Using physiology to guide time to cord clamping

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SUMMARY

Immediate clamping and cutting of the umbilical cord at birth has been the accepted standard of care for decades. The physiologic rationale relating umbilical cord clamping (UCC) to the events of the circulatory transition is not considered in arbitrarily recommended cord clamping times. Systematic review of early versus deferred UCC shows significant hemodynamic benefits to the deferred group. Mechanisms for this protective effect are considered in this review. The original concept of a placental transfusion with a volume load and prevention of low cardiac output relies on the physiological end point of the amount of blood transfused. The newer concept of an ordered physiological transition is increasingly supported. This model places aeration of the lungs and an increase in pulmonary blood flow back at the centre of the circulatory transition with timing of UCC being related to establishment of respiration. The need for “physiologically based” UCC is discussed.

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1. Introduction

Clamping and cutting of the umbilical cord at birth is much more than a symbolic separation of the infant from its mother [1]. While it is recognized that the transition to newborn life involves a sequence of physiological events, recent studies have now shown that the timing of umbilical cord clamping (UCC) within this sequence can have a major impact on the infant’s wellbeing [2]. In animal studies, UCC before ventilation onset results in a profound (~50%) reduction in venous return, ventricular preload and cardiac output [1,3]. Cardiac output is restored only after ventilation onset due to the resulting increase in pulmonary blood flow (PBF), which restores venous return and ventricular preload. Consequently, if there is a significant delay between UCC and ventilation onset, the newborn is exposed to a prolonged period of low cardiac output, placing the infant at risk of a hypoxic/ischemic insult. As this period of low cardiac output is immediately followed by a rapid increase in output, due to the increase in PBF [1], the risk of an intraventricular haemorrhage (IVH) caused by large swings in blood pressure and flow is also increased [2]. However, if ventilation onset precedes UCC, the increased PBF can immediately replace umbilical venous return as the primary source of ventricular preload without any loss of supply. Thus, cardiac output remains normal and stable throughout the transition sequence, thereby avoiding a reduction in output and large fluctuations in pressure and flow [1].

The concept of the need for “delayed cord clamping” has been an ongoing debate for centuries, but until recently has primarily focused on the potential for fetal-to-placental blood transfusion if delayed for 1–3 min [4,5]. This presumes that net placental-to-fetal blood transfusion is simply time dependent [6], but there are several other potential benefits apart from placental transfusion. These include: prevention of low cardiac output syndrome, keeping the transition in sequence and avoiding an overly vigorous resuscitation (suction, mask application, attempted intubation) in an infant who may transition and commence spontaneous breathing, given sufficient time. In view of recent findings, we believe that it is time to review our understanding of the transitional physiology at birth and how the timing of UCC could influence this. This review discusses the sequence of physiological events that underpin the transition to newborn life, the impact of UCC and effects on the postnatal cardiovascular system and how this knowledge can be translated into improving outcomes for newborn infants.

2. Physiological transition to newborn life

The primary event that underpins the transition to newborn life is lung aeration, which is commonly linked with the switch from placental to pulmonary gas exchange. However, lung aeration also initiates the circulatory changes at birth, by stimulating an increase...
in PBF. As such, lung aeration should be viewed as the central precipitating event that initiates a sequence of interdependent changes in physiological function that characterize the transition to newborn life.

Before birth, the fetal cardiovascular system is different from the adult circulation [7,8] mainly due to the presence of large vascular shunts, a high pulmonary vascular resistance (PVR) and a low-resistance placental circulation that is connected in parallel across the lower body. In the fetus, the majority of right ventricular output bypasses the lungs and flows from the main pulmonary artery into the descending aorta via the ductus arteriosus (DA). This is due to the high PVR, which in combination with a low placental vascular resistance results in low PBF during fetal life [7,8]. Thus, pulmonary venous return is also low and therefore left ventricular preload depends primarily on umbilical venous return. This passes from the placenta via the ductus venosus (DV), inferior vena cava and foramen ovale to directly enter the left atrium, therefore bypassing the right side of the heart and the lungs [7]. Thus, umbilical venous blood is the major source of preload for the left ventricle, with little derived from PBF. PVR decreases with increasing gestational age due to growth and development of the pulmonary vascular bed, but the small increases in PBF seen with these changes are insignificant compared to the much larger increases in PBF seen at birth.

Before birth, the liquid filling the future airways maintains the lungs in a distended state, which is vital for fetal lung growth and development [9]. However, at birth this liquid acts as an obstacle that restricts the entry of air and the onset of pulmonary gas exchange. As such, the airways must be cleared of liquid to allow air to enter the distal airways so that gas exchange can commence. Although a number of mechanisms likely contribute to airway liquid clearance [10,11], recent imaging studies in newborn rabbits demonstrate that airway liquid is predominantly cleared by transmural pressure gradients generated during inspiration [12–14]. Thus, inspiration drives liquid movement from the airways into peri-alveolar tissue, where it is cleared by the lymphatics and blood vessels [15].

Lung aeration at birth also triggers a large decrease in PVR and an increase in PBF [3], which along with UCC, drives the transition of the fetal circulation into the adult phenotype. As increases and decreases in fetal oxygenation can increase and decrease PBF, respectively [16], it is widely assumed that the increase in PBF at birth is mediated by an increase in oxygenation [8]. However, previous experimental studies have questioned whether increased oxygenation has an over-arching dominant role or is a contributor that provides the fine control for ventilation/perfusion matching after birth [17]. Indeed, ventilation of lambs can increase PBF in the absence of an increase in oxygenation [18] and when arterial oxygen levels both increase and decrease compared to the fetal state [19]. More recently, an imaging study in newborn rabbits has shown that unilateral aeration of the lung causes a global increase in PBF [17], resulting in a large ventilation perfusion mismatch in unventilated lung regions. Despite this mismatch, the lack of a spatial relationship between lung aeration and the increase in PBF at birth has some adaptive advantages (see below).

3. Cardiovascular consequences of UCC and lung aeration at birth

As the placental circulation is normally a low-resistance, highly compliant vascular bed that receives a large proportion (30–50%) of total cardiac output [20], UCC causes an immediate (stepwise) increase in systemic peripheral resistance. This results in a rapid (within four heart beats or ~1 s) increase (−30%) in arterial pressure [1] that drives a similar rapid increase in cerebral blood flow [1]. Thus, within this time frame, the cerebral circulation is pressure passive and vulnerable to large changes in flow in response to rapid fluctuations in pressure. As UCC also reduces cardiac output (see below) this elevation in systemic arterial pressure and cerebral blood flow is transient and followed by a rapid reduction and then a rapid increase again after ventilation onset [1].

UCC causes a profound reduction in venous return and ventricular preload because the umbilical circulation receives a large proportion of combined ventricular output in the fetus [20]. Consequently, both right and left ventricular output decreases by as much as 50% in lambs [13] and remains low until the lung aerates and PBF increases. This is because the increases in PBF restores venous return and preload to the left ventricle and possibly the right ventricle via left-to-right flow through the FO. This increase in PBF results from both a redirection of right ventricular output to entirely pass through the lungs and a reversal in net flow through the DA [3] because downstream resistance in the pulmonary circulation decreases below that in the lower body. As a result, blood preferentially flows left to right through the DA, from the aorta into the pulmonary circulation. While net flow is left to right, instantaneous flow is largely bidirectional, because the pressure waves emanating from the left and right ventricles reach either end of the DA at different times after ventricular contraction [3,21,22]. That is, the pressure wave traveling from the right ventricle reaches the pulmonary artery–DA junction before the pressure wave from the left ventricle reaches the DA–aorta junction. This creates a pulmonary artery-to-aorta pressure gradient that facilitates right-to-left flow early in systole, which is reversed when the pressure wave from the left ventricle reaches the DA–aorta junction, causing left-to-right flow during late systole and throughout diastole [3,21,22].

As UCC at birth causes a large reduction in cardiac output [1,2], if there is a significant delay between UCC and lung aeration after birth, the infant will not only be exposed to a hypoxic episode, but also to a protracted period of low cardiac output. The primary physiological mechanism that protects vital organs such as the brain from hypoxia involves an increase and redistribution in cardiac output, which results in a large increase in cerebral blood flow [20,23,24]. Consequently, during the period between UCC and ventilation onset, when cardiac output is compromised, the infant is at significant risk of hypoxic/ischemic brain injury. On the other hand, even normoxic infants will be exposed to large swings in arterial pressure and cerebral blood flow if UCC significantly precedes ventilation onset and the increase in PBF. This is because UCC causes a rapid increase in arterial pressure and cerebral blood flow, which is followed by a reduction in pressure and flow due to a reduction in preload and cardiac output, which in turn is followed by a rapid increase in cardiac output when PBF increases and restores ventricular preload [1]. These large swings in cardiac output and arterial pressure increase the risk of perinatal brain injury [2], but can be avoided if UCC occurs after the lungs have aerated and ventilation has commenced.

4. Lung aeration before UCC: a physiological approach to cord clamping

As venous return and left ventricular preload must switch from umbilical to pulmonary venous return after birth, it seems logical to initiate pulmonary ventilation and increase PBF before UCC. We have termed this “physiologically based cord clamping”. If the umbilical circulation remains intact while the lung aerates and PBF increases, then the reduction in venous return and cardiac output associated with UCC is minimized. This is because venous return and the supply of ventricular preload can immediately switch from umbilical to pulmonary venous return without any diminution to supply [1]. As a result, there is no loss in cardiac output and the
large swings in arterial pressure and cerebral blood flow associated with UCC are greatly mitigated. The rapid increase in arterial pressure (over four heart beats) caused by UCC is also greatly reduced [1], because a low-resistance pulmonary circulation can become an alternate pathway for left ventricular output due to left-to-right flow through the DA.

It is widely considered that the benefits of not immediately clamping the umbilical cord primarily concern the net transfusion of blood between the placenta and infant. Largely based on studies done in the late 1960s, it is assumed that placental-to-infant blood transfusion is a time-dependent process that commences within seconds and is completed within ~3 min of birth, resulting in the net transfer of up to 30 mL/kg of blood [6]. This has led to a time-based approach to “delayed cord clamping” in many resuscitation guidelines, irrespective of the infant’s physiology [25]. However, recent observations in humans have indicated that net blood flow into and out of the infant via the umbilical vessels is more complex than previously considered [26]. Flow continues for much longer than previously considered and can cease in the umbilical vein before the artery, potentially leading to blood loss for the infant. The flow is also heavily influenced by inspiratory efforts, with flow in the umbilical vein mostly occurring during inspiration [26]. Expiratory breath holds and crying can cause flow in both the umbilical artery and vein to cease and the bidirectional flow in the umbilical artery is thought to be due to uterine contractions [26]. Clearly, therefore, the infant’s physiology is important and the relationship with time is incidental and likely to be due to the fact that the underlying physiological changes take time to unfold after birth.

5. Physiological factors affecting umbilical blood flow after birth

Although there is considerable potential benefit for the infant if the lungs aerate and PBF increases before UCC, in addition to breathing and crying there are likely to be many factors that influence blood distribution between the placenta and infant after birth. For instance, as the placental circulation is connected in parallel with the infant’s lower body, if the infant has a vasoconstricted peripheral vascular bed then blood flow will be redirected towards the placental circulation [24]. This can arise in response to hypoxia or cooling and would increase the risk of blood loss from the infant to the placenta during “delayed cord clamping”. It is also unclear whether delaying UCC would be beneficial or detrimental in severely asphyxicated bradycardic infants requiring chest compressions. This is because the presence of a persisting low-resistance placental circulation may reduce or restrict the increase in diastolic pressure required to restore spontaneous circulation during resuscitation.

Several practical issues may also impact on the physiological benefits of “delayed cord clamping”, although none of these relate to the practicalities of resuscitating an infant next to the mother following either vaginal or cesarean section delivery. [27]. Instead, these relate to the vertical positioning of the infant, relative to the mother, and the timing of uterotonie administration, as this could greatly impact upon cardiovascular benefits of initiating lung aeration before UCC. Until recently, it was widely recommended that the mother be given a uterotonin (e.g. syntocinon) upon delivery of the infant’s anterior shoulder, which is followed by immediate UCC and gentle cord traction to hasten delivery of the placenta [28,29]. Whereas this active management strategy reduces the risk of postpartum haemorrhage (PPH), it is also associated with a significant reduction in infant birth weight, which is thought to be due to a reduction in infant blood volume [28]. As oxytocin is equally effective when given following delivery of the placenta [29], it may be preferential to administer it at the end of third stage to avoid interfering with the placental circulation as the lung aerates. Importantly the meta-analysis of delayed cord clamping shows no increased risk of postpartum haemorrhage in mothers of infants who received delayed cord clamping [30].

Clinical studies suggest that, while the umbilical circulation remains intact, uterine contractions enhance the blood transfusion between the placenta and infant by “squeezing” umbilical blood towards the infant [31]. However, this suggestion is not consistent with the interpretation of fetal heart rate variability associated with uterine contractions during the second stage of labour [32]. Differential occlusion of umbilical venous and arterial vessels (intraplacental) during a uterine contraction is thought to cause the placental accumulation of blood. This is due to the earlier occlusion and later release of the more compliant venous vessels, compared with the arteries, leading to increased venous return and an increase in heart rate at the end of the contraction [32]. As a sustained and intense uterine contraction causes umbilical blood flow to reduce or to cease, oxytocin administration may negate the benefits of this procedure.

The effect of positioning the infant above or below the placenta is another factor that could influence the cardiovascular transition if UCC is delayed. It is assumed that placing the infant above the placenta increases blood flow into the placenta, whereas placing the infant below the placenta increases blood flow into the infant. This assumption is supported by studies [6,33,34] showing that placental transfusion is maximized when neonates are placed below the placenta [33]. Although the effects were explained by the ability of gravity to assist or reduce the placental to infant blood transfusion, the hemodynamics are likely to be considerably more complex. Nevertheless, a recent non-inferiority clinical trial has found no adverse effects (on infant weight used as a proxy for placental transfusion) of placing the infant above the placenta [35], which is consistent with the current common practice of placing the infant on the mother’s abdomen or chest after birth. Whereas this does not appear to influence infant outcome, the science underpinning this practice has not been investigated.

Although numerous factors are likely to influence flow in the umbilical vessels after birth, previous studies have detected a time-dependent increase in blood transfer after birth. These changes were measured either by weight gain [36] or by direct measures of blood volume [6,31]. As we now know the impact that immediate cord clamping can have on cardiovascular function at birth, it is possible that the measurement technique (dilution of 131-labelled albumin) used by Yao et al. [6] was not optimized for newborn infants. Indeed, it is possible that the lower blood volumes measured in the early clamp group simply reflect lower cardiovascular function over the 5 min period between label injection and sampling time [31]. Reduced cardiovascular function will reduce the mixing efficiency of the labelled albumin throughout the circulation, which is required to obtain an accurate volume estimate. The weight gain technique of measuring increased blood volumes would appear more robust, although the authors do report the problem of movement artefact and unfortunately infants subjected to immediate UCC were not included for comparison [35].

6. Postnatal myocardial adaptation of the preterm infant

The effects of the timing of UCC manifest long beyond the immediate post-clamping period. The circulatory transition is a complex series of cardiorespiratory events occurring in a sequence that allows safe conversion from a fetus with placental-dependent circulation to a neonate with an independent circulation. In the term infant this sequence of events occurs rapidly, usually with spontaneous respiration established within a short period after
birth. In the preterm infant with more immature lungs and a more immature myocardium, the circulatory transition occurs more slowly. Consequently there is an increased risk of delay in establishing spontaneous respiration that can adversely affect the transiti-
onal sequence, with the cord being clamped during or even before the first breath. As discussed, this potentially creates an abnormal physiological state, which has more profound implications for the immature cardiorespiratory system of the preterm infant than the term infant. Following premature birth, a delay in UCC not only allows placental transfusion but gives more opportunity for the preterm infant to establish spontaneous respiration prior to UCC.

The newborn myocardium and cardiac function are more vulnerable to both preload and afterload changes than are older infants and adults [37], and this vulnerability is even greater in preterm infants (see also S. Noori and I. Seri, Chapter 4, this issue). They have a simpler structure with fewer mitochondria, and differences in the myofibrils themselves result in less reserve and ability to compensate for changes in blood volume and peripheral resistance [38]. Consequently, the increased afterload and decreased preload associated with UCC before lung aeration may result in significant physiological instability and severely restrict the infant's ability to compensate to any additional adverse events.

7. Loss of circulating blood volume and placental transfusion

Before birth, there is a shared blood volume between the placenta and fetus, and the distribution is determined by the relative resistances between the two circulations as well as the differential flow in the umbilical vein and arteries. Following def-
ered UCC, placental transfusion can be as much as an absolute increase in blood volume of the infant of 20% [35] corresponding to 80 mL of blood at 1 min and 100 mL after 3 min [6]. As discussed above, there is significant variability in how much blood is trans-
ferred from the placenta to the neonate in a given period of time. A single time point for cord clamping to maximize the benefits is unlikely to be physiologically feasible. Rather the time to UCC should be described as a physiological end point such as when a particular volume of blood has been transfused — possibly based on a change in weight or measured flow in the umbilical vessels. Further refinement of practical ways to measure these outcomes is needed — changes in weight require accurate scales that stabilize rapidly and allow for movement, and use of real-time ultrasound to detect flow is dependent on Doppler angle, separating arterial from venous flow, and user experience to prevent partial occlusion of the vessel. Further assessment of the adequacy of the transition may be via either non-invasive measurement of cardiac output during the period of postnatal transition or postnatal measurement of card-
diac output/systemic blood flow following UCC. Use of previously validated techniques to measure right ventricular output or super-
ior vena cava flow is subject to the limitations of these techniques, which include user variability and inter-observer variation of up to 20%.

One of the potential consequences of interrupting the placental transfusion by immediate UCC after birth is a reduced circulating blood volume in the newborn infant. Term infants who experience early UCC are less likely to be affected as they often start spontaneously breathing and crying before the cord is cut, thereby enhancing the amount of placental transfusion within a short time period [39]. In preterm infants, this is less likely to occur as they may require more time between birth and cord clamping before breathing or even initiation of resuscitation can commence. The presence of reduced circulating blood volume is more evident in the preterm infant. Systematic reviews show that preterm infants who received early versus later UCC have reduced haemoglobin levels, more hypotension requiring treatment and a higher use of inotropic support [30]. Many preterm infants who had early UCC, particularly if they are then mechanically ventilated, appear to be relatively hypovolemic and respond well to a volume bolus if they have hypotension or evidence of low cardiac output [40]. Addi-
tionally there is now a series of clinical studies suggesting lower systemic blood flow/cardiac output in preterm infants who had early UCC [41,42]. The consequences of increased hypotension treatment and reduced systemic blood flow are significant, with associations between adverse neurological outcome and other significant morbidities. Concerns regarding a higher incidence of polycythemia, hyperbilirubinemia or other respiratory disorders potentially associated with later UCC have not been confirmed in randomized controlled trials and systematic reviews [30].

8. Assessing cardiovascular impairment: hypotension and low systemic blood flow

As blood pressure in neonates provides limited information on cardiovascular function, there is much interest in measuring car-
diac output or systemic blood flow, particularly in preterm infants. Cardiac output is a direct determinant of systemic oxygen delivery, and therefore may be the more relevant measure to assess. Variable peripheral vascular resistance alters the relationship between systemic blood flow and blood pressure. An infant who is vasodi-
lated can have a low systemic blood pressure but have good perfusion, no evidence of acidosis, and have a cardiac output within or even higher than the normal range. Similarly, when an infant is ex-
posed to a sudden increase in SVR, although the blood pressure may be within a normal range, cardiac output may be low, resulting in reduced perfusion and eventually acidosis.

Consequently techniques to measure the cardiac output of an infant have become increasingly important. In newborn infants the use of catheters and thermodilution are problematic due to physical size and the presence of cardiac shunts. The use of non-invasive Doppler ultrasound to measure cardiac output has increased, and there are normative values for both left and right ventricular output in newborn infants with well-demonstrated validity [43]. In newborn infants, ventricular outputs are altered due to the presence of both a ductal and a patent foramen ovale (PFO) shunt, meaning that true systemic blood flow may be underestimated. The presence of a large left-to-right ductal shunt will increase left ventricular output, which means that true systemic blood flow is overestimated. If there is a PFO shunt, the right ventricular output will similarly overestimate systemic blood flow [44,45]. To avoid this, superior vena cava (SVC flow) has been used as a measure of sys-
temic blood flow [45]. This measure estimates systemic blood flow by assessing the inflow to the heart from the upper body, head and brain; it has been clinically validated; and low SVC flow has been demonstrated to be associated with significant adverse outcomes. The heart is dependent, among other factors, on filling to provide an output, so measures of inflow are a valid way to assess changes in cardiac output. SVC flow therefore is the presently available most-tested assessment tool for the adequacy of the postnatal cardiovas-
cular system immediately after birth when fetal shunts are patent. This measure has been utilized in several studies of early versus late cord clamping to assess the systemic blood flow, particularly in preterm infants where postnatal fetal shunts are most prominent. These studies have found evidence of reduced systemic blood flow in infants who had early UCC compared to those who had UCC after 45 s to 3 min of postnatal age [41,42]. Umbilical cord milking with UCC at an earlier time point has also been shown to have a similar effect on decreasing the incidence of low systemic blood flow [46]. However, cord milking provides a rapid transfusion over 10–20 s, often before the establishment of
spontaneous breathing. Proponents of cord milking argue that it allows a more rapid transfer of blood to the fetus and subsequently allows earlier UCC in a fetus judged to require resuscitation. However, the safety of a rapid placental transfusion in terms of both volume transfer and the risk of cell debris or vasoactive factors from the cord endothelial cells being transferred to the neonate is uncertain. The premise of cord milking is that the main benefit in the transition from umbilical/placental transfer strategies is the increased blood volume, rather than facilitation of the normal transitional sequence whereby respiration begins and PBF increases prior to UCC. In the case of cord milking, the cord is still likely to be clamped in a preterm infant prior to establishment of breathing.

9. Hemodynamic complications of reduced systemic blood flow including periventricular/intraventricular haemorrhage (P/I VH)

An important association with low cardiac output/SVC flow is periventricular/intraventricular haemorrhage (P/I VH), with low cardiac output and SVC flow being more frequent in infants who subsequently develop this significant complication of prematurity (see S. Noori and I. Seri, Chapter 4, this issue). The mechanism is thought to involve a period of postnatal ischemia/reduced blood flow, which impairs cerebral autoregulation, eventually leading to P/I VH after blood flow and blood pressure recovery [47]. It is of particular interest that, in systematic reviews, preterm infants who received later UCC had an overall decreased incidence of P/I VH [30]. This association may be explained by the link between interruption of the placental transfusion and improved myocardial adaptation and subsequent reduced systemic blood flow in preterm infants, increasing the risk of P/I VH in patients in the immediate UCC group. A large ongoing study – the Australian Placental Transfer Study – will assess this link more closely using early cardiac ultrasound to routinely assess the cardiovascular function of infants randomized to early UCC at 10 s or a deferral of 60 s.

10. The timing of resuscitation intervention

The new understanding of physiology surrounding the timing of UCC challenges the previous assumption that early UCC and separation of the mother and baby to allow resuscitation and initiation of respiration is the priority in an aneuploid infant. The intervention of early UCC was introduced into the care of the newborn infant without any physiologic rationale in the baby or systematic study as to the consequences. As mentioned earlier, the rationale was related more to concerns regarding protection of the mother from PPH, which was subsequently found to be not related to the timing of UCC [48]. Similarly, protection of the infant from exposure to maternal anesthetics and analgesics is also an untested assumption. Concerns regarding risks of polycythemia and an increased need for phototherapy were also cited but have been refuted in a series of clinical trials in preterm infants undergoing deferred UCC [30]. As a consequence of the belief that resuscitation of the newborn infant is more important than allowing a physiological transition, our labour wards, delivery suites and operating theatres have evolved with separate areas for newborn resuscitation, resulting in the need to cut the umbilical cord and separate mother and baby if resuscitation is to be provided.

Increasingly this model of resuscitation is being questioned. It is suggested that the first step in neonatal resuscitation should be delayed UCC and/or a placental transfusion and allowing the infant to initiate respirations while still attached to the placenta [49]. As reviewed in this article, allowing the more natural transitional sequence to occur may result in less physiological instability and subsequently a smoother transition. The initial steps of resuscitation may sometimes be counterproductive to a smooth cardiorespiratory transition with suctioning of the airway, application of a facemask and attempts at intubation; all potentially inhibiting attempts by the preterm infant to establish breathing. Deferring UCC may allow more time for the infant to commence respiration spontaneously, thus allowing a more physiological transition. Heart rate is one of the main determinants of the initiation of the various steps of resuscitation, and it has been demonstrated in both animals [1] and human infants [50] that early cord clamping, particularly in an aneuploid infant, will result in a significant reflex bradycardia. In infants who all received early UCC, 50% of the infants had HR < 100 bpm and 10% were < 40 bpm at 1 min. The decreased heart rate may lead a clinician to initiate resuscitation measures, whereas, if there had been a deferral of UCC, transition may have occurred without the need for resuscitation.

We have suggested the term “physiologically based cord clamping” to describe the process of allowing a more natural sequence of transition to occur. The timing of UCC is then not defined as a particular time period between birth and UCC, but rather clamping the umbilical cord after regular respiration has been established or after appropriate lung inflation has been achieved in depressed preterm or term neonates, at whatever time point this may be. A natural evolution of this approach is commencing resuscitation and initiating respiratory efforts while the infant is still attached to the placenta. Facilitating this will require a change in practice at the bedside with medical resuscitation equipment being brought to the place of birth. This is increasingly feasible and the development and testing of a resuscitation cot that can be brought to the bedside after the birth of a preterm infant has already commenced [27]. The use of new equipment to allow resuscitation and particularly lung inflation, of the preterm infant while still receiving the placental circulation with its oxygen and nutrient supply has the potential to substantially change the way we approach postnatal care. It is important to note that this suggested novel approach to neonatal resuscitation must be vigorously tested in large trials before routine clinical use can be recommended.

11. Conclusions

Professional bodies concerned with issuing guidelines concerning management of labour and delivery have recommended deferral of UCC in both term and preterm infants [49]. Despite this, the correct physiological time point to clamp the umbilical cord is still not clear. The benefits of deferring the time of UCC are dependent on two main mechanisms with a physiological rationale. The first is the receipt of a placental transfusion with subsequent benefits in terms of preventing low blood pressure and cardiac output with associated reduction in P/I VH, less inotropes and less iron deficiency anaemia. The time point of UCC would thus be related to a measured volume of transfusion, and the factors that contribute to the volume are many. Validated techniques to assess the volume of transfusion in real time are urgently needed. The second mechanism is allowing an ordered sequence of physiological events at birth with commencement of breathing and lung ventilation followed by a normal cardiovascular transition. In this case, the time point of UCC is related to initiation of breathing and lung inflation. To implement this physiological intervention requires rigorous testing of the approach and, if the approach is found to be effective, and in a rethinking of the design of our labour and delivery rooms to allow resuscitation of the infant with cord intact by the mother’s bedside.
Practice points

- The practice of immediate clamping of the umbilical cord in both term and preterm infants is increasingly being questioned, and systematic reviews suggest a range of benefits resulting from deferral of cord clamping.
- The mechanism resulting in these benefits is not clear — placental transfer is important but there is increasing evidence that the timing of the relationship between cord clamping and lung aeration is also important.
- The term physiologically based cord clamping recognizes the importance of using a physiological outcome to time cord clamping rather than an arbitrary time point.

Research directions

- More evidence is needed regarding the benefits and risks of deferred cord clamping in the setting of very preterm, asphyxiated and apneic infants who are in need of resuscitation. Several ongoing randomized clinical trials will address this question.
- The best physiological outcome on which to base the clamping of the cord is still not clear — more data on how to assess placental function, umbilical arterial blood flow, volume of blood transfused and commencement of the circulatory transition process in the immediate time after birth are needed to help define this.
- The benefits and risks of cord milking to enhance placental transfer and allow earlier cord clamping, possibly in an apneic infant, need more study.

Conflict of interest statement

None declared.

Funding sources

None.

References


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