capillary blood by (by Easy Touch GCHb device).

Outcome:

- The primary outcome measure of the study will be Neonatal Hemoglobin level after delivery.

- Secondary outcome
  1. Maximum time in seconds of delayed cord clamping to reach the maximum fetal weight to determine the optimum time for delayed cord clamping.
  2. Neonatal hemoglobin level after 6 months.
  3. Intubation.
  4. Respiratory distress (intercostal, subcostal retraction, tachypnea).
  5. Jaundice requiring phototherapy (by history after 6 weeks of delivery).
  6. Neonatal Intensive Care unit (NICU) admission (for causes other than photo therapy).
  7. Apgar score (after 5 minutes of delivery).
  8. Need for maternal blood transfusion.
  9. Additional need for therapeutic uterotonics (more than 20 units of oxytocin).
  10. Post partum hemorrhage (blood loss > 500cc).

Ethical and legal aspect.

Delegation of investigator responsibilities:

The investigator will ensure that all persons assisting with the trial are adequately informed about the protocol, any amendments to the protocol, their trial-related duties and functions. The investigator will maintain a list of sub-investigators and other appropriately qualified person to home he / she has delegated scientific trial-related duties.

Patient information and informed consent:

Before being admitted to the clinical study, the patient must consent to participate after the nature, scope, and possible consequences of the clinical studies has been explained in a form understandable to here. An informed consent document, in Arabiclanguage, contains all

locally required elements and specifies who informed the patient. After reading the informed consent document, the patient must give consent in writing. the patient`s consent must be confirmed at the time of consent by the personally dated signature of the patient and by the personally dated signature of the person conducting the informed consent discussions. If the patient is unableto read, oral presentation and explanation of the written informed consent form and information to be supplied to patients must take place in the presence of an impartial witness. Consent must be confirmed at the time of consent orally and by the personally dated signature of the patient or by local legally recognized.

Alternative (e.g., the patient`s thumbprint or mark) the witness and the person conducting the informed consent discussion must also sign and personally date the consent document.

The original signed consent document will be retained by the investigator. The investigator will not undertake any measures specifically required only for the clinical study until valid consent has been obtained.

Confidentiality:

Only the patient number and patient initials will be recorded in the CRF, and if the patient`s name appear in any other document (e.g., pathologist report), it must be kept in privacy by the investigator. The investigator will maintain personal patient identification List (patient numbers with the corresponding patient named to enable records to be identified.

Protocol approval:

Before the beginning of the study and in accordance with local regulation followed the protocol and all corresponding documents will be declared for ethical research approval by the council of OB/GYN department, Ain Shams University.