

REVIEW

Immediate or early cord clamping vs delayed clamping

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Over the past 40 years, there have been a number of review articles attempting to rationalise cord clamping practice. Early cord clamping was originally thought to be important in active management of the third stage of labour, but this was never evidence based. Without an evidence base to justify it, early cord clamping in clinical practice has remained very variable. There is good evidence that early cord clamping leads to hypovolaemia, anaemia and low iron stores in the neonate. We review all the evidence and discuss possible reasons why some obstetricians and midwives persevere with early clamping. We explain how a variable definition, defective education, deferred responsibility between obstetrician and paediatrician, variable guidelines and a lack of appreciation for the potential harm of the intervention, have all contributed. This study describes how the need for early cord clamping can be avoided in practically all clinical complications of birth.

Keywords: Circulation, cord clamping, delayed, early, immediate, placental transfusion, transition

Introduction

Over the past 40 years, there have been a number of review articles (Dunn 1964; Dunn 1967; Linderkamp 1982; Mercer 2001; Mercer and Skovgaard 2002; Philip and Saigal 2004; Merce et al. 2007; Weeks 2007; Hutchon 2008; Hutchon 2010) attempting to rationalise cord clamping practice. Practice is very variable both among practitioners and in different countries (Winter et al. 2007). To put it simply, some believe the baby does not get enough blood when the cord is clamped quickly, while others believe the baby may get too much blood when clamping is delayed or the cord vessels are allowed to close naturally. Covert factors may influence the view. What is the reality?

Definition

The precise timing of immediate or early cord clamping (ICC) varies between studies and guidelines but the principle of early clamping is the application of a clamp across the umbilical cord while there is a significant circulation. This is clearly an intervention. Delayed cord clamping (DCC) is sometime later, when physiological closure will have commenced or been completed. There will be less or no impact on the neonatal circulation. The time which the placental circulation ceases naturally is quite

variable, however it has been shown to be absent in 95% of babies after an interval of 5 min (Farrar et al. 2011). Thus, clamping after 5 min will rarely have any impact on the neonatal circulation. Earlier clamping will have an impact inversely proportional to the interval between birth and clamping. The RCOG defines ICC within 15 s of birth whereas DCC is defined as a delay of 30 s (RCOG 2009b). Using this definition, the impact on the circulation between clamping at 15 s (ICC) and clamping at 30 s (DCC) is likely to be small.

There is no question that given time, the umbilical vessels will constrict under the influence of physiological mechanisms and if left intact, will dry and break off a few days after birth, as in a Lotus birth (Lotus birth 2011). Cutting the cord provides convenience for the mother or other attendants while caring for the baby and the umbilical clamp provides additional protection against bleeding from the cut end. The tradition of using a linen tie around the cord goes back thousands of years, but Aristotle realised that the baby may be harmed if tying and cutting was performed too soon after birth (Cresswell 1862). In more recent years, Erasmus Darwin (1796) and Charles White (White 1773) proposed that the baby may be harmed if the cord is clamped too soon. The question is what is 'too soon'? The cord has no nerves or lymphatics, therefore once the circulation through the arteries and vein has ceased as a result of vessel constriction, it is simply a fleshy connection between the baby and the placenta. Cutting this fleshy connection should have no impact on the baby. Applying a clamp before cutting the cord seems a sensible precaution given the potentially large vessels within.

The first cord clamp (Magennis 1899) came with specific instructions that it should not be applied until cord pulsation has ceased. A readily available clamp allows easy application onto the cord within seconds of birth if the attendant wishes.

Education

The majority of English language textbooks do not provide an accurate description of physiological transition. During transition from placental to pulmonary respiration, the circulatory system of the neonate has to make significant changes. While the physiology of transition is only partly understood, natural closure of the placental circulation does occur within about 5 min. It does not require the outside intervention of a cord clamp. In the latest edition of *Ganong's Review of Medical Physiology* (Barret 2010), a popular teaching textbook, it is stated:

'Because of the patent ductus arteriosus and foramen ovale (figure 3-18), the left heart and right heart pump in parallel in the fetus rather than in series as they do in the adult. At birth, the placental circulation is cut off and the peripheral resistance suddenly rises. The pressure in the aorta rises until it exceeds that in the pulmonary artery. Meanwhile, because the placental circulation has been cut off, the infant becomes increasingly asphyxial. Finally, the infant gasps several times, and the lungs expand. The markedly negative intrapleural pressure (-30 to -50 mm Hg) during the gasps contributes to the expansion of the lungs, but other factors are likely also involved. The sucking action of the first breath plus constriction of the umbilical vein squeezes as much as 100 ml of blood from the placenta (the "placental transfusion").

We question that this is a description of physiological transition. Farrar et al. (2011) and Wiberg et al. (2008) clearly showed that there is no 'cut off' of the placental circulation at birth. They showed that the circulation continues, although there is steady closure over the first 5 min after birth. Every midwife knows that during a physiological 3rd stage, the cord continues to pulsate for several minutes. The Ganong author makes no attempt to explain the mechanism for the 'cut off' of the placental circulation which must be a sudden and external influence implied by the 'sudden rise in the peripheral resistance' and the passive voice 'is cut off'. A sudden rise in pressure has been shown to occur after early cord clamping (Hofmeyr 1988). The description that the infant becomes increasingly asphyxial is not supported by recent studies, although logically will occur if the cord has been clamped. Wiberg et al. (2008) showed a steady rise in the arterial PO₂ and a similar rise in venous PO₂ up to 45 s after birth.

The statement that the infant gasps because of the asphyxia from the loss of placental circulation is only true after cord clamping but it would not be true in a normal physiological transition, which the textbook is purporting to teach. The mechanism of the placental transfusion as 'constriction of the umbilical vein squeezes as much as 100 ml of blood from the placenta' is confusing, since earlier on the author tells us that the placental circulation has been cut off. How has it been opened up again? This is not the normal understanding of the placental transfusion (RCOG 2009b). *Gray's Anatomy* tells us that it is gas exchange within the neonatal lungs that leads to the rise in umbilical artery PO₂ and the high oxygen content of the blood leads to constriction of the arterial vessel walls, together with the production of bradykinins from the lungs and cord, which are potent vasoconstrictors of the umbilical vessels (Standring 2005).

Ganong's confusion with the common practice of early cord clamping and physiological transition is typical of many other textbook descriptions. Virtually every textbook of physiology (Berne and Levy 1996; Lindsay 1996), paediatrics (McMillan 1999; Behrman 2004; Campbell and McIntosh 1998) and cardiology (Braunwald 2001) describes the cord clamp as part of the physiological process. At best, these descriptions are confusing to a student, but they also affect research papers. A study to define the normal range heart rate in the first 10 min after birth of infants who did not receive any postnatal medical interventions, ignored the fact that all these babies had had the medical intervention of early cord clamping (Dawson et al. 2010). Strictly it might be considered that early cord clamping is not postnatal, but the study was clearly aimed at healthy babies who needed no intervention. A mini-symposium on heart failure described the adverse effect of cord clamping without further comment, implying that it was a normal physiological event (Hutchon and Bewley 2005).

The terms 'delayed cord clamping' and 'placental transfusion' also affect the understanding of neonatal transition which

has been affected students for several generations. Delayed cord clamping implies a delay in something which should be done sooner. Placental transfusion implies a specific volume of blood being transferred from the placenta to the baby. This blood is circulating and it is therefore a redistribution of blood due to the earlier constriction of the arterial flow and later the venous return. The blood is the baby's own blood. Even describing it as an autotransfusion is not strictly accurate, as the blood has never been out of the baby's circulation, as would be the case in the autotransfusion of intraoperative cell salvage (NICE 2005). The placental transfusion is not a transfusion as normally understood. However, by using this term, the known risk of over-transfusion is often used to raise concern about DCC. There is no logic in this comparison. The redistribution of blood from the placenta is thought to fill the new pulmonary circulation and other parts of the circulation which now need to be much more active such as the diaphragmatic and chest muscles, kidneys and gut. However, the required volume to fill the pulmonary circulation after birth has never been measured even in animal models, so it is impossible to know how much of the placental transfusion is critical. Logically, without the additional blood, the neonate has to steal from the rest of the circulation to allow the lung circulation to fill.

A recent article suggested that the cord clamp is a physiological necessity (Hutchon et al. 2010). It is true that when a clamp is applied to the umbilical cord it must be applied across the whole width. Teaching midwives that the cord clamp is a physiological necessity encourages the concept that DCC is the intervention needing evidence.

Responsibility

Cord clamping is carried out by the midwife or obstetrician, however, the impact is on the health of the baby who now becomes the responsibility of the paediatrician. The importance of dialogue between these two specialties has been realised and is now common practice in many problems such as pre-term birth. The timing of cord clamping however, is not discussed sufficiently in the care of individual births.

Evidence

The evidence about cord clamping is separated between pre-term babies and term babies. This is partly because of the high mortality of pre-term babies which it was thought might be reduced by DCC. From the evidence of two systematic reviews, it is now clear that there are short-term benefits of DCC in pre-term babies (Rabe et al. 2004; Rabe et al. 2008). These benefits are: less need for transfusion, less anaemia, less intraventricular haemorrhage and less late onset sepsis. DCC at birth seems to be protective of very low birth weight male infants against motor disability at 7 months corrected age (Mercer et al. 2010). One ongoing RCT shows significantly higher superior vena cava blood flow in pre-term babies after DCC (Sommers et al. 2012). This was also shown in an observational study (Meyer and Mildenhall 2011). In another study using near infra-red spectroscopy (NIRS) to measure mean regional tissue oxygenation, they found it was higher at the ages of 4 h and of 24 h in the babies who had DCC (Baenziger et al. 2007).

Term babies have a low mortality and morbidity and cord clamping has less of an impact. All the randomised controlled studies have been relatively small and excluded vulnerable babies which required resuscitation. Probably because of concern about the condition of the baby, there were many protocol violations

within the DCC arm with fewer in the ICC arm. Analysis was by intention to treat and a high number of protocol violations makes this analysis unreliable. However, there are two systematic reviews (one by Cochrane) and both show less anaemia and better iron stores after DCC (Hutton and Hassan 2007; McDonald and Middleton 2008). On the other side, the Cochrane review showed a slight increase in the use of phototherapy for jaundice in the babies after DCC. This was attributed to one unpublished trial and has been criticised because the paediatricians were not blinded to cord management and the bilirubin level for treatment was not predefined. A recent large RCT (published since the Cochrane review) has shown no impact on the need for phototherapy and there were actually fewer babies needing phototherapy after DCC (Andersson et al. 2011).

A number of factors affect the speed of the placental transfusion and the time taken before the circulation ceases. If the baby is elevated higher than the cord venous pressure (30 mmHg or 16 inches water) no blood will flow and there may be reverse flow if the baby is elevated high enough (Dawes 1968). Provided the baby is not elevated more than 6 inches above the placenta, adequate flow will continue. Skin-to-skin on the mother's abdomen meets this requirement (Chaparro and Lutter 2007). Flow will be more rapid if the baby is below the level of the placenta but the final size of the placental transfusion will remain unaltered (Yao and Lind 1969). The placental transfusion is also accelerated by the onset of breathing. At caesarean section, the open uterus might be expected to reduce the pressure on the placenta and reduce the rate of placental transfusion but Farrar et al. (2011) found no difference in the size of the placental transfusion in babies delivered by caesarean section. Prophylactic uterotonics would be expected to increase the intrauterine pressure and the umbilical venous pressure. Farrar's study showed little demonstrable effect (2011). The size of the placental transfusion is reduced if clamping occurs before the onset of respiration (Redmond et al. 1965).

All the studies compared DCC as the intervention or the experimental treatment with ICC as the control. This has the effect that when the difference is slight, evidence to support DCC is weak. The reality is that ICC is the intervention and all studies therefore show weak evidence of harm for ICC. If ICC was a medication it would be withdrawn immediately (Weeks 2007).

Guidelines

There are several international guidelines for the prevention of postpartum haemorrhage that have specifically withdrawn the need for early cord clamping as part of active management of the third stage of labour (ICM 2006). The recommendation for clamping at about 3 min is recommended by the World Health Organization for the health of the baby (WHO 2007). The RCOG added an addendum to the Green-top guideline (RCOG 2009a) stating:

'Evidence suggests that delayed cord clamping (more than 30 seconds) may benefit the neonate in reducing anaemia, and particularly the preterm neonate by allowing time for transfusion of placental blood to the newborn infant, which can provide an additional 30% blood volume. In the preterm infant (less than 37 + 0 weeks of gestation), this may reduce the need for transfusion and reduce intraventricular haemorrhage. Delayed cord clamping does not appear to increase the risk of postpartum haemorrhage'.

The NICE intrapartum care guideline (NICE 2007), which includes early cord clamping as part of active management is under review. The NICE caesarean section guideline (NICE 2011)

under the heading of 'Cord Clamping' misrepresents the review of Mercer (Hutchon 2007) by using it as a reference for the statement that there are possible harms for delayed cord clamping. Mercer's article specifically states that, 'The idea that delayed cord clamping is harmful is not supported by the findings from the 16 randomised controlled trials and 5 controlled trials completed over the last two decades involving term and preterm infants and reviewed here' (Mercer 2001).

The 2005 Newborn Life Support guidelines (NLS 2005) stated that very early clamping and clamping while the baby is held above the level of the placenta can cause hypovolaemia. It also stated that hypovolaemia needs to be considered in any baby that fails to respond to normal resuscitation measures. The 2010 NLS (NLS 2010) and ILCOR (Wyllie et al. 2010) guideline recommend for uncompromised babies, a delay in cord clamping of at least 1 minute from the complete delivery of the infant. As yet, there is insufficient evidence to recommend an appropriate time for clamping the cord in babies who are severely compromised at birth. The NLS and ILCOR guidelines are based on very robust evidence.

Drivers preventing widespread adoption of DCC

Cord blood gases, resuscitation, nuchal cord, cord blood banking and the need for neonatal blood group in rhesus negative mothers are all drivers preventing DCC becoming routine practice.

There is insufficient space to discuss in detail the value of cord blood gases, however it is commonly thought that ICC is necessary for a valid result, since the values change during a physiological transition. When normal ranges during a physiological transition are available, there will no longer be a conflict. The importance of cord blood gases is for audit and medico-legal purposes, neither of which benefits the individual baby.

As stated above, ILCOR advise that there is insufficient evidence to recommend a time of cord clamping for babies that require resuscitation. Current practice is to transfer the baby immediately to a remote resuscitator and this requires cord clamping. There is however, increasing opinion and evidence that maintaining a placental circulation in these babies will aid recovery (Dunn 1984; Hutchon and Thakur 2008; Mercer and Bewley 2009). Three babies with moderate and severe intrapartum hypoxia in the Wiberg (2008) series recovered quickly, with only an intact placental circulation. Initiation of resuscitation is possible at the side of the mother without clamping the cord (Hutchon and Thakur 2007; Van Rhee 2011).

It is standard practice to feel for a nuchal cord because it is thought that a tight shortened cord may prevent further descent of the baby and delivery of the body. It is advised that the cord may be clamped, although this is highly dangerous with the possibility of delay in delivery of the body from shoulder dystocia (Iffy and Varadi 1994; Vanhaesebrouck et al. 1987). Even in the absence of shoulder dystocia, clamping a nuchal cord can lead to cerebral palsy (Chow vs Wellesley Hospital 1999). The correct procedure is to deliver the baby using the somersault manoeuvre (Mercer et al. 2005). Often the baby's body will deliver in the presence of a nuchal cord without difficulty.

Current cord blood banking of stem cells relies on a sufficient volume of residual placental blood (Diaz-Rossello 2006). DCC results in much smaller volumes and after a physiological transition (Farrar et al. 2011), the volume is 20 ml (± 10), which is rarely sufficient for stem cell banking. Public banks will therefore need to consider other methods to harvest the billions of stem

cells left in the placenta if life-saving use of the cells is to continue (Hutchon 2012).

Consent, legality and ethics

If ICC is not thought of as an intervention, then obstetricians and midwives may well not discuss the issue, nor will they ask for consent when carrying out cord clamping. However, since the procedure is interfering with normal physiology, informed consent is legally required. Informed consent means that the mothers must have been given information about the procedure and this is available in several popular pregnancy information books (Blott 2010; Regan 2010). Both these books explain the advantages for the baby of DCC and tell readers that DCC is the usual practice. Some women may specifically request DCC in their birth plan, while others will assume that the usual practice will be carried out unless they are informed otherwise. Some women may be familiar with the latest ILCOR guideline referred to previously and expect it to be followed by any unit with at least CNST level 1 maternity standards. The question arises about the legality of the intervention if ICC is carried out without previous discussion and consent.

The importance of avoiding pain and distress during the care of neonates has recently been appreciated (Anand et al. 2001). One principle is that if a procedure is painful in adults, it should be considered painful in newborn infants. As discussed previously, ICC immediately stops the return of oxygenated blood and results in increasing asphyxia of the neonate. It also results in a degree of hypovolaemia, which sometimes can be severe. Both asphyxia and hypovolaemia would distress an adult and indeed may be fatal. Routine ICC may therefore be unethical.

Indications for ICC

There may be some situations where early clamping is indicated. A ruptured vasa praevia results in fetal blood loss and the need for urgent delivery. While the baby is likely to be hypovolaemic (Hutchon 2011a), waiting for a placental transfusion may be fruitless with continued loss of blood from the cord vein. However, it may be possible to accelerate venous blood flow and create a placental transfusion by cord milking and lowering the baby well below the placenta. These situations are rare and unlikely to be subjected to a RCT, however it should not be assumed that ICC will always be the best management.

Concern about polycythaemia has been raised repeatedly (NICE 2007), although symptomatic polycythaemia was not seen in any of the RTCs. There are however, a small group of fetuses at particular risk of polycythaemia and the possibility that ICC is beneficial in this group should be investigated. One problem with ICC being used as prophylaxis of the condition is that the volume of blood being denied to the baby is unknown and unpredictable. A baby with increased blood viscosity and a low blood pressure due to hypovolaemia may be just as harmful to the circulation as increased viscosity and a normal blood pressure.

Discussion

Although an RCT provides the most robust form of evidence, observational or retrospective reviews can provide useful information. However, this sort of study is not possible with cord clamping because of the lack of documentation. Failure to time or document is probably a reflection of the commonly held view that any effect of cord clamping is trivial. Anaemia and low iron stores

in a neonate is not immediately seen as serious or life-threatening. If more serious consequences of cord clamping were considered, the need for timing and documentation of the intervention would be obvious.

Studies have shown the extent of the placental transfusion by measuring the weight gain in the baby immediately after birth. This is a very simple and reliable approach and other studies using dye dilution methods have reached similar conclusions. The placental transfusion can account for up to 40% of the neonate's blood volume (Farrar et al. 2011). In any other situation, losing 40% of circulating blood volume would lead to serious hypovolaemia and possible death. The possibility that loss of such a large proportion of circulating blood volume leads to serious compromise in the neonate has been raised many years ago (Dunn 1988). In *Obstetrics by Ten Teachers* (Rennie 2011), the author states that a failure of an adequate placental transfusion due to extreme cord compression can be a reason for birth depression and explains that an emergency transfusion of uncross-matched O-negative blood may be life-saving. From Farrar's data (Farrar et al. 2011), one out of 26 babies could lose as much as 204 ml (representing 45–60% of a baby BW 3.5–5 kg) from failure of the placental transfusion. Studies in pre-term babies have shown ICC has an adverse effect on cerebral circulation (Sommers et al. 2012; Meyer 2011; Baenziger et al. 2007). It is not unreasonable that ICC has a similar effect on cerebral circulation in the term baby. This has never been investigated but absence of evidence is not evidence of absence (Altman and Bland 1995).

The evidence currently available from randomised controlled trials is not considered strong enough to change clinical practice by some researchers (Farrar 2011) who point out that the studies to date have been underpowered for serious adverse effects, and there was a lack of adequate long-term follow-up of the women or children. They agree however, that immediate cord clamping should have been rigorously evaluated decades ago before it became normal clinical practice. If ideal standards are applied to the evidence base, equally ideal standards should be applied to the intervention. An intervention which is shown to cause even minor short-term harm and no benefit should be removed from clinical practice until ongoing research shows clear evidence of benefit. This principle has been applied to medication prescribed during pregnancy.

A routine intervention, which is not documented cannot be audited or investigated retrospectively. A routine intervention, which is thought to be necessary when there is concern about the condition of the neonate delivered because of fetal distress, is unlikely to be considered to be the cause in any adverse outcome. Documentation has now been recommended by the RCOG (2009a).

The results of ongoing studies in pre-term babies will be important to show how these fragile neonates can be cared for close enough to the mother for the cord to remain intact. The challenge is maintaining a satisfactory temperature, initiating ventilation if necessary and the administration of surfactant. The possibility that there may be some rare indications for ICC needs to be investigated.

Declaration of interest: I convened a meeting in 2010 in Worcester to discuss resuscitation with the cord intact. From this meeting, the Bedside Assessment, Stabilisation and Initial Cardiorespiratory Support (BASICS) trolley was conceived, which allows resuscitation at the bedside. All royalties from the development of the trolley are to be donated to a children's charity and the author has no financial interest in the sale of the trolley.

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