A practical approach to timing cord clamping in resource poor settings

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There is little agreement among doctors and midwives about the optimal time to clamp the umbilical cord after birth. The most important points of difference relate to maternal and infant safety. Many healthcare workers worldwide tend to clamp the cord and pass the baby off as quickly as possible. Infants in resource poor settings are the main victims of immediate clamping, as this prevents a cost-free means of boosting their small iron stores.

Infant anaemia is common in poor communities, especially where malaria is endemic. In sub-Saharan Africa more than 75% of infants are anaemic before 6 months of age.[w1-w3] Infant anaemia is associated with increased mortality[w4 w5] and with impaired mental and motor development.[w6] Its prevention is of critical importance, and delaying clamping of the umbilical cord could be an effective strategy to reduce anaemia and improve child survival.

We propose a practice guideline on cord clamping for resource poor countries for singleton vaginal deliveries, based on published systematic reviews, randomised controlled trials, and biological evidence. Taking account of the safety of mothers and infants, we provide evidence about inclusion and exclusion criteria for delayed cord clamping, optimal timing of clamping, infant position during placental-fetal transfusion, and potential side effects. We present the evidence as a series of structured clinical questions, which identify the population concerned (mothers and infants from resource poor countries), the options being compared (mostly delayed versus immediate cord clamping), and the outcome measures used to measure effectiveness and safety of delayed cord clamping. We also present a practical and simple flow chart for quick reference.

Summary points

- There is little agreement about the optimal time to clamp the umbilical cord after birth
- Delaying clamping of the umbilical cord is a cheap and effective strategy to reduce infant anaemia and improve child survival in resource poor settings
- This practice guideline for singleton vaginal deliveries takes into account the safety of both mothers and infants
- Delayed cord clamping should be considered in every infant born in a resource poor setting, regardless of gestational age
- It should be combined with the administration of oxytocin immediately after delivery to reduce maternal blood loss in the third stage of labour
- Cord clamping should be delayed for at least three minutes for optimal placental transfusion, regardless of fetal weight
- When the state of the infant does not allow a clamping delay of three minutes, aim for a delay of at least 60 seconds with the infant placed between the mother's legs

Clinical questions

Is delayed cord clamping associated with improved haematological status in infancy?

Four randomised controlled trials, all from developing countries, evaluated haemoglobin concentrations in term infants 2-4 months after birth.[2–5] Meta-analysis showed that haemoglobin concentrations were significantly higher after delayed cord clamping (317 infants, weighted mean difference 4.9 g/l (95% confidence interval 2.6 to 7.2 g/l)). The proportion of infants with anaemia was lower with delayed cord clamping (three trials, 127 infants, relative risk 0.53 (95% confidence interval 0.40 to 0.69)).[2 3 5] A large randomised controlled trial from Mexico showed a beneficial effect of delayed cord clamping on infant iron status could be measured six months after birth, although haemoglobin levels were no longer different.[6]

The haematological effects of delayed cord clamping in preterm infants were studied in four randomised controlled trials from industrialised countries.[7–10] The observation period lasted four to six weeks and comprised the time the infants were admitted to the neonatal intensive care unit. Many of these infants born before 30 weeks of gestation would not have

References w1-w29 are on bmj.com

survived in resource poor countries. After delayed cord clamping, fewer of these infants required blood transfusion in the first six weeks after birth (183 infants, relative risk 0.64 (0.46 to 0.88)).

Is delayed cord clamping associated with side effects that require treatment?

Four controlled trials and one randomised controlled trial, all from industrialised countries,[11–16] and two randomised controlled trials from resource poor countries[5 17] evaluated the incidence of hyperbilirubinaemia and hyperviscosity in term neonates. Packed cell volume was significantly higher after delayed cord clamping, but infants showed no evidence of hyperviscosity syndrome and partial exchange transfusion was never needed. Although peak bilirubin concentrations tended to be higher after delayed cord clamping, the phototherapy threshold was never exceeded and none required exchange transfusion. Meta-analysis showed that delayed cord clamping in healthy term infants caused no side effects requiring treatment (seven trials, 583 infants, relative risk 0.20 (0.01 to 3.97)).

Three randomised trials and one quasi-randomised controlled trial in preterm neonates, all from industrialised countries, measured peak bilirubin and found significantly higher concentrations after delayed cord clamping (259 infants, weighted mean difference 25 μmol/l (14 to 36 μmol/l)).[8–10 15] Two of these four trials reported the incidence of hyperbilirubinaemia necessitating treatment and found no difference between delayed cord clamping and immediate clamping (138 infants, relative risk 1.09 (0.66 to 1.81)).[10 15] It is unclear whether these results can be extrapolated to resource poor countries, where low birth weight babies are predominantly growth retarded. About a third of the preterm infants in the study by Rabe et al[10] were growth retarded and equally distributed between delayed cord clamping and immediate clamping. Necrotising enterocolitis was examined in two trials, and the incidence did not differ between delayed and immediate clamping (111 infants, relative risk 0.76 (0.37 to 1.58)).[9 10]

Body temperature on admission to the neonatal intensive care unit was studied in only one trial, which found no difference between delayed and immediate clamping (39 infants, weighted mean difference 0.20°C (−0.03 to 0.43)).[10] This should be studied further and advice is required about keeping the baby wrapped and warm.

Recommendation

- Delayed cord clamping should be considered in every infant born in a resource poor setting, regardless of gestational age

  Grade of recommendation: Strong

Is delayed cord clamping associated with increased maternal blood loss?

Two randomised controlled trials (one from a resource poor country[5]) evaluated the effect of cord clamping on maternal blood loss.[5 16] Major limitations of these trials were the differences in the method of measuring blood loss (visual estimation versus measuring jar), the mode of delivery (100% vaginal versus >25% caesarean section), and the definition of delayed cord clamping. The risk of postpartum haemorrhage, defined as blood loss of >500 ml, was not different after delayed cord clamping or immediate clamping (363 participants, relative risk 0.89 (0.58 to 1.36)). A Mexican trial did not quantitatively measure maternal blood loss but classified the bleeding as normal, high, or severe, and found no differences between delayed cord clamping and immediate clamping.[6]

How does delayed cord clamping affect obstetric management of the third stage of labour?

The third stage of labour is defined as the period from expulsion of the fetus to the expulsion of the placenta. In active management the aim is to keep this period as short as possible to reduce maternal blood loss, but the time frame is not exactly specified. In expectant management the aim is to deliver the placenta within one hour without medical interference. A Cochrane review compared active management with expectant

Methods

Search strategy

We identified systematic reviews from the *Cochrane Library* (issue 2, 2006). We identified randomised controlled trials from the *Cochrane Library*, PubMed (1966 to June 2006), and EMBASE (1988 to June 2006) using the terms "umbilical cord" and "clamp*." We examined related articles and reference lists of published trials, and hand searched major journals on perinatal and tropical medicine. Any new evidence was used to update existing meta-analyses. When a systematic review or meta-analysis did not exist, we completed our own following published methods.[w7]

Criteria for considering trials for meta-analysis

We included randomised and quasi-randomised trials comparing immediate cord clamping (within 20 seconds of birth) with delayed clamping in infants born vaginally at 30-42 weeks' gestation and with birth weight >1000 g. We excluded infants born before 30 completed weeks' gestation or with birth weights <1000 g because their mortality is high in resource poor countries.[w8-w10]

Quality assessment

To minimise bias and to aid interpretation of the guidelines, we used the systematic approach to grading the strength of recommendations developed by the GRADE working group[1]:

- Levels of evidence

  High—Further research is unlikely to change our confidence in the estimate of effect

  Moderate—Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate

  Low—Further research is highly likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate

  Very low—Any estimate of effect is very uncertain
- Grades of recommendations

  The strength of a recommendation indicates the extent to which one can be confident that adherence to the recommendation will do more good than harm

  Strong—Do it

  Weak—Probably do it

management and included five randomised controlled trials from industrialised countries.[18] Active management involves clamping the cord as soon as possible, as well as routinely using prophylactic uterotonic drugs and controlled cord traction. Expectant management is a "hands off" policy, in which signs of placental separation are awaited and spontaneous delivery of the placenta is allowed. Active management was associated with a reduction in clinically estimated maternal blood loss (two trials, 2941 participants, weighted mean difference −79 ml (−94 to −64))[w11 w12] and a reduced risk of postpartum haemorrhage (four trials, 6284 participants, relative risk 0.38 (0.32 to 0.46)).[w11-w14]

The administration of uterotonic drugs immediately after delivery of the baby, which forms the mainstay of active management, would hasten the transfer of blood into the baby and increase the infant's red cell mass.[w15 w16] Immediately after placental transfusion is completed, after about three minutes, the cord can be clamped and cut, and delivery of the placenta by controlled cord traction can commence.

The authors of the Cochrane review concluded that routine "active management is superior to expectant management" in terms of maternal complications but considered that research was needed in the developing world, with its higher incidence of maternal and infant mortality. Whether all the components of full active management are useful should also be investigated.[w17] The International Confederation of Midwives and the International Federation of Gynaecologists and Obstetricians have not waited for these studies before acting and have removed immediate cord clamping from their recommendations.[w18] Oxytocin is the uterotonic drug of choice, but there are problems with its universal availability and storage conditions.

Recommendation

- Delayed cord clamping should be combined with the administration of oxytocin immediately after delivery of the infant to reduce maternal blood loss in the third stage of labour

Grade of recommendation: Strong

Is delayed cord clamping in growth retarded infants associated with more adverse effects?

A systematic review has established the safety of delayed cord clamping in normal birthweight babies,[19] but there is little information about growth retarded babies.[20] Those born in industrialised countries often have an increased incidence of polycythaemia due to chronic hypoxaemia in utero and increased fetal erythropoiesis. In the presence of sufficient iron this leads to increased packed cell volume, although half of growth retarded newborn babies have ferritin concentrations below the fifth centile.[w19] Most polycythaemic infants remain asymptomatic, although growth retarded babies may be at greater risk of symptoms and the clinical consequences of altered blood viscosity.[w20]

The baseline risk for polycythaemia and hyperviscosity in growth retarded babies in resource poor countries should be low because many infants have low cord haemoglobin concentration in areas where malaria and maternal iron deficiency anaemia are common.[w21-w23] In these areas up to 30% of babies have fetal anaemia, defined as cord haemoglobin concentration below 125 g/l.[w21]

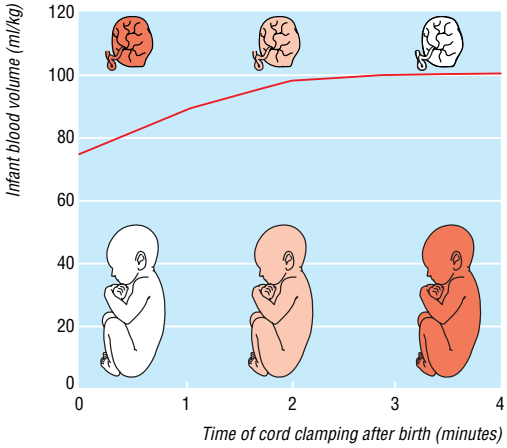

Fig 1 Distribution of blood between infant and placenta depending on time of cord clamping after birth (adapted from Linderkamp[w24] and Yao et al[w25]). The term infants are at the level of the introitus, about 10 cm below the placenta

What is the optimal delay for cord clamping in infants in relation to their position during placental transfusion?

Vaginally born, normal birthweight infants

The total fetoplacental blood volume is about 120 ml/kg of fetal weight.[w24-w27] At birth, the distribution of blood between fetus and placenta is roughly in a ratio of 2:1, and this distribution remains unchanged if the cord is clamped immediately. Figure 1 shows that allowing placental transfusion to occur for at least three minutes results in a larger infant blood volume (ratio 5:1).[w24 w25] The rate of placental transfusion is markedly influenced by the position of the delivered infant. An infant held 50-60 cm above the placenta will not receive any blood from the placenta. From 10 cm above to 10 cm below the level of the placenta, infants receive the maximum possible amount after at least three minutes of birth. Keeping the infant 40 cm below the placenta hastens placental transfusion to near completion within one minute.[w24 w28]

The randomised and quasi-randomised controlled trials that studied delayed cord clamping in vaginally born, healthy, term infants differed in clamping time and infant position before clamping (see table). All the trials showed that placental transfusion occurred after

Position of infant in relation to timing of cord clamping in trials that studied vaginally born, healthy, term infants

Position of infant in relation to placenta	Time to cord clamping (minutes)			
	1-2	3	5	>5
>10 cm above	Ceriani Cernadas et al[16]	Nelle et al[12-14]; Ceriani Cernadas et al[16]	—	—
0-10 cm below	Chaparro et al[6]	Linderkamp et al[11]	Grajeda et al[2]; van Rheenen et al[5]; Pao-Chen et al[22]	Gupta et al[3]; Lanzkowsky et al[4]; Geethanath et al[21]
30 cm below	Saigal et al[15]	—	Saigal et al[15]	—

delayed cord clamping by showing higher packed cell volume or haemoglobin concentration in the first 24 hours after birth compared with immediate clamping.[2–6 11–16 21 22]

Recommendation

- Cord clamping should be delayed for at least three minutes for the optimal volume of placental transfusion, regardless of fetal weight

Grade of recommendation: Weak

Vaginally born, low birthweight infants

Most of the low birthweight infants in the cord clamping trials were born by caesarean section. Six trials had a sufficient number of vaginally born preterm infants.[7–9 15 23–25] There was considerable heterogeneity in clamping time and infant position before clamping. In five trials the cord was clamped after a delay of 30-60 seconds,[7–9 23 25] and all but one compensated for the relatively short delay by lowering the infant as much as cord length permitted to ensure placental transfusion. The trial in which infants were not lowered failed to show placental transfusion.[8] In the trial with a clamping delay of 1-2 minutes the infants were also not lowered, but the longer delay was sufficient for placental transfusion.[24]

What is the optimal time of clamping when neonatal resuscitation is required?

The vast majority of newborn infants do not require resuscitation—immediate drying and keeping them warm is all that is required. Less than 10% of newborns require help to start breathing at birth (stimulation, positioning, clearing the airway), and about 1% require extensive resuscitation. When respiratory efforts are absent or inadequate despite initial stabilisation, positive pressure ventilation with a self inflating bag is the priority.[w29] The earliest time to assess whether ventilation is successful is about 60 seconds after delivery.

All these steps can be done while the umbilical cord is intact. When resuscitation is required the preferred position for the infant should be between the mother's legs, as bag-mask ventilation is not feasible if the infant is placed on the mother's abdomen. Immediate cord clamping to enable resuscitation away from the mother could deprive the infant of much needed extra blood volume, and the resulting hypovolaemia might adversely affect tissue perfusion. Furthermore, as long as the uterus is not contracting and the placenta has not been detached, the infant may still receive oxygen via the intact placental-fetal circulation.

Recommendation

- When the state of the infant does not allow a clamping delay of three minutes, aim for a delay of at least 60 seconds with the infant placed between the mother's legs

Grade of recommendation: Weak

Conclusions

The evidence we reviewed can be summarised as follows:

1. Delayed cord clamping in term infants is safe and, compared with immediate clamping, is associated with higher haemoglobin concentrations and lower incidence of anaemia in the first 4 months of life, and higher iron stores up to at least 6 months

   Level of evidence: Moderate

2. Although delayed cord clamping in preterm infants is associated with higher peak bilirubin concentrations, the need to give treatment for hyperbilirubinaemia was not different after immediate clamping. Delayed cord clamping is safe in preterm infants and is associated with fewer blood transfusions in the first 6 weeks of life compared with immediate clamping

   Level of evidence: Moderate

3. Delayed cord clamping in combination with administration of oxytocin immediately after delivery of the baby is safe for mothers

   Level of evidence: Moderate

4. There is little information on delayed cord clamping in growth retarded babies, but the presumed baseline risk for polycythaemia in these infants is probably lower in resource poor countries than in industrialised countries

   Level of evidence: Low

5. In normal birthweight babies, for the maximum possible volume of placental transfusion cord clamping should be delayed for at least three minutes, provided that the position of the baby before clamping is on the mother's abdomen or lower

   Level of evidence: Moderate

6. In low birthweight babies delaying clamping for 30-60 seconds without lowering the baby is probably not effective

   Level of evidence: Moderate

7. When immediate neonatal resuscitation is required, place the child between the legs of the mother, start positive pressure ventilation with the umbilical cord intact and delay clamping for at least 60 seconds

   Level of evidence: Very low

We also provide a flow chart of our guidelines on cord clamping in resource poor settings for quick reference (fig 2).

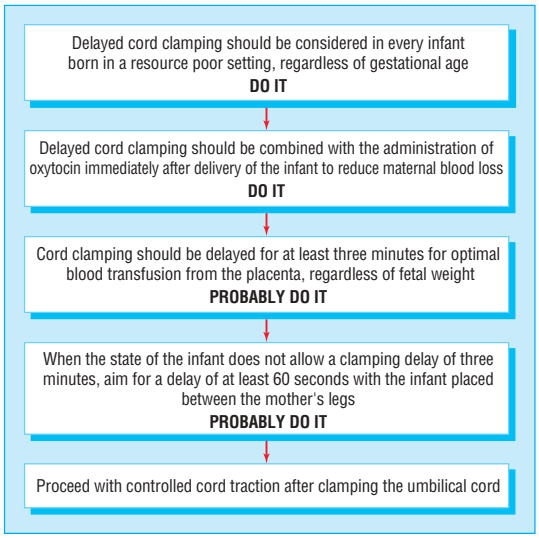

Fig 2 Guidelines for cord clamping in resource poor settings

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A consultation that changed my practice

Doctors often get so set in their roles that they fail to see matters from their patients' perspective. Hence, an occasional role reversal has its benefits, as I learnt from my recent consultation with my dentist. The treatment itself was uneventful, but what struck me when I sat in the patient's chair—on the "other side of the table"—was the many gifts from drug companies that adorned his desk and walls, mostly by the manufacturer of a particular brand of toothpaste, X. "Nothing unusual for a consulting room," I thought: mine's not very different—a penholder, a box of tissues, and a calendar given by a friendly drug representative, that's all. At the end of my consultation, I asked him which toothpaste he would recommend for my sensitive gums. He said, "Of course, X is the best one available." That made me think about my own practice and the potential message it sends to patients.

Gifts from drug companies occupy many consulting rooms and, on the face of it, seem innocuous. The Royal College of Psychiatrists in a guidance note states: "Educational gifts worth less than £6 per gift (note pads, pens, etc) may be accepted if their purpose is genuinely educational." And doctors would argue that receiving such gifts does not in any way compromise the independence of their professional judgment.

From a patient's perspective, however, there might well seem to be a conflict of interest. How likely is it that a patient would trust a doctor's decision if he or she prescribed a drug, using a pen and note pad gifted by the same company that manufactures that drug? Not the best start to a therapeutic alliance and ensuring long term compliance with drug treatment. Would our consulting rooms not look more professional if we were to rid them of such gifts, unless their purpose was "genuinely educational"? It took me less than five minutes to clear my consulting room. When will you?

Sanju George *consultant in addiction psychiatry, Birmingham and Solihull Mental Health NHS Trust (sanju.george@talk21.com)*

We welcome articles up to 600 words on topics such as *A memorable patient, A paper that changed my practice, My most unfortunate mistake,* or any other piece conveying instruction, pathos, or humour. Please submit the article on http://submit.bmj.com Permission is needed from the patient or a relative if an identifiable patient is referred to. We also welcome contributions for "Endpieces," consisting of quotations of up to 80 words (but most are considerably shorter) from any source, ancient or modern, which have appealed to the reader.