Alexandria University
Faculty of Medicine
Department of Pediatrics

COMPARATIVE STUDY OF THE SHORT TERM OUTCOME OF EARLY VERSUS DELAYED CORD CLAMPING IN PRETERM NEWBORN INFANTS

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In

Pediatrics

By

Walaa Ibrahim Abd Elrazek Ghonim

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AHA	:	American Heart Association
AMTSL	:	Active management of the third stage of labor
AMUH	:	Alexandria university maternity hospital
BPD	:	Broncho-pulmonary dysplasia
BW	:	Birth weight
CBC	:	Complete Blood Count
CLD	:	Chronic lung disease
COP	:	Cardiac output
CRP	:	C-reactive protein
DCC	:	Delayed cord clamping
ECC	:	Early cord clamping
EOS	:	Early onset sepsis
Epo	:	Erythropoietin
ERC	:	European Resuscitation Council
FiO2	:	Fraction inspired oxygen
FPBV	:	Fetal - placental blood volume
FTT	:	Failure to thrive
GA	:	Gestational age
HbF	:	Hemoglobin F
Hct	:	Hematocrit
Hgb	:	Hemoglobin
HIE	:	Hypoxic-ischemic encephalopathy
HIV	:	Human immune deficiency virus
HR	:	Heart rate
IDA	:	Iron deficiency anemia
IVH	:	Intra-ventricular hemorrhage
LOS	:	Late-onset sepsis
NEC	:	Necrotizing entero-colitis
NICU	:	Neonatal intensive care unit
NIHB	:	Neonatal indirect hyperbilirubinemia
NK	:	Natural Killer cells
NRP	:	Neonatal resuscitation program
PFT	:	Placental fetal transfusion
PPH	:	Postpartum hemorrhage
PPHN	:	Persistent pulmonary hypertension
PROM	:	Premature rupture of membrane
PT	:	Preterm

PTLP	:	Preterm labor pains
PVL	:	Periventricular leukomalacia
RBCs	:	Red blood cells
RDS	:	RESPIRATORY distress syndrome
ROP	:	Retinopathy of prematurity
SNEC	:	Suspected necrotizing entero- colitis
SVC	:	Superior vena cava
TPN	:	Total parenteral nutrition
UK	:	United kingdom
UNICEF	:	United Nations Children's Fund
VE	:	Volume expander
VLBW	:	Very low birth weight
WHO	:	World Health Organization

INTRODUCTION

The incidence of prematurity has risen drastically over the last twenty-five years. In 2010, WHO stated that approximately 15 million babies are born prematurely each year worldwide, accounting for more than one in each ten of all newborn babies. The incidence of preterm deliveries has increased from 9.4% in 1980 to 11.1% in 2012.[1] Over 60% of preterm births occur in Africa and South Asia with average of 12% in the poorest countries compared to 9% in the higher income countries.[2] In 2013, Unicef reported 44% of the under- five deaths worldwide occur in the neonatal period accounting for 2.8 million death per year. Prematurity and its complications is the first leading cause of neonatal mortality (35%), intrapartum-related complications (24%), sepsis (15%), pneumonia (5%), tetanus (2%) and diarrhea (1%).[3]

All newborns are generally fragile and more so premature babies, making them in continuous need for special care just to remain alive. Advances in medical technology have contributed to smaller infants surviving past the neonatal period. This survival, however, is fraught by many complications including respiratory distress syndrome (RDS), intra-ventricular hemorrhage (IVH), neonatal indirect hyperbilirubinemia (NIHB), sepsis either early onset (EOS) or late onset (LOS), apnea and anemia of prematurity, necrotizing entero-colitis (NEC), bronchopulmonary dysplasia (BPD) and retinopathy of prematurity (ROP).[4] Most of these complications may end up a preterm life or make him suffering all through it. So, ongoing efforts are aiming to prevention of prematurity and its complications rather than treatment, aiming to a better outcome together with the least expenses.

In the last few years delayed cord clamping (DCC) has been resurrected again after centuries of being dormant to be scaled up and integrated in the management of those vulnerable premature babies. After decades of discussion, debate and dialogue, DCC is assumed to have many benefits especially in case of premature infants. Meanwhile, there is still little unanimous about the optimal timing of cord clamping. In 2009, the Royal College of Obstetricians and Gynecologists issued an opinion paper about this practice. Their document didn't make any recommendations about the exact timing for cord clamping, but it firmly recommend that large randomized trials are needed in order to understand the substantive outcomes of this alternative strategy.[5]

In 1875, the great French obstetrician Pierre Budin [6] wrote a paper entitled "A Quel Moment Doit On Pratiquer La Ligature du Cordon Ombilical?" that literally translation is "At what moment ought one practice tying off the umbilical cord?". In that era early cord clamping (ECC) was considered to be within 1 minute after birth while DCC after 5 minutes. Later in the 1960s a series of blood volume measurements and other observations were made by John Lind et al. Their studies suggested that ECC should be defined as occurring within 15 seconds and DCC within 1 minute, because a significant proportion of blood is already transferred from the placenta to the baby by this time.[7,8]

In 2010, a review of literature defined DCC as clamping after 30 seconds and ECC before 30 seconds.[9] However, nowadays, although clear clinical guidelines based on solid data have not been yet adopted, the latest neonatal resuscitation program (NRP) developed by the American Heart Association (AHA) and the European Resuscitation Council (ERC) in 2010, recommended that for uncompromised babies, i.e. not in need for immediate

resuscitation, there may be benefits in delaying the clamping of the umbilical cord for at least 1 minute from the complete delivery of the infant.[10]

Furthermore, on October 2010, the new UK newborn resuscitation guidelines were published simultaneously with the European guidelines, one of the major changes in these guidelines is the endorsement of DCC in resuscitation management plan.[10] In 2011, a web based questionnaire to the heads of departments in all maternity units in Norway was performed. The study revealed that ten of sixteen (62.5%) large obstetric department reported to practice DCC of full term neonates, while only seven (43.7%) of these do so for premature infants.[11]

Delayed versus early cord clamping

At any point of time, during the fetal state one third and one half of the fetal placental blood volume (FPBV) is present in the placenta of a full term and preterm fetus, respectively. Out of these about 15-20 ml of blood is circulating in the umbilical vein carrying out the process of gas exchange, nutrition, elimination of waste products and many other essential functions that the placenta is responsible for.[12]

Before delivery the pulmonary circulation receives only 8%of the fetal cardiac output (COP). After birth for extra- uterine respiration to occur a dramatic increase in the pulmonary circulation should happen demanding 40%-55% of neonatal COP. This transition requires a redirection of the COP and increase in blood volume. So, if adequate perfusion of both the respiratory and systemic circulation is to be maintained, a partial transfusion of the placental blood volume to the neonate is required.[12]

Naturally during the second stage of labor, uterine contractions generates an intra-uterine pressure of 80-100 mmHg forcing blood transfusion from the placenta to the fetus. Compression of the placenta continues as the uterus empties, transferring more of the placental-fetal blood to the baby. At delivery, when the baby is taking his first breath while the umbilical cord is left unclamped, the oxygen level in the newborn's venous blood rises from 15 to 36 mm Hg leading to closure of the umbilical arteries, preventing any further blood flow from the infant's body to the placenta.[12]

The next few uterine contractions may squeeze a small amount of additional remaining blood through the umbilical vein to the infant, ensuring maximum RBCs for oxygenation and normal infant blood volume.[12]

Yao and colleagues [7] clearly documented a substantial increase in the neonate's blood volume that occurs when the umbilical circulation is left intact for few minutes after delivery. They estimated that 50% of the placental transfusion occurs within 1minute and 100% by 3 minutes while the infant position is at the level of the introitus. The same workers found that lowering the baby 30 cm speeds the transfusion reaching its maximum by 1 minute.

In another study Ceriani Cernadas et al calculated a placental transfusion up to 80 ml after 1 minute and 100 ml after 3 minutes. This volume of extra blood has been shown to increase perfusion, raise blood pressure and increase RBC delivery to the vital organs.[13]

The rise in fetal/neonatal blood volume boosts the increase in the systemic blood pressure to override the high pulmonary vascular resistance to begin the process of lung

recruitment via capillary erection. When the unclamped umbilical cord continues to pulsate, it allows the newborn to equilibrate blood volume, oxygen levels and pH through ongoing placental exchange. The increased red blood cell flow raises the oxygen level in the newborn's blood stimulating the respiratory center to initiate breathing.[12]

However, it appears that ECC became a common practice in the last century despite evidence that clamping before the first breath may cause momentarily fetal bradycardia. Dawes'graph of heart rate (HR) showed that the fall in HR occurred very rapidly after cord occlusion. A proposed cause for this bradycardia is a reduction in venous return to the right side of the heart following clamping of the cord. Furthermore, if the cord is cut before the lung has been aerated and pulmonary blood flow has increased, venous return to the left side of the heart will also be low. The resulting reduction in venous return to both sides of the heart causes a reflex decrease in ventricular output, resulting in reflex vegal stimulation and reduction in HR.[14]Based on these physiological changes, ECC may interfere theoretically with the normal neonatal transition by reducing the expected blood volume of the newborn by 25- 40% in combination with bradycardia. Such a massive restriction, especially in a preterm, may be responsible for untoward consequences.[12]

Concerns exist regarding universally adopting DCC that it may jeopardize timely resuscitation efforts, when needed, especially in preterm infants. The latest WHO guidelines on basic newborn resuscitation state that, the cord should be clamped and cut to allow for effective ventilation in term or preterm babies requiring positive pressure ventilation. However, as long as the placenta continues to perform gas exchange after delivery and sick preterm infants are likely to benefit most from the additional blood volume, they recommended that, whenever the clinician has experience in providing effective positive-pressure ventilation without cutting the cord, it can be initiated at the perineum to allow for placental transfusion.[15]

Difficulty of performing the procedure of resuscitation with the infant placed at or below the level of the placenta was also bypassed, a specialized resuscitation unit has already been produced to be attached to the delivery bed enabling the baby to be placed in a stable, warmed position without the need to cut the umbilical cord and still allow the clinical staff the necessary access. (figure1)[16]

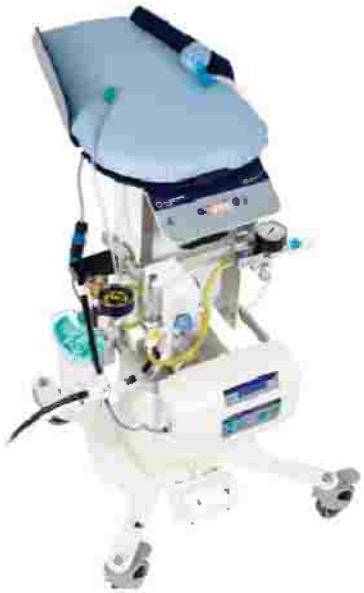

Figure (1): The feature of the Life Start design ressusciter.[16]

An alternative method for achieving active placental transfusion without delaying resuscitation was studied. Milking the umbilical cord toward the baby before clamping should take less than 5 seconds and therefore should not interfere with neonatal resuscitation. This has been found to result in a similar amount of placento-fetal blood transfusion. Although some practitioners have adopted this practice in preterm deliveries, there is a paucity of data to support this practice.[17]

The complications for excessive placental transfusion secondary to DCC have also been raised. This can lead to neonatal polycythemia, especially in the presence of risk factors such as maternal diabetes, severe intrauterine growth restriction (IUGR) and fetal and/or maternal hypoxia. During the latter, increased levels of catecholamines in both circulations will induce vasoconstriction of the umbilical vessels that is more prominent in the arteries leading to transfer of blood from the placenta to the baby prior to delivery.[18]

Philip and Saigal and colleagues found that the increased breakdown of RBC's in infants who have higher Hct levels secondary to DCC had contributed to an increased bilirubin load. The incidence of hyperbilirubinemia >15mg/100ml was significantly greater with DCC group. It reached 14% after 1 minute and 38% after 5 minutes with some preterm infants required exchange transfusion. On the other hand, ECC group had only a 6% increase. [19]

Hyper viscosity resulting from excessive placental transfusion in case of preterm neonate was refuted by Linderkamp et al who observed that the large erythrocytes of preterm neonates are not associated with higher blood viscosity. Although the red cells are much larger than those of term neonates, they are much elastic. In addition the lower plasma proteins concentration in preterm infants makes the overall blood viscosity less than that of a term neonate. This makes worries for developing complications of polythycemia in a preterm baby negligible.[20]

Nowadays, a new protest is raised against DCC that it might interfere with attempts to collect cord blood for banking. However, ethically talking, the routine practice of umbilical cord clamping should not be altered for collection of umbilical cord blood for banking.[15]

HIV transmission has been less worried for after the WHO 2012 recommendations which stated that delayed cord clamping is recommended even among women living with HIV or women with unknown HIV status. During the time between birth and cord clamping, blood flow from the placenta to the newborn baby is the same as during pregnancy. There is no evidence that 1 to 3 minutes of additional placental blood flow after birth increases the possibility of HIV transmission from mother to baby.[15]

Early clamping appears to have been an unintended consequence of the introduction of active management of the third stage of labor (AMTSL) in the 1970s to reduce the risk of postpartum hemorrhage (PPH). However, the new 2012 WHO guidelines includes the use of uterotonics, controlled cord traction, uterine tone assessment and delayed cord clamping for all babies as it benefits the baby and does not interfere with the practice of AMTSL.[15]

Finally, several recent studies had emphasized many benefits of DCC especially in preterm babies, including smoother postnatal transition, more stable blood pressure during the first day of life, reduced use of inotrops and fewer subsequent blood transfusions.[12] In a Cochrane review of 738 infants born between 24 and 36 weeks gestation these benefits were emphasized in addition to decreased incidence of both NEC and IVH.[21] In addition, Mercer et al. Reported lower incidence of LOS and IVH in babies with DCC. Additional possible benefit in the same study were the reduction of (BPD) and ROP.[22]

Benefits of DCC in preterm infants

Hemoglobin (Hgb) concentrations gradually rise during gestation. At 10 weeks gestation, the average concentration is approximately 9 g/dl. By the start of the third trimester it reaches 11 to 12 g/dl and by the 30_{th} week it ranges from 13 to 14 g/dl. From the 22nd week onward, the Hgb increases by approximately 0.2 g/dl/ week.[23]

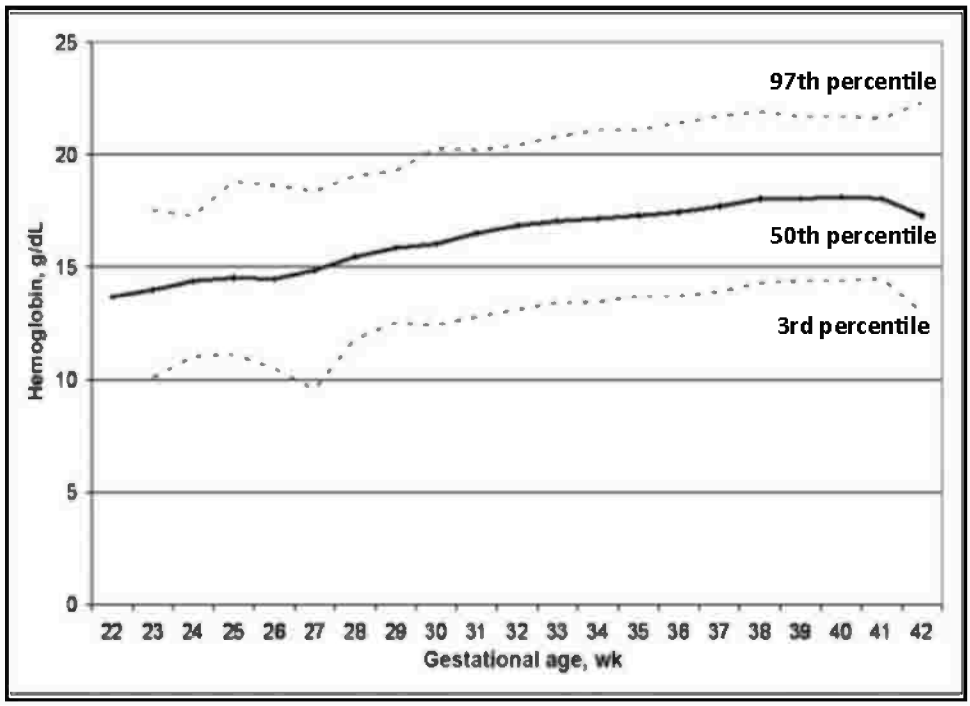

Figure (2): Reference ranges for blood hemoglobin concentrations at birth in babies at 22 to 42 weeks' gestation.[23]

During the first day of life in term and late preterm infants, Hgb concentrations increase by approximately 4% at 4 hours of postnatal age, resulting from the physiological shifting in fluid distribution with a decrease in plasma volume. By 8-12 hours of age, the concentration achieves a relatively constant level. On the contrary, in preterm infants a decrease in Hgb of approximately 6% does occur at 4 hours of age.[23]Many workers explained this drop to be due to lack of placental transfusion as the umbilical cord in preterm infants, most of the time, is clamped early to expedite resuscitation. This decrement, however, could be easily overcome by DCC.[24]

Deprivation of the potentially sick PT infant of the sizable placental RBCs reservoir by ECC could reduce their blood oxygen carrying capacity. This aggravates conditions whereby oxygen delivery is the primary concern. These include RDS, persistent pulmonary hypertension (PPHN), NEC, and hypoxic-ischemic encephalopathy (HIE).[12]

Later on during the neonatal period RBCs production decreases significantly, primarily as a result of the increased availability of oxygen, that greatly reduces the production of the already deficient erythropoietin (Epo). In addition, the shortened erythrocyte life span, deficient iron stores and phlebotomy losses makes preterm infant more at risk of developing anemia of prematurity.[25]

Even a mild anemia in the sick PT infant is no doubt a confounding factor complicating the course of diseases these babies could suffer during their NICU admission such as, chronic lung disease (CLD), infection, NEC and other common neonatal morbidities. In addition, reduced Hgb levels are associated with more apneic episodes, pathologic tachycardia and tachypnea, increased oxygen consumption and increased incidence of failure to thrive (FTT). A 1-2 g / dl rise of Hgb base line when DCC is performed may help alleviating the severity of anemia and its complications.[26]

Furthermore, knowing that iron storage takes place mainly in the last 8 weeks of gestation, this makes preterm infants more liable to iron deficiency anemia (IDA). Placental transfusion of 30 ml/kg of blood supplies the infant with 35-75 mg of iron. This amount is sufficient to maintain the desirable levels of tissue and circulating iron for 4-6 months of life protecting infants from iron deficiency anemia (IDA).[27]

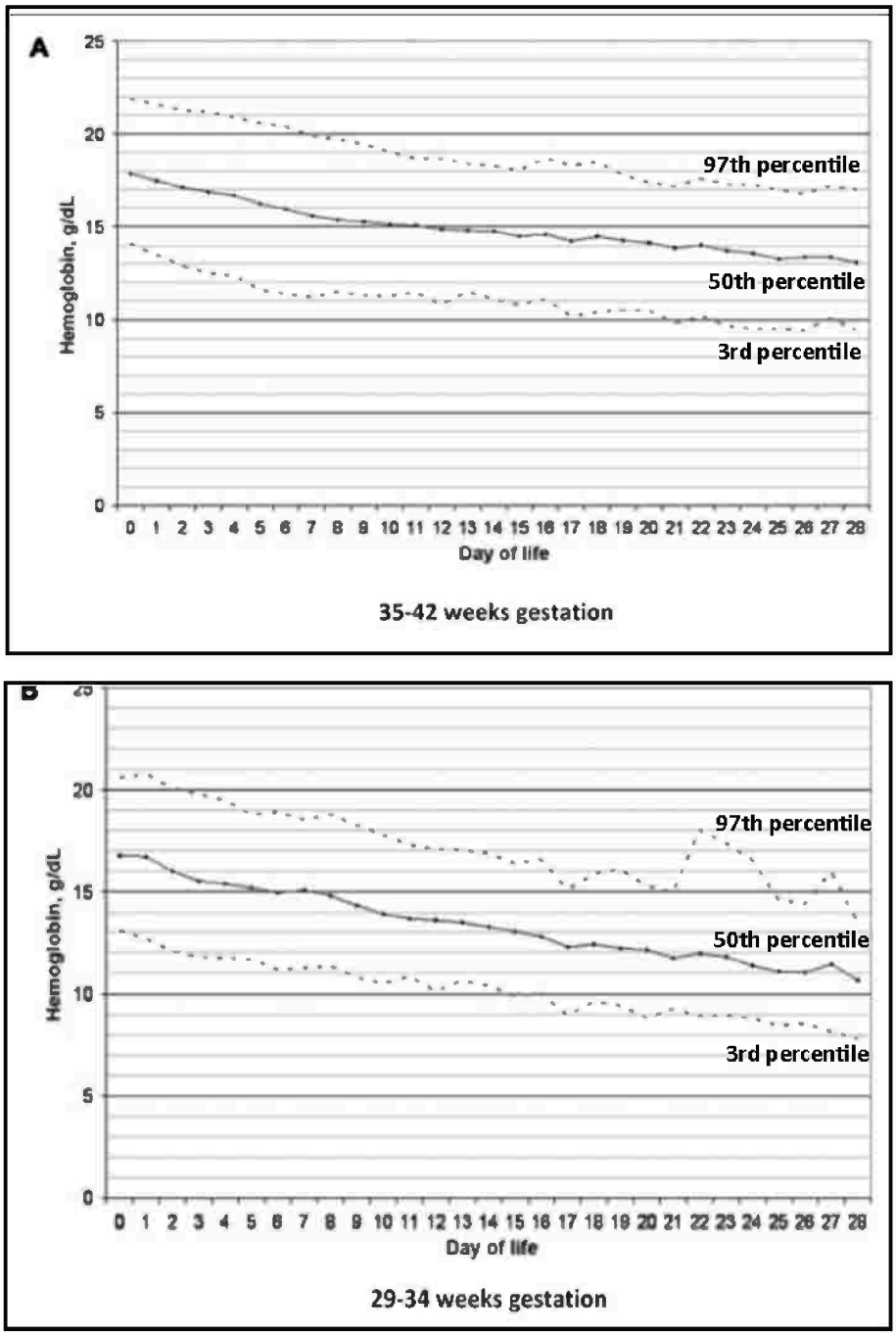

Figure (3): Reference ranges for blood hemoglobin concentrations in babies during the 28 days after birth in late preterm and term infants 35 to 42 weeks' gestation (panel A) and in preterm infants 29 to 34 weeks' gestation (panel B).[23]

An estimated 60% to 80% of very low-birth weight (VLBW) infants usually receive one or more RBC transfusions during the NICU admission as treatment for anemia and /or suspected hypovolemia. Researchers observed that approximately 50% of administered transfusions occurs in the first 2 weeks of life and up to 70% by the first month.[26]

Rabe et al. pointed out that delaying cord clamping was associated with fewer premature infants requiring transfusions for anemia. Needless to say that, reducing the frequency of blood transfusion reduces the risk of transfusion related infections, graft-versus-host disease and transfusion-related lung and gut injuries and their long term morbidities.[21]

When the cord is clamped before an adequate placental transfusion to the infant has occurred, the required blood volume may be taken from other capillary beds resulting in relative hypo perfusion. The potential circulatory effect of this may be disruption of the auto regulation essential to stabilize cerebral blood flow and prevent a pressure-passive circulation, ending up into ischemic injury to the brain and similarly to the gastrointestinal tract, the kidneys, the lung and other vital organs.[28] Cochrane review of studies documented that DCC stabilizes the circulatory system of the newborn during the first day of life allowing less transfusion for treatment of hypovolemia. Optimizing tissue perfusion by PFT also influences cerebral perfusion and potentially reduces the risk of hypoxic ischemic brain damage.[21] This may play a role in protection against the development of periventricular leukomalacia (PVL).[28]

Under normal situations reduced blood volume does not necessarily results in immediate reduction of blood pressure. This is attributed to auto regulation mechanisms of the cardiovascular system, increasing the vascular resistance to stabilize blood pressure. However, these mechanisms are defective in case of preterm infants besides increased capillary permeability that allows rapid fluid shift between intra and extra vascular spaces.[28]

In a comparative randomized study on the timing of cord clamping (ECC versus DCC), Aladangady and colleagues reported a statistically significant change in blood volume between the two groups corresponding to 18% increase with DCC. The authors concluded that a cord clamping time of 30- 40 seconds would achieve euvolemia defined as a blood volume of approximately 75-100ml /kg. In another study comparing superior vena cava (SVC) blood flow, DCC group had significantly higher caval blood flow and greater right ventricular output and stroke volumes that persisted up to 48 hours after birth.[29] In addition, Baenziger et al showed higher values for mean regional cerebral tissue oxygenation in DCC group at 4 hours of age, which persisted for 24 hours of age.[28]

Therefore, the additional volume of extra blood received as a result of DCC would help to reduce neonatal morbidity by providing more intravascular volume that is required to maintain adequate perfusion and improving cardiovascular stability during this critical period of transition from fetal to neonatal life.[12]

The incidence of IVH is inversely related to gestational age and / or birth weight. Approximately 90% of IVH take place during the first week of life, out of them 78% occurs by 72 hours of age and only a small proportion of IVH is visible on scans performed immediately after birth.[30]

Because of its multifactorial etiology and pathogenesis, the "silver bullet" that will prevent IVH still does not exist. However, numerous studies have addressed various modalities for prevention of this event in both antenatal and postnatal periods. The apparent impairment of auto regulation of cerebral blood flow in distressed preterm infants denotes the importance of preventing both hypotension and rapid increase in blood pressure. Not only hypotension but also its treatment with volume expanders and vasopressor has shown variable effect on cerebral blood flow and increased incidence of periventricular and intraventricular hemorrhage.[31]

Postnatal measures are directed primarily at preventing neonatal factors that are associated with an increased risk of hemorrhages including maintenance of adequate oxygenation, ventilation, and acid-base balance, slow infusion of volume expanders to treat hypotension and if needed judicious use of vasopressor to maintain a stable normal range blood pressure and circulation. Most of these could be achieved by DCC providing a stable circulatory system during the first 48 hours of life, improving the postnatal transition and reducing the use of volume expanders and vasopressor.[31]

Many studies have shown that one of the important clinical benefits of DCC for preterm infants is reduction of the incidence of IVH down to 50%.[9,22,32] The apparent protective effect of DCC especially for the male infants, suggests the hypothesis that this additional blood volume may have a gender-specific neuro-protective effects.[28]

Decreased incidence of NEC is also one of the important suggested benefits of DCC. Although the pathogenesis of NEC remains elusive, the multifactorial theory suggests four key risk factors for the initiation of intestinal injury in neonates namely prematurity, formula feeding, intestinal ischemia, and bacterial colonization. Current hypotheses suggest that these risk factors stimulate activation of the inflammatory cascade that ultimately results in the final common pathway of bowel necrosis that is the hallmark of neonatal NEC.[33]

In previous studies, clinical suspicion of NEC occurred less frequently in babies undergone DCC. Counting on this observation the initial increase in systemic perfusion might result in better capillary distension, similar to capillary erection occurring in the lung, and thereby modeling of the gastrointestinal mucosa.[34]

Moreover babies who are more stressed by low blood volume in ECC may have a double insult viz decreased blood flow to the gut as a result of activation of the sympathetic nervous system causing redistribution of cardiac output to more vital organs in addition to the original hypovolemia.[34]

There is increasing evidence that oxidative stress is implicated in the development of BPD. Several important factors contribute to augmented oxidative stress in the newborn and especially the preterm infant. Because of immaturity, the lung of preterm infants is frequently exposed to oxygen and hyperoxic oxidative stress. This is augmented by the impairment of the antioxidant defense stores and the free iron which catalyzes the

production of toxic reactive oxygen species. Also infection and inflammation are common complications preterm infants experience which increases oxidative stress.[35]

Hemoglobin, especially HbF, may protect against oxidative stress because its high affinity for oxygen makes it possible to oxygenate with a lower FiO2. The only available source of extra HbF is the blood in his own placenta, making DCC a possible factor contributing to decreasing the incidence of this condition.[36] From another point of view, repeated postnatal blood transfusions have been implicated in the development and worsening of BPD. This was explained by increasing the non-transferrin bound iron and inflammatory mediators that present in stored blood, causing an oxidative injury to the lungs. This can be reduced if the number of these transfusions has been cut down by DCC.[37]

A high concentration of oxygen therapy was previously thought to be the major contributory factor in the development of ROP. However, reports have found cases without oxygen therapy. This evidence suggests that factors other than oxygen play an important role in its development. Among infants of similar gestations, those who have the more unstable hospital course have the higher risk of serious retinal pathology.[38,39] Bassiouny reported that lower BW, GA, apnoea, blood transfusion, mechanical ventilation, metabolic acidosis, TPN, IVH and sepsis were associated with development of ROP.[40]

Although there is no direct relationship between the timing of cord clamping and ROP, it is plausible that the attended reduction of morbidities predisposing to it by DCC can reduce the incidence of its occurrence or at least mitigates its severity.[40]

Placental transfusion not only gives the infant extra blood volume, it also provides him with important cellular components. The cord blood, especially that of a preterm (24-31weeks) infant, contains the highest concentration of primitive hematopoietic progenitor cells when compared to that of infants closer to term. These cells belong to the mononuclear fraction composed of mononcytes and lymphocytes, beside the Natural Killer cells (NK) that highly exist in the cord blood.[41] Mercer et al.explained the increased incidence of LOS in infants who had ECC in previous studies by the presumed state of immunocompromisation induced by deprivation of the infant of these cells.[22]

In addition to red blood cells, fetal blood contains large numbers of highly activated hematopoietic stem cells along with endothelial cell precursors, mesenchymal progenitors, and multipotent/pluripotent lineage stem cells. Obviously obtaining this lifelong regenerative reservoir is an invaluable gift that could be lost when ECC is practiced.[41]

Stem cells play an essential role in organ development of the central nervous, respiratory, cardiovascular, hematologic, immunologic, and endocrine systems. Only at birth a human being will get the chance to have such a high number of circulating stem cells. These cells have incredible potential for healing of different organs. In animal models, they have been found to repair heart, brain, liver, lung, muscle, and endothelial cells, and can prevent cerebral palsy when administered within 24 hours of brain injury in rats. In addition, they have been used successfully to treat a wide variety of hemoglobinopathies, metabolic and hematologic disorders, immune deficiencies, and cancers. [27]

Furthermore, Tolosa et al argued that “artificial loss of stem cells at birth could predispose infants to diseases such as chronic lung disease, asthma, diabetes, cerebral palsy,

infection, and neoplasm". The authors of this article suggested the hypothesis that a newborn should obtain his full allotment of available stem cells at birth and this could be facilitated by placental transfusion (DCC) or by milking the cord. If the labor and birth was in anyway traumatic for the infant, it is possible that the stem cells may assist with healing.[41]

To the best of our knowledge the short term outcome of preterm babies with variable timing of cord clamping has not been studied in Egyptian medical institutes. However, at Ain Shams University a study was done for monitoring the effect of DCC on iron status of full term infants. Another study was conducted in El Minia University targeting term infants for multiple outcomes, the most important of which is anemia. In Tanta University another study compared the effect of timing of cord clamping on Hgb level, Apgar score, blood sugar level and total serum billirubin in term babies.

AIM OF THE WORK

The aim of this work is to assess the short term outcome of two groups of preterm neonates (who do not need immediate resuscitation other than routine care) according to the timing of cord clamping.

SUBJECTS AND METHODS

Study design:

Prospective true experimental study to compare the short term outcomes of early versus delayed cord clamping among two groups of preterm neonates who don't need immediate resuscitation.

Study setting:

- This study was conducted in the delivery room and neonatal intensive care unit at Alexandria University Maternity Hospital (AUMH).
- AUMH is a tertiary obstetric center that has about (142) beds and its NICU have 70 incubators and beds.

Target population:

Ninety six preterm newborn infants less than 32 weeks of gestation not in need for immediate resuscitation (other than routine care with or without oxygen therapy) delivered at AUMH and admitted to its neonatal intensive care unit.

We attended 154 preterm births; fifty eight neonates were excluded for the following reasons: 4 were referred to another NICU after delivery, 11 had been diagnosed to have ABO incompatibility, 41 needed immediate resuscitation and 2 proved EOS after being enrolled in the study.

The study was carried out over the period from June 2012 to July 2014 (one year pause for unavailability of transcrainial US screening).

Methodology

The study was carried out in 3 phases:

1- First phase: enrollment phase.
2- Second phase: intervention and monitoring phase.
3- Third phase: collected data analysis and results.

First phase (Enrollment phase):

Inclusion criteria

Apparently healthy preterm baby delivered at gestational age less than 32 completed weeks who don't need immediate resuscitation at birth.

Exclusion criteria

- Babies who needs immediate resuscitation (according to NRP 2011).[42]
- Severe maternal illness.
- Pre-eclampsia & eclampsia.
- Chrioamnionitis.
- Monochorionic twins.
- Ante partum hemorrhage.
- Major congenital anomalies.
- Infant of diabetic mother.
- Intrauterine growth retardation.
- Blood group & RH incompatibility.
- Early neonatal anemia due to any other cause

Data collection:

1- Detailed maternal, obstetric and perinatal history was documented in a predesigned sheet (appendix 1).
2- Assessment of gestational age using modified Ballard score.[43]
3- Full resuscitation data according to NRP 2011 were obtained.[42]
4- Assessment of Apgar score at 1st and 5th minute.

Second phase: intervention and monitoring phase:

- Randomization of babies into the two groups was done before the beginning of the study. Closed envelop technique was used to determine to which group belongs the first baby of the study (baby no 1 belonged to ECC group). After that babies were distributed equally, those with an odd number in the ECC group and those of an even one in the DCC group.
- Once the newborns are delivered either by cesarean section or normal vaginal delivery they were held at the same level of the incision or introitus, respectively, to negate the effect of gravity on the flow of blood.
- Time elapsing between delivery of the baby and cord clamping was estimated using digital stopwatch by the researcher who is not one of the resuscitation team.

- Early cord clamping (ECC) was done within the first 30 seconds after complete delivery of the baby. Delayed cord clamping (DCC) was performed after 30 second and up to 45 seconds.
- Following cord clamping the newborn was be placed on an already switched on radiant warmer where the usual steps of resuscitation was carried out according to the latest NRP by the resuscitation team already present in the resuscitation room.
- Assessment of birth weight and vital signs on admission to the NICU including:
    a. HR&SPO2 using Nellcor pulse oximeter.
    b. MAP using none invasive Dynamap (blood pressure was compared to normal reference range for age and sex).[43]
    c. Temperature using rectal thermometer (temperature was compared to normal reference range for age and sex).[43]
    d. Both groups were monitored during the duration of admission for:

Primary objectives (during the first day of life):

- Initial venous hematocrit value: venous samples were withdrawn from babies upon NICU admission within the first 4 hours of life. Samples were withdrawn from a peripheral vein and CBC was analyzed using ADVIA automated analyzer. Value was compared to normal reference range for age and sex.[43]
- Mean arterial blood pressure, upon admission and after stabilization of the infants, was measured using a none-invasive DINAMAP (procare auscultatory 100). Value was compared to normal reference range for age and sex.[43]
- Need for volume expanders and or vasopressor was decided by the treating doctors depending on signs of hypotension (tachycardia, mottling, blood pressure less than the 3rd percentile for gestational age, poor peripheral pulsations and oliguria).

Secondary objectives (during the period of NICU admission):

- Need of blood transfusion either packed RBCs or whole blood and number of transfusions was assessed from the babies' files.
- Occurrence of (LOS) documented by bacteriological blood cultures after 72 hours of age. CBC and C Reactive Protein (CRP) laboratory markers screening for sepsis were ordered by NICU residents as routine investigations or upon clinical suspension of sepsis. (CBC was analyzed using ADVIA automated analyzer and CRP (quantitative) analyzed by DADE BEHRING Dimension RXL clinical chemistry auto analyzer). Cases of EOS documented by blood culture on day One were excluded from the study.
- Occurrence of (IVH) and its grades was screened for using trans cranial ultrasound done by experienced NICU staff members on day 1, 3 and 7 as the followed protocol in the NICU.
- Occurrence of (NIHB) was screened for by total serum billirubin done to all studied neonates upon routine NICU investigations on day 2 and later on clinical suspension using a venous sample and analyzed by DADE BEHRING Dimension RXL clinical chemistry auto analyzer. Need for phototherapy and or exchange transfusion as treatment for NIHB was assessed using the patients' files. Decision of commencing phototherapy or exchange transfusion was taken by NICU residents using a time and age guided curves for treatment of hyperbilirubinemia.(appendix 2)

- Occurrence of suspected necrotizing entero-colitis (SNEC) was assessed from the babies' files by the orders of abdominal films and or laboratory investigations to exclude NEC in cases of feeding intolerance using the Bell's staging system.[44]
- Occurrence of (BPD) was assessed from the babies' files by the duration of oxygen therapy when exceeding 28 day and radiological findings of plane chest x ray.[45]
- Occurrence of (ROP) was assessed from the babies' files and it was done by an ophthalmologist in routine visits as the followed protocol in the unit.
- Final outcome: discharge /death and duration of admission were assessed from the babies' files.

Third phase: Statistical analysis of the data.[46]

Data were fed to the computer and analyzed using IBM *SPSS software package version 20.0.*[47] Qualitative data were described using number and percent. Quantitative data were described using Range (minimum and maximum), mean, standard deviation and median. Comparison between different groups regarding categorical variables was tested using Chi-square test. When more than 20% of the cells have expected count less than 5, correction for chi-square was conducted using Fisher's Exact test or Monte Carlo correction. The distributions of quantitative variables were tested for normality using *Kolmogorov-Smirnov test, Shapiro-Wilk test and D'Agstino test, also Histogram and QQ plot were used for vision test.* If it reveals normal data distribution, parametric tests was applied. If the data were abnormally distributed, non-parametric tests were used. For normally distributed data, comparison between two independent populations was done using independent t-test. For abnormally distributed data, comparison between two independent populations were done using Mann Whitney test. Significance of the obtained results was judged at the 5% level.

Ethical consideration:

Approval for the study was obtained from the department and Faculty Ethical Review Committee. Moreover, an informed consent was obtained from all parents.

RESULTS

Table (1): Demographic and perinatal data of the studied neonates

	Groups				Test of sig.	p
	ECC (n=48)		DCC (n=48)			
	No.	%	No.	%		
Gestational age						
<28 weeks	0	0.0	1	2.1	FE	$^{FE}p = 1.000$
28 – 32 weeks	48	100.0	47	97.9		
Gender						
Male	25	52.1	24	50.0	$\chi^2 = 0.042$	0.835
Female	23	47.9	24	50.0		
Ante natal steroid	21	43.8	26	54.2	$\chi^2 = 1.042$	0.307
Mode of delivery						
CS	34	70.8	39	81.3	$\chi^2 = 1.429$	0.232
NVD	14	29.2	9	18.8		
Cause of preterm labour						
Tender scar	14	31.3	20	41.7	MCP	0.782
PROM	6	12.5	6	12.5		
PTLP	15	29.2	11	22.9		
Drained liquor	10	20.8	7	14.6		
Oligohydraminous	3	6.6	4	8.3		
Apgar score (Mean ± SD)						
1 min	5.50 ± 1.19		6.50 ± 0.68		$t = 5.063^*$	$<0.001^*$
5 min	7.15 ± 0.95		7.83 ± 0.69		$t = 4.061^*$	$<0.001^*$
Birth weight (Mean ± SD)	1.18 (0.80 – 1.59)		1.20 (0.87 – 1.35)		Z =1.184	0.236

χ^2: Chi square test MC: Monte Carlo test
FE: Fisher Exact test t: Student t-test
Z: Z for Mann Whitney test
*: Statistically significant at $p \leq 0.05$

Table (1) shows that there was no significant difference between both groups regarding demographic and perinatal data of all studied neonates except for Apgar score at both 1 and 5 min that was significantly higher in the DCC group.

Table (2): Clinical data on admission

	Groups				χ^2	p
	ECC (n=48)		DCC (n=48)			
	No.	%	No.	%		
Temp						
Hypothermic (<36.5°C)	34	70.8	29	60.4	1.154	0.283
HR						
Tachycardia	23	47.9	3	6.3	21.099*	<0.001*
Mean arterial BP						
Hypotensive	16	33.3	5	10.4	7.375*	0.007*
Respiratory rate						
Tachypnia	30	62.5	25	52.1	1.064	0.302
Respiratory support						
Off oxygen	15	31.3	9	18.8		
Oxygen therapy	13	27.1	24	50.0	5.485	0.064
Ventilation	20	41.7	15	31.3		
Surfactant administration	18	37.5	11	22.9	2.421	0.120

χ^2: Chi square test
*: Statistically significant at $p \leq 0.05$

Table (2) displays clinical data of the studied neonates on admission to the NICU. There were a significantly greater number of neonates that had hypotension and tachycardia in the ECC group.

Table (3): Primary objectives of the study

	Groups				χ^2	p
	ECC (n=48)		DCC (n=48)			
	No.	%	No.	%		
Initial venous HCT value						
65% – 45%	21	43.8	46	95.8	30.880*	<0.001*
<45%	27	56.3	2	4.2		
MAP after stabilization in NICU						
Hypotension	18	37.5	5	10.4	9.663*	0.002*
VE (normal saline)						
Once	7	14.6	5	10.4		
Twice	7	14.6	0	0.0	MCP	0.002*
>Twice	4	8.3	0	0.0		
VE and inotrops "vasopressor"	13	27.1	0	0.0	15.036*	<0.001*

χ^2: Chi square test
MC: Monte Carlo test
*: Statistically significant at $p \leq 0.05$

Table (3) demonstrates results of the primary objectives of the study. It shows that both initial venous HCT and MAP were significantly higher in the DCC group. None of the babies had either polythycemia or hypertension. Also need for volume expanders and vasopressor was significantly lower among babies in the DCC group.

Table (4): Secondary objectives of the studied neonates

	Groups				χ^2	p
	ECC (n=48)		DCC (n=48)			
	No.	%	No.	%		
Need of blood transfusion						
Once	22	45.8	13	27.1	MCP	<0.001*
Twice	10	20.8	1	2.1		
>Twice	6	12.5	1	2.1		
LOS						
Positive blood culture	20	41.7	5	10.4	12.169*	<0.001*
Negative blood culture	14	29.2	16	33.3	0.194	0.660
Jaundice						
Not requiring phototherapy	30	62.5	16	33.3	8.181*	0.004*
Requiring phototherapy	18	37.5	32	66.7		
Need exchange transfusion	0	0.0	0	0.0		
IVH and grade						
GI	2	4.2	1	2.1	MCP	<0.001*
GII	13	27.1	2	4.2		
GIII	6	12.5	0	0.0		
GIV	4	8.3	0	0.0		
Occurrence of suspected NEC	19	39.6	2	2.1	23.688*	<0.001*
Occurrence of BPD	6	12.5	2	4.2	FE	0.268
Occurrence of ROP	3	6.3	1	2.1	FE	0.617

χ^2: Chi square test
MC: Monte Carlo test
FE: Fisher Exact test
*: Statistically significant at $p \leq 0.05$

Table (4) demonstrates the results of secondary objectives of the study. The frequency of blood transfusion is significantly lower in the DCC group with most of babies who received PRBCS of them had it for once or twice only. 4 out of 38 babies in the ECC who received transfusions had it during the first 48 hours of life. Incidence of LOS, IVH and suspected NEC were significantly lower in the DCC group. Jaundice was significantly higher among babies of the DCC with most of them needed phototherapy and none had undergone exchange transfusion.

Table (5): Final outcome of the studied neonates

	Groups				χ^2	p
	ECC (n=48)		DCC (n=48)			
	No.	%	No.	%		
Outcome						
Discharge	30	62.5	44	91.7	$\chi^2 = 11.558^*$	0.001^*
Death	18	37.5	4	8.3		
Duration of admission Median (Min. – Max.)	26.50 (1.0 – 102.0)		28.50 (14.0 – 95.0)		Z = 0.422	0.673

χ^2: Chi square test
Z: Z for Mann Whitney test
*: Statistically significant at $p \leq 0.05$

Table (5) displays the final outcome of the studied neonates during the period of their NICU admission. Mortality was significantly lower among babies of the DCC group.

DISCUSSION

Recommendations concerning the optimal time to clamp the umbilical cord have varied since antiquity, and the topic still remains controversial. Although systematic reviews of controlled clinical trials have concluded that cord clamping between 30 and 180 seconds after birth has significant health benefits, this practice is not widely performed nowadays.[9]

Until the early decades of the 20th century, most pregnant women delivered in their homes, where midwives tended to cut the umbilical cord several minutes after birth or wait until the cord ceased pulsating. Coinciding with the improvements in obstetric and neonatal care, more women delivered in hospital. In the 1960s the practice of active management of the third stage of labor was introduced to reduce postpartum hemorrhage and to prevent placental retention. Some experts believe that the practice of immediate cord clamping was an unintended addition to this management, and has not been shown to benefit the infant or the mother. Management of the umbilical cord at the time of birth is probably most frequently done without thought, and clamping of the cord is often seen as merely a task.[43] Finally the current typical practice of immediate cord clamping, especially of those infants potentially in most need of additional red blood cells, needs to be reconsidered. The lack of evidence to guide practice, the assumption that early cord clamping can "do no harm," and the relative connection that the RBC is the only transporter of oxygen lead to the conclusion that reexamination of the consequences of early versus delayed cord clamping is warranted.[12]

In the present study, the mean gestational age and birth weight of the 2 studied groups showed no statistical difference (table 1). The majority of babies were delivered by C-section. Preterm labor pain, preterm rupture of the membranes were the most common causes of this mode of delivery long time before reaching term. Reflecting the poor antenatal care and services, only 50% of the mothers of the studied babies did receive a full course of corticosteroids (4 dexamethasone shots), a treatment that exceeds the usual task of lung maturity to preservation of the preterm infant white matter.[49]

Apgar score at both 1 and 5 minutes was significantly higher among babies of the DCC group (table 1). Kaempf et al.[50] found a significantly higher score only at the 1 minute score while Dunn [51] reported a higher score at 5 minutes in their DCC groups. Other workers denied any relation between the timing of cord clamping and the Apgar score.[22,52] The discrepancies between the results of these studies and the present one are probably attributed to the different gestational age of the studied babies as the current study tested the relation of the timing of cord clamping and Apgar score in preterm babies while the others included both preterm and term neonates.

In the present study, the majority of the studied babies were hypothermic upon admission to the NICU with no significant difference between the 2 studied groups, albeit the number of neonates in the ECC group was greater. In similar studies, the same observation was reported by McDonnell, Mercer and Rabe and their colleagues.[53,22,54]The low core temperature of the preterm in this work is attributed - among many other causes - to the unavailability of radiant warm and low ambient temperature in the operation theater, reluctance in wrapping the babies in polyethylene bag and the frequent delayed admission to the NICU.

A significantly greater number of babies in the DCC group had a heart rate and mean arterial blood pressure within normal gestational age related reference range upon admission to the NICU(table 2) and they required less volume expanders and vasopressors (table 3). Similar results were reported by Mercer and associates. These latter examined the effect of ECC versus DCC on blood pressure in a cohort of infants born between 24 and 34 weeks of gestation. The workers observed that infants in the DCC group were 3 times more likely to have mean blood pressure above 30 mmHg.[34] Kugelman et al. pointed out that DCC for at least 30 seconds increases the baby's blood volume that is reflected by a higher blood pressure and initial hematocrit value.[55] It is to be noted that a normal blood pressure and a greater blood volume optimize the heart rate and reduce the incidence of ROP and cerebral palsy.[34]

In the present work, the respiratory status of the studied babies did not differ according to the timing of cord clamping (table 2). No significant difference was noted in the proportion of babies in both groups suffering respiratory distress, needing supplemental oxygen, requiring respiratory support or surfactant administration. Coggins and Mercer, on the other hand, stated that DCC is associated with better respiratory function.[56] Rabe et al. reviewed 7 randomized controlled studies comparing early with delayed cord clamping in preterm babies. The authors commented that these trials were too small for any firm conclusion about possible respiratory effects of these alternative strategies.[21]

A significantly greater number of babies in the ECC group had a Hct level <45%. These findings were consistent with the studies of Kinmond, Kugelman, Ultee and associates.[57,55,58] In the latter study, the difference in Hct value was documented till the age of 10 weeks. This was not the case in other studies that didn't find difference between both groups as regards to the initial Hct value, Mercer attributed his results to the small sample size,[34] while Aldangady suggested that the lack of difference in Hct value between the two groups in his study is due to the proportionate transfer of plasma along with RBCS increasing the blood volume without a selective rise in the Hct value.[29] It is to be noted that not a single baby in both groups had polycythemia (Hct >65%)

A significantly higher proportion of infants among the DCC had mean arterial blood pressure reading within normal range for gestational age after stabilization within 4 hours of delivery (table3). Consequently, treatment by volume expanders and / or vassopressors during the first 24 hour of life were needed in a significantly smaller number of babies in the delayed clamped group. Similarly, Ibrahim et al. documented higher mean arterial blood pressure in the first 4 hours of life among delayed clamped preterm infants and subsequent reduced requirements for blood and albumin transfusion in the first 24 hours.[59]

The frequency of blood transfusion among babies in the present study was significantly lower in the DCC group (table 4). In agreement, Rabe et al. reported that 50% of infants without transfusions several weeks after delivery belong to DCC group while 15% in ECC one.[54] Similar results were documented by Kinmond et al. who stated that the initial greater endowment of red blood cells and the consequent milder course of illness with less investigational blood loss during the NICU stay are behind the lower incidence of transfusion requirement among babies of the DCC group.[57] On the contrary, Kugelman et al. study did not show significant decrease in blood transfusions among DCC group. The authors commented that this could be due to the strict criteria of transfusion in their study center that reduced overall blood transfusions.[55]

In the present study, the incidence of late onset sepsis proved by blood culture (table 4) was significantly higher among babies of the ECC group. Mercer and associates documented similar results among a group of preterm infants less than 32 weeks. They speculated this resulted from the deprivation of babies of stem cells progenitors namely lymphocytes, NK cells and monocytes along with RBCs when the umbilical cord is clamped early. They added that cord blood of preterm infants (24–31 weeks) contains the highest concentration of primitive hematopoietic progenitor cells and long-term culture-initiating cells when compared with the cord blood of infants closer to term.[22]

A significantly greater number of infants among the DCC group in the present study required phototherapy for treatment of hyperbilirubinemia (table 4), while no babies in both groups underwent exchange transfusion. After exclusion of most causes of pathological jaundice this can be explained by the higher initial Hct levels though not reaching levels of polycythemia. A meta-analysis performed by McDonald and Middleton reported that delaying clamping increased significantly the risk of jaundice requiring treatment in full term infants.[60] On the other hand, Kugelman, Kinmond, Ultee and their associates found no relation between the timing of cord clamping and development of significant hyperbilirubinemia. [55, 57, 58]

In the present work, the incidence of IVH (table 4) was significantly higher among the ECC group. Also the severity of IVH was significantly different; grades III&IV occurred only among ECC group. Kinmond and associates reported that the immediate hemodynamic effect of interrupting blood flow to the low resistance placental circulation while the umbilical arteries are still pulsating lead to an abrupt rise in systemic arterial pressure with possible deleterious effects including IVH.[57] Hofmeyr et al demonstrated this pressure surge in term infants and postulated that this could contribute to the development of periventricular and intra-ventricular hemorrhage in preterm infants. Mercer in his study documented similar results.[32]

The incidence of suspected NEC (table 4) during the course of NICU admission was significantly higher among babies of the ECC group. A Cochrane review of 5 trials studying 241 preterm infants showed a lower risk for NEC when cord clamping is delayed.[21] Mercer documented reduced incidence of NEC when DCC is performed but he couldn't confirm these results in a similar study few years later.[22,34] Kugelman et al. noticed a low frequency of NEC among their studied neonates that didn't allow them to suggest the influence of DCC on this complication.[55]

The incidence of BPD and ROP in the present study (table 4) was higher among the ECC group, although statistically insignificant. In a similar study by Mercer et al the workers reported insignificant difference in the incidence of both conditions among their studied neonates. Mercer and co- workers suggested that the extra amount of blood offered by DCC prevents ischemic hypo perfusion injury to the lungs and retina respectively.[61]

Table (5) demonstrates the final outcomes of the studied babies. No significant difference was found between both groups as regards the mean duration of stay in the NICU. Kinmond and his colleges reported similar results.[57] As regards to incidence of death (table 5) it was significantly lower among babies of the DCC. Mc Donnell and Henderson-Smart reported similar results.[53] Although this was not the case in Mercer, Kugelman and Hosono[34, 55, 62] studies who reported that DCC didn't has an effect on mortality among their studied neonates.

SUMMARY

Delayed cord clamping (DCC) has been an established step in the resuscitation management of all newborn infants according to the latest NRP guidelines. The optimal time for gaining the benefits of such intervention together with avoiding the risk of excessive transfusion is the issue of controversy. The time of delayed clamping has varied between 30-180 seconds in most previous studies. Benefits of DCC have been studied since centuries. They include stabilization of the cardiovascular system of the newborn during the first 48 hours of life and hence reducing the need for volume expanders and vassopressors and their possible side effects and thus providing a smooth transition from fetal to neonatal life. DCC seems to Protect the infant, either preterm or full term, from early neonatal anemia or later iron deficiency anemia and hence reducing the incidence of blood transfusion and protecting the infant from its related complications. Till now researches about the influence of DCC on these diseases, namely RDS, NEC, BPD, ROP, IVH and LOS are still running. Worries about delayed resuscitation and excessive placental transfusion with its possible complications of polycythemia; jaundice and hyper viscosity are the main alleges against the implication of DCC in the actual practice.

This study was conducted at AUMH and its NICU to determine the short term benefits and hazards of delaying cord clamping for 30-45 seconds while ECC was done before 30 seconds after complete delivery of the infant in a group of 96 preterm neonates less than 32 completed weeks of gestation. DCC was conducted with the infant held by the obstetrician at the level of the placenta. Infants were randomly assigned into the two equal groups by the closed envelop technique. Babies were then followed up during their course of NICU admission.

Clinical, laboratory data and radiological examination were collected from the babies' files in the NICU. DCC was associated with a higher initial venous Hct value, less blood transfusion requirement and less hypotension episodes during the first 24 hour and less use of volume expander and vassopressors. IVH and suspected NEC, LOS were significantly lower among babies of the DCC group. Although statistically insignificant but a greater proportion of babies among ECC group suffered from BPD & ROP. There was a higher incidence of pathological jaundice requiring treatment by phototherapy in the DCC group but no baby developed polythycemia or needed exchange transfusion. Final outcome of the study showed less proportion of babies in the DCC group died before discharge from the NICU.

CONCLUSIONS

- DCC seems to improve neonatal transition that can be suggested by the better APGAR scores at 1 and 5 minutes.
- DCC improves and stabilizes the cardiovascular status of the preterm infants at birth and up to 24 hours of life.
- DCC is associated with reduction of cases of early neonatal anemia and frequency of blood transfusion.
- DCC protects premature babies from IVH and reducing its severity.
- DCC seems to be a protective intervention against LOS and suspected NEC.
- DCC seems to improve the final outcome of preterm babies and reduces the number of deaths before NICU discharge.
- DCC is not associated with increased incidence of polythycemia
- DCC didn't reduce the use of surfactant.
- DCC may be responsible for increased incidence of NIHB requiring treatment by phototherapy.
- DCC don't specifically affect the baby's temperature on admission to the NICU as it is affected by many confounding factors.
- No protective effect of DCC from BDP or ROP was found among the DCC studied neonates.

RECOMMENDATIONS

- DCC for at least 30-45 seconds should be an established practice in the resuscitation of all none compromised preterm babies.
- Further studies about relation of DCC and HMD, baby's temperature, BDP and ROP should be conducted.
- Further researches to confirm the practicality and benefits of DCC on both full term and compromised babies need to be carried out.

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الملخص العربى

إن الربط المتأخر للحبل السرى قد أصبح خطوه معترف بها فى إنعاش الأطفال حديثى الولاده حسب أحدث إصدارات المبادئ التوجيهيه لبرنامج إنعاش الأطفال.أفضل توقيت لإجراء هذا التداخل مع إكتساب فوائده وتجنب خطوره نقل الدم الزائد من المشيمه لازال محط إختلاف حتى الأن.تراوح توقيت ربط الحبل السرى فى معظم الدراسات السابقه ما بين ثلاثون إلى مائه وثمانون ثانيه. إن فوائد الربط المتأخر للحبل السرى لا تزال تحت الدراسه منذ قرون ومن ضمنها تحسين حاله الدوره الدمويه للأطفال حديثى الولاده أثناء أول ٤٨ ساعه من عمرهم مما يؤدى إلى تقليل إستخدام موسعات الحجم الدموى وقوابض الأوعيه الدمويه وما لهم من أثار جانبيه. تؤدى هذه الفوائد إلى فتره أنتقاليه سلسه من الحياه داخل الرحم إلى خارجه. الربط المتأخر للحبل السرى يحمى الطفل حديث الولاده سواء كاملى النمو أو الخدج من فقر الدم المبكر أو الناتج عن نقص الحديد لاحقا مما يقلل من إحتياجه إلى نقل الدم ويحميه من مخاطره. لا تزال الدراسات جاريه حول تأثير الربط المتأخر للحبل السرى على الأمراض التاليه : متلازمه الضائقه التنفسيه للأطفال الخدج ، الإلتهاب المعوى القولونى الناخر، خلل النسيج القصبى الرئوى، إعتلال الشبكيه عند الخدج، النزيف داخل البطينى، وتعفن الدم المتأخر. القلق من التأخير فى إنعاش الطفل و نقل الدم الزائد من المشيمه المؤدى إلى كثره الحمر وإرتفاع نسبه لزوجه الدم واليرقان هما اكثر ألاسباب ضد التطبيق العملى لهذا التداخل.

أجريت الدراسه الحاليه بمستشفى النسا والولاده جامعه الاسكندريه ووحده العنايه المركزه للأطفال المبتسرين التابعه لها على ٩٦ طفل مبتسرعمرهم الرحمى أقل من ٣٢ إسبوع بهدف تحديد النتائج قصيره المدى المترتبه على تأخير ربط الحبل السرى لفتره تتراوح من ٣٠ إلى ٤٥ ثانيه بعد ولاده الطفل وهو على نفس مستوى المشيمه بينما تم الربط المبكر للحبل السرى فى فتره أقل من ٣٠ ثانيه. تم توزيع الأطفال بالتساوى عشوائيا بين المجموعتين. تم متابعه الأطفال طوال فتره حجزهم بوحده العنايه المركزه. تم تجميع البيانات الخاصه بالأطفال من فحصوات إكلينيكيه وتحاليل معمليه وإشاعات بإستخدام الملفات الخاصه بهم فى وحده العنايه المركزه.

أظهرت النتائج أن الربط المتأخر للحبل السرى مصحوب بإرتفاع قيمه الهيماتوكريت الأوليه وإنخفاض فى عدد مرات نقل الدم أثناء فتره الحجز بالعنايه المركزه وكذلك استقرار فى حاله الجهاز الدورى تظهر فى صوره عدم إنخفاض ضغط الدم وقله إستخدام موسعات الحجم الدموى و قوابض الأوعيه الدمويه.أثبتت الدراسه أيضا أن الربط المتأخر للحبل السرى يقلل من نسبه حدوث الأمراض التاليه:النزيف داخل البطينى و الإلتهاب المعوى القولونى الناخر و تعفن الدم المتأخر. على الرغم من أن النتائج لم تثبت دلاله إحصائيه ولكن عدد الأطفال المصابين بخلل النسيج القصبى الرئوى و إعتلال الشبكيه عند الخدج كان أقل فى الأطفال المنتمين إلى مجموعه الربط المتأخر. نسبه الأطفال اللذين عانو من ارتفاع نسبه اليرقان لدرجه تستلزم العلاج الضوئى كانت أعلى ما بين الاطفال فى مجموعه الربط المتاخر على الرغم من عدم حدوث حالات كثره الحمر أو إحتياج أيا منهم إلى تغير الدم الكلى. أدى الربط المتأخر للحبل السرى الى تحسين النتيجه النهائيه للأطفال بالنسبه إلى عدد حالات الوفيات أثناء الحجز بالعنايه المركزه.

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دراسة النتائج قصيرة المدى لربط الحبل السرى المبكر مقارنه بالربط المتأخر فى الأطفال الخدج حديثى الولادة

رسالة مقدمة

لقسم طب الأطفال ـ كلية الطب ـ جامعة الإسكندرية
ضمن متطلبات درجة

الماجستير

فى

طب الأطفال

مـــن

ولاء ابراهيم عبد الرازق غنيم
بكالوريوس الطب والجراحة ، ٢٠٠٧
كلية الطب، جامعة الإسكندرية

[٢٠١٥]

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رسالة مقدمة من

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للحصول على درجة

الماجستير

فى

طب الأطفال

لجنة المناقشة والحكم على الرسالة	التوقيع
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